

Supporting Information

Synthesis of Pyrimidine-Fused Skeletons through Copper-Catalyzed Consecutive Sonogashira Coupling and Aminocyclization

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Table of Contents

I. General information	S1
II. Crystallography	S1
III. Synthesis and analytical data of compounds 1, 3, 4, 5, 6 and 7	S5
2-(2-bromo-5-fluorophenyl)-1 <i>H</i> -perimidine (1d)	S5
2-(2-bromo-6-fluorophenyl)-1 <i>H</i> -perimidine (1g).....	S5
2-(6-bromobenzo[<i>d</i>][1,3]dioxol-5-yl)-1 <i>H</i> -perimidine (1h).....	S6
2-(1-bromonaphthalen-2-yl)-1 <i>H</i> -perimidine (1i).....	S6
2-(2-bromopyridin-3-yl)-1 <i>H</i> -perimidine (1j)	S6
5-(2-bromo-4-fluorophenyl)-1-methyl-3-propyl-1,6-dihydro-7 <i>H</i> -pyrazolo[4,3- <i>d</i>]pyrimidin-7-one (4b)	S7
5-(2-bromo-4-chlorophenyl)-1-methyl-3-propyl-1,6-dihydro-7 <i>H</i> -pyrazolo[4,3- <i>d</i>]pyrimidin-7-one (4c).....	S8
5-(2-bromo-4-methylphenyl)-1-methyl-3-propyl-1,6-dihydro-7 <i>H</i> -pyrazolo[4,3- <i>d</i>]pyrimidin-7-one (4d)	S8
5-(2-bromo-5-fluorophenyl)-1-methyl-3-propyl-1,6-dihydro-7 <i>H</i> -pyrazolo[4,3- <i>d</i>]pyrimidin-7-one (4e)	S8
5-(2-bromo-5-chlorophenyl)-1-methyl-3-propyl-1,6-dihydro-7 <i>H</i> -pyrazolo[4,3- <i>d</i>]pyrimidin-7-one (4f)	S9
5-(2-bromo-5-methoxyphenyl)-1-methyl-3-propyl-1,6-dihydro-7 <i>H</i> -pyrazolo[4,3- <i>d</i>]pyrimidin-7-one (4g)	S9
5-(2-bromo-6-fluorophenyl)-1-methyl-3-propyl-1,6-dihydro-7 <i>H</i> -pyrazolo[4,3- <i>d</i>]pyrimidin-7-one (4h)	S9
5-(1-bromonaphthalen-2-yl)-1-methyl-3-propyl-1,6-dihydro-7 <i>H</i> -pyrazolo[4,3- <i>d</i>]pyrimidin-7-one (4i)	S10
5-(6-bromobenzo[<i>d</i>][1,3]dioxol-5-yl)-1-methyl-3-propyl-1,6-dihydro-7 <i>H</i> -pyrazolo[4,3- <i>d</i>]pyrimidin-7-one (4j)	S10
5-(2-bromo-4,5-dimethoxyphenyl)-1-methyl-3-propyl-1,6-dihydro-7 <i>H</i> -pyrazolo[4,3- <i>d</i>]pyrimidin-7-one (4k)	S11
2-(2-bromo-5-methoxyphenyl)-5,6,7,8-tetrahydrobenzo[4,5]thieno[2,3- <i>d</i>]pyrimidin-4(3 <i>H</i>)-one (7)	S11
(<i>E</i>)-12-benzylidene-12 <i>H</i> -isoindolo[2,1- <i>a</i>]perimidine (3a).....	S12

(<i>E</i>)-12-benzylidene-10-fluoro-12 <i>H</i> -isoindolo[2,1- <i>a</i>]perimidine (3b)	S12
(<i>E</i>)-12-benzylidene-10-chloro-12 <i>H</i> -isoindolo[2,1- <i>a</i>]perimidine (3c)	S13
(<i>E</i>)-12-benzylidene-9-fluoro-12 <i>H</i> -isoindolo[2,1- <i>a</i>]perimidine (3d)	S14
(<i>E</i>)-12-benzylidene-9-chloro-12 <i>H</i> -isoindolo[2,1- <i>a</i>]perimidine (3e)	S14
(<i>E</i>)-12-benzylidene-9-methoxy-12 <i>H</i> -isoindolo[2,1- <i>a</i>]perimidine (3f)	S15
(<i>E</i>)-12-benzylidene-8-fluoro-12 <i>H</i> -isoindolo[2,1- <i>a</i>]perimidine (3g)	S16
(<i>E</i>)-13-benzylidene-13 <i>H</i> -[1,3]dioxolo[4',5':5,6]isoindolo[2,1- <i>a</i>]perimidine (3h)	S16
(<i>E</i>)-14-benzylidene-14 <i>H</i> -benzo[5,6]isoindolo[2,1- <i>a</i>]perimidine (3i)	S17
(<i>E</i>)-12-benzylidene-12 <i>H</i> -pyrido[3',2':3,4]pyrrolo[1,2- <i>a</i>]perimidine (3j)	S18
(<i>E</i>)-12-(naphthalen-1-ylmethylene)-12 <i>H</i> -isoindolo[2,1- <i>a</i>]perimidine (3k)	S18
(<i>E</i>)-12-(2-methoxybenzylidene)-12 <i>H</i> -isoindolo[2,1- <i>a</i>]perimidine (3l)	S19
(<i>E</i>)-12-(2-fluorobenzylidene)-12 <i>H</i> -isoindolo[2,1- <i>a</i>]perimidine (3m)	S20
(<i>E</i>)-12-(2-chlorobenzylidene)-12 <i>H</i> -isoindolo[2,1- <i>a</i>]perimidine (3n)	S20
(<i>E</i>)-12-(2-methylbenzylidene)-12 <i>H</i> -isoindolo[2,1- <i>a</i>]perimidine (3o)	S21
(<i>E</i>)-12-(3-methoxybenzylidene)-12 <i>H</i> -isoindolo[2,1- <i>a</i>]perimidine (3p)	S22
(<i>E</i>)-12-(3-fluorobenzylidene)-12 <i>H</i> -isoindolo[2,1- <i>a</i>]perimidine (3q)	S23
(<i>E</i>)-12-(3-chlorobenzylidene)-12 <i>H</i> -isoindolo[2,1- <i>a</i>]perimidine (3r)	S23
(<i>E</i>)-12-(3-methylbenzylidene)-12 <i>H</i> -isoindolo[2,1- <i>a</i>]perimidine (3s)	S24
(<i>E</i>)-12-(3-nitrobenzylidene)-12 <i>H</i> -isoindolo[2,1- <i>a</i>]perimidine (3t)	S25
(<i>E</i>)-12-(4-bromobenzylidene)-12 <i>H</i> -isoindolo[2,1- <i>a</i>]perimidine (3u)	S25
(<i>E</i>)-12-(4-chlorobenzylidene)-12 <i>H</i> -isoindolo[2,1- <i>a</i>]perimidine (3v)	S26
(<i>E</i>)-9-benzylidene-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5a)	S27
(<i>E</i>)-9-benzylidene-7-fluoro-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5b)	S27
(<i>E</i>)-9-benzylidene-7-chloro-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5c)	S28
(<i>E</i>)-9-benzylidene-1,7-dimethyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5d)	S29
(<i>E</i>)-9-benzylidene-6-fluoro-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5e)	S29

(<i>E</i>)-9-benzylidene-6-chloro-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5f).....	S30
(<i>E</i>)-9-benzylidene-6-methoxy-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5g)	S31
(<i>E</i>)-9-benzylidene-5-fluoro-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5h)	S32
(<i>E</i>)-13-benzylidene-10-methyl-8-propyl-10,13-dihydro-11 <i>H</i> -benzo[<i>e</i>]pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5i)	S32
(<i>E</i>)-10-benzylidene-1-methyl-3-propyl-1,10-dihydro-12 <i>H</i> -[1,3]dioxolo[4,5- <i>f</i>]pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-12-one (5j).....	S33
(<i>E</i>)-9-benzylidene-6,7-dimethoxy-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5k)	S34
(<i>E</i>)-6,7-dimethoxy-9-(2-methoxybenzylidene)-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5l)	S35
(<i>E</i>)-1-methyl-9-(naphthalen-2-ylmethylene)-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5m)	S36
(<i>E</i>)-1-methyl-3-propyl-9-(thiophen-2-ylmethylene)-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5n)	S36
(<i>E</i>)-9-(4-fluorobenzylidene)-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5o)	S37
(<i>E</i>)-9-(4-chlorobenzylidene)-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5p)	S38
(<i>E</i>)-1-methyl-9-(4-methylbenzylidene)-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5q)	S38
(<i>E</i>)-9-(4-methoxybenzylidene)-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5r).....	S39
(<i>E</i>)-9-(4-ethylbenzylidene)-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5s)	S40
(<i>E</i>)-9-(4-ethoxybenzylidene)-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5t).....	S40
(<i>E</i>)-1-methyl-3-propyl-9-(4-propylbenzylidene)-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5u)	S41

(<i>E</i>)-9-(4-butylbenzylidene)-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5v)	S42
(<i>E</i>)-1-methyl-9-(4-pentylbenzylidene)-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5w)	S42
(<i>E</i>)-9-(2-fluorobenzylidene)-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5x)	S43
(<i>E</i>)-9-(2-chlorobenzylidene)-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5y)	S44
(<i>E</i>)-1-methyl-9-(2-methylbenzylidene)-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5z)	S45
(<i>E</i>)-9-(2-methoxybenzylidene)-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5aa)	S45
(<i>E</i>)-9-(3-fluorobenzylidene)-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5ab)	S46
(<i>E</i>)-9-(3-chlorobenzylidene)-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5ac)	S47
(<i>E</i>)-1-methyl-9-(3-methylbenzylidene)-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5ad)	S47
(<i>E</i>)-9-(3-methoxybenzylidene)-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5ae)	S48
(<i>E</i>)-11-benzylidene-8-methoxy-2,3,4,11-tetrahydrobenzo[4',5']thieno[2',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-13(1 <i>H</i>)-one (5af)	S49
(<i>Z</i>)-9-benzylidene-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6a)	S50
(<i>Z</i>)-9-benzylidene-7-fluoro-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6b)	S50
(<i>Z</i>)-9-benzylidene-7-chloro-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6c)	S51
(<i>Z</i>)-9-benzylidene-1,7-dimethyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6d)	S52
(<i>Z</i>)-9-benzylidene-6-fluoro-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6e)	S52
(<i>Z</i>)-9-benzylidene-6-chloro-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6f)	S53

(Z)-9-benzylidene-6-methoxy-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6g)	S54
(Z)-9-benzylidene-5-fluoro-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6h)	S55
(Z)-11-benzylidene-1-methyl-3-propyl-1,11-dihydro-13H-benzo[<i>f</i>]pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-13-one (6i)	S56
(Z)-10-benzylidene-1-methyl-3-propyl-1,10-dihydro-12H-[1,3]dioxolo[4,5- <i>f</i>]pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-12-one (6j)	S56
(Z)-9-benzylidene-6,7-dimethoxy-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6k)	S57
(Z)-6,7-dimethoxy-9-(2-methoxybenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6l)	S58
(Z)-1-methyl-9-(naphthalen-2-ylmethylene)-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6m)	S59
(Z)-1-methyl-3-propyl-9-(thiophen-2-ylmethylene)-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6n)	S59
(Z)-9-(4-fluorobenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6o)	S60
(Z)-9-(4-chlorobenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6p)	S61
(Z)-1-methyl-9-(4-methylbenzylidene)-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6q)	S62
(Z)-9-(4-methoxybenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6r)	S62
(Z)-9-(4-ethylbenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6s)	S63
(Z)-9-(4-ethoxybenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6t)	S64
(Z)-1-methyl-3-propyl-9-(4-propylbenzylidene)-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6u)	S65
(Z)-9-(4-butylbenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6v)	S66
(Z)-1-methyl-9-(4-pentylbenzylidene)-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6w)	S66

(Z)-9-(2-fluorobenzylidene)-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6x)	S67
(Z)-9-(2-chlorobenzylidene)-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6y)	S68
(Z)-1-methyl-9-(2-methylbenzylidene)-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6z)	S69
(Z)-9-(2-methoxybenzylidene)-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6aa)	S70
(Z)-9-(3-fluorobenzylidene)-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6ab)	S70
(Z)-9-(3-chlorobenzylidene)-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6ac)	S71
(Z)-1-methyl-9-(3-methylbenzylidene)-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6ad)	S72
(Z)-9-(3-methoxybenzylidene)-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6ae)	S73
2,2'-di(1 <i>H</i> -perimidin-2-yl)-1,1'-biphenyl (3')	S73
IV. NMR spectra	S75
2-(2-bromo-5-fluorophenyl)-1 <i>H</i> -perimidine (1d)	S75
2-(2-bromo-6-fluorophenyl)-1 <i>H</i> -perimidine (1g).....	S76
2-(6-bromobenzo[<i>d</i>][1,3]dioxol-5-yl)-1 <i>H</i> -perimidine (1h).....	S77
2-(1-bromonaphthalen-2-yl)-1 <i>H</i> -perimidine (1i).....	S78
2-(2-bromopyridin-3-yl)-1 <i>H</i> -perimidine (1j)	S79
5-(2-bromo-4-fluorophenyl)-1-methyl-3-propyl-1,6-dihydro-7 <i>H</i> -pyrazolo[4,3- <i>d</i>]pyrimidin-7-one (4b)	S80
5-(2-bromo-4-chlorophenyl)-1-methyl-3-propyl-1,6-dihydro-7 <i>H</i> -pyrazolo[4,3- <i>d</i>]pyrimidin-7-one (4c).....	S81
5-(2-bromo-4-methylphenyl)-1-methyl-3-propyl-1,6-dihydro-7 <i>H</i> -pyrazolo[4,3- <i>d</i>]pyrimidin-7-one (4d)	S82
5-(2-bromo-5-fluorophenyl)-1-methyl-3-propyl-1,6-dihydro-7 <i>H</i> -pyrazolo[4,3- <i>d</i>]pyrimidin-7-one (4e)	S83
5-(2-bromo-5-chlorophenyl)-1-methyl-3-propyl-1,6-dihydro-7 <i>H</i> -pyrazolo[4,3- <i>d</i>]pyrimidin-7-one (4f)	S84

5-(2-bromo-5-methoxyphenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3- <i>d</i>]pyrimidin-7-one (4g)	S85
5-(2-bromo-6-fluorophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3- <i>d</i>]pyrimidin-7-one (4h)	S86
5-(1-bromonaphthalen-2-yl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3- <i>d</i>]pyrimidin-7-one (4i)	S87
5-(6-bromobenzo[<i>d</i>][1,3]dioxol-5-yl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3- <i>d</i>]pyrimidin-7-one (4j)	S88
5-(2-bromo-4,5-dimethoxyphenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3- <i>d</i>]pyrimidin-7-one (4k)	S89
2-(2-bromo-5-methoxyphenyl)-5,6,7,8-tetrahydrobenzo[4,5]thieno[2,3- <i>d</i>]pyrimidin-4(3 <i>H</i>)-one (7)	S90
(<i>E</i>)-12-benzylidene-12 <i>H</i> -isoindolo[2,1- <i>a</i>]perimidine (3a).....	S91
(<i>E</i>)-12-benzylidene-10-fluoro-12 <i>H</i> -isoindolo[2,1- <i>a</i>]perimidine (3b)	S92
(<i>E</i>)-12-benzylidene-10-chloro-12 <i>H</i> -isoindolo[2,1- <i>a</i>]perimidine (3c)	S93
(<i>E</i>)-12-benzylidene-9-fluoro-12 <i>H</i> -isoindolo[2,1- <i>a</i>]perimidine (3d)	S94
(<i>E</i>)-12-benzylidene-9-chloro-12 <i>H</i> -isoindolo[2,1- <i>a</i>]perimidine (3e).....	S95
(<i>E</i>)-12-benzylidene-9-methoxy-12 <i>H</i> -isoindolo[2,1- <i>a</i>]perimidine (3f).....	S96
(<i>E</i>)-12-benzylidene-8-fluoro-12 <i>H</i> -isoindolo[2,1- <i>a</i>]perimidine (3g)	S97
(<i>E</i>)-13-benzylidene-13 <i>H</i> -[1,3]dioxolo[4',5':5,6]isoindolo[2,1- <i>a</i>]perimidine (3h)	S98
(<i>E</i>)-14-benzylidene-14 <i>H</i> -benzo[5,6]isoindolo[2,1- <i>a</i>]perimidine (3i)	S99
(<i>E</i>)-12-benzylidene-12 <i>H</i> -pyrido[3',2':3,4]pyrrolo[1,2- <i>a</i>]perimidine (3j)	S100
(<i>E</i>)-12-(naphthalen-1-ylmethylene)-12 <i>H</i> -isoindolo[2,1- <i>a</i>]perimidine (3k).....	S101
(<i>E</i>)-12-(2-methoxybenzylidene)-12 <i>H</i> -isoindolo[2,1- <i>a</i>]perimidine (3l).....	S102
(<i>E</i>)-12-(2-fluorobenzylidene)-12 <i>H</i> -isoindolo[2,1- <i>a</i>]perimidine (3m)	S103
(<i>E</i>)-12-(2-chlorobenzylidene)-12 <i>H</i> -isoindolo[2,1- <i>a</i>]perimidine (3n).....	S104
(<i>E</i>)-12-(2-methylbenzylidene)-12 <i>H</i> -isoindolo[2,1- <i>a</i>]perimidine (3o).....	S105
(<i>E</i>)-12-(3-methoxybenzylidene)-12 <i>H</i> -isoindolo[2,1- <i>a</i>]perimidine (3p).....	S106
(<i>E</i>)-12-(3-fluorobenzylidene)-12 <i>H</i> -isoindolo[2,1- <i>a</i>]perimidine (3q)	S107
(<i>E</i>)-12-(3-chlorobenzylidene)-12 <i>H</i> -isoindolo[2,1- <i>a</i>]perimidine (3r)	S108
(<i>E</i>)-12-(3-methylbenzylidene)-12 <i>H</i> -isoindolo[2,1- <i>a</i>]perimidine (3s)	S109
(<i>E</i>)-12-(3-nitrobenzylidene)-12 <i>H</i> -isoindolo[2,1- <i>a</i>]perimidine (3t).....	S110

(<i>E</i>)-12-(4-bromobenzylidene)-12 <i>H</i> -isoindolo[2,1- <i>a</i>]perimidine (3u)	S111
(<i>E</i>)-12-(4-chlorobenzylidene)-12 <i>H</i> -isoindolo[2,1- <i>a</i>]perimidine (3v)	S112
(<i>E</i>)-9-benzylidene-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5a)	S113
(<i>E</i>)-9-benzylidene-7-fluoro-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5b)	S114
(<i>E</i>)-9-benzylidene-7-chloro-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5c)	S115
(<i>E</i>)-9-benzylidene-1,7-dimethyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5d)	S116
(<i>E</i>)-9-benzylidene-6-fluoro-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5e)	S117
(<i>E</i>)-9-benzylidene-6-chloro-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5f)	S118
(<i>E</i>)-9-benzylidene-6-methoxy-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5g)	S119
(<i>E</i>)-9-benzylidene-6-fluoro-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5h)	S120
(<i>E</i>)-13-benzylidene-10-methyl-8-propyl-10,13-dihydro-11 <i>H</i> -benzo[<i>e</i>]pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5i)	S121
(<i>E</i>)-10-benzylidene-1-methyl-3-propyl-1,10-dihydro-12 <i>H</i> -[1,3]dioxolo[4,5- <i>f</i>]pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-12-one (5j)	S122
(<i>E</i>)-9-benzylidene-6,7-dimethoxy-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5k)	S123
(<i>E</i>)-6,7-dimethoxy-9-(2-methoxybenzylidene)-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5l)	S124
(<i>E</i>)-1-methyl-9-(naphthalen-2-ylmethylene)-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5m)	S125
(<i>E</i>)-1-methyl-3-propyl-9-(thiophen-2-ylmethylene)-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5n)	S126
(<i>E</i>)-9-(4-fluorobenzylidene)-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5o)	S127
(<i>E</i>)-9-(4-chlorobenzylidene)-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5p)	S128

(<i>E</i>)-1-methyl-9-(4-methylbenzylidene)-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5q)	S129
(<i>E</i>)-9-(4-methoxybenzylidene)-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5r)	S130
(<i>E</i>)-9-(4-ethylbenzylidene)-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5s)	S131
(<i>E</i>)-9-(4-ethoxybenzylidene)-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5t)	S132
(<i>E</i>)-1-methyl-3-propyl-9-(4-propylbenzylidene)-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5u)	S133
(<i>E</i>)-9-(4-butylbenzylidene)-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5v)	S134
(<i>E</i>)-1-methyl-9-(4-pentylbenzylidene)-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5w)	S135
(<i>E</i>)-9-(2-fluorobenzylidene)-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5x)	S136
(<i>E</i>)-9-(2-chlorobenzylidene)-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5y)	S137
(<i>E</i>)-1-methyl-9-(2-methylbenzylidene)-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5z)	S138
(<i>E</i>)-9-(2-methoxybenzylidene)-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5aa)	S139
(<i>E</i>)-9-(3-fluorobenzylidene)-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5ab)	S140
(<i>E</i>)-9-(3-chlorobenzylidene)-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5ac)	S141
(<i>E</i>)-1-methyl-9-(3-methylbenzylidene)-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5ad)	S142
(<i>E</i>)-9-(3-methoxybenzylidene)-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (5ae)	S143
(<i>E</i>)-11-benzylidene-8-methoxy-2,3,4,11-tetrahydrobenzo[4',5']thieno[2',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-13(1 <i>H</i>)-one (5af)	S144
(<i>Z</i>)-9-benzylidene-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6a)	S145

(Z)-9-benzylidene-7-fluoro-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6b)	S146
(Z)-9-benzylidene-7-chloro-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6c)	S147
(Z)-9-benzylidene-1,7-dimethyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6d)	S148
(Z)-9-benzylidene-6-fluoro-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6e)	S149
(Z)-9-benzylidene-6-chloro-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6f)	S150
(Z)-9-benzylidene-6-methoxy-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6g)	S151
(Z)-9-benzylidene-5-fluoro-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6h)	S152
(Z)-11-benzylidene-1-methyl-3-propyl-1,11-dihydro-13 <i>H</i> -benzo[<i>f</i>]pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-13-one (6i)	S153
(Z)-10-benzylidene-1-methyl-3-propyl-1,10-dihydro-12 <i>H</i> -[1,3]dioxolo[4,5- <i>f</i>]pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-12-one (6j)	S154
(Z)-9-benzylidene-6,7-dimethoxy-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6k)	S155
(Z)-6,7-dimethoxy-9-(2-methoxybenzylidene)-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6l)	S156
(Z)-1-methyl-9-(naphthalen-2-ylmethylene)-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6m)	S157
(Z)-1-methyl-3-propyl-9-(thiophen-2-ylmethylene)-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6n)	S158
(Z)-9-(4-fluorobenzylidene)-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6o)	S159
(Z)-9-(4-chlorobenzylidene)-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6p)	S160
(Z)-1-methyl-9-(4-methylbenzylidene)-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6q)	S161
(Z)-9-(4-methoxybenzylidene)-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6r)	S162

(Z)-9-(4-ethylbenzylidene)-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6s)	S163
(Z)-9-(4-ethoxybenzylidene)-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6t).....	S164
(Z)-1-methyl-3-propyl-9-(4-propylbenzylidene)-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6u)	S165
(Z)-9-(4-butylbenzylidene)-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6v)	S166
(Z)-1-methyl-9-(4-pentylbenzylidene)-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6w)	S167
(Z)-9-(2-fluorobenzylidene)-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6x)	S168
(Z)-9-(2-chlorobenzylidene)-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6y)	S169
(Z)-1-methyl-9-(2-methylbenzylidene)-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6z)	S170
(Z)-9-(2-methoxybenzylidene)-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> - pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6aa)	S171
(Z)-9-(3-fluorobenzylidene)-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6ab)	S172
(Z)-9-(3-chlorobenzylidene)-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6ac)	S173
(Z)-1-methyl-9-(3-methylbenzylidene)-3-propyl-1,9-dihydro-11 <i>H</i> -pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6ad)	S174
(Z)-9-(3-methoxybenzylidene)-1-methyl-3-propyl-1,9-dihydro-11 <i>H</i> - pyrazolo[4',3':4,5]pyrimido[2,1- <i>a</i>]isoindol-11-one (6ae)	S175
2,2'-di(1 <i>H</i> -perimidin-2-yl)-1,1'-biphenyl (3')	S176
V. References	S177

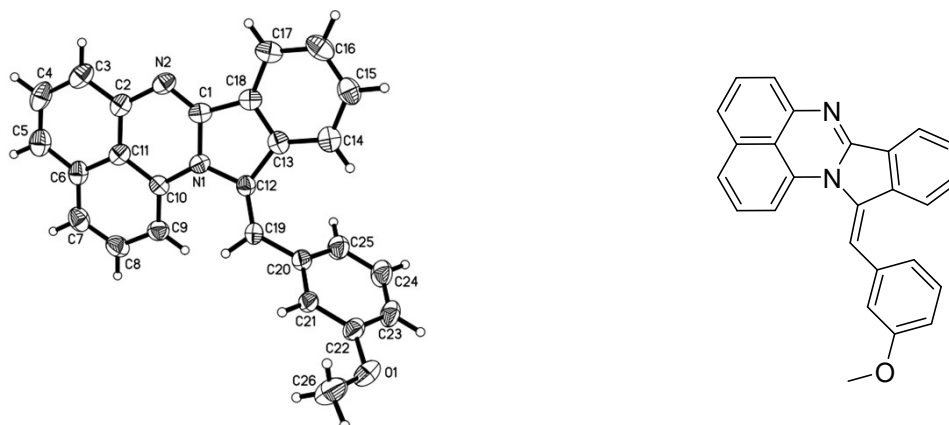
I. General information

All reagents were purchased from commercial sources and used without treatment unless otherwise indicated. The products were purified by column chromatography over silica gel. ^1H NMR and ^{13}C NMR spectra were recorded at 25 °C on a Varian spectrometer at 400 MHz and 101 MHz, respectively, with TMS as the internal standard. Mass spectra were recorded on a BRUKER AutoflexIII Smartbeam MS-spectrometer. High resolution mass spectra (HRMS) were recorded on Bruker microTof using ESI-TOF method.

II. Crystallography

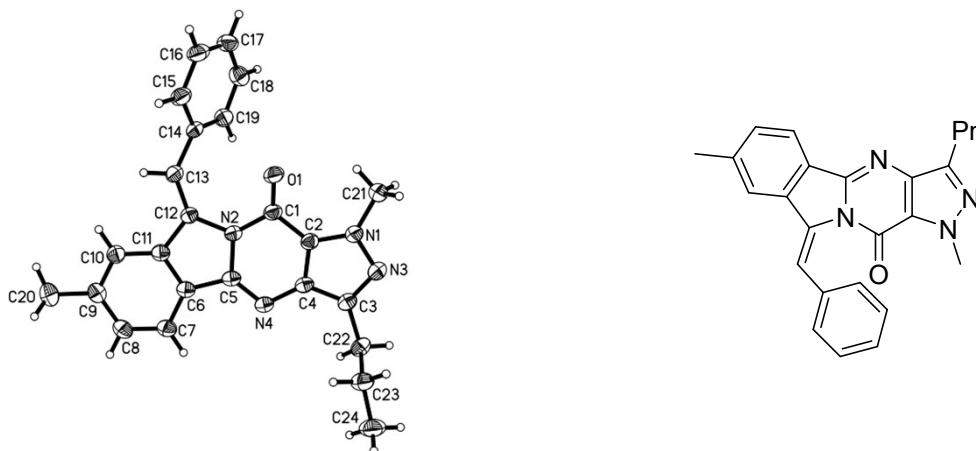
Compound **3p** (50 mg) was dissolved in a centrifuge tube in 150 μL CDCl_3 . Upon standing for several days (seven days), crystals suitable for X-ray diffraction of **3p**, **6d** and **5aa** were obtained. The structures of the *N*-fused heterocyclic scaffolds were further established by X-ray diffraction. Single-crystal X-ray diffraction data for the reported compound was recorded at a temperature of 296(2) K on an Oxford Diffraction Gemini R Ultra diffractometer using a ω scan technique with Mo-K α radiation ($\lambda = 0.71073 \text{ \AA}$). The structures were solved by the Direct Method of SHELXS-97 and refined by full-matrix least-squares techniques using the SHELXL-97 program.¹ Non-hydrogen atoms were refined with anisotropic temperature parameters, and hydrogen atoms of the ligands were refined as rigid groups. Basic information pertaining to crystal parameters and structure refinement is summarized in Tables S1, S2 and S3.

Table S1. Crystal structure and refinement data for compound **3p** (thermal ellipsoids at 30% probability).



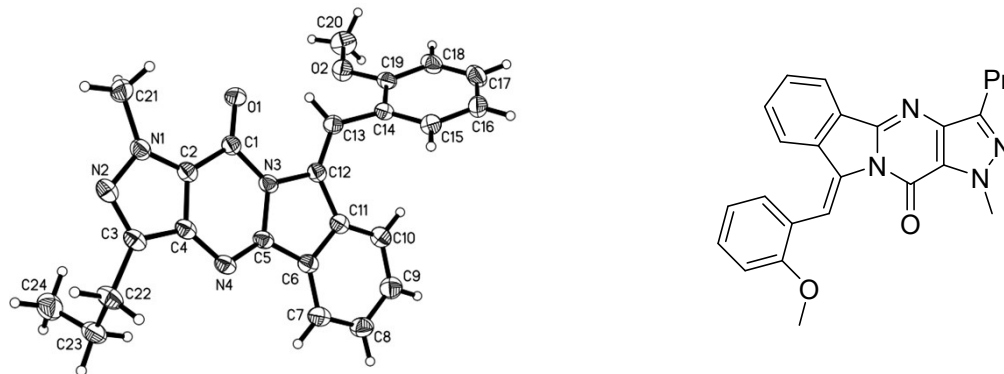
Empirical formula	C ₂₆ H ₁₈ N ₂ O
Temperature	296(2) K
Wavelength	0.71073 Å
Space group	P2(1)/n
Unit cell dimensions	a = 11.023(4) Å b = 14.004(6) Å c = 13.233(5) Å alpha = 90 deg. beta = 114.61 deg. gamma = 90 deg.
Volume	1856.9(13) Å ³
Z	4
Calculated density	1.339 Mg/m ³
Absorption coefficient	0.082 mm ⁻¹
F(000)	784
Crystal size	0.122 x 0.100 x 0.089 mm
Theta range for data collection	2.50 to 22.77 deg.
Reflections collected / unique	4758 / 1784 [R(int) = 0.0515]
Data / restraints / parameters	1784 / 0 / 263
Goodness-of-fit on F ²	0.969
Final R indices [I>2sigma(I)]	R1 = 0.0441, wR2 = 0.0802
R indices (all data)	R1 = 0.0762, wR2 = 0.0854

Table S2. Crystal structure and refinement data for compound **6d** (thermal ellipsoids at 30% probability).



Empirical formula	C ₂₄ H ₂₂ N ₄ O
Temperature	296(2) K
Wavelength	0.71073 Å
Space group	P2(1)/c
Unit cell dimensions	a = 9.810(7) Å b = 10.948(8) Å c = 11.015(8) Å alpha = 61.711(8) deg. beta = 82.606(9) deg. gamma = 76.072(9) deg.
Volume	1011.0(12) Å ³
Z	2
Calculated density	1.256 Mg/m ³
Absorption coefficient	0.079 mm ⁻¹
F(000)	404
Crystal size	0.134 x 0.122 x 0.088 mm
Theta range for data collection	3.024 to 25.017 deg.
Reflections collected / unique	5137 / 3508 [R(int) = 0.0139]
Data / restraints / parameters	3508 / 0 / 262
Goodness-of-fit on F ²	1.040
Final R indices [I > 2sigma(I)]	R1 = 0.0482, wR2 = 0.1320
R indices (all data)	R1 = 0.0578, wR2 = 0.1420

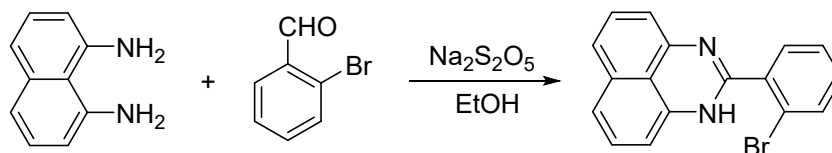
Table S3. Crystal structure and refinement data for compound **5aa** (thermal ellipsoids at 30% probability).



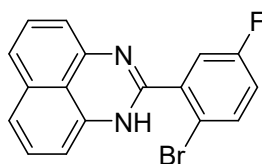
Empirical formula	C ₂₄ H ₂₂ N ₄ O ₂
Temperature	296(2) K
Wavelength	0.71073 Å
Space group	P-1
Unit cell dimensions	a = 8.8519(9) Å b = 9.9144(11) Å c = 12.8442(14) Å alpha = 108.2800(10) deg. beta = 93.0630(10) deg. gamma = 108.3660(10) deg.
Volume	1001.21(19) Å ³
Z	2
Calculated density	1.322 Mg/m ³
Absorption coefficient	0.087 mm ⁻¹
F(000)	420
Crystal size	0.142 x 0.123 x 0.088 mm
Theta range for data collection	2.309 to 25.018 deg.
Reflections collected / unique	5053 / 3473 [R(int) = 0.0183]
Data / restraints / parameters	3473 / 0 / 272
Goodness-of-fit on F ²	1.057
Final R indices [I > 2sigma(I)]	R1 = 0.0415, wR2 = 0.1137
R indices (all data)	R1 = 0.0474, wR2 = 0.1201

III. Synthesis and analytical data of compounds 1, 3, 4, 5, 6 and 7

Note: Compound 1 can be synthesized by the cited literature method, where 1d, 1g, 1h, 1i and 1j are new.

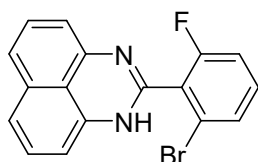


General procedure for preparation of 2-(2-bromophenyl)-1H-perimidine²: A mixture of the 1,8-diaminonaphthalene (158.20 mg, 1 mmol) and the 2-bromobenzaldehyde (194.27 mg, 1.05 mmol) in anhydrous ethanol (20 mL) was prepared in a round-bottom flask (100 mL) equipped with a magnetic stirrer. Then, the mixture was heated up to 50 °C in an oil bath and sodium pyrosulfite (380.18 mg, 2 eq.) was added. The resulting mixture was monitored by TLC and stirred for the appropriate time. Upon completion of the reaction, the reaction mixture was poured into water (60 mL). The precipitate was filtered, rinsed with water (6 mL × 2) and dried under air.



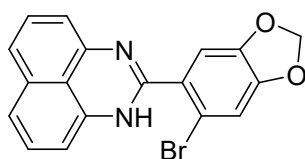
2-(2-bromo-5-fluorophenyl)-1H-perimidine (1d)

Orange solid; mp 117-119 °C; ¹H NMR (DMSO-*d*₆, 400 MHz): δ_H 10.99 (s, 1H), 7.83–7.79 (m, 1H), 7.61–7.58 (m, 1H), 7.39–7.34 (m, 1H), 7.17–7.12 (m, 2H), 7.09–7.06 (m, 2H), 6.50–6.47 (m, 2H); ¹³C NMR (DMSO-*d*₆, 101 MHz): δ_C 161.2 (d, *J*_{C-F} = 244.8 Hz), 153.0, 144.8, 138.2 (d, *J*_{C-F} = 8.1 Hz), 135.1, 134.7 (d, *J*_{C-F} = 8.1 Hz), 128.9, 128.0, 121.8, 119.7, 118.5 (d, *J*_{C-F} = 22.2 Hz), 118.0, 117.6 (d, *J*_{C-F} = 24.0 Hz), 115.6 (d, *J*_{C-F} = 3.3 Hz), 114.0, 102.4; HRMS (ESI-TOF, *m/z*): calcd for C₁₇H₁₁BrFN₂ [M + H]⁺, 341.0084; found, 341.0095.



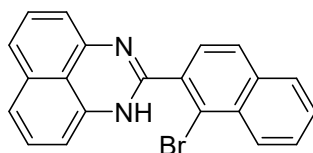
2-(2-bromo-6-fluorophenyl)-1H-perimidine (1g)

White solid; mp 127-129 °C; ^1H NMR (DMSO- d_6 , 400 MHz): δ_{H} 11.03 (s, 1H), 7.64 (d, J = 8.0 Hz, 1H), 7.55–7.43 (m, 2H), 7.21–7.16 (m, 1H), 7.12–7.08 (m, 2H), 7.05 (d, J = 8.0 Hz, 1H), 6.62 (d, J = 7.2 Hz, 1H), 6.30 (d, J = 7.2 Hz, 1H); ^{13}C NMR (DMSO- d_6 , 101 MHz): δ_{C} 158.7 (d, $J_{\text{C-F}}$ = 246.8 Hz), 148.4, 143.7, 137.1, 134.2, 131.6 (d, $J_{\text{C-F}}$ = 2.3 Hz), 127.8 (d, $J_{\text{C-F}}$ = 22.3 Hz), 127.1 (d, $J_{\text{C-F}}$ = 1.1 Hz), 124.0, 121.2, 120.8, 118.9, 117.1, 114.3 (d, $J_{\text{C-F}}$ = 21.9 Hz), 113.0, 101.4; HRMS (ESI-TOF, m/z): calcd for $\text{C}_{17}\text{H}_{11}\text{BrFN}_2$ [$\text{M} + \text{H}$] $^+$, 341.0084; found, 341.0088.



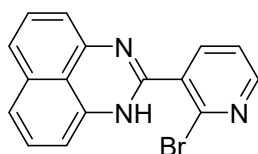
2-(6-bromobenzo[*d*][1,3]dioxol-5-yl)-1H-perimidine (1h)

White solid; mp 131-132 °C; ^1H NMR (DMSO- d_6 , 400 MHz): δ_{H} 10.78 (s, 1H), 7.35 (s, 1H), 7.21 (s, 1H), 7.14–7.11 (m, 2H), 7.05–7.03 (m, 2H), 6.45–6.44 (m, 2H), 6.16 (s, 2H); ^{13}C NMR (DMSO- d_6 , 101 MHz): δ_{C} 154.4, 149.7, 147.2, 139.4, 135.0, 128.5, 126.9, 121.5, 119.7, 112.8, 112.2, 110.1, 108.2, 102.7; HRMS (ESI-TOF, m/z): calcd for $\text{C}_{18}\text{H}_{12}\text{BrO}_2\text{N}_2$ [$\text{M} + \text{H}$] $^+$, 367.0077; found, 367.0102.



2-(1-bromonaphthalen-2-yl)-1H-perimidine (1i)

White solid; mp 203-205 °C; ^1H NMR (DMSO- d_6 , 400 MHz): δ_{H} 11.77 (s, 1H), 8.32 (d, J = 8.4 Hz, 1H), 8.17–8.11 (m, 2H), 7.83–7.72 (m, 3H), 7.23–7.15 (m, 4H), 6.61–5.59 (m, 2H); ^{13}C NMR (DMSO- d_6 , 101 MHz): δ_{C} 155.2, 135.0, 134.3, 133.3, 131.1, 130.1, 128.8, 128.6, 128.53, 128.50, 128.1, 127.0, 126.4, 123.8, 121.6, 121.4, 119.5; HRMS (ESI-TOF, m/z): calcd for $\text{C}_{21}\text{H}_{14}\text{BrN}_2$ [$\text{M} + \text{H}$] $^+$, 373.0335; found, 373.0356.

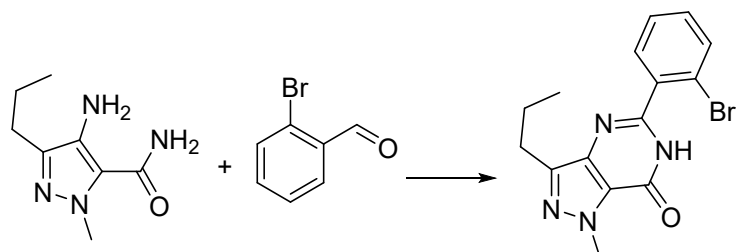


2-(2-bromopyridin-3-yl)-1H-perimidine (1j)

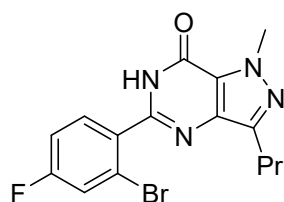
White solid; mp 122-123 °C; ^1H NMR (DMSO- d_6 , 400 MHz): δ_{H} 11.09 (s, 1H), 8.55–8.54 (m, 1H), 8.09–8.07 (m, 1H), 7.64–7.60 (m, 1H), 7.18–7.14 (m, 2H), 7.10–7.08 (m, 2H), 6.51–6.49

(m, 2H); ^{13}C NMR (DMSO- d_6 , 101 MHz): δ_{C} 152.9, 151.2, 139.9, 139.2, 135.1, 133.4, 128.5, 123.5, 121.8, 119.1; HRMS (ESI-TOF, m/z): calcd for $\text{C}_{16}\text{H}_{11}\text{BrN}_3$ [$\text{M} + \text{H}$] $^+$, 324.0131; found, 324.0137.

Note: Compound 4 can be synthesized by the cited literature method, where 4b-4k are new.



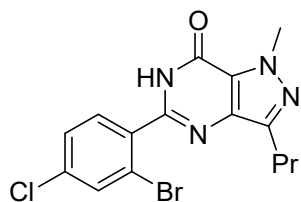
General procedure for preparation of 5-(2-bromophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one³: A mixture of the 4-Amino-1-methyl-3-*n*-propyl-1*H*-pyrazole-5-formamide (1.0 g, 5.5 mmol) and the *o*-bromobenzaldehyde (2.02 g, 11 mmol) in xylene (10.0 mL) was prepared in a round-bottom flask (50 mL) equipped with a magnetic stirrer. Then, the mixture was refluxed in an oil bath and methylsulfonic acid (1 drop) was added. The resulting mixture was monitored by TLC and stirred for the appropriate time. Upon completion of the reaction, the reaction mixture was cooled. The precipitate was filtered, rinsed with water (4 mL \times 2) and dried under air.



5-(2-bromo-4-fluorophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one

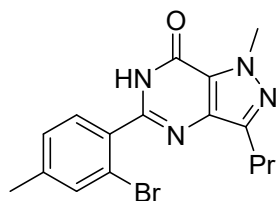
(4b)

White solid; mp 173-174 °C; ^1H NMR (CDCl_3 , 400 MHz): δ_{H} 11.02 (s, 1H), 7.70–7.66 (m, 1H), 7.45 (dd, $J = 8.0$ Hz, 2.0 Hz, 1H), 7.19 (t, $J = 8.4$ Hz, 1H), 4.21 (s, 3H), 2.90 (t, $J = 7.6$ Hz, 2H), 1.87–1.78 (m, 2H), 1.01 (t, $J = 7.6$ Hz, 3H); ^{13}C NMR (CDCl_3 , 101 MHz): δ_{C} 163.3 (d, $J_{\text{C-F}} = 254.2$ Hz), 155.1, 148.6, 147.0, 138.5, 133.0 (d, $J_{\text{C-F}} = 8.9$ Hz), 131.4 (d, $J_{\text{C-F}} = 3.4$ Hz), 124.3, 122.3 (d, $J_{\text{C-F}} = 9.7$ Hz), 120.9 (d, $J_{\text{C-F}} = 24.7$ Hz), 115.2 (d, $J_{\text{C-F}} = 21.2$ Hz), 38.2, 27.6, 22.5, 14.0; HRMS (ESI-TOF, m/z): calcd for $\text{C}_{15}\text{H}_{15}\text{BrFON}_4$ [$\text{M} + \text{H}$] $^+$, 365.0408; found, 365.0416.



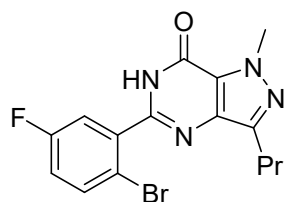
5-(2-bromo-4-chlorophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one (4c)

White solid; mp 179-182 °C; ^1H NMR (CDCl_3 , 400 MHz): δ_{H} 11.14 (s, 1H), 7.71 (s, 1H), 7.63–7.60 (m, 1H), 7.45–7.42 (m, 1H), 4.19 (s, 3H), 2.89 (t, $J = 8.0$ Hz, 2H), 1.87–1.77 (m, 2H), 1.00 (t, $J = 7.6$ Hz, 3H); ^{13}C NMR (CDCl_3 , 101 MHz): δ_{C} 155.0, 148.5, 147.0, 138.5, 137.1, 133.5, 133.2, 132.3, 128.1, 124.3, 122.1, 38.2, 27.6, 22.5, 14.0; HRMS (ESI-TOF, m/z): calcd for $\text{C}_{15}\text{H}_{15}\text{BrClON}_4$ [$\text{M} + \text{H}$] $^+$, 381.0112; found, 381.0116.



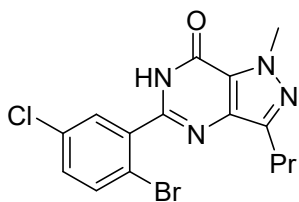
5-(2-bromo-4-methylphenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one (4d)

White solid; mp 189-191 °C; ^1H NMR (CDCl_3 , 400 MHz): δ_{H} 11.03(s, 1H), 7.56 (d, $J = 7.6$ Hz, 1H), 7.51 (s, 1H), 7.27–7.23 (m, 1H), 4.23 (s, 3H), 2.90 (t, $J = 8.0$ Hz, 2H), 2.40 (s, 3H), 1.88–1.77 (m, 2H), 1.00 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (CDCl_3 , 101 MHz): δ_{C} 154.6, 149.5, 146.9, 142.5, 138.5, 134.0, 132.1, 131.3, 128.6, 124.4, 121.0, 38.2, 27.7, 22.5, 21.0, 14.0; HRMS (ESI-TOF, m/z): calcd for $\text{C}_{16}\text{H}_{18}\text{BrON}_4$ [$\text{M} + \text{H}$] $^+$, 361.0659; found, 361.0668.



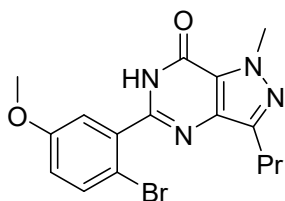
5-(2-bromo-5-fluorophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one (4e)

White solid; mp 172-174 °C; ^1H NMR (CDCl_3 , 400 MHz): δ_{H} 10.71 (s, 1H), 7.68–7.65 (m, 1H), 7.46–7.43 (m, 1H), 7.15–7.09 (m, 1H), 4.21 (s, 3H), 2.91 (t, $J = 7.6$ Hz, 2H), 1.88–1.78 (m, 2H), 1.01 (t, $J = 7.6$ Hz, 3H); ^{13}C NMR (CDCl_3 , 101 MHz): δ_{C} 161.7 (d, $J_{\text{C-F}} = 248.2$ Hz), 155.1, 148.2 (d, $J_{\text{C-F}} = 2.0$ Hz), 147.1, 138.4, 136.4 (d, $J_{\text{C-F}} = 7.9$ Hz), 135.1 (d, $J_{\text{C-F}} = 8.0$ Hz), 124.4, 119.1 (d, $J_{\text{C-F}} = 6.1$ Hz), 118.8 (d, $J_{\text{C-F}} = 8.3$ Hz), 115.9 (d, $J_{\text{C-F}} = 3.4$ Hz), 38.2, 27.6, 22.5, 14.0; HRMS (ESI-TOF, m/z): calcd for $\text{C}_{15}\text{H}_{15}\text{BrFON}_4$ [$\text{M} + \text{H}$] $^+$, 365.0408; found, 365.0431.



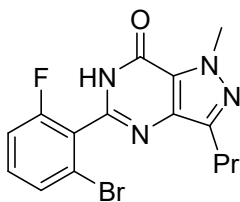
5-(2-bromo-5-chlorophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one (4f)

White solid; mp 176-177 °C; ^1H NMR (CDCl_3 , 400 MHz): δ_{H} 11.16 (s, 1H), 7.68 (s, 1H), 7.64–7.61 (m, 1H), 7.36 (d, $J = 8.4$ Hz, 1H), 4.22 (s, 3H), 2.91 (t, $J = 7.6$ Hz, 2H), 1.88–1.78 (m, 2H), 1.01 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (CDCl_3 , 101 MHz): δ_{C} 155.1, 148.1, 147.1, 138.4, 136.2, 134.8, 134.0, 131.7, 131.5, 124.4, 119.6, 38.3, 27.6, 22.5, 14.0; HRMS (ESI-TOF, m/z): calcd for $\text{C}_{15}\text{H}_{15}\text{BrClN}_4$ [$\text{M} + \text{H}$] $^+$, 381.0112; found, 381.0123.



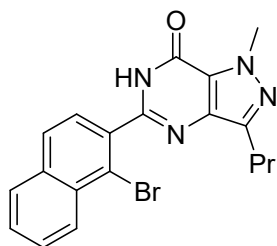
5-(2-bromo-5-methoxyphenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one (4g)

White solid; mp 180-181 °C; ^1H NMR (CDCl_3 , 400 MHz): δ_{H} 10.71 (s, 1H), 7.55 (d, $J = 9.2$ Hz, 1H), 7.20 (s, 1H), 6.91 (d, $J = 8.8$ Hz, 1H), 4.21 (s, 3H), 3.84 (s, 3H), 2.91 (t, $J = 7.6$ Hz, 2H), 1.88–1.78 (m, 2H), 1.01 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (CDCl_3 , 101 MHz): δ_{C} 159.1, 154.8, 149.3, 146.9, 138.4, 135.5, 134.4, 124.4, 117.9, 116.8, 111.6, 55.7, 38.2, 27.6, 22.5, 14.0; HRMS (ESI-TOF, m/z): calcd for $\text{C}_{16}\text{H}_{18}\text{BrN}_4\text{O}_2$ [$\text{M} + \text{H}$] $^+$, 377.0608; found, 377.0627.



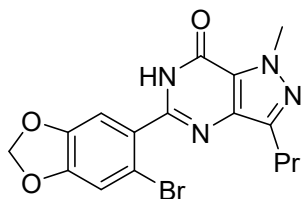
5-(2-bromo-6-fluorophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one (4h)

White solid; mp 127-130 °C; ^1H NMR (CDCl_3 , 400 MHz): δ_{H} 11.15 (s, 1H), 7.50 (d, $J = 8.4$ Hz, 1H), 7.39–7.34 (m, 1H), 7.20–7.16 (m, 1H), 4.17 (s, 3H), 2.90 (t, $J = 7.6$ Hz, 2H), 1.86–1.78 (m, 2H), 0.99 (t, $J = 7.6$ Hz, 3H); ^{13}C NMR (CDCl_3 , 101 MHz): δ_{C} 160.8 (d, $J_{\text{C-F}} = 252.6$ Hz), 155.4, 147.0, 144.5, 138.4, 132.4 (d, $J_{\text{C-F}} = 9.0$ Hz), 128.9 (d, $J_{\text{C-F}} = 3.7$ Hz), 124.6, 124.2 (d, $J_{\text{C-F}} = 18.3$ Hz), 123.6 (d, $J_{\text{C-F}} = 2.8$ Hz), 115.2 (d, $J_{\text{C-F}} = 21.5$ Hz), 38.1, 27.6, 22.6, 13.9; HRMS (ESI-TOF, m/z): calcd for $\text{C}_{15}\text{H}_{15}\text{BrFN}_4$ [$\text{M} + \text{H}$] $^+$, 365.0408; found, 365.0415.



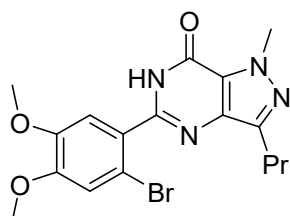
5-(1-bromonaphthalen-2-yl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-*d*]pyrimidin-7-one (4i)

White solid; mp 207-209 °C; ^1H NMR (CDCl_3 , 400 MHz): δ_{H} 10.12 (s, 1H), 8.38 (d, $J = 8.4$ Hz, 1H), 7.95–7.89 (m, 2H), 7.71–7.62 (m, 3H), 4.16 (s, 3H), 2.91 (t, $J = 7.6$ Hz, 2H), 1.88–1.79 (m, 2H), 1.01 (t, $J = 7.6$ Hz, 3H); ^{13}C NMR (CDCl_3 , 101 MHz): δ_{C} 154.4, 150.1, 147.0, 138.5, 134.9, 133.1, 132.1, 128.5, 128.4, 128.4, 128.1, 128.0, 127.0, 124.5, 122.7, 38.2, 27.7, 22.5, 14.0; HRMS (ESI-TOF, m/z): calcd for $\text{C}_{19}\text{H}_{18}\text{BrON}_4$ [$\text{M} + \text{H}$] $^+$, 397.0659; found, 397.0675.



5-(6-bromobenzo[*d*][1,3]dioxol-5-yl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-*d*]pyrimidin-7-one (4j)

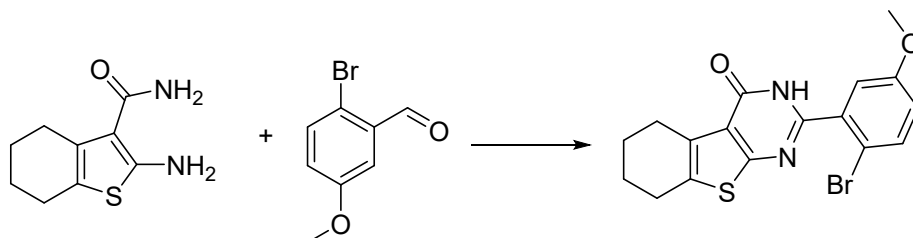
White solid; mp 122-123 °C; ^1H NMR (CDCl_3 , 400 MHz): δ_{H} 11.39 (s, 1H), 7.99–7.95 (m, 1H), 7.56 (d, $J = 7.6$ Hz, 1H), 7.50–7.44 (m, 1H), 7.22–7.16 (m, 1H), 4.22–4.16 (m, 3H), 2.93–2.88 (m, 2H), 1.87–1.78 (m, 2H), 1.02–0.97 (m, 3H); ^{13}C NMR (CDCl_3 , 101 MHz): δ_{C} 155.4, 151.3, 147.0, 140.1, 138.8, 138.4, 131.5, 130.4, 128.3, 124.4, 95.8, 38.2, 27.7, 22.6, 14.0; HRMS (ESI-TOF, m/z): calcd for $\text{C}_{16}\text{H}_{16}\text{BrO}_3\text{N}_4$ [$\text{M} + \text{H}$] $^+$, 391.0400; found, 391.0419.



5-(2-bromo-4,5-dimethoxyphenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-*d*]pyrimidin-7-one (4k)

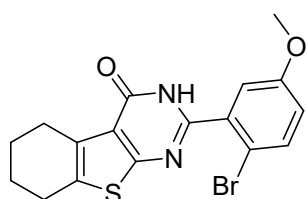
White solid; mp 194-196 °C; ^1H NMR (CDCl_3 , 400 MHz): δ_{H} 10.20 (s, 1H), 7.21 (s, 1H), 7.10 (s, 1H), 4.24 (s, 3H), 3.94–3.93 (m, 6H), 2.91 (t, $J = 7.6$ Hz, 2H), 1.89–1.79 (m, 2H), 1.02 (t, $J = 7.2$

Hz, 3H); ^{13}C NMR (CDCl_3 , 101 MHz): δ_{C} 154.7, 151.1, 149.3, 148.6, 146.8, 138.5, 126.8, 124.3, 116.0, 113.9, 111.9, 56.4, 56.2, 38.2, 27.6, 22.5, 14.0; HRMS (ESI-TOF, m/z): calcd for $\text{C}_{17}\text{H}_{20}\text{BrO}_3\text{N}_4$ [$\text{M} + \text{H}$] $^+$, 407.0713; found, 407.0737.



General procedure for preparation of 2-(2-bromo-5-methoxyphenyl)-5,6,7,8-tetrahydrobenzo[4,5]thieno[2,3-d]pyrimidin-4(3H)-one

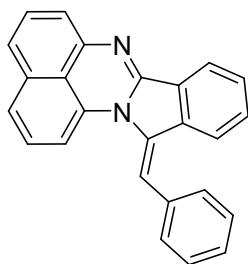
: A mixture of the 2-amino-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-formamide (0.39 g, 2.0 mmol), the anhydrous ammonium chloride (0.01 g, 0.2 mmol) and the 2-bromo-5-methoxybenzaldehyde (0.43 g, 2.0 mmol) in EtOH (10.0 mL) was prepared in a round-bottom flask (50 mL) equipped with a magnetic stirrer. The resulting mixture was monitored by TLC and stirred for the appropriate time. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4 and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 3:1) afforded **7**.



2-(2-bromo-5-methoxyphenyl)-5,6,7,8-tetrahydrobenzo[4,5]thieno[2,3-d]pyrimidin-4(3H)-one (7)

Yellow solid; mp 187–189 °C; ^1H NMR (CDCl_3 , 400 MHz): δ_{H} 11.17 (s, 1H), 7.55 (d, $J = 9.2$ Hz, 1H), 7.23 (d, $J = 3.2$ Hz, 1H), 6.93 (dd, $J = 8.8, 3.2$ Hz, 1H), 3.85 (s, 3H), 2.94 (t, $J = 6.4$ Hz, 2H), 2.81 (t, $J = 6.4$ Hz, 2H), 1.93–1.81 (m, 4H); ^{13}C NMR (CDCl_3 , 101 MHz): δ_{C} 163.6, 159.3, 159.0, 151.3, 134.8, 134.6, 134.5, 131.5, 121.6, 118.4, 116.3, 111.4, 55.7, 25.4, 25.2, 23.0, 22.2; HRMS (ESI-TOF, m/z): calcd for $\text{C}_{17}\text{H}_{16}\text{BrN}_2\text{O}_2\text{S}$ [$\text{M} + \text{H}$] $^+$, 391.0110; found, 391.0136.

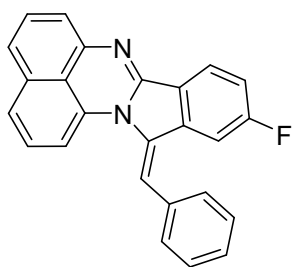
Note: All ethynylbenzene 2 are commercially available.



(E)-12-benzylidene-12H-isoindolo[2,1-a]perimidine (3a)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 2-(2-bromophenyl)-1H-perimidine **1a** (162 mg, 0.5 mmol, 1.0 equiv), ethynylbenzene **2a** (61 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 8:1) afforded **3a** in 85% yield (146 mg).

Red solid; mp 191 °C⁴; ¹H NMR (CDCl₃, 400 MHz): δ_H 8.09 (d, *J* = 8.0 Hz, 1H), 7.71 (s, 1H), 7.51–7.39 (m, 8H), 7.36–7.27 (m, 4H), 7.25–7.20 (m, 2H); ¹³C NMR (CDCl₃, 101 MHz): δ_C 152.3, 142.0, 136.7, 135.6, 135.5, 134.9, 131.1, 130.6, 129.5, 129.1, 128.8, 128.5, 127.9, 126.9, 123.1, 122.3, 122.0, 121.6, 121.0, 117.8, 111.6, 105.3; HRMS (ESI-TOF, *m/z*): calcd for C₂₅H₁₇N₂ [M + H]⁺, 345.1386; found, 345.1376.

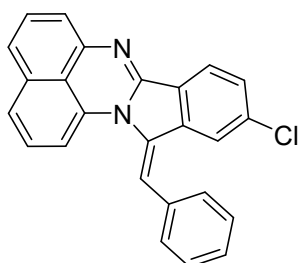


(E)-12-benzylidene-10-fluoro-12H-isoindolo[2,1-a]perimidine (3b)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 2-(2-bromo-4-fluorophenyl)-1H-perimidine **1b** (170 mg, 0.5 mmol, 1.0 equiv), ethynylbenzene **2a** (61 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic

layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 8:1) afforded **3b** in 70% yield (127 mg).

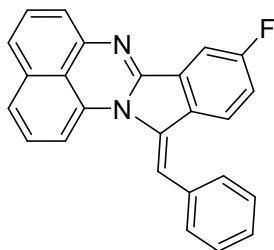
Red solid; mp 164-165 °C; ¹H NMR (CDCl₃, 400 MHz): δ_H 8.06 (dd, *J* = 8.4, 5.2 Hz, 1H), 7.72 (s, 1H), 7.52–7.39 (m, 7H), 7.37–7.29 (m, 3H), 7.21–7.15 (m, 2H), 6.87 (d, *J* = 8.4 Hz, 1H); ¹³C NMR (CDCl₃, 101 MHz): δ_C 164.5 (d, *J*_{C-F} = 248.2 Hz), 151.3, 141.8, 136.7 (d, *J*_{C-F} = 10.6 Hz), 135.9 (d, *J*_{C-F} = 3.6 Hz), 135.4, 134.9, 129.3, 129.0, 128.5, 128.3, 126.9, 126.7 (d, *J*_{C-F} = 1.4 Hz), 124.1 (d, *J*_{C-F} = 9.7 Hz), 122.2, 121.24, 121.16, 117.9, 117.1 (d, *J*_{C-F} = 23.9 Hz), 112.6, 110.1 (d, *J*_{C-F} = 26.2 Hz), 105.3; HRMS (ESI-TOF, *m/z*): calcd for C₂₅H₁₆FN₂ [M + H]⁺, 363.1292; found, 363.1282.



(*E*)-12-benzylidene-10-chloro-12*H*-isoindolo[2,1-*a*]perimidine (**3c**)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 2-(2-bromo-4-chlorophenyl)-1*H*-perimidine **1c** (179 mg, 0.5 mmol, 1.0 equiv), ethynylbenzene **2a** (61 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 8:1) afforded **3c** in 76% yield (144 mg).

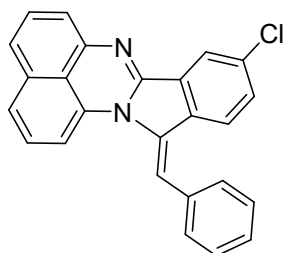
Red solid; mp 228-230 °C; ¹H NMR (CDCl₃, 400 MHz): δ_H 8.00 (d, *J* = 8.4 Hz, 1H), 7.72 (s, 1H), 7.52–7.29 (m, 11H), 7.20–7.17 (m, 2H); ¹³C NMR (CDCl₃, 101 MHz): δ_C 151.4, 141.8, 137.1, 136.2, 135.7, 135.44, 135.40, 134.8, 129.5, 129.4, 128.99, 128.98, 128.6, 128.3, 126.9, 123.4, 123.3, 122.3, 121.4, 121.2, 118.0, 112.6, 105.3; HRMS (ESI-TOF, *m/z*): calcd for C₂₅H₁₆ClN₂ [M + H]⁺, 379.0997; found, 379.0981.



(E)-12-benzylidene-9-fluoro-12H-isoindolo[2,1-a]perimidine (3d)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 2-(2-bromo-5-fluorophenyl)-1H-perimidine **1d** (170 mg, 0.5 mmol, 1.0 equiv), ethynylbenzene **2a** (61 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 8:1) afforded **3d** in 70% yield (127 mg).

Red solid; mp 195–197 °C; ¹H NMR (CDCl₃, 400 MHz): δ_H 7.74–7.63 (m, 2H), 7.50–7.28 (m, 10H), 7.20–7.13 (m, 2H), 7.00–6.93 (m, 1H); ¹³C NMR (CDCl₃, 101 MHz): δ_C 163.1 (d, J_{C-F} = 248.7 Hz), 151.4, 141.7, 136.0, 135.5 (d, J_{C-F} = 3.8 Hz), 135.3, 132.8 (d, J_{C-F} = 9.6 Hz), 130.9, 129.5, 128.9, 128.5, 128.0, 126.9, 125.1 (d, J_{C-F} = 8.1 Hz), 122.3, 121.6, 121.1, 118.8 (d, J_{C-F} = 23.0 Hz), 118.0, 111.2, 108.7 (d, J_{C-F} = 23.9 Hz), 105.3; HRMS (ESI-TOF, *m/z*): calcd for C₂₅H₁₆FN₂ [M + H]⁺, 363.1292; found, 363.1282.

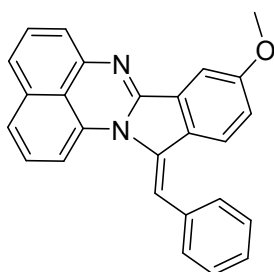


(E)-12-benzylidene-9-chloro-12H-isoindolo[2,1-a]perimidine (3e)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 2-(2-bromo-5-chlorophenyl)-1H-perimidine **1e** (179 mg, 0.5 mmol, 1.0 equiv), ethynylbenzene **2a** (61 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h.

The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 8:1) afforded **3e** in 83% yield (157 mg).

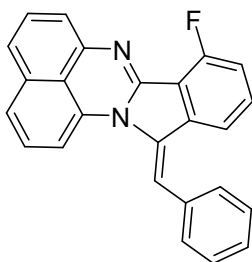
Red solid; mp 164-170 °C; ¹H NMR (CDCl₃, 400 MHz): δ_H 8.06 (s, 1H), 7.69 (s, 1H), 7.48–7.28 (m, 10H), 7.24–7.19 (m, 2H), 7.13–7.10 (m, 1H); ¹³C NMR (CDCl₃, 101 MHz): δ_C 151.2, 141.8, 136.0, 135.5, 135.3, 135.2, 133.2, 132.2, 131.3, 129.5, 128.9, 128.6, 128.1, 126.9, 124.4, 122.4, 122.2, 121.6, 121.2, 118.1, 111.9, 105.4; HRMS (ESI-TOF, *m/z*): calcd for C₂₅H₁₆ClN₂ [M + H]⁺, 379.0997; found, 379.0981.



(E)-12-benzylidene-9-methoxy-12H-isoindolo[2,1-a]perimidine (3f)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 2-(2-bromo-5-methoxyphenyl)-1*H*-perimidine **1f** (176 mg, 0.5 mmol, 1.0 equiv), ethynylbenzene **2a** (61 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 8:1) afforded **3f** in 83% yield (155 mg).

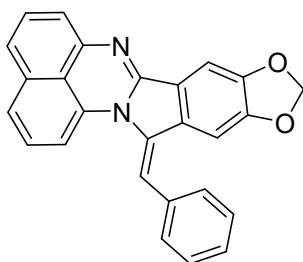
Red solid; mp 89-94 °C; ¹H NMR (CDCl₃, 400 MHz): δ_H 7.59 (s, 1H), 7.52–7.44 (m, 6H), 7.42–7.38 (m, 2H), 7.35–7.26 (m, 3H), 7.22–7.18 (m, 1H), 7.12 (d, *J* = 8.8 Hz, 1H), 6.84 (dd, *J* = 8.8, 2.0 Hz, 1H), 3.90 (s, 3H); ¹³C NMR (CDCl₃, 101 MHz): δ_C 160.6, 152.4, 142.0, 136.5, 135.7, 135.6, 135.5, 132.3, 129.6, 128.8, 128.5, 128.0, 127.7, 126.9, 124.4, 122.0, 121.6, 120.8, 120.1, 117.6, 110.1, 105.2, 104.1, 55.8; HRMS (ESI-TOF, *m/z*): calcd for C₂₆H₁₉N₂O [M + H]⁺, 375.1492; found, 375.1475.



(E)-12-benzylidene-8-fluoro-12H-isoindolo[2,1-a]perimidine (3g)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 2-(2-bromo-6-fluorophenyl)-1H-perimidine **1g** (170 mg, 0.5 mmol, 1.0 equiv), ethynylbenzene **2a** (61 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 8:1) afforded **3g** in 72% yield (130 mg).

Red solid; mp 205-207 °C; ¹H NMR (CDCl₃, 400 MHz): δ_H 7.74 (s, 1H), 7.48–7.27 (m, 11H), 7.25–7.21 (m, 1H), 7.13 (t, *J* = 8.8 Hz, 1H), 7.04 (d, *J* = 8.0 Hz, 1H); ¹³C NMR (CDCl₃, 101 MHz): δ_C 158.3 (d, *J*_{C-F} = 259.3 Hz), 150.1, 141.8, 137.4 (d, *J*_{C-F} = 1.0 Hz), 136.1, 135.33, 135.29 (d, *J*_{C-F} = 3.0 Hz), 132.4 (d, *J*_{C-F} = 7.8 Hz), 129.5, 129.0, 128.6, 128.1, 126.8, 122.5, 121.2 (d, *J*_{C-F} = 3.0 Hz), 119.20, 119.16, 118.8, 118.1, 118.0, 116.3 (d, *J*_{C-F} = 19.1 Hz), 112.0, 105.4; HRMS (ESI-TOF, *m/z*): calcd for C₂₅H₁₆FN₂ [M + H]⁺, 363.1292; found, 363.1282.

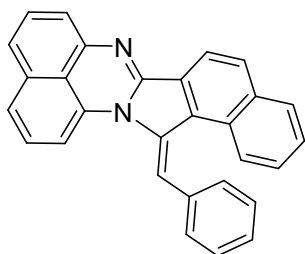


(E)-13-benzylidene-13H-[1,3]dioxolo[4',5':5,6]isoindolo[2,1-a]perimidine (3h)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 2-(6-bromobenzo[*d*][1,3]dioxol-5-yl)-1H-perimidine **1h** (184 mg, 0.5 mmol, 1.0 equiv), ethynylbenzene **2a** (61 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in

an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 8:1) afforded **3h** in 79% yield (153 mg).

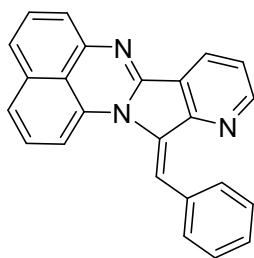
Red solid; mp 148-153 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.62 (s, 1H), 7.47–7.38 (m, 8H), 7.35–7.29 (m, 3H), 7.18 (d, *J* = 7.2 Hz, 1H), 6.58 (s, 1H), 6.00 (s, 2H); ¹³C NMR (CDCl₃, 101 MHz): δ 152.3, 142.1, 136.7, 135.6, 135.5, 134.9, 131.1, 130.6, 129.5, 129.1, 128.8, 128.5, 127.9, 126.9, 123.1, 122.3, 122.0, 121.6, 121.0, 117.8, 111.6, 105.3; HRMS (ESI-TOF, *m/z*): calcd for C₂₆H₁₇N₂O₂ [M + H]⁺, 398.1285; found, 389.1266.



(E)-14-benzylidene-14H-benzo[5,6]isoindolo[2,1-a]perimidine (3i)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 2-(3-bromonaphthalen-2-yl)-1H-perimidine **1i** (187 mg, 0.5 mmol, 1.0 equiv), ethynylbenzene **2a** (61 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 8:1) afforded **3i** in 75% yield (148 mg).

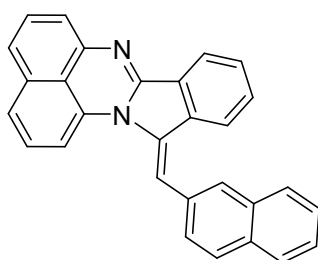
Red solid; mp 227-229 °C; ¹H NMR (CDCl₃, 400 MHz): δ_H 8.71 (d, *J* = 8.4 Hz, 1H), 8.18 (d, *J* = 8.4 Hz, 1H), 8.02–7.96 (m, 2H), 7.56–7.72 (m, 1H), 7.64 (t, *J* = 7.6 Hz, 1H), 7.59 (s, 1H), 7.48–7.35 (m, 3H), 7.25–7.18 (m, 4H), 7.08–7.06 (m, 2H), 6.83 (t, *J* = 8.0 Hz, 1H), 5.65 (d, *J* = 7.6 Hz, 1H); ¹³C NMR (CDCl₃, 101 MHz): δ_C 153.6, 142.1, 136.0, 135.7, 135.2, 134.8, 134.5, 132.4, 130.2, 130.1, 130.0, 128.2, 127.9, 127.8, 127.6, 127.3, 126.4, 125.8, 124.2, 122.4, 120.0, 119.9, 118.9, 118.0, 113.9, 110.0; HRMS (ESI-TOF, *m/z*): calcd for C₂₉H₁₉N₂ [M + H]⁺, 395.1543; found, 395.1525.



(E)-12-benzylidene-12H-pyrido[3',2':3,4]pyrrolo[1,2-a]perimidine (3j)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 2-(2-bromopyridin-3-yl)-1H-perimidine **1j** (162 mg, 0.5 mmol, 1.0 equiv), ethynylbenzene **2a** (61 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 8:1) afforded **3j** in 82% yield (142 mg).

Red solid; mp 172-174 °C; ¹H NMR (CDCl₃, 400 MHz): δ_H 8.70 (d, *J* = 4.8 Hz, 1H), 8.35 (d, *J* = 6.4 Hz, 1H), 7.90–7.88 (m, 2H), 7.76 (s, 1H), 7.51 (d, *J* = 7.2 Hz, 1H), 7.45–7.26 (m, 8H), 7.17 (d, *J* = 7.2 Hz, 1H); ¹³C NMR (CDCl₃, 101 MHz): 153.7, 152.6, 150.1, 141.7, 135.5, 135.2, 134.5, 133.8, 131.1, 130.0, 128.5, 128.0, 127.7, 126.9, 124.1, 123.6, 122.4, 121.9, 121.2, 117.9, 114.5, 105.5; HRMS (ESI-TOF, *m/z*): calcd for C₂₄H₁₆N₃ [M + H]⁺, 346.1339; found, 346.1322.

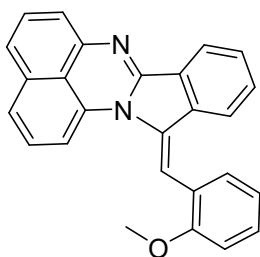


(E)-12-(naphthalen-1-ylmethylene)-12H-isoindolo[2,1-a]perimidine (3k)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 2-(2-bromophenyl)-1H-perimidine **1a** (162 mg, 0.5 mmol, 1.0 equiv), 1-ethynyl-naphthalene **2u** (91 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic

layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 8:1) afforded **3k** in 78% yield (154 mg).

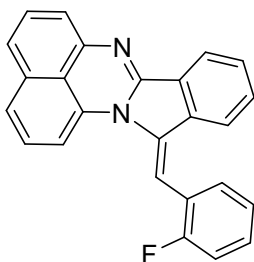
Red solid; mp 221-223 °C; ¹H NMR (CDCl₃, 400 MHz): δ_H 8.11 (d, *J* = 7.6 Hz, 1H), 8.01 (s, 1H), 7.96–7.92 (m, 2H), 7.88–7.84 (m, 2H), 7.60–7.53 (m, 4H), 7.48–7.31 (m, 6H), 7.26–7.21 (m, 2H); ¹³C NMR (CDCl₃, 101 MHz): δ_C 152.3, 142.0, 136.8, 135.6, 135.5, 134.9, 133.4, 132.9, 132.8, 131.2, 130.6, 129.2, 128.6, 128.5, 128.4, 128.0, 127.9, 127.5, 126.9, 126.6, 126.4, 123.1, 122.3, 122.1, 121.6, 121.1, 117.9, 111.7, 105.3; HRMS (ESI-TOF, *m/z*): calcd for C₂₉H₁₉N₂ [M + H]⁺, 395.1543; found, 395.1525.



(E)-12-(2-methoxybenzylidene)-12H-isoindolo[2,1-a]perimidine (3l)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 2-(2-bromophenyl)-1H-perimidine **1a** (162 mg, 0.5 mmol, 1.0 equiv), 1-ethynyl-2-methoxybenzene **2e** (79 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 8:1) afforded **3l** in 75% yield (140 mg).

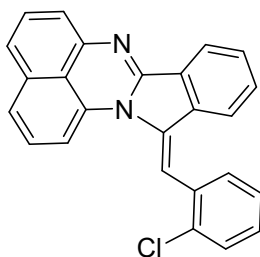
Red solid; mp 203-205 °C; ¹H NMR (CDCl₃, 400 MHz): δ_H 8.08 (d, *J* = 7.6 Hz, 1H), 7.64 (s, 1H), 7.60–7.53 (m, 2H), 7.48–7.27 (m, 8H), 7.19 (d, *J* = 7.2 Hz, 1H), 7.08–6.99 (m, 2H), 3.84 (s, 3H); ¹³C NMR (CDCl₃, 101 MHz): δ_C 157.1, 152.4, 142.2, 136.1, 135.7, 135.5, 135.1, 131.8, 131.1, 130.5, 129.7, 128.9, 128.5, 126.9, 123.9, 122.9, 122.2, 121.8, 121.7, 120.8, 120.5, 117.5, 110.8, 108.8, 105.3, 55.5; HRMS (ESI-TOF, *m/z*): calcd for C₂₆H₁₉N₂O [M + H]⁺, 375.1492; found, 375.1475.



(E)-12-(2-fluorobenzylidene)-12H-isoindolo[2,1-a]perimidin-12-ylidene (3m)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 2-(2-bromophenyl)-1H-perimidine **1a** (162 mg, 0.5 mmol, 1.0 equiv), 1-ethynyl-2-fluorobenzene **2b** (72 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 8:1) afforded **3m** in 75% yield (136 mg).

Red solid; mp 127-130 °C; ¹H NMR (CDCl₃, 400 MHz): δ_H 8.10 (d, *J* = 7.6 Hz, 1H), 7.56 (t, *J* = 7.6 Hz, 1H), 7.52–7.47 (m, 3H), 7.45–7.28 (m, 7H), 7.26–7.19 (m, 3H); ¹³C NMR (CDCl₃, 101 MHz): δ_C 160.2 (d, *J*_{C-F} = 246.3 Hz), 152.1, 141.8, 137.7, 135.4, 134.7, 132.0 (d, *J*_{C-F} = 2.8 Hz), 131.2, 130.7, 130.0 (d, *J*_{C-F} = 8.2 Hz), 129.3, 128.5, 126.9, 124.3, 124.2, 123.2 (d, *J*_{C-F} = 15.8 Hz), 122.8, 122.3 (d, *J*_{C-F} = 9.1 Hz), 121.5, 121.1, 118.0, 116.0 (d, *J*_{C-F} = 21.5 Hz), 105.5, 103.7; HRMS (ESI-TOF, *m/z*): calcd for C₂₅H₁₆FN₂ [M + H]⁺, 363.1292; found, 363.1282.

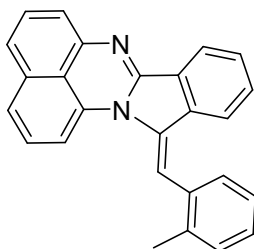


(E)-12-(2-chlorobenzylidene)-12H-isoindolo[2,1-a]perimidin-12-ylidene (3n)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 2-(2-bromophenyl)-1H-perimidine **1a** (162 mg, 0.5 mmol, 1.0 equiv), 1-chloro-2-ethynylbenzene **2c** (82 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about

12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 8:1) afforded **3n** in 82% yield (155 mg).

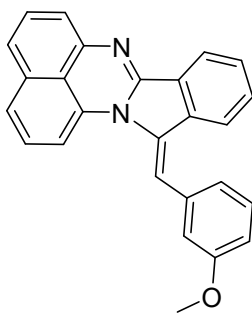
Red solid; mp 184-186 °C; ¹H NMR (CDCl₃, 400 MHz): δ_H 8.11 (d, *J* = 7.6 Hz, 1H), 7.63–7.52 (m, 4H), 7.51–7.47 (m, 1H), 7.44–7.29 (m, 7H), 7.23 (d, *J* = 7.2 Hz, 1H), 7.13 (d, *J* = 8.0 Hz, 1H); ¹³C NMR (CDCl₃, 101 MHz): δ_C 152.2, 141.9, 137.2, 135.4, 134.7, 134.2, 134.1, 131.9, 131.2, 130.8, 129.9, 129.5, 129.3, 128.5, 127.0, 126.9, 123.0, 122.4, 122.3, 121.5, 121.1, 118.0, 108.1, 105.5; HRMS (ESI-TOF, *m/z*): calcd for C₂₅H₁₆ClN₂ [M + H]⁺, 379.0997; found, 379.0981.



(E)-12-(2-methylbenzylidene)-12H-isoindolo[2,1-a]perimidine (3o)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 2-(2-bromophenyl)-1H-perimidine **1a** (162 mg, 0.5 mmol, 1.0 equiv), 1-ethynyl-2-methylbenzene **2d** (70 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.10 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 8:1) afforded **3o** in 79% yield (142 mg).

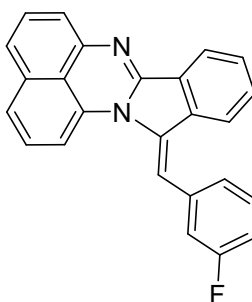
Red solid; mp 160-163 °C; ¹H NMR (CDCl₃, 400 MHz): δ_H 8.09 (d, *J* = 7.6 Hz, 1H), 7.62 (s, 1H), 7.50–7.25 (m, 11H), 7.23–7.20 (m, 1H), 6.92 (d, *J* = 8.0 Hz, 1H), 2.32 (s, 3H); ¹³C NMR (CDCl₃, 101 MHz): δ_C 152.4, 142.1, 136.7, 136.6, 135.7, 135.5, 135.1, 134.6, 131.3, 130.5, 130.4, 130.2, 129.0, 128.5, 128.3, 126.9, 126.2, 123.1, 122.2, 122.0, 121.6, 120.9, 117.7, 110.7, 105.1, 20.4; HRMS (ESI-TOF, *m/z*): calcd for C₂₆H₁₉N₂ [M + H]⁺, 359.1543; found, 359.1527.



(E)-12-(3-methoxybenzylidene)-12H-isoindolo[2,1-a]perimidin-12-ylidene (3p)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 2-(2-bromophenyl)-1H-perimidine **1a** (162 mg, 0.5 mmol, 1.0 equiv), 1-ethynyl-3-methoxybenzene **2i** (79 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 8:1) afforded **3p** in 82% yield (154 mg).

Red solid; mp 158-160 °C; ¹H NMR (CDCl₃, 400 MHz): δ_H 8.09 (d, *J* = 7.6 Hz, 1H), 7.68 (s, 1H), 7.49–7.45 (m, 2H), 7.43–7.37 (m, 3H), 7.35–7.29 (m, 4H), 7.21 (d, *J* = 7.6 Hz, 1H), 7.10 (d, *J* = 7.6 Hz, 1H), 7.02 (s, 1H), 6.96 (dd, *J* = 8.4, 2.8 Hz, 1H), 3.85 (s, 3H); ¹³C NMR (CDCl₃, 101 MHz): δ_C 159.9, 152.3, 142.0, 136.8, 135.6, 135.5, 134.9, 131.2, 130.6, 129.9, 129.1, 128.5, 126.9, 123.3, 122.3, 122.1, 121.9, 121.6, 121.0, 117.8, 114.5, 113.8, 111.4, 105.3, 55.3; HRMS (ESI-TOF, *m/z*): calcd for C₂₆H₁₉N₂O [M + H]⁺, 375.1492; found, 375.1475.

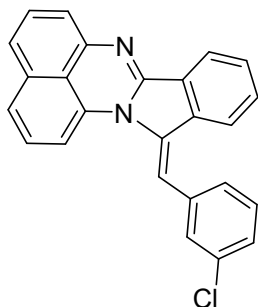


(E)-12-(3-fluorobenzylidene)-12H-isoindolo[2,1-a]perimidin-12-ylidene (3q)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 2-(2-bromophenyl)-1H-perimidine **1a** (162 mg, 0.5 mmol, 1.0 equiv), 1-ethynyl-3-fluorobenzene **2f** (72 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv),

CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 8:1) afforded **3q** in 76% yield (138 mg).

Red solid; mp 146-149 °C; ¹H NMR (CDCl₃, 400 MHz): δ_H 8.11 (d, *J* = 7.6 Hz, 1H), 7.63 (s, 1H), 7.52–7.26 (m, 10H), 7.24–7.19 (m, 2H), 7.15–7.10 (m, 1H); ¹³C NMR (CDCl₃, 101 MHz): δ_C 163.0 (d, *J*_{C-F} = 245.8 Hz), 152.1, 141.8, 137.7 (d, *J*_{C-F} = 8.0 Hz), 137.3, 135.4, 134.6, 131.2, 130.7, 130.4 (d, *J*_{C-F} = 8.5 Hz), 129.4, 128.6, 126.9, 125.4 (d, *J*_{C-F} = 2.9 Hz), 123.1, 122.4, 122.3, 121.5, 121.2, 118.0, 116.4 (d, *J*_{C-F} = 21.5 Hz), 114.8 (d, *J*_{C-F} = 20.8 Hz), 109.780, 109.775, 105.4; HRMS (ESI-TOF, *m/z*): calcd for C₂₅H₁₆FN₂ [M + H]⁺, 363.1292; found, 363.1282.

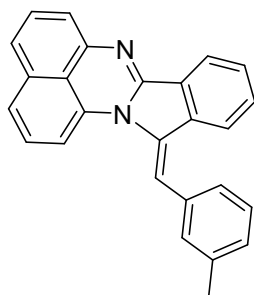


(E)-12-(3-chlorobenzylidene)-12H-isoindolo[2,1-a]perimidine (3r)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 2-(2-bromophenyl)-1H-perimidine **1a** (162 mg, 0.5 mmol, 1.0 equiv), 1-chloro-3-ethynylbenzene **2g** (82 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 8:1) afforded **3r** in 76% yield (144 mg).

Red solid; mp 94-96 °C; ¹H NMR (CDCl₃, 400 MHz): δ_H 8.11 (d, *J* = 7.6 Hz, 1H), 7.60 (s, 1H), 7.52–7.29 (m, 11H), 7.26–7.22 (m, 2H); ¹³C NMR (CDCl₃, 101 MHz): δ_C 152.1, 141.8, 137.4, 137.3, 135.39, 135.36, 134.7, 134.6, 131.2, 130.7, 130.1, 129.5, 129.4, 128.5, 127.9, 127.8,

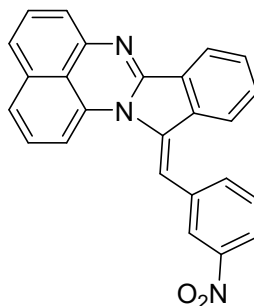
126.8, 123.0, 122.4, 122.3, 121.4, 121.2, 118.1, 109.5, 105.4; HRMS (ESI-TOF, m/z): calcd for $C_{25}H_{16}ClN_2$ [$M + H$] $^+$, 379.0997; found, 379.0981.



(E)-12-(3-methylbenzylidene)-12H-isoindolo[2,1-a]perimidine (3s)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 2-(2-bromophenyl)-1H-perimidine **1a** (162 mg, 0.5 mmol, 1.0 equiv), 1-ethynyl-3-methylbenzene **2h** (70 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs_2CO_3 (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4 and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 8:1) afforded **3s** in 80% yield (143 mg).

Red solid; mp 156-158 °C; 1H NMR ($CDCl_3$, 400 MHz): δ_H 8.09 (d, $J = 7.6$ Hz, 1H), 7.68 (s, 1H), 7.50–7.26 (m, 11H), 7.24–7.20 (m, 2H), 2.42 (s, 3H); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 152.4, 142.1, 136.7, 136.6, 135.7, 135.5, 135.1, 134.6, 131.3, 130.5, 130.4, 130.2, 129.0, 128.5, 128.3, 126.9, 126.2, 123.1, 122.2, 122.0, 121.6, 120.9, 117.7, 110.7, 105.1, 20.4; HRMS (ESI-TOF, m/z): calcd for $C_{26}H_{19}N_2$ [$M + H$] $^+$, 359.1543; found, 359.1527.

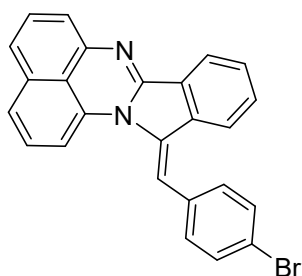


(E)-12-(3-nitrobenzylidene)-12H-isoindolo[2,1-a]perimidine (3t)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 2-(2-bromophenyl)-1H-perimidine **1a** (162 mg, 0.5 mmol, 1.0 equiv), 1-ethynyl-3-nitrobenzene **2j** (88 mg, 0.6 mmol, 1.2

equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 8:1) afforded **3t** in 77% yield (150 mg).

Red solid; mp 158-161 °C; ¹H NMR (CDCl₃, 400 MHz): δ_H 8.39 (s, 1H), 8.27 (dd, *J* = 8.4, 2.4 Hz, 1H), 8.12 (d, *J* = 7.6 Hz, 1H), 7.85 (d, *J* = 7.6 Hz, 1H), 7.68–7.62 (m, 2H), 7.53–7.30 (m, 7H), 7.25 (d, *J* = 8.0 Hz, 1H), 7.14 (d, *J* = 8.0 Hz, 1H); ¹³C NMR (CDCl₃, 101 MHz): δ_C 151.9, 148.6, 141.5, 138.1, 137.5, 135.8, 135.4, 135.2, 134.2, 131.3, 130.9, 129.79, 129.76, 128.6, 126.8, 124.6, 122.7, 122.6, 121.4, 121.3, 118.4, 107.7, 105.6; HRMS (ESI-TOF, *m/z*): calcd for C₂₅H₁₆N₃O₂ [M + H]⁺, 390.1237; found, 390.1264.

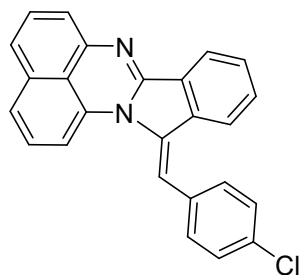


(E)-12-(4-bromobenzylidene)-12H-isoindolo[2,1-a]perimidine (3u)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 2-(2-bromophenyl)-1H-perimidine **1a** (162 mg, 0.5 mmol, 1.0 equiv), 1-bromo-4-ethynylbenzene **2m** (109 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 8:1) afforded **3u** in 79% yield (167 mg).

Red solid; mp 214-217 °C; ¹H NMR (CDCl₃, 400 MHz): δ_H 8.09 (d, *J* = 7.6 Hz, 1H), 7.61–7.56 (m, 3H), 7.50–7.36 (m, 7H), 7.33–7.27 (m, 3H), 7.25–7.21 (m, 1H); ¹³C NMR (CDCl₃, 101 MHz): δ_C 152.1, 141.9, 137.1, 135.4, 134.7, 134.5, 133.8, 132.0, 131.8, 131.3, 130.7, 129.3, 128.6,

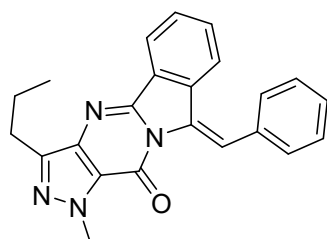
126.9, 123.0, 122.4, 122.2, 121.9, 121.5, 121.2, 118.0, 109.9, 105.4; HRMS (ESI-TOF, m/z): calcd for $C_{25}H_{16}BrN_2$ $[M + H]^+$, 423.0491; found, 423.0470.



(E)-12-(4-chlorobenzylidene)-12H-isoindolo[2,1-a]perimidine (3v)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 2-(2-bromophenyl)-1H-perimidine **1a** (162 mg, 0.5 mmol, 1.0 equiv), 1-chloro-4-ethynylbenzene **2l** (82 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs_2CO_3 (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4 and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 8:1) afforded **3v** in 80% yield (152 mg).

Red solid; mp 198–201 °C; 1H NMR ($CDCl_3$, 400 MHz): δ_H 8.10 (d, $J = 7.6$ Hz, 1H), 7.60 (s, 1H), 7.51–7.44 (m, 6H), 7.41–7.29 (m, 6H), 7.24–7.21 (m, 1H); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 152.1, 141.9, 137.1, 135.5, 135.4, 134.7, 134.0, 133.8, 133.7, 131.2, 130.9, 130.7, 129.3, 129.1, 128.9, 128.6, 126.9, 123.0, 122.4, 122.2, 121.5, 121.1, 118.0, 109.9, 105.3; HRMS (ESI-TOF, m/z): calcd for $C_{25}H_{16}ClN_2$ $[M + H]^+$, 379.0997; found, 379.0981.

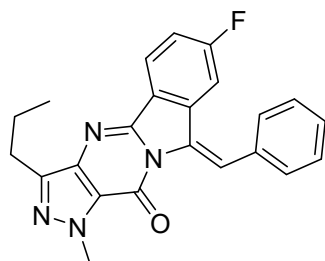


(E)-9-benzylidene-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (5a)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one **4a** (174 mg, 0.5 mmol, 1.0 equiv), ethynylbenzene **2a** (61 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs_2CO_3 (163 mg, 0.5 mmol, 1.0

equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **5a** in 27% yield (50 mg).

Yellow solid; mp 193–194 °C; ¹H NMR (CDCl₃, 400 MHz): δ_H 9.08 (s, 1H), 8.11 (d, *J* = 7.6 Hz, 1H), 7.51–7.40 (m, 6H), 7.28–7.24 (m, 1H), 7.22–7.19 (m, 1H), 4.35 (s, 3H), 2.96 (t, *J* = 7.6 Hz, 2H), 1.94–1.85 (m, 2H), 1.05 (t, *J* = 7.6 Hz, 3H); ¹³C NMR (CDCl₃, 101 MHz) δ_C 154.2, 150.0, 146.1, 137.2, 135.5, 135.4, 134.1, 130.9, 130.5, 129.5, 129.0, 128.8, 128.2, 124.9, 123.7, 122.7, 122.3, 38.6, 27.7, 22.4, 14.1; HRMS (ESI-TOF, *m/z*): calcd for C₂₃H₂₁N₄O [M + H]⁺, 369.1710; found, 369.1707.

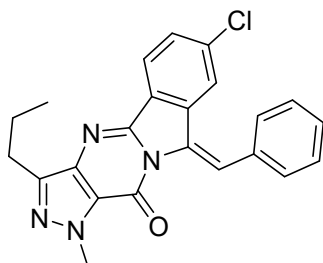


(*E*)-9-benzylidene-7-fluoro-1-methyl-3-propyl-1,9-dihydro-11*H*-pyrazolo[4',3':4,5]pyrimido[2,1-*a*]isoindol-11-one (5b**)**

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromo-4-fluorophenyl)-1-methyl-3-propyl-1,6-dihydro-7*H*-pyrazolo[4,3-*d*]pyrimidin-7-one **4b** (183 mg, 0.5 mmol, 1.0 equiv), ethynylbenzene **2a** (61 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **5b** in 25% yield (48 mg).

Yellow solid; mp 181–182 °C; ¹H NMR (CDCl₃, 400 MHz): δ_H 9.09 (s, 1H), 8.09–8.05 (m, 1H), 7.51–7.43 (m, 5H), 7.18–7.13 (m, 1H), 6.83 (d, *J* = 9.6 Hz, 1H), 4.34 (s, 3H), 2.94 (t, *J* = 7.6 Hz, 2H), 1.93–1.84 (m, 2H), 1.05 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (CDCl₃, 101 MHz) δ_C 164.1 (d, *J*_{C-F} = 248.2 Hz), 154.1, 149.0, 146.0, 137.1, 135.9 (d, *J*_{C-F} = 10.5 Hz), 134.75, 134.67 (d, *J*_{C-F} = 4.2 Hz),

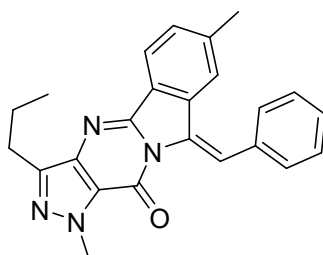
128.9 (d, $J_{C-F} = 22.1$ Hz), 128.5, 126.7 (d, $J_{C-F} = 2.2$ Hz), 124.6, 124.2 (d, $J_{C-F} = 14.1$ Hz), 123.9, 117.6 (d, $J_{C-F} = 24.2$ Hz), 110.8, 110.5, 38.6, 27.7, 22.4, 14.0; HRMS (ESI-TOF, m/z): calcd for $C_{23}H_{20}FN_4O$ [$M + H$] $^+$, 387.1616; found, 387.1616.



(E)-9-benzylidene-7-chloro-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (5c)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromo-4-chlorophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one **4c** (191 mg, 0.5 mmol, 1.0 equiv), ethynylbenzene **2a** (61 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs_2CO_3 (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4 and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **5c** in 20% yield (40 mg).

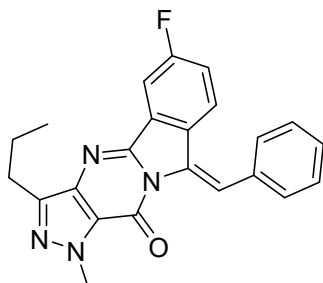
Yellow solid; mp 186–187 °C; 1H NMR ($CDCl_3$, 400 MHz): δ_H 9.10 (s, 1H), 8.04 (dd, $J = 8.0, 1.6$ Hz, 1H), 7.52–7.41 (m, 6H), 7.15 (s, 1H), 4.35 (s, 3H), 2.94 (t, $J = 8.0$ Hz, 2H), 1.93–1.84 (m, 2H), 1.05 (t, $J = 7.6$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 101 MHz) δ_C 154.0, 149.0, 146.1, 137.0, 135.4, 134.7, 134.4, 130.0, 129.0, 128.9, 128.8, 128.6, 124.8, 124.0, 123.7, 123.4, 38.6, 27.7, 22.4, 14.0; HRMS (ESI-TOF, m/z): calcd for $C_{23}H_{20}ClN_4O$ [$M + H$] $^+$, 403.1320; found, 403.1325.



(E)-9-benzylidene-1,7-dimethyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1- α]isoindol-11-one (5d)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromo-4-methylphenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-*d*]pyrimidin-7-one **4d** (181 mg, 0.5 mmol, 1.0 equiv), ethynylbenzene **2a** (61 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **5d** in 25% yield (48 mg).

Yellow solid; mp 204–205 °C; ¹H NMR (CDCl₃, 400 MHz): δ_{H} 9.04 (s, 1H), 7.97 (d, *J* = 7.6 Hz, 1H), 7.50–7.40 (m, 5H), 7.27–7.25 (m, 1H), 6.98 (s, 1H), 4.34 (s, 3H), 2.94 (t, *J* = 7.6 Hz, 2H), 2.22 (s, 3H), 1.94–1.84 (m, 2H), 1.05 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (CDCl₃, 101 MHz) δ_{C} 154.3, 150.1, 145.9, 141.4, 137.2, 135.6, 135.5, 134.4, 130.7, 129.0, 128.7, 128.1, 124.8, 124.0, 122.5, 122.0, 38.6, 27.7, 22.4, 22.0, 14.1; HRMS (ESI-TOF, *m/z*): calcd for C₂₄H₂₃N₄O [M + H]⁺, 383.1866; found, 383.1875.

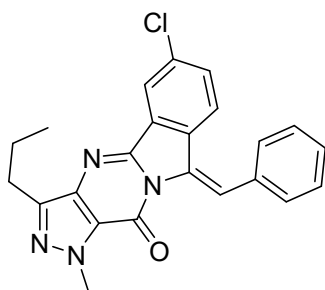


(E)-9-benzylidene-6-fluoro-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1- α]isoindol-11-one (5e)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromo-5-fluorophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-*d*]pyrimidin-7-one **4e** (183 mg, 0.5 mmol, 1.0 equiv), ethynylbenzene **2a** (61 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄

and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **5e** in 24% yield (46 mg).

Yellow solid; mp 183–184 °C; ^1H NMR (CDCl_3 , 400 MHz): δ_{H} 9.03 (s, 1H), 7.76–7.73 (m, 1H), 7.50–7.40 (m, 5H), 7.15 (dd, $J = 8.8, 4.4$ Hz, 1H), 6.95 (t, $J = 8.8$ Hz, 1H), 4.35 (s, 3H), 2.94 (t, $J = 7.6$ Hz, 2H), 1.93–1.84 (m, 2H), 1.05 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (CDCl_3 , 101 MHz) δ_{C} 163.3 (d, $J_{\text{C-F}} = 249.3$ Hz), 154.0, 148.93, 148.89, 146.3, 137.0, 135.2, 134.7, 132.7 (d, $J_{\text{C-F}} = 10.1$ Hz), 130.2 (d, $J_{\text{C-F}} = 2.6$ Hz), 128.9 (d, $J_{\text{C-F}} = 3.4$ Hz), 128.3, 125.7 (d, $J_{\text{C-F}} = 8.5$ Hz), 124.9, 122.2 (d, $J_{\text{C-F}} = 1.0$ Hz), 118.7 (d, $J_{\text{C-F}} = 23.5$ Hz), 108.7 (d, $J_{\text{C-F}} = 24.1$ Hz), 38.6, 27.7, 22.4, 14.0; HRMS (ESI-TOF, m/z): calcd for $\text{C}_{23}\text{H}_{20}\text{FN}_4\text{O}$ [$\text{M} + \text{H}$] $^+$, 387.1616; found, 387.1616.

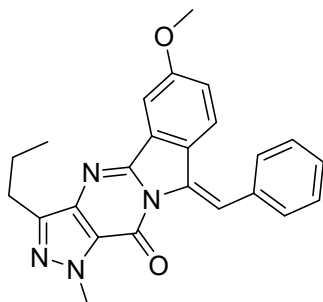


(E)-9-benzylidene-6-chloro-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (5f)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromo-5-chlorophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one **4f** (191 mg, 0.5 mmol, 1.0 equiv), ethynylbenzene **2a** (61 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs_2CO_3 (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4 and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **5f** in 20% yield (40 mg).

Yellow solid; mp 200–201 °C; ^1H NMR (CDCl_3 , 400 MHz): δ_{H} 9.06 (s, 1H), 8.10–8.08 (m, 1H), 7.50–7.43 (m, 5H), 7.22–7.20 (m, 1H), 7.13–7.10 (m, 1H), 4.35 (s, 3H), 2.95 (t, $J = 7.2$ Hz, 2H), 1.93–1.84 (m, 2H), 1.05 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (CDCl_3 , 101 MHz) δ_{C} 154.0, 148.7, 146.3, 137.0, 135.7, 135.1, 134.8, 132.4, 132.1, 131.1, 130.0, 128.9, 128.4, 124.9, 123.7, 123.1,

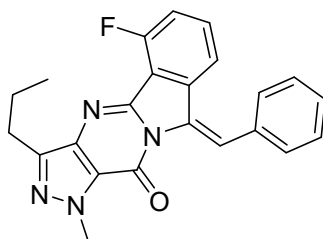
122.2, 38.6, 27.7, 22.4, 14.0; HRMS (ESI-TOF, m/z): calcd for $C_{23}H_{20}ClN_4O$ $[M + H]^+$, 403.1320; found, 403.1325.



(E)-9-benzylidene-6-methoxy-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (5g)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromo-5-methoxyphenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one **4g** (188 mg, 0.5 mmol, 1.0 equiv), ethynylbenzene **2a** (61 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs_2CO_3 (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4 and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **5g** in 30% yield (60 mg).

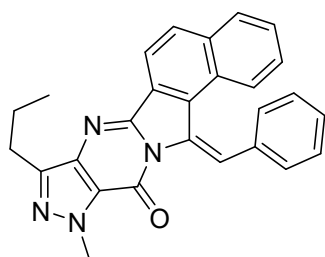
Yellow solid; mp 155–156 °C; 1H NMR ($CDCl_3$, 400 MHz): δ_H 8.94 (s, 1H), 7.54–7.53 (m, 1H), 7.49–7.38 (m, 5H), 7.10 (d, $J = 8.8$ Hz, 1H), 6.84–6.81 (m, 1H), 4.35 (s, 3H), 3.92 (s, 3H), 2.96 (t, $J = 7.6$ Hz, 2H), 1.94–1.85 (m, 2H), 1.06 (t, $J = 7.6$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 101 MHz) δ_C 160.9, 154.2, 150.0, 146.0, 137.0, 135.6, 135.3, 132.2, 129.1, 128.8, 128.0, 127.2, 125.0, 120.7, 119.8, 104.3, 55.7, 38.6, 27.7, 22.4, 14.1; HRMS (ESI-TOF, m/z): calcd for $C_{24}H_{23}N_4O_2$ $[M + H]^+$, 399.1816; found, 399.1824.



(E)-9-benzylidene-5-fluoro-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-*a*]isoindol-11-one (5h)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromo-6-fluorophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-*d*]pyrimidin-7-one **4h** (183 mg, 0.5 mmol, 1.0 equiv), ethynylbenzene **2a** (61 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **5h** in 25% yield (48 mg).

Yellow solid; mp 209–210 °C; ¹H NMR (CDCl₃, 400 MHz): δ_H 9.12 (s, 1H), 7.50–7.40 (m, 5H), 7.23–7.18 (m, 1H), 7.14–7.10 (m, 1H), 6.99 (d, *J* = 8.0 Hz, 1H), 4.35 (s, 3H), 2.97 (t, *J* = 7.6 Hz, 2H), 1.95–1.86 (m, 2H), 1.05 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (CDCl₃, 101 MHz) δ_C 158.1 (d, *J*_{C-F} = 259.1 Hz), 153.9, 147.25, 147.19, 146.5, 137.2, 136.5 (d, *J*_{C-F} = 2.7 Hz), 135.2, 134.9 (d, *J*_{C-F} = 1.9 Hz), 132.2 (d, *J*_{C-F} = 7.4 Hz), 128.9 (d, *J*_{C-F} = 8.7 Hz), 128.3, 124.5, 123.7, 119.6 (d, *J*_{C-F} = 4.2 Hz), 118.0 (d, *J*_{C-F} = 12.6 Hz), 116.5 (d, *J*_{C-F} = 18.7 Hz), 38.6, 27.7, 22.2, 14.0; HRMS (ESI-TOF, *m/z*): calcd for C₂₃H₂₀FN₄O [M + H]⁺, 387.1616; found, 387.1616.

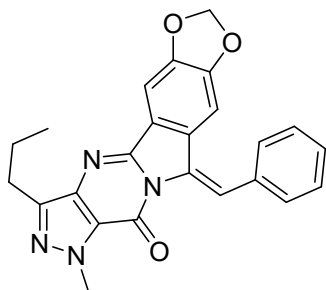


(E)-13-benzylidene-10-methyl-8-propyl-10,13-dihydro-11H-benzo[*e*]pyrazolo[4',3':4,5]pyrimido[2,1-*a*]isoindol-11-one (5i)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(1-bromonaphthalen-2-yl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-*d*]pyrimidin-7-one **4i** (198 mg, 0.5 mmol, 1.0 equiv), ethynylbenzene **2a** (61 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄

and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **5i** in 28% yield (59 mg).

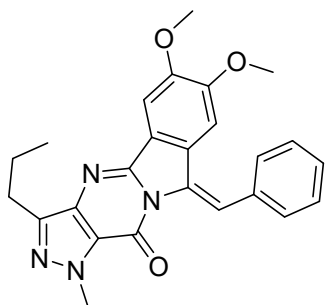
Yellow solid; mp 159–160 °C; ^1H NMR (CDCl_3 , 400 MHz): δ_{H} 9.41 (d, J = 3.6 Hz, 1H), 8.18–8.14 (m, 1H), 7.98–7.95 (m, 1H), 7.84–7.82 (m, 1H), 7.39–7.36 (m, 1H), 7.31–7.20 (m, 6H), 7.00–6.96 (m, 1H), 4.36 (s, 3H), 3.00–2.96 (m, 2H), 1.96–1.87 (m, 2H), 1.07 (t, J = 7.6 Hz, 3H); ^{13}C NMR (CDCl_3 , 101 MHz) δ_{C} 153.8, 150.1, 146.0, 137.1, 136.2, 136.0, 135.5, 132.10, 132.07, 131.8, 130.9, 130.5, 128.8, 128.6, 128.3, 127.7, 127.0, 126.4, 126.2, 124.9, 122.0, 118.65, 118.62, 38.6, 27.8, 22.4, 14.1; HRMS (ESI-TOF, m/z): calcd for $\text{C}_{27}\text{H}_{23}\text{N}_4\text{O}$ [$\text{M} + \text{H}$] $^+$, 419.1866; found, 419.1870.



(E)-10-benzylidene-1-methyl-3-propyl-1,10-dihydro-12H-[1,3]dioxolo[4,5-f]pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-12-one (5j**)**

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(6-bromobenzo[*d*][1,3]dioxol-5-yl)-1-methyl-3-propyl-1,6-dihydro-7*H*-pyrazolo[4,3-*d*]pyrimidin-7-one **4j** (195 mg, 0.5 mmol, 1.0 equiv), ethynylbenzene **2a** (61 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs_2CO_3 (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4 and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **5j** in 23% yield (47 mg).

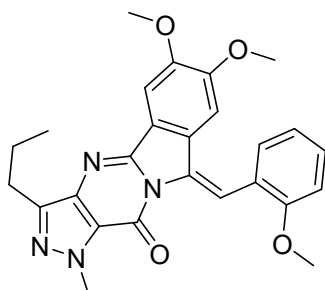
Yellow solid; mp 236–237 °C; ^1H NMR (CDCl_3 , 400 MHz): δ_{H} 8.96 (s, 1H), 7.48–7.38 (m, 6H), 6.52 (s, 1H), 6.00 (s, 2H), 4.33 (s, 3H), 2.93 (t, J = 7.6 Hz, 2H), 1.92–1.83 (m, 2H), 1.04 (t, J = 7.6 Hz, 3H); ^{13}C NMR (CDCl_3 , 101 MHz) δ_{C} 154.1, 150.6, 149.8, 149.5, 145.8, 137.1, 135.23, 135.16, 129.4, 128.9, 128.8, 128.1, 125.6, 124.5, 121.4, 103.5, 102.0, 101.5, 38.5, 27.7, 22.4, 14.1; HRMS (ESI-TOF, m/z): calcd for $\text{C}_{24}\text{H}_{21}\text{N}_4\text{O}_3$ [$\text{M} + \text{H}$] $^+$, 413.1609; found, 413.1623.



(E)-9-benzylidene-6,7-dimethoxy-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (5k)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromo-4,5-dimethoxyphenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one **4k** (203 mg, 0.5 mmol, 1.0 equiv), ethynylbenzene **2a** (61 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **5k** in 30% yield (64 mg).

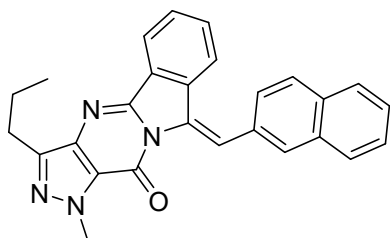
Yellow solid; mp 208–209 °C; ¹H NMR (CDCl₃, 400 MHz): δ_H 8.93 (s, 1H), 7.52–7.44 (m, 5H), 7.41–7.38 (m, 1H), 6.53 (s, 1H), 4.33 (s, 3H), 4.01 (s, 3H), 3.49 (s, 3H), 2.94 (t, *J* = 6.8 Hz, 2H), 1.94–1.84 (m, 2H), 1.06 (t, *J* = 7.6 Hz, 3H); ¹³C NMR (CDCl₃, 101 MHz) δ_C 154.2, 151.6, 151.0, 150.3, 145.7, 137.2, 135.6, 135.5, 129.2, 128.7, 128.0, 127.9, 124.6, 123.7, 120.9, 105.6, 103.1, 56.3, 55.6, 38.6, 27.7, 22.5, 14.1; HRMS (ESI-TOF, *m/z*): calcd for C₂₅H₂₅N₄O₃ [M + H]⁺, 429.1921; found, 429.1947.



(E)-6,7-dimethoxy-9-(2-methoxybenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (5l)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromo-4,5-dimethoxyphenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one **4k** (203 mg, 0.5 mmol, 1.0 equiv), 1-ethynyl-2-methoxybenzene **2e** (79 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **5l** in 30% yield (69 mg).

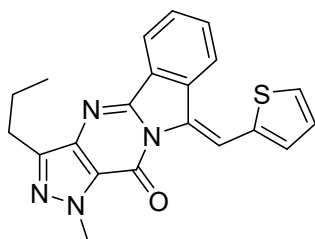
Yellow solid; mp 203–205 °C; ¹H NMR (CDCl₃, 400 MHz): δ_H 8.86 (s, 1H), 7.53–7.47 (m, 2H), 7.40 (t, *J* = 8.0 Hz, 1H), 7.05–7.01 (m, 2H), 6.76 (s, 1H), 4.35 (s, 3H), 4.02 (s, 3H), 3.86 (s, 3H), 3.55 (s, 3H), 2.95 (t, *J* = 8.0 Hz, 2H), 1.94–1.85 (m, 2H), 1.06 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (CDCl₃, 101 MHz) δ_C 157.4, 154.2, 151.7, 151.0, 150.4, 145.7, 137.2, 135.0, 131.0, 130.0, 128.2, 124.7, 124.1, 123.7, 120.2, 117.7, 111.0, 105.5, 103.1, 56.3, 55.62, 55.59, 38.6, 27.7, 22.4, 14.1; HRMS (ESI-TOF, *m/z*): calcd for C₂₆H₂₇N₄O₄ [M + H]⁺, 459.2027; found, 459.2057.



(E)-1-methyl-9-(naphthalen-2-ylmethylene)-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (5m)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one **4a** (174 mg, 0.5 mmol, 1.0 equiv), 2-ethynyl-naphthalene **2u** (91 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **5m** in 35% yield (73 mg).

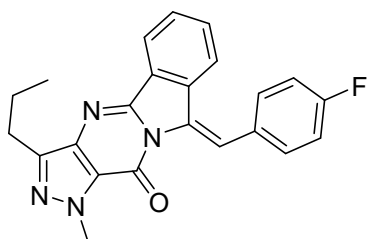
Yellow solid; mp 196–197 °C; ^1H NMR (CDCl_3 , 400 MHz): δ_{H} 9.22 (s, 1H), 8.13 (d, $J = 8.0$ Hz, 1H), 7.99 (s, 1H), 7.95–7.90 (m, 2H), 7.86–7.84 (m, 1H), 7.60–7.52 (m, 3H), 7.47–7.43 (m, 1H), 7.29–7.26 (m, 1H), 7.22–7.18 (m, 1H), 4.36 (s, 3H), 2.97 (t, $J = 7.6$ Hz, 2H), 1.95–1.86 (m, 2H), 1.06 (t, $J = 8.0$ Hz, 3H); ^{13}C NMR (CDCl_3 , 101 MHz) δ_{C} 154.3, 150.0, 146.1, 137.2, 135.6, 134.2, 133.4, 132.9, 132.8, 131.0, 130.6, 129.6, 128.5, 128.2, 128.1, 127.8, 127.0, 126.54, 126.52, 124.9, 123.7, 122.7, 122.4, 38.6, 27.7, 22.4, 14.0; HRMS (ESI-TOF, m/z): calcd for $\text{C}_{27}\text{H}_{23}\text{N}_4\text{O}$ $[\text{M} + \text{H}]^+$, 419.1866; found, 419.1870.



(*E*)-1-methyl-3-propyl-9-(thiophen-2-ylmethylene)-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-*a*]isoindol-11-one (5n)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromophenyl)-1-methyl-3-propyl-1,6-dihydro-7*H*-pyrazolo[4,3-*d*]pyrimidin-7-one **4a** (174 mg, 0.5 mmol, 1.0 equiv), 2-ethynylthiophene **2v** (65 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs_2CO_3 (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4 and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **5n** in 35% yield (66 mg).

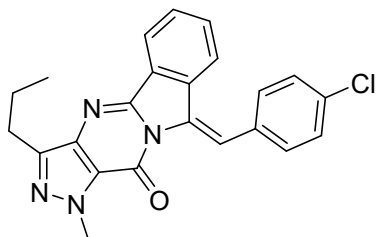
Yellow solid; mp 189–190 °C; ^1H NMR (CDCl_3 , 400 MHz): δ_{H} 8.99 (s, 1H), 8.11 (dd, $J = 7.6$ Hz, 2.8 Hz, 1H), 7.64 (d, $J = 8.0$ Hz, 1H), 7.52–7.47 (m, 2H), 7.38–7.34 (m, 1H), 7.28–7.27 (m, 1H), 7.16–7.14 (m, 1H), 4.34 (s, 3H), 2.95 (t, $J = 7.6$ Hz, 2H), 1.94–1.84 (m, 2H), 1.05 (t, $J = 8.0$ Hz, 3H); ^{13}C NMR (CDCl_3 , 101 MHz) δ_{C} 154.1, 149.7, 146.1, 137.1, 137.0, 136.6, 133.8, 131.1, 130.6, 129.8, 128.1, 127.6, 127.5, 124.8, 123.6, 122.3, 114.7, 38.6, 27.7, 22.4, 14.0; HRMS (ESI-TOF, m/z): calcd for $\text{C}_{21}\text{H}_{19}\text{N}_4\text{OS}$ $[\text{M} + \text{H}]^+$, 375.1274; found, 375.1280.



(E)-9-(4-fluorobenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1- α]isoindol-11-one (5o)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one **4a** (174 mg, 0.5 mmol, 1.0 equiv), 1-ethynyl-4-fluorobenzene **2k** (72 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **5o** in 27% yield (52 mg).

Yellow solid; mp 238–239 °C; ¹H NMR (CDCl₃, 400 MHz): δ_{H} 9.00 (s, 1H), 8.12 (d, J = 7.6 Hz, 1H), 7.49–7.45 (m, 3H), 7.31–7.27 (m, 1H), 7.21–7.15 (m, 3H), 4.34 (s, 3H), 2.95 (t, J = 7.6 Hz, 2H), 1.94–1.85 (m, 2H), 1.05 (t, J = 7.2 Hz, 3H); ¹³C NMR (CDCl₃, 101 MHz) δ_{C} 162.6 (d, $J_{\text{C-F}}$ = 246.8 Hz), 154.2, 149.9, 146.1, 137.2, 135.8, 134.0, 131.3 (d, $J_{\text{C-F}}$ = 4.1 Hz), 131.0, 130.8 (d, $J_{\text{C-F}}$ = 8.0 Hz), 130.6, 129.7, 124.9, 123.5, 122.4, 121.4, 116.0 (d, $J_{\text{C-F}}$ = 21.6 Hz), 38.6, 27.7, 22.4, 14.0; HRMS (ESI-TOF, m/z): calcd for C₂₃H₂₀FN₄O [M + H]⁺, 387.1616; found, 387.1616.

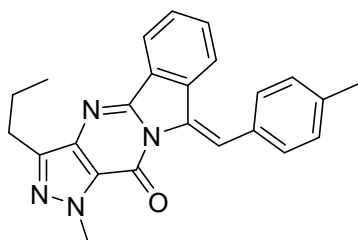


(E)-9-(4-chlorobenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1- α]isoindol-11-one (5p)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one **4a** (174 mg, 0.5 mmol, 1.0 equiv), 1-chloro-4-ethynylbenzene **2l** (82 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture

was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **5p** in 20% yield (40 mg).

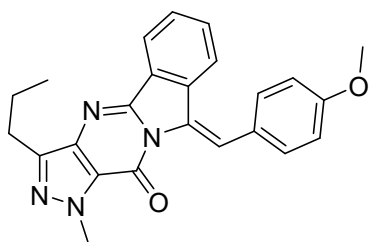
Yellow solid; mp 229–230 °C; ¹H NMR (CDCl₃, 400 MHz): δ_H 8.99 (s, 1H), 8.12 (d, *J* = 7.6 Hz, 1H), 7.51–7.42 (m, 5H), 7.31 (t, *J* = 7.6 Hz, 1H), 7.24 (d, *J* = 8.0 Hz, 1H), 4.35 (s, 3H), 2.96 (t, *J* = 7.6 Hz, 2H), 1.94–1.85 (m, 2H), 1.05 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (CDCl₃, 101 MHz) δ_C 154.2, 149.9, 146.2, 137.2, 135.9, 134.1, 133.9, 133.8, 131.0, 130.7, 130.4, 129.8, 129.1, 124.9, 123.6, 122.5, 121.1, 38.6, 27.7, 22.4, 14.0; HRMS (ESI-TOF, *m/z*): calcd for C₂₃H₂₀ClN₄O [M + H]⁺, 403.1320; found, 403.1325.



(E)-1-methyl-9-(4-methylbenzylidene)-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (5q)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-*d*]pyrimidin-7-one **4a** (174 mg, 0.5 mmol, 1.0 equiv), 1-ethynyl-4-methylbenzene **2n** (70 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **5q** in 30% yield (57 mg).

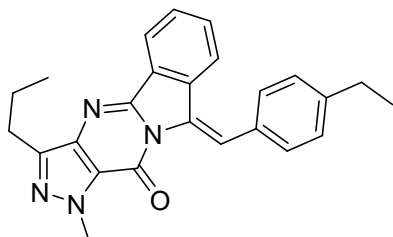
Yellow solid; mp 202–203 °C; ¹H NMR (CDCl₃, 400 MHz): δ_H 9.04 (s, 1H), 8.10 (d, *J* = 7.6 Hz, 1H), 7.47–7.37 (m, 3H), 7.33–7.26 (m, 4H), 4.34 (s, 3H), 2.95 (t, *J* = 7.6 Hz, 2H), 2.44 (s, 3H), 1.94–1.85 (m, 2H), 1.05 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (CDCl₃, 101 MHz) δ_C 154.2, 150.0, 146.0, 138.1, 137.2, 135.2, 134.2, 132.3, 130.8, 130.5, 129.5, 129.4, 128.9, 124.9, 123.7, 123.0, 122.3, 38.6, 27.7, 22.4, 21.4, 14.0; HRMS (ESI-TOF, *m/z*): calcd for C₂₄H₂₃N₄O [M + H]⁺, 383.1866; found, 383.1875.



(E)-9-(4-methoxybenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1- α]isoindol-11-one (5r)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-*d*]pyrimidin-7-one **4a** (174 mg, 0.5 mmol, 1.0 equiv), 1-ethynyl-4-methoxybenzene **2o** (79 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **5r** in 25% yield (50 mg).

Yellow solid; mp 206–207 °C; ¹H NMR (CDCl₃, 400 MHz): δ_{H} 9.02 (s, 1H), 8.11 (d, *J* = 7.6 Hz, 1H), 7.48–7.42 (m, 3H), 7.38 (d, *J* = 8.0 Hz, 1H), 7.31–7.26 (m, 1H), 7.01–6.99 (m, 2H), 4.35 (s, 3H), 3.90 (s, 3H), 2.96 (t, *J* = 7.6 Hz, 2H), 1.94–1.85 (m, 2H), 1.05 (t, *J* = 7.6 Hz, 3H); ¹³C NMR (CDCl₃, 101 MHz) δ_{C} 159.6, 154.3, 150.0, 146.0, 137.2, 135.1, 134.3, 130.9, 130.5, 129.4, 127.5, 124.9, 123.5, 122.8, 122.3, 114.2, 55.3, 38.6, 27.7, 22.4, 14.1; HRMS (ESI-TOF, *m/z*): calcd for C₂₄H₂₃N₄O₂ [M + H]⁺, 399.1816; found, 399.1824.

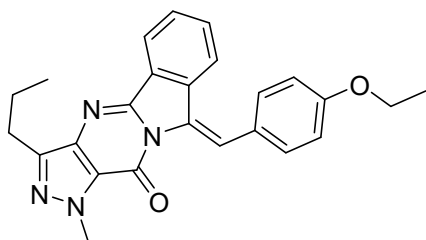


(E)-9-(4-ethylbenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1- α]isoindol-11-one (5s)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-*d*]pyrimidin-7-one **4a** (174 mg, 0.5 mmol, 1.0 equiv), 1-ethyl-4-ethynylbenzene **2p** (78 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture

was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **5s** in 30% yield (59 mg).

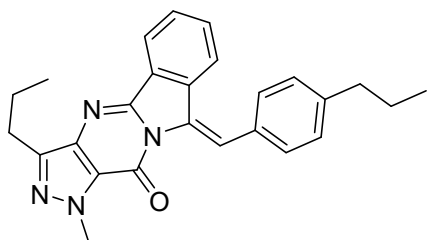
Yellow solid; mp 170–171 °C; ¹H NMR (CDCl₃, 400 MHz): δ_H 9.05 (s, 1H), 8.11 (d, *J* = 8.0 Hz, 1H), 7.48–7.40 (m, 3H), 7.34–7.26 (m, 4H), 4.35 (s, 3H), 2.95 (t, *J* = 8.4 Hz, 2H), 2.77–2.72 (m, 2H), 1.94–1.85 (m, 2H), 1.32 (t, *J* = 7.6 Hz, 3H), 1.05 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (CDCl₃, 101 MHz) δ_C 154.2, 150.0, 146.0, 144.4, 137.2, 135.2, 134.3, 132.5, 130.9, 130.5, 129.4, 129.0, 128.3, 124.9, 123.7, 123.0, 122.3, 38.6, 28.7, 27.7, 22.4, 15.4, 14.1; HRMS (ESI-TOF, *m/z*): calcd for C₂₅H₂₅N₄O [M + H]⁺, 397.2023; found, 397.2034.



(E)-9-(4-ethoxybenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (5t)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-*d*]pyrimidin-7-one **4a** (174 mg, 0.5 mmol, 1.0 equiv), 1-ethoxy-4-ethynylbenzene **2q** (88 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **5t** in 26% yield (54 mg).

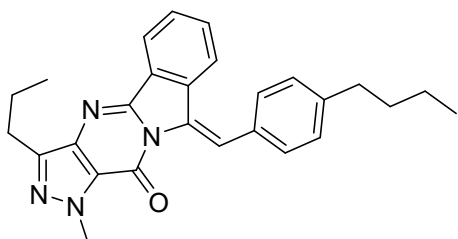
Yellow solid; mp 196–197 °C; ¹H NMR (CDCl₃, 400 MHz): δ_H 9.03 (s, 1H), 8.12 (d, *J* = 7.6 Hz, 1H), 7.48–7.39 (m, 4H), 7.32–7.26 (m, 1H), 7.00–6.97 (m, 2H), 4.35 (s, 3H), 4.15–4.10 (m, 2H), 2.96 (t, *J* = 7.6 Hz, 2H), 1.94–1.85 (m, 2H), 1.48 (t, *J* = 7.2 Hz, 3H), 1.05 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (CDCl₃, 101 MHz) δ_C 159.0, 154.3, 150.0, 146.0, 137.2, 135.0, 134.3, 130.9, 130.49, 130.45, 129.3, 127.3, 124.9, 123.5, 122.9, 122.3, 114.7, 63.5, 38.6, 27.7, 22.4, 14.9, 14.1; HRMS (ESI-TOF, *m/z*): calcd for C₂₅H₂₅N₄O₂ [M + H]⁺, 413.1972; found, 413.1984.



(E)-1-methyl-3-propyl-9-(4-propylbenzylidene)-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1- α]isoindol-11-one (5u)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-*d*]pyrimidin-7-one **4a** (174 mg, 0.5 mmol, 1.0 equiv), 1-ethynyl-4-propylbenzene **2r** (87 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **5u** in 24% yield (49 mg).

Yellow solid; mp 142–143 °C; ¹H NMR (CDCl₃, 400 MHz): δ_{H} 9.06 (s, 1H), 8.12–8.10 (m, 1H), 7.47–7.39 (m, 3H), 7.32–7.26 (m, 4H), 4.35 (s, 3H), 2.96 (t, *J* = 7.6 Hz, 2H), 2.68 (t, *J* = 7.6 Hz, 2H), 1.94–1.85 (m, 2H), 1.77–1.68 (m, 2H), 1.07–0.99 (m, 6H); ¹³C NMR (CDCl₃, 101 MHz) δ_{C} 154.2, 150.0, 146.0, 142.9, 137.2, 135.3, 134.3, 132.6, 130.8, 130.5, 129.4, 128.92, 128.87, 124.9, 123.7, 123.1, 122.3, 38.6, 37.9, 27.7, 24.4, 22.4, 14.1, 13.8; HRMS (ESI-TOF, *m/z*): calcd for C₂₆H₂₇N₄O [M + H]⁺, 411.2179; found, 411.2188.

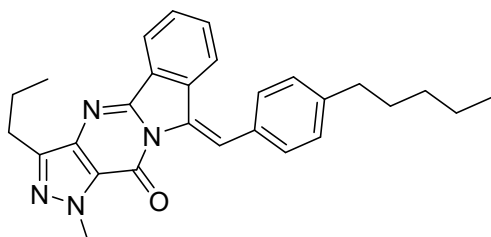


(E)-9-(4-butylbenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1- α]isoindol-11-one (5v)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-*d*]pyrimidin-7-one **4a** (174 mg, 0.5 mmol, 1.0 equiv), 1-butyl-4-ethynylbenzene **2s** (95 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0

equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **5v** in 21% yield (45 mg).

Yellow solid; mp 207–208 °C; ¹H NMR (CDCl₃, 400 MHz): δ_H 9.05 (s, 1H), 8.11 (d, *J* = 7.6 Hz, 1H), 7.47–7.39 (m, 3H), 7.32–7.25 (m, 4H), 4.35 (s, 3H), 2.96 (t, *J* = 7.6 Hz, 2H), 2.70 (t, *J* = 7.6 Hz, 2H), 1.94–1.85 (m, 2H), 1.72–1.68 (m, 2H), 1.47–1.38 (m, 2H), 1.05 (t, *J* = 7.2 Hz, 3H), 0.98 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (CDCl₃, 101 MHz) δ_C 154.2, 150.0, 146.0, 143.2, 137.2, 135.2, 134.3, 132.5, 130.8, 130.5, 129.4, 128.9, 128.8, 124.9, 123.7, 123.1, 122.3, 38.6, 35.5, 33.5, 27.7, 22.41, 22.39, 14.05, 13.98; HRMS (ESI-TOF, *m/z*): calcd for C₂₇H₂₉N₄O [M + H]⁺, 425.2336; found, 425.2352.

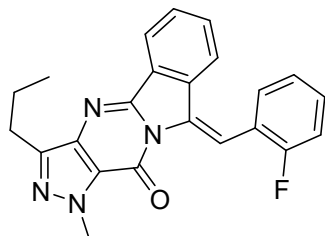


(E)-1-methyl-9-(4-pentylbenzylidene)-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1- α]isoindol-11-one (5w**)**

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-*d*]pyrimidin-7-one **4a** (174 mg, 0.5 mmol, 1.0 equiv), 1-ethynyl-4-pentylbenzene **2t** (103 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **5w** in 28% yield (61 mg).

Yellow solid; mp 154–155 °C; ¹H NMR (CDCl₃, 400 MHz): δ_H 9.06 (s, 1H), 8.11 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.48–7.44 (m, 1H), 7.41–7.39 (m, 2H), 7.32–7.26 (m, 4H), 4.35 (s, 3H), 2.96 (t, *J* = 7.6 Hz, 2H), 2.69 (t, *J* = 7.6 Hz, 2H), 1.94–1.85 (m, 2H), 1.73–1.66 (m, 2H), 1.41–1.36 (m, 4H),

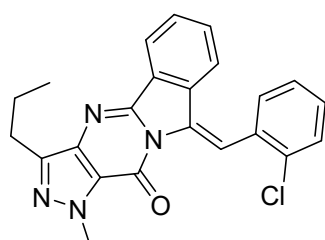
1.05 (t, $J = 7.6$ Hz, 3H), 0.95–0.91 (m, 3H); ^{13}C NMR (CDCl_3 , 101 MHz) δ_{C} 154.2, 150.0, 146.0, 143.2, 137.2, 135.2, 134.3, 132.5, 130.8, 130.5, 129.4, 128.9, 128.8, 124.9, 123.7, 123.1, 122.3, 38.6, 35.8, 31.5, 31.1, 27.7, 22.6, 22.4, 14.08, 14.06; HRMS (ESI-TOF, m/z): calcd for $\text{C}_{28}\text{H}_{31}\text{N}_4\text{O}$ [$\text{M} + \text{H}$] $^+$, 439.2492; found, 439.2513.



(*E*)-9-(2-fluorobenzylidene)-1-methyl-3-propyl-1,9-dihydro-11*H*-pyrazolo[4',3':4,5]pyrimido[2,1-*a*]isoindol-11-one (5x)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromophenyl)-1-methyl-3-propyl-1,6-dihydro-7*H*-pyrazolo[4,3-*d*]pyrimidin-7-one **4a** (174 mg, 0.5 mmol, 1.0 equiv), 1-ethynyl-2-fluorobenzene **2b** (72 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs_2CO_3 (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4 and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **5x** in 26% yield (50 mg).

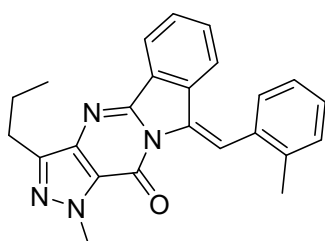
Yellow solid; mp 193–194 °C; ^1H NMR (CDCl_3 , 400 MHz): δ_{H} 8.91 (s, 1H), 8.12 (d, $J = 7.6$ Hz, 1H), 7.54–7.41 (m, 3H), 7.33–7.29 (m, 1H), 7.24–7.19 (m, 3H), 4.35 (s, 3H), 2.96 (t, $J = 7.6$ Hz, 2H), 1.94–1.85 (m, 2H), 1.05 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (CDCl_3 , 101 MHz) δ_{C} 160.0 (d, $J_{\text{C-F}} = 246.8$ Hz), 154.2, 149.9, 146.2, 137.2, 136.6, 134.0, 131.2 (d, $J_{\text{C-F}} = 2.7$ Hz), 131.1, 130.7, 130.3 (d, $J_{\text{C-F}} = 7.9$ Hz), 129.8, 124.9, 124.3 (d, $J_{\text{C-F}} = 3.6$ Hz), 123.4, 123.1 (d, $J_{\text{C-F}} = 15.9$ Hz), 122.4, 116.1 (d, $J_{\text{C-F}} = 21.4$ Hz), 115.1 (d, $J_{\text{C-F}} = 20.0$ Hz), 38.6, 27.7, 22.4, 14.0; HRMS (ESI-TOF, m/z): calcd for $\text{C}_{28}\text{H}_{31}\text{N}_4\text{O}$ [$\text{M} + \text{H}$] $^+$, 439.2492; found, 439.2513.



(E)-9-(2-chlorobenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1- α]isoindol-11-one (5y)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-*d*]pyrimidin-7-one **4a** (174 mg, 0.5 mmol, 1.0 equiv), 1-chloro-2-ethynylbenzene **2c** (82 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **5y** in 28% yield (56 mg).

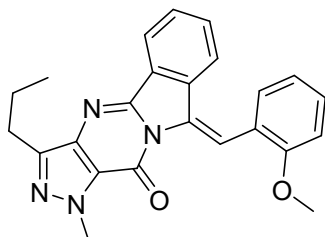
Yellow solid; mp 163–164 °C; ¹H NMR (CDCl₃, 400 MHz): δ_{H} 8.96 (s, 1H), 8.12 (d, *J* = 7.6 Hz, 1H), 7.56–7.53 (m, 2H), 7.50–7.46 (m, 1H), 7.41–7.33 (m, 2H), 7.30–7.26 (m, 1H), 7.04 (d, *J* = 8.0 Hz, 1H), 4.36 (s, 3H), 2.96 (t, *J* = 7.6 Hz, 2H), 1.94–1.85 (m, 2H), 1.05 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (CDCl₃, 101 MHz) δ_{C} 154.2, 150.0, 146.2, 137.2, 136.1, 134.1, 134.0, 133.9, 131.1, 131.0, 130.7, 130.0, 129.8, 129.7, 126.9, 125.0, 123.5, 122.4, 119.4, 38.6, 27.7, 22.4, 14.0; HRMS (ESI-TOF, *m/z*): calcd for C₂₃H₂₀ClN₄O [M + H]⁺, 403.1320; found, 403.1325.



(E)-1-methyl-9-(2-methylbenzylidene)-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1- α]isoindol-11-one (5z)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-*d*]pyrimidin-7-one **4a** (174 mg, 0.5 mmol, 1.0 equiv), 1-ethynyl-2-methylbenzene **2d** (70 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **5z** in 35% yield (67 mg).

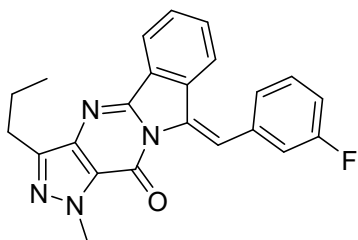
Yellow solid; mp 149–151 °C; ^1H NMR (CDCl_3 , 400 MHz): δ_{H} 9.00 (s, 1H), 8.12 (d, $J = 8.0$ Hz, 1H), 7.45 (t, $J = 7.6$ Hz, 1H), 7.40–7.35 (m, 3H), 7.30–7.23 (m, 2H), 6.92 (d, $J = 8.0$ Hz, 1H), 4.36 (s, 3H), 2.97 (t, $J = 7.6$ Hz, 2H), 2.35 (s, 3H), 1.95–1.85 (m, 2H), 1.05 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (CDCl_3 , 101 MHz) δ_{C} 154.3, 150.0, 146.1, 137.2, 136.5, 135.4, 134.7, 134.4, 131.1, 130.5, 130.4, 129.4, 129.1, 128.4, 126.1, 125.0, 123.6, 122.24, 122.16, 38.6, 27.7, 22.4, 20.2, 14.0; HRMS (ESI-TOF, m/z): calcd for $\text{C}_{24}\text{H}_{23}\text{N}_4\text{O}$ [$\text{M} + \text{H}$] $^+$, 383.1866; found, 383.1875.



(*E*)-9-(2-methoxybenzylidene)-1-methyl-3-propyl-1,9-dihydro-11*H*-pyrazolo[4',3':4,5]pyrimido[2,1-*a*]isoindol-11-one (5aa)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromophenyl)-1-methyl-3-propyl-1,6-dihydro-7*H*-pyrazolo[4,3-*d*]pyrimidin-7-one **4a** (174 mg, 0.5 mmol, 1.0 equiv), 1-ethynyl-2-methoxybenzene **2e** (79 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs_2CO_3 (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4 and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **5aa** in 32% yield (64 mg).

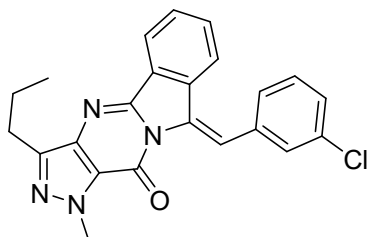
Yellow solid; mp 144–145 °C; ^1H NMR (CDCl_3 , 400 MHz): δ_{H} 8.99 (s, 1H), 8.11 (d, $J = 7.6$ Hz, 1H), 7.50–7.35 (m, 4H), 7.30–7.26 (m, 1H), 7.04–7.00 (m, 2H), 4.35 (s, 3H), 3.84 (s, 3H), 2.96 (t, $J = 7.6$ Hz, 2H), 1.94–1.85 (m, 2H), 1.05 (t, $J = 8.8$ Hz, 3H); ^{13}C NMR (CDCl_3 , 101 MHz) δ_{C} 157.3, 154.2, 150.0, 146.0, 137.1, 135.1, 134.4, 130.84, 130.79, 130.5, 130.0, 129.3, 125.0, 123.9, 123.5, 122.2, 120.5, 119.5, 110.9, 55.5, 38.6, 27.7, 22.4, 14.0; HRMS (ESI-TOF, m/z): calcd for $\text{C}_{24}\text{H}_{23}\text{N}_4\text{O}_2$ [$\text{M} + \text{H}$] $^+$, 399.1816; found, 399.1824.



(E)-9-(3-fluorobenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (5ab)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one **4a** (174 mg, 0.5 mmol, 1.0 equiv), 1-ethynyl-3-fluorobenzene **2f** (72 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **5ab** in 25% yield (48 mg).

Yellow solid; mp 175–176 °C; ¹H NMR (CDCl₃, 400 MHz): δ_H 9.00 (s, 1H), 8.11 (dd, *J* = 8.4, 3.2 Hz, 1H), 7.50–7.42 (m, 2H), 7.31–7.26 (m, 2H), 7.21–7.18 (m, 2H), 7.15–7.11 (m, 1H), 4.34 (s, 3H), 2.95 (t, *J* = 8.4 Hz, 2H), 1.94–1.84 (m, 2H), 1.05 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (CDCl₃, 101 MHz) δ_C 163.0 (d, *J*_{C-F} = 245.7 Hz), 154.2, 149.8, 146.2, 137.5 (d, *J*_{C-F} = 8.0 Hz), 137.2, 136.0, 133.8, 131.0, 130.7, 130.5 (d, *J*_{C-F} = 8.4 Hz), 129.8, 124.84, 124.79 (d, *J*_{C-F} = 3.0 Hz), 123.7, 122.4, 120.9 (d, *J*_{C-F} = 2.0 Hz), 115.9 (d, *J*_{C-F} = 21.5 Hz), 115.1 (d, *J*_{C-F} = 20.9 Hz), 38.6, 27.7, 22.4, 14.0; HRMS (ESI-TOF, *m/z*): calcd for C₂₃H₂₀FN₄O [M + H]⁺, 387.1616; found, 387.1616.

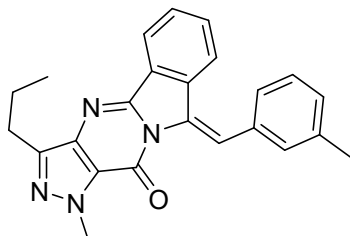


(E)-9-(3-chlorobenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (5ac)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one **4a** (174 mg, 0.5 mmol, 1.0 equiv), 1-chloro-3-ethynylbenzene **2g** (82 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0

equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **5ac** in 30% yield (60 mg).

Yellow solid; mp 140–143 °C; ¹H NMR (CDCl₃, 400 MHz): δ_H 8.98 (s, 1H), 8.12 (d, *J* = 8.0 Hz, 1H), 7.50–7.46 (m, 2H), 7.42–7.36 (m, 3H), 7.32–7.27 (m, 1H), 7.18 (d, *J* = 8.0 Hz, 1H), 4.34 (s, 3H), 2.95 (t, *J* = 7.6 Hz, 2H), 1.94–1.84 (m, 2H), 1.05 (t, *J* = 7.6 Hz, 3H); ¹³C NMR (CDCl₃, 101 MHz) δ_C 154.2, 149.8, 146.2, 137.2, 137.1, 136.1, 134.7, 133.8, 131.1, 130.7, 130.1, 129.8, 129.0, 128.2, 127.2, 124.8, 123.6, 122.4, 120.7, 38.6, 27.7, 22.4, 14.0; HRMS (ESI-TOF, *m/z*): calcd for C₂₃H₂₀ClN₄O [M + H]⁺, 403.1320; found, 403.1325.

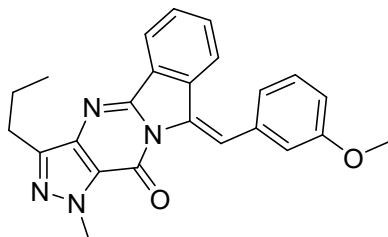


(E)-1-methyl-9-(3-methylbenzylidene)-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (5ad)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-*d*]pyrimidin-7-one **4a** (174 mg, 0.5 mmol, 1.0 equiv), 1-ethynyl-3-methylbenzene **2h** (70 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **5ad** in 30% yield (57 mg).

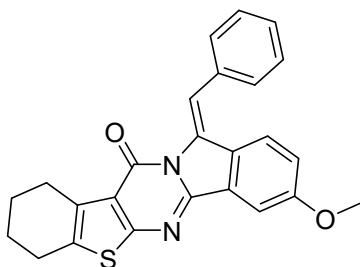
Yellow solid; mp 144–145 °C; ¹H NMR (CDCl₃, 400 MHz): δ_H 9.05 (s, 1H), 8.11 (d, *J* = 7.6 Hz, 1H), 7.48–7.44 (m, 1H), 7.36 (t, *J* = 7.6 Hz, 1H), 7.30–7.22 (m, 5H), 4.35 (s, 3H), 2.96 (t, *J* = 7.6 Hz, 2H), 2.41 (s, 3H), 1.94–1.85 (m, 2H), 1.05 (t, *J* = 7.6 Hz, 3H); ¹³C NMR (CDCl₃, 101 MHz) δ_C 154.2, 150.0, 146.0, 138.5, 137.2, 135.4, 135.3, 134.3, 130.9, 130.5, 129.5, 129.4, 128.9,

128.7, 126.0, 124.9, 123.8, 123.0, 122.3, 38.6, 27.7, 22.4, 21.4, 14.0; HRMS (ESI-TOF, m/z): calcd for $C_{24}H_{23}N_4O$ $[M + H]^+$, 383.1866; found, 383.1875.



(E)-9-(3-methoxybenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (5ae)

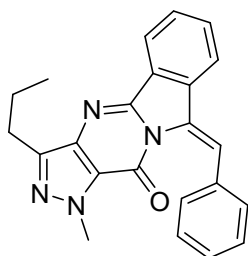
To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one **4a** (174 mg, 0.5 mmol, 1.0 equiv), 1-ethynyl-3-methoxybenzene **2i** (79 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs_2CO_3 (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4 and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **5ae** in 34% yield (68 mg). Yellow solid; mp 145–148 °C; 1H NMR ($CDCl_3$, 400 MHz): δ_H 9.04 (s, 1H), 8.11 (d, $J = 8.0$ Hz, 1H), 7.49–7.45 (m, 1H), 7.40–7.36 (m, 1H), 7.31–7.27 (m, 2H), 7.08 (d, $J = 7.2$ Hz, 1H), 7.02 (s, 1H), 6.97 (dd, $J = 8.0, 2.4$ Hz, 1H), 4.35 (s, 3H), 3.84 (s, 3H), 2.96 (t, $J = 8.0$ Hz, 2H), 1.94–1.85 (m, 2H), 1.05 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 101 MHz) δ_C 159.9, 154.2, 150.0, 146.1, 137.2, 136.7, 135.6, 134.1, 131.0, 130.6, 129.9, 129.6, 124.9, 123.9, 122.5, 122.3, 121.3, 114.0, 55.3, 38.6, 27.7, 22.4, 14.0; HRMS (ESI-TOF, m/z): calcd for $C_{24}H_{23}N_4O_2$ $[M + H]^+$, 399.1816; found, 399.1824.



(E)-11-benzylidene-8-methoxy-2,3,4,11-tetrahydrobenzo[4',5']thieno[2',3':4,5]pyrimido[2,1-*a*]isoindol-13(1*H*)-one (5af)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 2-(2-bromo-5-methoxyphenyl)-5,6,7,8-tetrahydrobenzo[4,5]thieno[2,3-*d*]pyrimidin-4(3*H*)-one **7** (78 mg, 0.2 mmol, 1.0 equiv), phenylacetylene **2a** (31 mg, 0.3 mmol, 1.5 equiv), DMF (4.0 mL), Cs₂CO₃ (65 mg, 0.2 mmol, 1.0 equiv), *o*-phen (7 mg, 0.04 mmol, 0.2 equiv), CuI (4 mg, 0.02 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 10:1) afforded **5af** in 85% yield (70 mg).

Yellow solid; mp 213–215 °C; ¹H NMR (CDCl₃, 400 MHz): δ_H 9.11 (s, 1H), 7.50–7.38 (m, 6H), 7.16 (d, *J* = 8.8 Hz, 1H), 6.86–6.83 (m, 1H), 3.89 (s, 3H), 3.16–3.13 (m, 2H), 2.84–2.81 (m, 2H), 1.93–1.88 (m, 4H); ¹³C NMR (CDCl₃, 101 MHz): δ_C 161.4, 161.0, 158.4, 151.1, 135.6, 135.4, 133.7, 132.5, 131.8, 129.2, 128.8, 128.1, 127.2, 125.1, 122.5, 121.6, 120.4, 104.1, 55.8, 26.0, 25.5, 22.9, 22.4; HRMS (ESI-TOF, *m/z*): calcd for C₂₅H₂₁O₂N₂S [M + H]⁺, 413.1318; found, 413.1347.

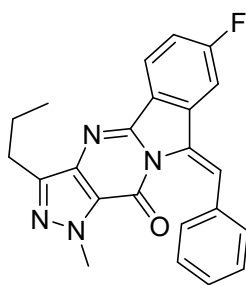


(Z)-9-benzylidene-1-methyl-3-propyl-1,9-dihydro-11*H*-pyrazolo[4',3':4,5]pyrimido[2,1-*a*]isoindol-11-one (6a)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromophenyl)-1-methyl-3-propyl-1,6-dihydro-7*H*-pyrazolo[4,3-*d*]pyrimidin-7-one **4a** (174 mg, 0.5 mmol, 1.0 equiv), ethynylbenzene **2a** (61 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄

and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **6a** in 55% yield (101 mg).

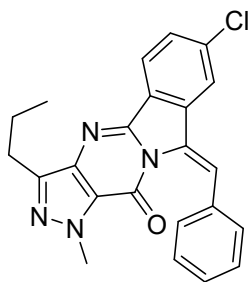
Yellow solid; mp 141–143 °C; **6a** : **5a** = 96 : 4; ¹H NMR (CDCl₃, 400 MHz, Major Product **6a**): δ_H 8.13 (d, *J* = 7.6 Hz, 1H), 7.86 (d, *J* = 7.6 Hz, 1H), 7.61–7.52 (m, 2H), 7.39–7.31 (m, 3H), 7.27–7.21 (m, 3H), 4.18 (s, 3H), 2.96 (t, *J* = 7.6 Hz, 2H), 1.94–1.85 (m, 2H), 1.07 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (CDCl₃, 101 MHz) δ_C 151.8, 151.1, 146.1, 138.1, 136.9, 136.2, 131.3, 130.3, 129.9, 129.3, 129.2, 127.9, 127.2, 124.8, 122.5, 119.6, 115.9, 38.4, 27.7, 22.5, 14.1; HRMS (ESI-TOF, *m/z*): calcd for C₂₃H₂₁N₄O [M + H]⁺, 369.1710; found, 369.1707.



(Z)-9-benzylidene-7-fluoro-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (6b)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromo-4-fluorophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-*d*]pyrimidin-7-one **4b** (183 mg, 0.5 mmol, 1.0 equiv), ethynylbenzene **2a** (61 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **6b** in 59% yield (114 mg).

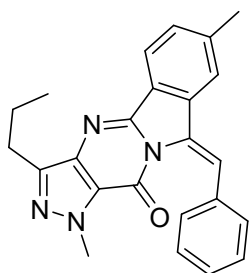
Yellow solid; mp 140–143 °C; **6b** : **5b** = 93 : 7; ¹H NMR (CDCl₃, 400 MHz, Major Product **6b**): δ_H 8.13–8.10 (m, 1H), 7.53–7.50 (m, 1H), 7.40–7.33 (m, 3H), 7.27–7.21 (m, 4H), 4.18 (s, 3H), 2.94 (t, *J* = 7.6 Hz, 2H), 1.93–1.84 (m, 2H), 1.08–1.04 (m, 3H); ¹³C NMR (CDCl₃, 101 MHz) δ_C 165.0 (d, *J*_{C-F} = 249.8 Hz), 151.0 (d, *J*_{C-F} = 6.8 Hz), 146.1, 140.2 (d, *J*_{C-F} = 10.0 Hz), 136.8, 135.8, 130.1, 129.5 (d, *J*_{C-F} = 4.0 Hz), 128.9 (d, *J*_{C-F} = 23.5 Hz), 128.2, 127.3, 125.4, 124.6 (d, *J*_{C-F} = 9.5 Hz), 124.5, 117.4 (d, *J*_{C-F} = 24.0 Hz), 116.9, 106.5 (d, *J*_{C-F} = 24.9 Hz), 38.4, 27.8, 22.5, 14.1; HRMS (ESI-TOF, *m/z*): calcd for C₂₃H₂₀FN₄O [M + H]⁺, 387.1616; found, 387.1616.



(Z)-9-benzylidene-7-chloro-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1- α]isoindol-11-one (6c)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromo-4-chlorophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-*d*]pyrimidin-7-one **4c** (191 mg, 0.5 mmol, 1.0 equiv), ethynylbenzene **2a** (61 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **6c** in 64% yield (129 mg).

Yellow solid; mp 165–166 °C; **6c** : **5c** = 95 : 5; ¹H NMR (CDCl₃, 400 MHz, Major Product **6c**): δ_{H} 8.09 (d, *J* = 8.0 Hz, 1H), 7.84 (s 1H), 7.52–7.49 (m, 1H), 7.40–7.35 (m, 3H), 7.26–7.20 (m, 3H), 4.18 (s, 3H), 2.95 (t, *J* = 7.6 Hz, 2H), 1.93–1.84 (m, 2H), 1.06 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (CDCl₃, 101 MHz) δ_{C} 150.9, 146.2, 139.5, 137.7, 136.5, 135.7, 130.1, 129.7, 129.2, 128.3, 127.5, 127.3, 124.6, 123.9, 119.9, 117.1, 38.4, 27.7, 22.5, 14.1. HRMS (ESI-TOF, *m/z*): calcd for C₂₃H₂₀ClN₄O [M + H]⁺, 403.1320; found, 403.1325.

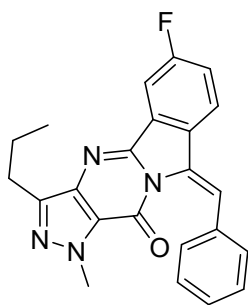


(Z)-9-benzylidene-1,7-dimethyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1- α]isoindol-11-one (6d)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromo-4-methylphenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-*d*]pyrimidin-7-one **4d** (181 mg, 0.5 mmol, 1.0 equiv),

ethynylbenzene **2a** (61 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **6d** in 56% yield (107 mg).

Yellow solid; mp 148–151 °C; ¹H NMR (CDCl₃, 400 MHz): δ_H 8.01 (d, *J* = 8.0 Hz, 1H), 7.66 (s, 1H), 7.38–7.31 (m, 4H), 7.26–7.20 (m, 3H), 4.17 (s, 3H), 2.95 (t, *J* = 7.6 Hz, 2H), 2.53 (s, 3H), 1.94–1.84 (m, 2H), 1.06 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (CDCl₃, 101 MHz) δ_C 152.0, 151.2, 146.0, 142.0, 138.4, 136.9, 136.3, 130.5, 130.3, 129.9, 127.8, 127.2, 126.9, 124.7, 122.3, 119.8, 115.6, 38.4, 27.7, 22.5, 22.1, 14.1; HRMS (ESI-TOF, *m/z*): calcd for C₂₄H₂₃N₄O [M + H]⁺, 383.1866; found, 383.1875.

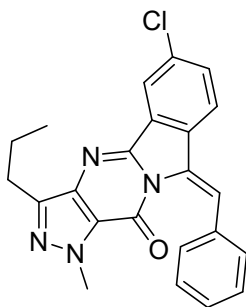


(Z)-9-benzylidene-6-fluoro-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1- α]isoindol-11-one (6e)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromo-5-fluorophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-*d*]pyrimidin-7-one **4e** (183 mg, 0.5 mmol, 1.0 equiv), ethynylbenzene **2a** (61 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **6e** in 63% yield (122 mg).

Yellow solid; mp 154–155 °C; **6e** : **5e** = 97 : 3; ¹H NMR (CDCl₃, 400 MHz, Major Product **6e**): δ_H 7.84–7.77 (m, 2H), 7.39–7.26 (m, 4H), 7.21–7.20 (m, 3H), 4.18 (s, 3H), 2.95 (t, *J* = 7.6 Hz,

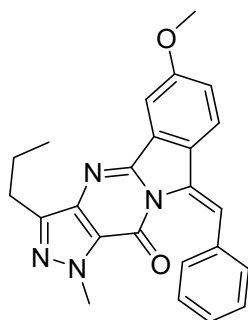
2H), 1.93–1.84 (m, 2H), 1.06 (t, $J = 7.6$ Hz, 3H); ^{13}C NMR (CDCl_3 , 101 MHz) δ_{C} 163.4 (d, $J_{\text{C-F}} = 247.9$ Hz), 150.9, 150.7 (d, $J_{\text{C-F}} = 4.1$ Hz), 146.3, 136.7, 136.1, 134.0 (d, $J_{\text{C-F}} = 2.4$ Hz), 131.1 (d, $J_{\text{C-F}} = 9.8$ Hz), 129.9, 129.6, 128.0, 127.2, 124.8, 121.5 (d, $J_{\text{C-F}} = 8.7$ Hz), 119.3 (d, $J_{\text{C-F}} = 24.2$ Hz), 115.7 (d, $J_{\text{C-F}} = 2.1$ Hz), 108.9 (d, $J_{\text{C-F}} = 24.2$ Hz), 38.4, 27.7, 22.5, 14.0; HRMS (ESI-TOF, m/z): calcd for $\text{C}_{23}\text{H}_{20}\text{FN}_4\text{O}$ [$\text{M} + \text{H}$] $^+$, 387.1616; found, 387.1616.



(Z)-9-benzylidene-6-chloro-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (6f)

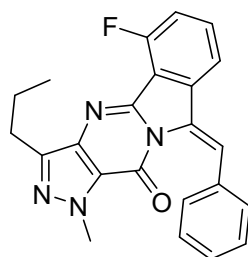
To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromo-5-chlorophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one **4f** (191 mg, 0.5 mmol, 1.0 equiv), ethynylbenzene **2a** (61 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs_2CO_3 (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4 and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **6f** in 59% yield (119 mg).

Yellow solid; mp 186–188 °C; **6f** : **5f** = 93 : 7; ^1H NMR (CDCl_3 , 400 MHz, Major Product **6f**): δ_{H} 8.12 (s, 1H), 7.79–7.77 (m, 1H), 7.54 (d, $J = 8.4$ Hz, 1H), 7.40–7.32 (m, 3H), 7.26–7.20 (m, 3H), 4.18 (s, 3H), 2.94 (t, $J = 7.6$ Hz, 2H), 1.93–1.84 (m, 2H), 1.06 (t, $J = 7.6$ Hz, 3H); ^{13}C NMR (CDCl_3 , 101 MHz) δ_{C} 150.9, 150.4, 146.3, 136.6, 136.3, 135.9, 135.3, 131.6, 130.6, 130.0, 129.5, 128.9, 128.1, 127.2, 124.8, 122.4, 120.9, 116.4, 38.4, 27.7, 22.5, 14.0; HRMS (ESI-TOF, m/z): calcd for $\text{C}_{23}\text{H}_{20}\text{ClN}_4\text{O}$ [$\text{M} + \text{H}$] $^+$, 403.1320; found, 403.1325.



(Z)-9-benzylidene-6-methoxy-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (6g)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromo-5-methoxyphenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one **4g** (188 mg, 0.5 mmol, 1.0 equiv), ethynylbenzene **2a** (61 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **6g** in 54% yield (108 mg). Yellow solid; mp 164–168 °C; **6g** : **5g** = 96 : 4; ¹H NMR (CDCl₃, 400 MHz, Major Product **6g**): δ_H 7.74 (d, *J* = 8.8 Hz, 1H), 7.55 (d, *J* = 2.4 Hz, 1H), 7.38–7.31 (m, 3H), 7.21–7.13 (m, 4H), 4.18 (s, 3H), 3.97 (s, 3H), 2.96 (t, *J* = 7.6 Hz, 2H), 1.94–1.85 (m, 2H), 1.07 (t, *J* = 7.6 Hz, 3H); ¹³C NMR (CDCl₃, 101 MHz) δ_C 160.9, 151.8, 151.1, 146.0, 136.7, 136.4, 131.1, 130.6, 130.2, 129.9, 127.6, 127.2, 124.8, 120.9, 120.7, 114.3, 104.2, 55.9, 38.4, 27.7, 22.5, 14.1; HRMS (ESI-TOF, *m/z*): calcd for C₂₄H₂₃N₄O₂ [M + H]⁺, 399.1816; found, 399.1824.

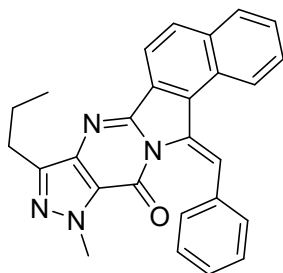


(Z)-9-benzylidene-5-fluoro-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (6h)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromo-6-fluorophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one **4h** (183 mg, 0.5 mmol, 1.0 equiv),

ethynylbenzene **2a** (61 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **6h** in 57% yield (110 mg).

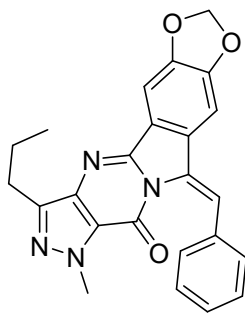
Yellow solid; mp 192–193 °C; **6h** : **5h** = 96 : 4; ¹H NMR (CDCl₃, 400 MHz, Major Product **6h**): δ_H 7.67 (d, *J* = 8.0 Hz, 1H), 7.57–7.52 (m, 1H), 7.40–7.32 (m, 3H), 7.29 (s, 1H), 7.22–7.18 (m, 3H), 4.18 (s, 3H), 2.97 (t, *J* = 7.2 Hz, 2H), 1.95–1.85 (m, 2H), 1.06 (t, *J* = 7.6 Hz, 3H); ¹³C NMR (CDCl₃, 101 MHz) δ_C 158.2 (d, *J*_{C-F} = 259.6 Hz) 150.8, 149.0 (d, *J*_{C-F} = 5.5 Hz), 146.6, 140.6 (d, *J*_{C-F} = 3.0 Hz), 137.0, 135.9, 132.6 (d, *J*_{C-F} = 7.6 Hz), 130.0, 129.6 (d, *J*_{C-F} = 1.9 Hz), 128.9 (d, *J*_{C-F} = 9.5 Hz), 128.2, 127.2, 124.4, 117.0 (d, *J*_{C-F} = 13.4 Hz), 116.9, 116.1 (d, *J*_{C-F} = 19.1 Hz), 115.4 (d, *J*_{C-F} = 4.1 Hz), 38.4, 27.7, 22.3, 14.0; HRMS (ESI-TOF, *m/z*): calcd for C₂₃H₂₀FN₄O [M + H]⁺, 387.1616; found, 387.1616.



(Z)-11-benzylidene-1-methyl-3-propyl-1,11-dihydro-13H-benzo[*f*]pyrazolo[4',3':4,5]pyrimido[2,1-*a*]isoindol-13-one (6i**)**

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(1-bromonaphthalen-2-yl)-1-methyl-3-propyl-1,6-dihydro-7*H*-pyrazolo[4,3-*d*]pyrimidin-7-one **4i** (198 mg, 0.5 mmol, 1.0 equiv), ethynylbenzene **2a** (61 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **6i** in 58% yield (121 mg).

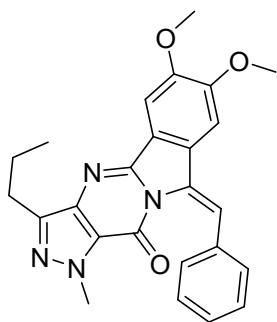
Yellow solid; mp 202–203 °C; ^1H NMR (CDCl_3 , 400 MHz): δ_{H} 8.64 (d, J = 8.8 Hz, 1H), 8.20–8.17 (m, 1H), 8.02–7.95 (m, 2H), 7.82 (s, 1H), 7.76–7.72 (m, 1H), 7.64 (t, J = 7.6 Hz, 1H), 7.40–7.31 (m, 5H), 4.16 (s, 3H), 2.99 (t, J = 7.6 Hz, 2H), 1.97–1.88 (m, 2H), 1.09 (t, J = 7.2 Hz, 3H); ^{13}C NMR (CDCl_3 , 101 MHz) δ_{C} 152.1, 151.1, 146.1, 137.0, 136.7, 135.8, 134.8, 132.5, 130.7, 130.1, 129.1, 128.5, 128.3, 127.7, 127.4, 126.7, 124.7, 124.2, 121.3, 118.8, 38.3, 27.8, 22.5, 14.1; HRMS (ESI-TOF, m/z): calcd for $\text{C}_{27}\text{H}_{23}\text{N}_4\text{O}$ [$\text{M} + \text{H}$] $^+$, 419.1866; found, 419.1870.



(Z)-10-benzylidene-1-methyl-3-propyl-1,10-dihydro-12H-[1,3]dioxolo[4,5-f]pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-12-one (6j)

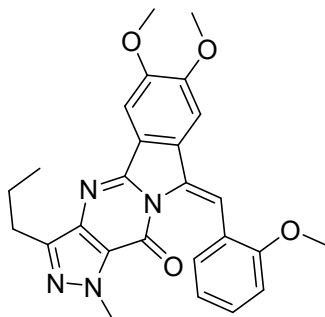
To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(6-bromobenzo[*d*][1,3]dioxol-5-yl)-1-methyl-3-propyl-1,6-dihydro-7*H*-pyrazolo[4,3-*d*]pyrimidin-7-one **4j** (195 mg, 0.5 mmol, 1.0 equiv), ethynylbenzene **2a** (61 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs_2CO_3 (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4 and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **6j** in 60% yield (124 mg).

Yellow solid; mp 164–166 °C; **6j** : **5j** = 91 : 9; ^1H NMR (CDCl_3 , 400 MHz, Major Product **6j**): δ_{H} 7.46 (s, 1H), 7.38–7.32 (m, 3H), 7.20–7.18 (m, 3H), 7.05 (s, 1H), 6.12 (s, 2H), 4.16 (s, 3H), 2.93 (t, J = 7.6 Hz, 2H), 1.92–1.83 (m, 2H), 1.07–1.04 (m, 3H); ^{13}C NMR (CDCl_3 , 101 MHz) δ_{C} 151.7, 151.5, 151.0, 149.6, 145.9, 136.9, 136.2, 133.8, 130.2, 129.9, 129.0, 128.9, 127.8, 127.2, 124.4, 123.9, 114.9, 102.2, 101.6, 99.5, 38.3, 27.7, 22.5, 14.1; HRMS (ESI-TOF, m/z): calcd for $\text{C}_{24}\text{H}_{21}\text{N}_4\text{O}_3$ [$\text{M} + \text{H}$] $^+$, 413.1609; found, 413.1623.



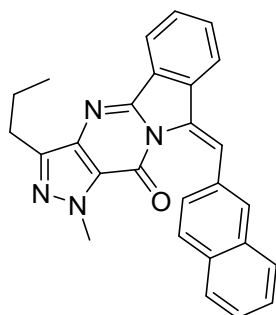
(Z)-9-benzylidene-6,7-dimethoxy-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (6k)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromo-4,5-dimethoxyphenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one **4k** (203 mg, 0.5 mmol, 1.0 equiv), ethynylbenzene **2a** (61 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **6k** in 55% yield (118 mg). Yellow solid; mp 229–232 °C; **6k** : **5k** = 91 : 9; ¹H NMR (CDCl₃, 400 MHz, Major Product **6k**): δ_H 7.51–7.49 (m, 1H), 7.38–7.30 (m, 3H), 7.24–7.21 (m, 3H), 7.10 (d, *J* = 2.4 Hz, 1H), 4.17 (s, 3H), 4.05 (s, 6H), 2.94 (t, *J* = 8.0 Hz, 2H), 1.94–1.84 (m, 2H), 1.07 (t, *J* = 7.6 Hz, 3H); ¹³C NMR (CDCl₃, 101 MHz) δ_C 152.8, 152.1, 151.2, 151.1, 145.7, 136.8, 136.3, 131.8, 130.3, 129.9, 129.1, 128.7, 127.7, 127.2, 124.5, 122.1, 114.5, 103.4, 101.2, 56.4, 56.3, 38.3, 27.7, 22.5, 14.1; HRMS (ESI-TOF, *m/z*): calcd for C₂₅H₂₅N₄O₃ [M + H]⁺, 429.1921; found, 429.1947.



(Z)-6,7-dimethoxy-9-(2-methoxybenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (6l)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromo-4,5-dimethoxyphenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one **4k** (203 mg, 0.5 mmol, 1.0 equiv), 1-ethynyl-2-methoxybenzene **2e** (79 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **6l** in 49% yield (112 mg). Yellow solid; mp 163–166 °C; **6l** : **5l** = 94 : 6; ¹H NMR (CDCl₃, 400 MHz, Major Product **6l**): δ_H 7.51 (s, 1H), 7.38–7.33 (m, 1H), 7.27 (s, 1H), 7.15–7.13 (m, 2H), 6.99–6.91 (m, 2H), 4.16 (s, 3H), 4.06–4.05 (m, 6H), 3.74 (s, 3H), 2.94 (t, *J* = 7.6 Hz, 2H), 1.94–1.85 (m, 2H), 1.07 (t, *J* = 7.6 Hz, 3H); ¹³C NMR (CDCl₃, 101 MHz) δ_C 156.7, 152.7, 151.8, 151.0, 150.9, 145.7, 136.9, 131.9, 131.2, 130.9, 129.5, 125.8, 124.7, 121.9, 119.4, 110.2, 109.8, 103.3, 101.5, 56.4, 56.3, 55.0, 38.3, 27.8, 22.5, 14.1; HRMS (ESI-TOF, *m/z*): calcd for C₂₆H₂₇N₄O₄ [M + H]⁺, 459.2027; found, 459.2057.

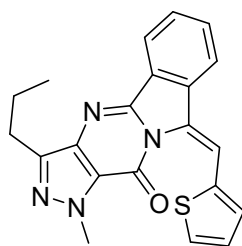


(Z)-1-methyl-9-(naphthalen-2-ylmethylene)-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (6m)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one **4a** (174 mg, 0.5 mmol, 1.0 equiv), 2-ethynyl-naphthalene **2u** (91 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the

residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **6m** in 48% yield (100 mg).

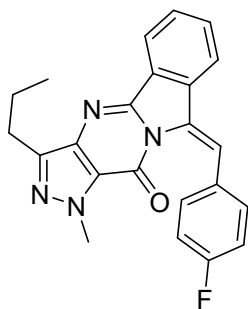
Yellow solid; mp 208–209 °C; **6m** : **5m** = 97 : 3; ¹H NMR (CDCl₃, 400 MHz, Major Product **6m**): δ_H 8.17 (d, *J* = 7.6 Hz, 1H), 7.91 (d, *J* = 7.6 Hz, 1H), 7.86–7.84 (m, 1H), 7.81–7.78 (m, 2H), 7.66–7.46 (m, 5H), 7.43 (s, 1H), 7.37–7.34 (m, 1H), 4.12 (s, 3H), 2.98 (t, *J* = 7.6 Hz, 2H), 1.96–1.87 (m, 2H), 1.08 (t, *J* = 7.6 Hz, 3H); ¹³C NMR (CDCl₃, 101 MHz) δ_C 151.8, 151.2, 146.2, 138.1, 136.9, 133.7, 132.8, 132.5, 131.4, 130.5, 129.6, 129.3, 129.2, 128.2, 127.72, 127.65, 126.5, 126.4, 126.2, 124.8, 122.6, 119.6, 115.9, 38.3, 27.8, 22.5, 14.1; HRMS (ESI-TOF, *m/z*): calcd for C₂₇H₂₃N₄O [M + H]⁺, 419.1866; found, 419.1870.



(Z)-1-methyl-3-propyl-9-(thiophen-2-ylmethylene)-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (6n)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one **4a** (174 mg, 0.5 mmol, 1.0 equiv), 2-ethynylthiophene **2v** (65 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **6n** in 50% yield (94 mg).

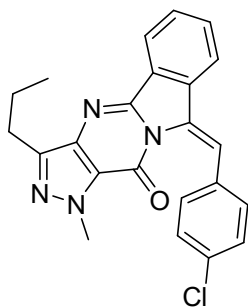
Yellow solid; mp 128–131 °C; **6n** : **5n** = 93 : 7; ¹H NMR (CDCl₃, 400 MHz, Major Product **6n**): δ_H 8.13 (d, *J* = 7.6 Hz, 1H), 7.84–7.82 (m, 1H), 7.61–7.50 (m, 3H), 7.34 (s, 1H), 7.13–7.10 (m, 1H), 6.94 (d, *J* = 4.0 Hz, 1H), 4.29 (s, 3H), 2.97 (t, *J* = 7.6 Hz, 2H), 1.95–1.86 (m, 2H), 1.06 (t, *J* = 7.6 Hz, 3H); ¹³C NMR (CDCl₃, 101 MHz) δ_C 151.5, 151.0, 146.1, 138.2, 138.1, 136.9, 131.5, 131.3, 129.0, 128.9, 128.7, 126.9, 124.7, 122.6, 119.4, 108.7, 38.4, 27.7, 22.5, 14.0; HRMS (ESI-TOF, *m/z*): calcd for C₂₁H₁₉N₄OS [M + H]⁺, 375.1274; found, 375.1280.



(Z)-9-(4-fluorobenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (6o)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one **4a** (174 mg, 0.5 mmol, 1.0 equiv), 1-ethynyl-4-fluorobenzene **2k** (72 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **6o** in 59% yield (114 mg).

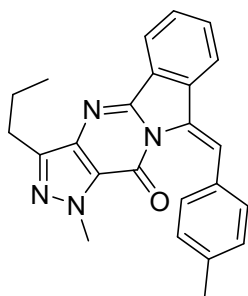
Yellow solid; mp 165–169 °C; **6o** : **5o** = 98 : 2; ¹H NMR (CDCl₃, 400 MHz, Major Product **6o**): δ_H 8.14 (d, *J* = 7.6 Hz, 1H), 7.86 (d, *J* = 7.6 Hz, 1H), 7.63–7.53 (m, 2H), 7.22–7.18 (m, 3H), 7.06 (t, *J* = 8.4 Hz, 2H), 4.20 (s, 3H), 2.96 (t, *J* = 7.6 Hz, 2H), 1.94–1.85 (m, 2H), 1.06 (t, *J* = 7.6 Hz, 3H); ¹³C NMR (CDCl₃, 101 MHz) δ_C 162.1 (d, *J*_{C-F} = 247.4 Hz), 151.7, 151.1, 146.2, 138.0, 136.9, 132.3 (d, *J*_{C-F} = 3.4 Hz), 131.7 (d, *J*_{C-F} = 8.3 Hz), 131.4, 130.3 (d, *J*_{C-F} = 1.1 Hz), 129.3, 129.2, 124.7, 122.6, 119.6, 114.7, 114.3 (d, *J*_{C-F} = 21.9 Hz), 38.4, 27.7, 22.5, 14.1; HRMS (ESI-TOF, *m/z*): calcd for C₂₃H₂₀FN₄O [M + H]⁺, 387.1616; found, 387.1616.



(Z)-9-(4-chlorobenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1- α]isoindol-11-one (6p)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-*d*]pyrimidin-7-one **4a** (174 mg, 0.5 mmol, 1.0 equiv), 1-chloro-4-ethynylbenzene **2l** (82 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **6p** in 60% yield (121 mg).

Yellow solid; mp 224–227 °C; ¹H NMR (CDCl₃, 400 MHz): δ_{H} 8.13 (d, *J* = 7.6 Hz, 1H), 7.84 (d, *J* = 7.6 Hz, 1H), 7.62–7.53 (m, 2H), 7.34–7.32 (m, 2H), 7.18 (s, 1H), 7.14–7.12 (m, 2H), 4.20 (s, 3H), 2.95 (t, *J* = 7.6 Hz, 2H), 1.94–1.84 (m, 2H), 1.06 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (CDCl₃, 101 MHz) δ_{C} 151.6, 151.1, 146.2, 137.8, 136.9, 134.7, 133.6, 131.4, 131.2, 130.7, 129.4, 129.3, 127.4, 124.6, 122.6, 119.6, 114.4, 38.4, 27.7, 22.5, 14.1; HRMS (ESI-TOF, *m/z*): calcd for C₂₃H₂₀ClN₄O [M + H]⁺, 403.1320; found, 403.1325.

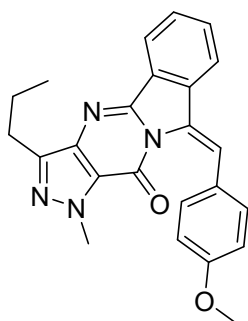


(Z)-1-methyl-9-(4-methylbenzylidene)-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1- α]isoindol-11-one (6q)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-*d*]pyrimidin-7-one **4a** (174 mg, 0.5 mmol, 1.0 equiv), 1-ethynyl-4-methylbenzene **2n** (70 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over

Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **6q** in 56% yield (107 mg).

Yellow solid; mp 139–142 °C; **6q** : **5q** = 98 : 2; ¹H NMR (CDCl₃, 400 MHz, Major Product **6q**): δ_H 8.13 (d, *J* = 7.6 Hz, 1H), 7.85 (d, *J* = 8.0 Hz, 1H), 7.60–7.50 (m, 2H), 7.26–7.24 (m, 1H), 7.18–7.10 (m, 4H), 4.21 (s, 3H), 2.96 (t, *J* = 7.6 Hz, 2H), 2.41 (s, 3H), 1.95–1.85 (m, 2H), 1.07 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (CDCl₃, 101 MHz) δ_C 151.8, 151.1, 146.1, 138.3, 138.0, 136.9, 133.2, 131.3, 130.1, 129.6, 129.1, 128.9, 128.0, 124.8, 122.5, 119.5, 116.1, 38.4, 27.8, 22.5, 21.6, 14.1; HRMS (ESI-TOF, *m/z*): calcd for C₂₄H₂₃N₄O [M + H]⁺, 383.1866; found, 383.1875.

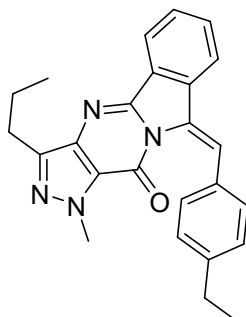


(Z)-9-(4-methoxybenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1- α]isoindol-11-one (6r**)**

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-*d*]pyrimidin-7-one **4a** (174 mg, 0.5 mmol, 1.0 equiv), 1-ethynyl-4-methoxybenzene **2o** (79 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **6r** in 63% yield (126 mg).

Yellow solid; mp 135–137 °C; **6r** : **5r** = 91 : 9; ¹H NMR (CDCl₃, 400 MHz, Major Product **6r**): δ_H 8.14 (d, *J* = 7.6 Hz, 1H), 7.86 (d, *J* = 8.0 Hz, 1H), 7.61–7.50 (m, 2H), 7.27–7.24 (m, 1H), 7.20–7.17 (m, 2H), 6.93–6.89 (m, 2H), 4.22 (s, 3H), 3.87 (s, 3H), 3.00–2.95 (m, 2H), 1.94–1.87 (m, 2H), 1.10–1.05 (m, 3H). ¹³C NMR (CDCl₃, 101 MHz) δ_C 159.4, 151.9, 151.1, 146.1, 138.4, 136.9, 131.8, 131.3, 128.9, 128.82, 128.77, 128.7, 124.7, 122.5, 119.4, 116.0, 112.7, 55.2,

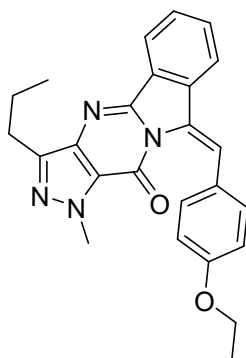
38.4, 27.8, 22.5, 14.1; HRMS (ESI-TOF, m/z): calcd for $C_{24}H_{23}N_4O_2$ $[M + H]^+$, 399.1816; found, 399.1824.



(Z)-9-(4-ethylbenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (6s)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one **4a** (174 mg, 0.5 mmol, 1.0 equiv), 1-ethyl-4-ethynylbenzene **2p** (78 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs_2CO_3 (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4 and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **6s** in 63% yield (125 mg).

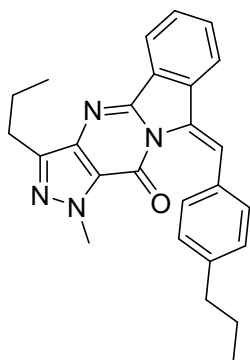
Yellow solid; mp 115–118 °C; 1H NMR ($CDCl_3$, 400 MHz): δ_H 8.13 (d, $J = 7.6$ Hz, 1H), 7.84 (d, $J = 6.8$ Hz, 1H), 7.60–7.50 (m, 2H), 7.24 (s, 1H), 7.21–7.13 (m, 4H), 4.20 (s, 3H), 2.96 (t, $J = 7.6$ Hz, 2H), 2.74–2.68 (m, 2H), 1.95–1.85 (m, 2H), 1.28 (t, $J = 7.6$ Hz, 3H), 1.07 (t, $J = 7.6$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 101 MHz) δ_C 151.8, 151.1, 146.1, 144.2, 138.3, 136.9, 133.4, 131.3, 130.2, 129.6, 129.1, 128.9, 126.7, 124.8, 122.5, 119.5, 116.1, 38.4, 28.8, 27.8, 22.5, 15.1, 14.1; HRMS (ESI-TOF, m/z): calcd for $C_{25}H_{25}N_4O$ $[M + H]^+$, 397.2023; found, 397.2034.



(Z)-9-(4-ethoxybenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1- α]isoindol-11-one (6t)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-*d*]pyrimidin-7-one **4a** (174 mg, 0.5 mmol, 1.0 equiv), 1-ethoxy-4-ethynylbenzene **2q** (88 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **6t** in 60% yield (124 mg).

Yellow solid; mp 91–93 °C; **6t** : **5t** = 91 : 9; ¹H NMR (CDCl₃, 400 MHz, Major Product **6t**): δ_{H} 8.13 (d, *J* = 7.6 Hz, 1H), 7.85–7.83 (m, 1H), 7.60–7.49 (m, 2H), 7.22 (s, 1H), 7.16–7.14 (m, 2H), 6.89–6.87 (m, 2H), 4.22 (s, 3H), 4.12–4.06 (m, 2H), 2.97 (t, *J* = 6.8 Hz, 2H), 1.95–1.86 (m, 2H), 1.45 (t, *J* = 6.8 Hz, 3H), 1.07 (t, *J* = 7.6 Hz, 3H); ¹³C NMR (CDCl₃, 101 MHz) δ_{C} 158.8, 151.8, 151.1, 146.0, 138.4, 136.9, 131.9, 131.2, 130.5, 128.9, 128.7, 128.4, 124.7, 122.5, 119.3, 116.0, 114.7, 113.2, 63.4, 38.4, 27.8, 22.5, 14.8, 14.1; HRMS (ESI-TOF, *m/z*): calcd for C₂₅H₂₅N₄O₂ [M + H]⁺, 413.1972; found, 413.1984.

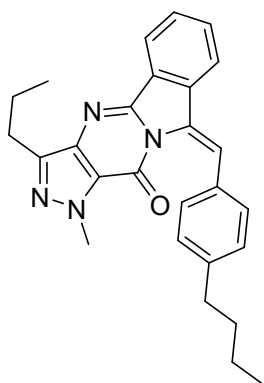


(Z)-1-methyl-3-propyl-9-(4-propylbenzylidene)-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1- α]isoindol-11-one (6u)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-*d*]pyrimidin-7-one **4a** (174 mg, 0.5 mmol, 1.0 equiv), 1-ethynyl-4-propylbenzene **2r** (87 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated

and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4 and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **6u** in 60% yield (123 mg).

Yellow solid; mp 120–121 °C; **6u** : **5u** = 93 : 7; ^1H NMR (CDCl_3 , 400 MHz, Major Product **6u**): δ_{H} 8.13 (d, J = 7.6 Hz, 1H), 7.85 (d, J = 8.0 Hz, 1H), 7.61–7.57 (m, 1H), 7.54–7.51 (m, 1H), 7.26 (s, 1H), 7.19–7.12 (m, 4H), 4.20 (s, 3H), 2.96 (t, J = 7.6 Hz, 2H), 2.64 (t, J = 7.6 Hz, 2H), 1.95–1.85 (m, 2H), 1.73–1.64 (m, 2H), 1.07 (t, J = 7.6 Hz, 3H), 0.97 (t, J = 7.2 Hz, 3H); ^{13}C NMR (CDCl_3 , 101 MHz) δ_{C} 151.8, 151.1, 146.1, 142.8, 138.3, 136.9, 133.5, 131.3, 130.1, 129.6, 129.1, 128.9, 127.4, 124.8, 122.5, 119.5, 116.2, 38.4, 38.0, 27.8, 24.3, 22.5, 14.1, 13.9; HRMS (ESI-TOF, m/z): calcd for $\text{C}_{26}\text{H}_{27}\text{N}_4\text{O}$ [$\text{M} + \text{H}$] $^+$, 411.2179; found, 411.2188.

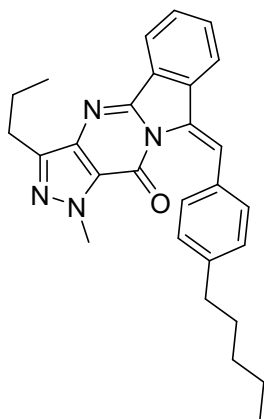


(Z)-9-(4-butylbenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (6v)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one **4a** (174 mg, 0.5 mmol, 1.0 equiv), 1-butyl-4-ethynylbenzene **2s** (95 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs_2CO_3 (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4 and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **6v** in 64% yield (136 mg).

Yellow solid; mp 105–106 °C; ^1H NMR (CDCl_3 , 400 MHz): δ_{H} 8.13 (d, J = 7.6 Hz, 1H), 7.86–7.83 (m, 1H), 7.60–7.50 (m, 2H), 7.25 (s, 1H), 7.19–7.12 (m, 4H), 4.20 (s, 3H), 2.96 (t, J = 7.6 Hz, 2H), 2.67 (t, J = 7.6 Hz, 2H), 1.95–1.85 (m, 2H), 1.68–1.60 (m, 2H), 1.43–1.34 (m, 2H), 1.07 (t,

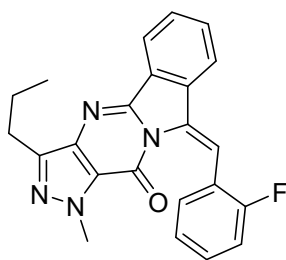
$J = 7.6$ Hz, 3H), 0.94 (t, $J = 7.6$ Hz, 3H); ^{13}C NMR (CDCl_3 , 101 MHz) δ_{C} 151.8, 151.1, 146.1, 143.0, 138.3, 136.9, 133.5, 131.3, 130.1, 129.6, 129.1, 128.9, 127.3, 124.8, 122.5, 119.5, 116.2, 38.3, 35.6, 33.3, 27.8, 22.5, 22.4, 14.1, 14.0; HRMS (ESI-TOF, m/z): calcd for $\text{C}_{27}\text{H}_{29}\text{N}_4\text{O}$ $[\text{M} + \text{H}]^+$, 425.2336; found, 425.2352.



(Z)-1-methyl-9-(4-pentylbenzylidene)-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (6w)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one **4a** (174 mg, 0.5 mmol, 1.0 equiv), 1-ethynyl-4-pentylbenzene **2t** (103 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs_2CO_3 (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4 and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **6w** in 62% yield (136 mg).

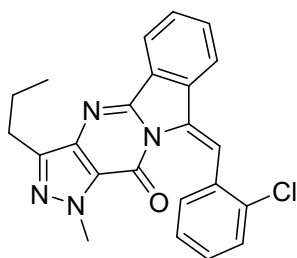
Yellow solid; mp 88–89 °C; **6w** : **5w** = 98 : 2; ^1H NMR (CDCl_3 , 400 MHz, Major Product **6w**): δ_{H} 8.13 (d, $J = 7.6$ Hz, 1H), 7.85 (d, $J = 8.0$ Hz, 1H), 7.61–7.51 (m, 2H), 7.26 (s, 1H), 7.19–7.12 (m, 4H), 4.20 (s, 3H), 2.96 (t, $J = 7.6$ Hz, 2H), 2.66 (t, $J = 8.0$ Hz, 2H), 1.95–1.85 (m, 2H), 1.70–1.62 (m, 2H), 1.37–1.33 (m, 4H), 1.07 (t, $J = 8.0$ Hz, 3H), 0.93–0.87 (m, 3H); ^{13}C NMR (CDCl_3 , 101 MHz) δ_{C} 151.8, 151.1, 146.1, 143.0, 138.3, 136.9, 133.5, 131.3, 130.1, 129.6, 129.2, 128.9, 127.3, 124.8, 122.5, 119.5, 116.2, 38.3, 35.9, 31.5, 30.8, 27.8, 22.53, 22.50, 14.1, 14.0; HRMS (ESI-TOF, m/z): calcd for $\text{C}_{28}\text{H}_{31}\text{N}_4\text{O}$ $[\text{M} + \text{H}]^+$, 439.2492; found, 439.2513.



(Z)-9-(2-fluorobenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (6x)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one **4a** (174 mg, 0.5 mmol, 1.0 equiv), 1-ethynyl-2-fluorobenzene **2b** (72 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **6x** in 57% yield (110 mg).

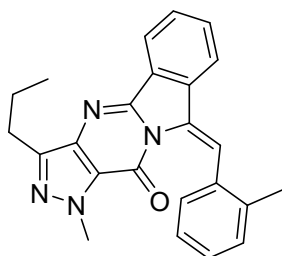
Yellow solid; mp 186–189 °C; ¹H NMR (CDCl₃, 400 MHz): δ_H 8.13 (d, *J* = 7.2 Hz, 1H), 7.87 (d, *J* = 7.6 Hz, 1H), 7.61–7.53 (m, 2H), 7.38–7.28 (m, 2H), 7.20–7.15 (m, 2H), 7.08–7.03 (m, 1H), 4.17 (s, 3H), 2.95 (t, *J* = 7.6 Hz, 2H), 1.94–1.85 (m, 2H), 1.06 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (CDCl₃, 101 MHz) δ_C 160.0 (d, *J*_{C-F} = 248.2 Hz), 151.3, 151.2, 146.2, 137.6, 137.0, 132.7 (d, *J*_{C-F} = 1.8 Hz), 131.3, 130.6 (d, *J*_{C-F} = 3.3 Hz), 129.9 (d, *J*_{C-F} = 8.6 Hz), 129.5, 129.4, 125.1, 124.9 (d, *J*_{C-F} = 7.0 Hz), 122.9 (d, *J*_{C-F} = 3.2 Hz), 122.5, 119.8, 114.6 (d, *J*_{C-F} = 22.0 Hz), 108.4, 38.4, 27.7, 22.5, 14.1; HRMS (ESI-TOF, *m/z*): calcd for C₂₃H₂₀FN₄O [M + H]⁺, 387.1616; found, 387.1616.



(Z)-9-(2-chlorobenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1- α]isoindol-11-one (6y)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-*d*]pyrimidin-7-one **4a** (174 mg, 0.5 mmol, 1.0 equiv), 1-chloro-2-ethynylbenzene **2c** (82 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **6y** in 52% yield (105 mg).

Yellow solid; mp 154–157 °C; ¹H NMR (CDCl₃, 400 MHz): δ_{H} 8.13 (d, *J* = 7.2 Hz, 1H), 7.91 (d, *J* = 7.6 Hz, 1H), 7.64–7.55 (m, 2H), 7.46 (d, *J* = 8.0 Hz, 1H), 7.30–7.19 (m, 3H), 7.10 (d, *J* = 7.6 Hz, 1H), 4.13 (s, 3H), 2.94 (t, *J* = 7.6 Hz, 2H), 1.93–1.84 (m, 2H), 1.06 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (CDCl₃, 101 MHz) δ_{C} 151.5, 151.0, 146.2, 137.5, 136.9, 135.4, 133.5, 132.3, 131.4, 131.3, 129.6, 129.5, 128.9, 128.6, 125.2, 124.8, 122.5, 120.0, 112.1, 38.4, 27.7, 22.5, 14.1; HRMS (ESI-TOF, *m/z*): calcd for C₂₃H₂₀ClN₄O [M + H]⁺, 403.1320; found, 403.1325.

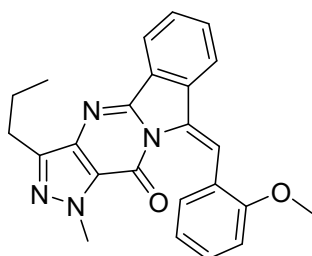


(Z)-1-methyl-9-(2-methylbenzylidene)-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1- α]isoindol-11-one (6z)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-*d*]pyrimidin-7-one **4a** (174 mg, 0.5 mmol, 1.0 equiv), 1-ethynyl-2-methylbenzene **2d** (70 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over

Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **6z** in 54% yield (103 mg).

Yellow solid; mp 134–135 °C; **6z** : **5z** = 97 : 3; ¹H NMR (CDCl₃, 400 MHz, Major Product **6z**): δ_H 8.13 (d, *J* = 7.2 Hz, 1H), 7.87 (d, *J* = 8.0 Hz, 1H), 7.62–7.52 (m, 2H), 7.29–7.22 (m, 3H), 7.11 (t, *J* = 7.2 Hz, 1H), 6.96 (d, *J* = 7.6 Hz, 1H), 4.12 (s, 3H), 2.94 (t, *J* = 7.6 Hz, 2H), 2.42 (s, 3H), 1.94–1.84 (m, 2H), 1.06 (t, *J* = 7.6 Hz, 3H); ¹³C NMR (CDCl₃, 101 MHz) δ_C 151.7, 150.9, 146.1, 137.8, 136.9, 136.0, 135.9, 131.3, 129.9, 129.4, 129.3, 129.2, 128.0, 124.9, 124.4, 122.5, 119.7, 114.7, 38.3, 27.7, 22.5, 20.4, 14.1; HRMS (ESI-TOF, *m/z*): calcd for C₂₄H₂₃N₄O [M + H]⁺, 383.1866; found, 383.1875.

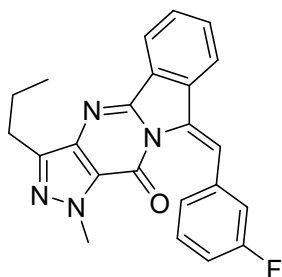


(Z)-9-(2-methoxybenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (6aa)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-*d*]pyrimidin-7-one **4a** (174 mg, 0.5 mmol, 1.0 equiv), 1-ethynyl-2-methoxybenzene **2e** (79 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **6aa** in 59% yield (118 mg).

Yellow solid; mp 178–182 °C; ¹H NMR (CDCl₃, 400 MHz): δ_H 8.13 (d, *J* = 7.6 Hz, 1H), 7.88 (d, *J* = 7.6 Hz, 1H), 7.60–7.50 (m, 2H), 7.38–7.30 (m, 2H), 7.17 (d, *J* = 7.6 Hz, 1H), 7.00–6.96 (m, 1H), 6.91 (d, *J* = 8.0 Hz, 1H), 4.17 (s, 3H), 3.70 (s, 3H), 2.97 (t, *J* = 7.6 Hz, 2H), 1.95–1.86 (m, 2H), 1.06 (t, *J* = 7.6 Hz, 3H); ¹³C NMR (CDCl₃, 101 MHz) δ_C 156.9, 151.5, 150.8, 146.1, 138.1, 136.9, 131.21, 131.18, 130.9, 129.7, 129.1, 128.9, 125.7, 124.9, 122.4, 119.7, 119.4, 111.6,

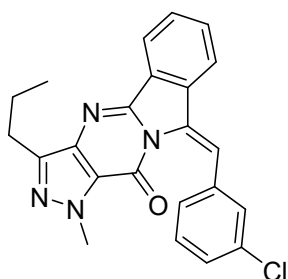
109.8, 55.0, 38.3, 27.8, 22.4, 14.1; HRMS (ESI-TOF, m/z): calcd for $C_{24}H_{23}N_4O_2$ $[M + H]^+$, 399.1816; found, 399.1824.



(Z)-9-(3-fluorobenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1- α]isoindol-11-one (6ab)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-*d*]pyrimidin-7-one **4a** (174 mg, 0.5 mmol, 1.0 equiv), 1-ethynyl-3-fluorobenzene **2f** (72 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs_2CO_3 (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na_2SO_4 and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **6ab** in 57% yield (110 mg).

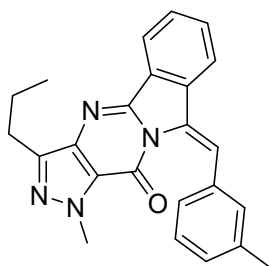
Yellow solid; mp 186–187 °C; **6ab** : **5ab** = 97 : 3; 1H NMR ($CDCl_3$, 400 MHz, Major Product **6ab**): δ_H 8.13 (d, $J = 7.6$ Hz, 1H), 7.85 (d, $J = 7.6$ Hz, 1H), 7.63–7.54 (m, 2H) 7.35–7.29 (m, 1H), 7.20 (s, 1H), 7.06–7.00 (m, 2H), 6.90 (d, $J = 9.6$ Hz, 1H), 4.19 (s, 3H), 2.95 (t, $J = 7.6$ Hz, 2H), 1.94–1.85 (m, 2H), 1.06 (t, $J = 7.6$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 101 MHz) δ_C 161.8 (d, $J_{C-F} = 243.6$ Hz), 151.7, 151.2, 146.2, 138.4 (d, $J_{C-F} = 8.2$ Hz), 137.8, 136.9, 131.4, 131.2, 129.5, 129.4, 128.5 (d, $J_{C-F} = 8.4$ Hz), 125.6 (d, $J_{C-F} = 2.9$ Hz), 124.7, 122.6, 119.7, 116.6 (d, $J_{C-F} = 21.9$ Hz), 114.7 (d, $J_{C-F} = 21.2$ Hz), 114.2 (d, $J_{C-F} = 2.8$ Hz), 38.4, 27.7, 22.5, 14.0; HRMS (ESI-TOF, m/z): calcd for $C_{23}H_{20}FN_4O$ $[M + H]^+$, 387.1616; found, 387.1616.



(Z)-9-(3-chlorobenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1- α]isoindol-11-one (6ac)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-*d*]pyrimidin-7-one **4a** (174 mg, 0.5 mmol, 1.0 equiv), 1-chloro-3-ethynylbenzene **2g** (82 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **6ac** in 49% yield (99 mg).

Yellow solid; mp 181–183 °C; ¹H NMR (CDCl₃, 400 MHz): δ_{H} 8.14 (d, *J* = 7.6 Hz, 1H), 7.85 (d, *J* = 7.6 Hz, 1H), 7.63–7.54 (m, 2H), 7.30–7.29 (m, 2H), 7.17–7.10 (m, 3H), 4.20 (s, 3H), 2.96 (t, *J* = 7.6 Hz, 2H), 1.94–1.85 (m, 2H), 1.07 (t, *J* = 8.0 Hz, 3H); ¹³C NMR (CDCl₃, 101 MHz) δ_{C} 151.6, 151.2, 146.2, 137.9, 137.7, 136.9, 133.1, 131.4, 131.2, 129.9, 129.6, 129.4, 128.3, 128.0, 127.8, 124.7, 122.6, 119.7, 113.9, 38.4, 27.7, 22.5, 14.1; HRMS (ESI-TOF, *m/z*): calcd for C₂₃H₂₀ClN₄O [M + H]⁺, 403.1320; found, 403.1325.

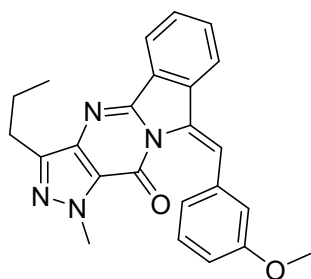


(Z)-1-methyl-9-(3-methylbenzylidene)-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1- α]isoindol-11-one (6ad)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-*d*]pyrimidin-7-one **4a** (174 mg, 0.5 mmol, 1.0 equiv), 1-ethynyl-3-methylbenzene **2h** (70 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over

Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **6ad** in 56% yield (107 mg).

Yellow solid; mp 157–158 °C; **6ad** : **5ad** = 97 : 3; ¹H NMR (CDCl₃, 400 MHz, Major Product **6ad**): δ_H 8.13 (d, *J* = 7.6 Hz, 1H), 7.85 (d, *J* = 8.0 Hz, 1H), 7.61–7.51 (m, 2H), 7.27–7.23 (m, 2H), 7.15 (d, *J* = 7.6 Hz, 1H), 7.06 (s, 1H), 7.00 (d, *J* = 7.6 Hz, 1H), 4.19 (s, 3H), 2.96 (t, *J* = 6.8 Hz, 2H), 2.37 (s, 3H), 1.95–1.85 (m, 2H), 1.09–1.05 (m, 3H); ¹³C NMR (CDCl₃, 101 MHz) δ_C 151.8, 151.1, 146.1, 138.2, 136.9, 136.6, 136.0, 131.3, 130.8, 130.1, 129.2, 129.1, 128.8, 127.4, 127.0, 124.8, 122.5, 119.5, 116.0, 38.3, 27.8, 22.5, 21.4, 14.1; HRMS (ESI-TOF, *m/z*): calcd for C₂₄H₂₃N₄O [M + H]⁺, 383.1866; found, 383.1875.

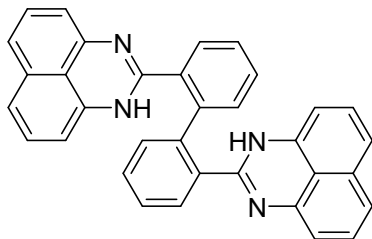


(Z)-9-(3-methoxybenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (6ae)

To a 10 mL Schlenk tube equipped with a magnetic stir bar was added 5-(2-bromophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-*d*]pyrimidin-7-one **4a** (174 mg, 0.5 mmol, 1.0 equiv), 1-ethynyl-3-methoxybenzene **2i** (79 mg, 0.6 mmol, 1.2 equiv), DMF (4.0 mL), Cs₂CO₃ (163 mg, 0.5 mmol, 1.0 equiv), *o*-phen (18 mg, 0.1 mmol, 0.2 equiv), CuI (10 mg, 0.05 mmol, 0.1 equiv). The reaction mixture was stirred at 80 °C in an oil bath for about 12 h. The resulting mixture was concentrated and the residue was taken up in ethyl acetate. The organic layer was washed with brine, dried over Na₂SO₄ and concentrated. Purification of the crude product by column chromatography (silica gel; petroleum ether/ethyl acetate = 13:1) afforded **6ae** in 55% yield (110 mg).

Yellow solid; mp 124–125 °C; **6ae** : **5ae** = 96 : 4; ¹H NMR (CDCl₃, 400 MHz, Major Product **6ae**): δ_H 8.13 (d, *J* = 7.6 Hz, 1H), 7.86 (d, *J* = 8.0 Hz, 1H), 7.62–7.52 (m, 2H), 7.30–7.24 (m, 2H), 6.89 (d, *J* = 8.4 Hz, 1H), 6.83 (d, *J* = 8.0 Hz, 1H), 6.78 (s, 1H), 4.19 (s, 3H), 3.80 (s, 3H), 2.96 (t, *J* = 7.6 Hz, 2H), 1.94–1.85 (m, 2H), 1.07 (t, *J* = 7.6 Hz, 3H); ¹³C NMR (CDCl₃, 101 MHz) δ_C 158.5, 151.8, 151.1, 146.2, 138.1, 137.4, 136.9, 131.4, 130.5, 129.3, 129.2, 128.1, 124.8, 122.8,

122.6, 119.6, 115.7, 115.4, 113.8, 55.2, 38.4, 27.8, 22.5, 14.1; HRMS (ESI-TOF, m/z): calcd for $C_{24}H_{23}N_4O_2$ $[M + H]^+$, 399.1816; found, 399.1824.

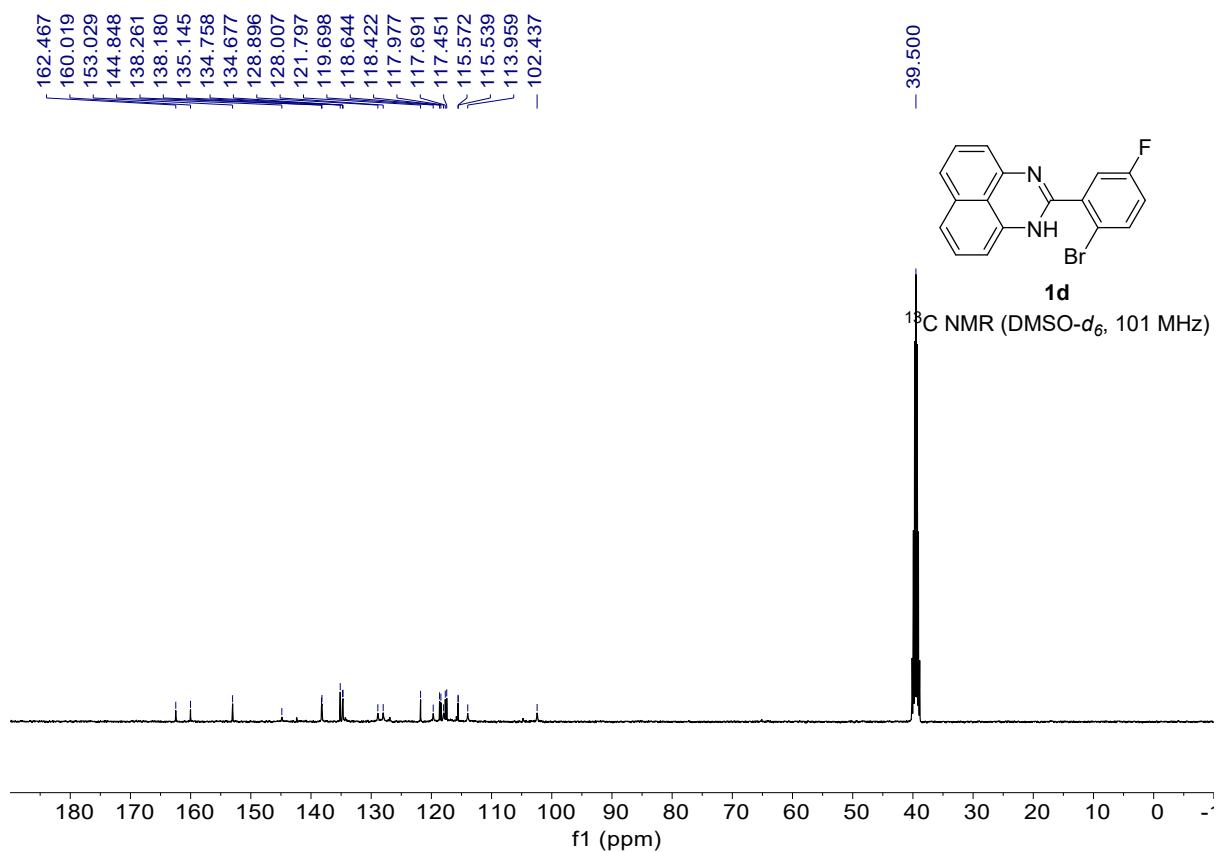
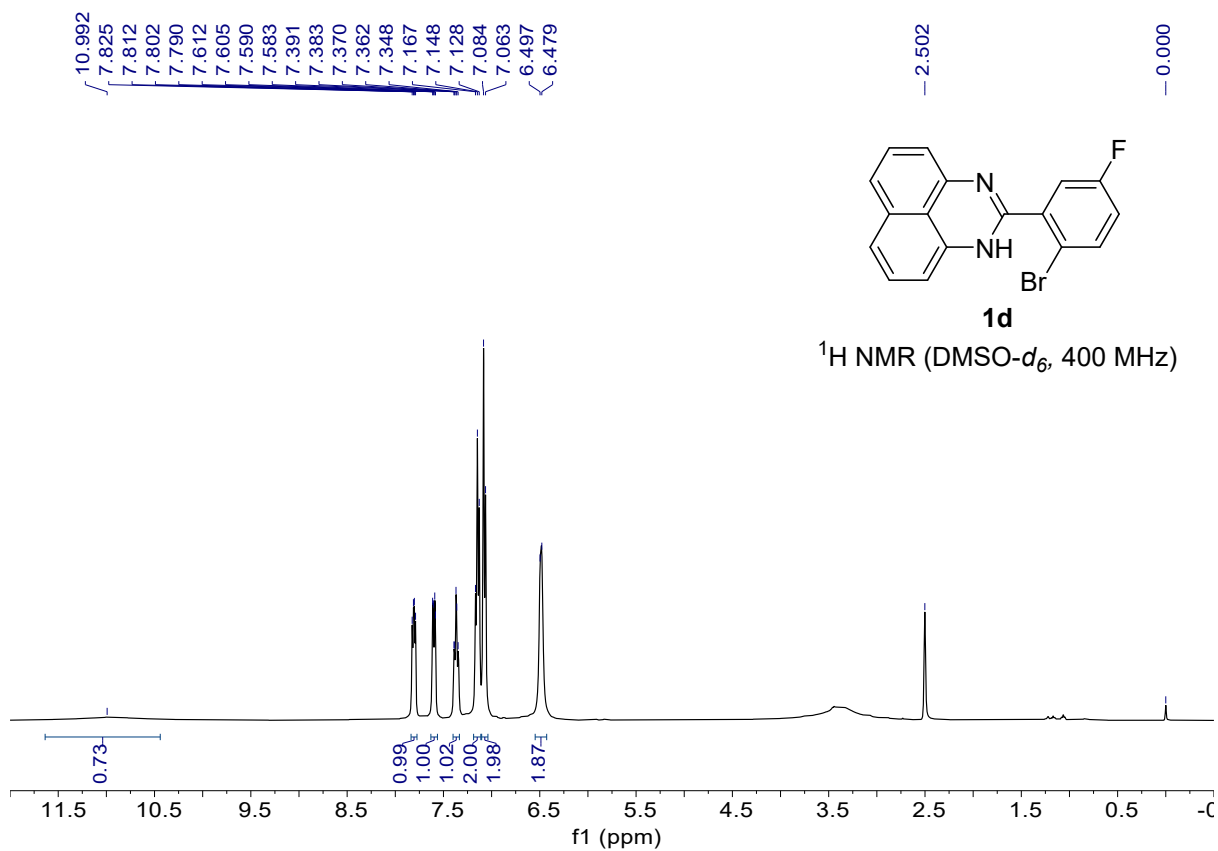


2,2'-di(1H-perimidin-2-yl)-1,1'-biphenyl (3')

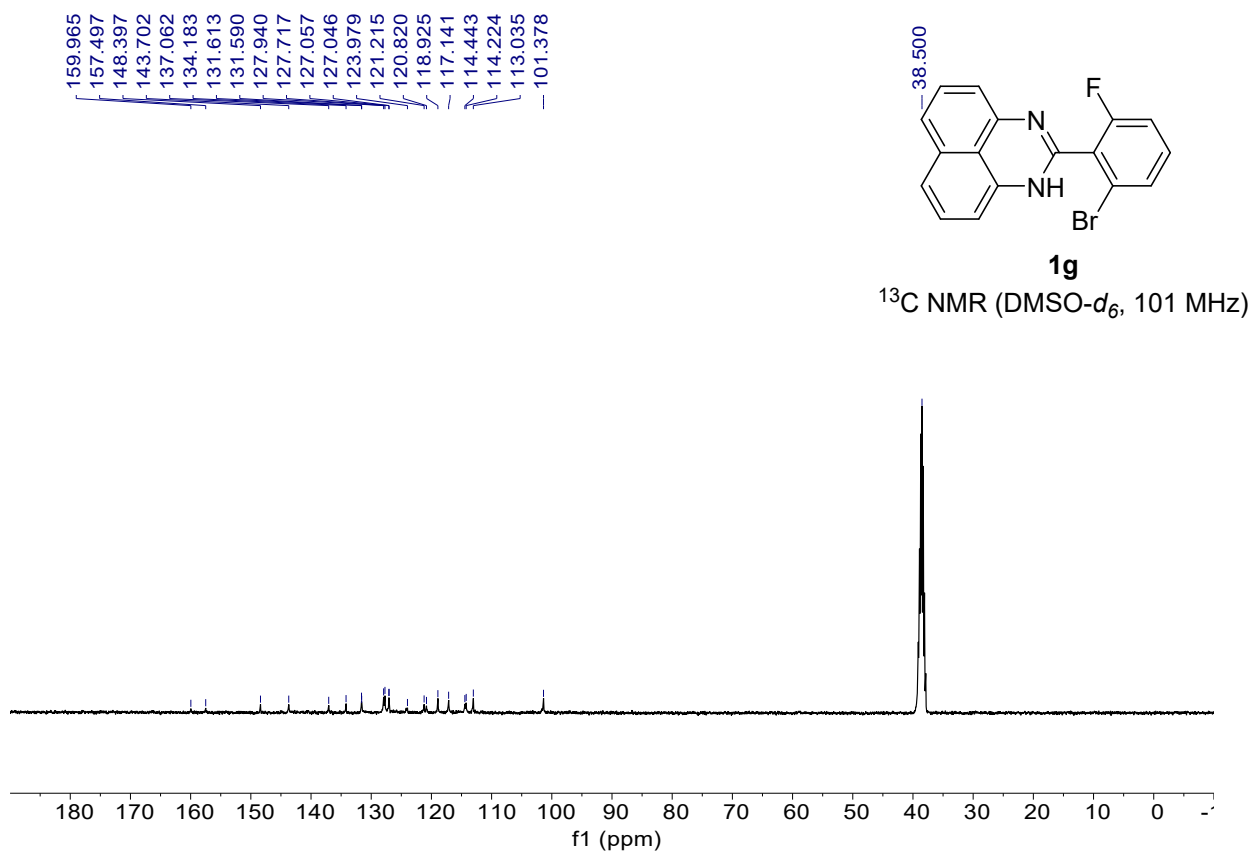
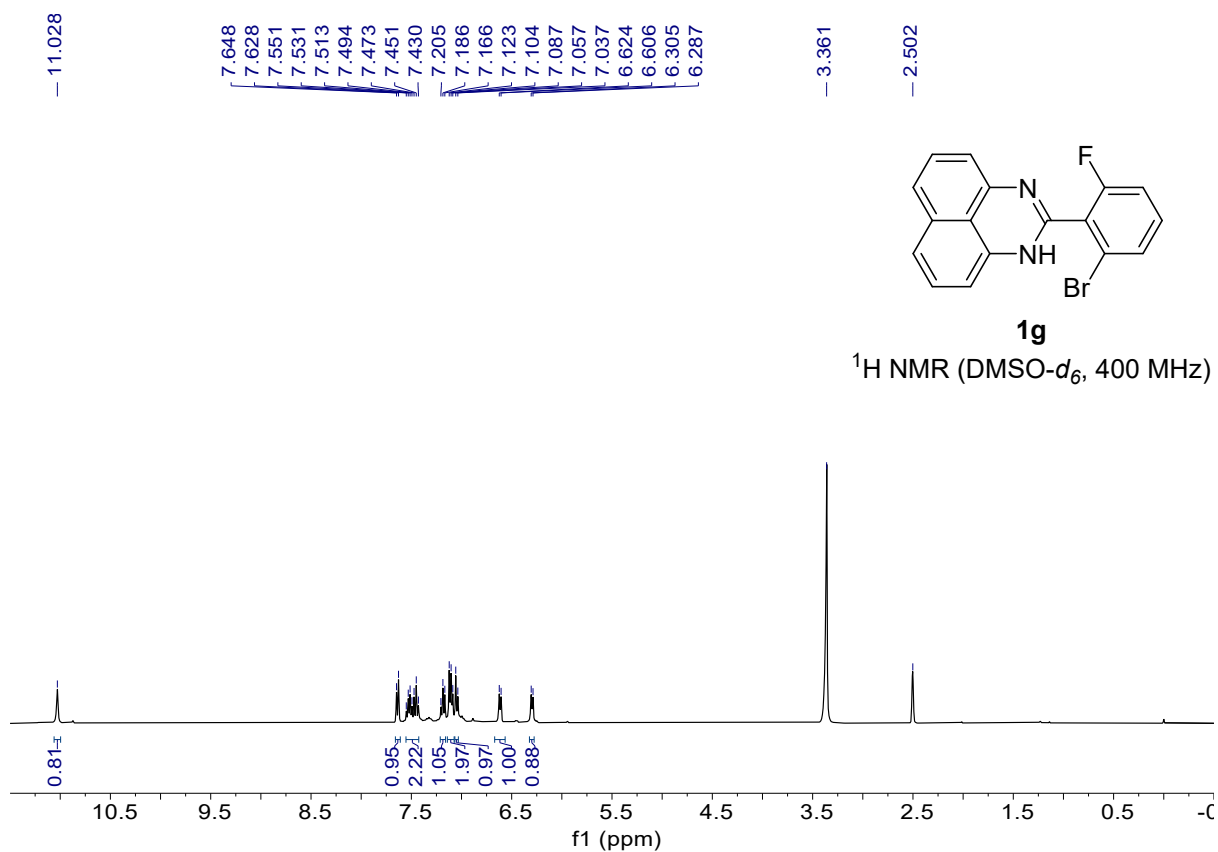
White oil; 1H NMR ($CDCl_3$, 400 MHz): δ_H 13.94 (s, 2H), 9.19 (d, $J = 4.4$ Hz, 1H), 8.26 (d, $J = 8.0$ Hz, 1H), 7.80 (s, 1H), 7.67–7.63 (m, 3H), 7.31–7.25 (m, 3H), 7.18–7.02 (m, 11H); ^{13}C NMR ($CDCl_3$, 101 MHz) δ_C 156.1, 150.3, 146.3, 140.0, 136.0, 135.6, 132.8, 129.6, 129.1, 128.7, 128.6, 127.9, 127.8, 126.6, 123.1, 122.4, 119.2; HRMS (ESI-TOF, m/z): calcd for $C_{34}H_{23}N_4$ $[M + H]^+$, 487.1917; found, 487.1934.

IV. NMR spectra

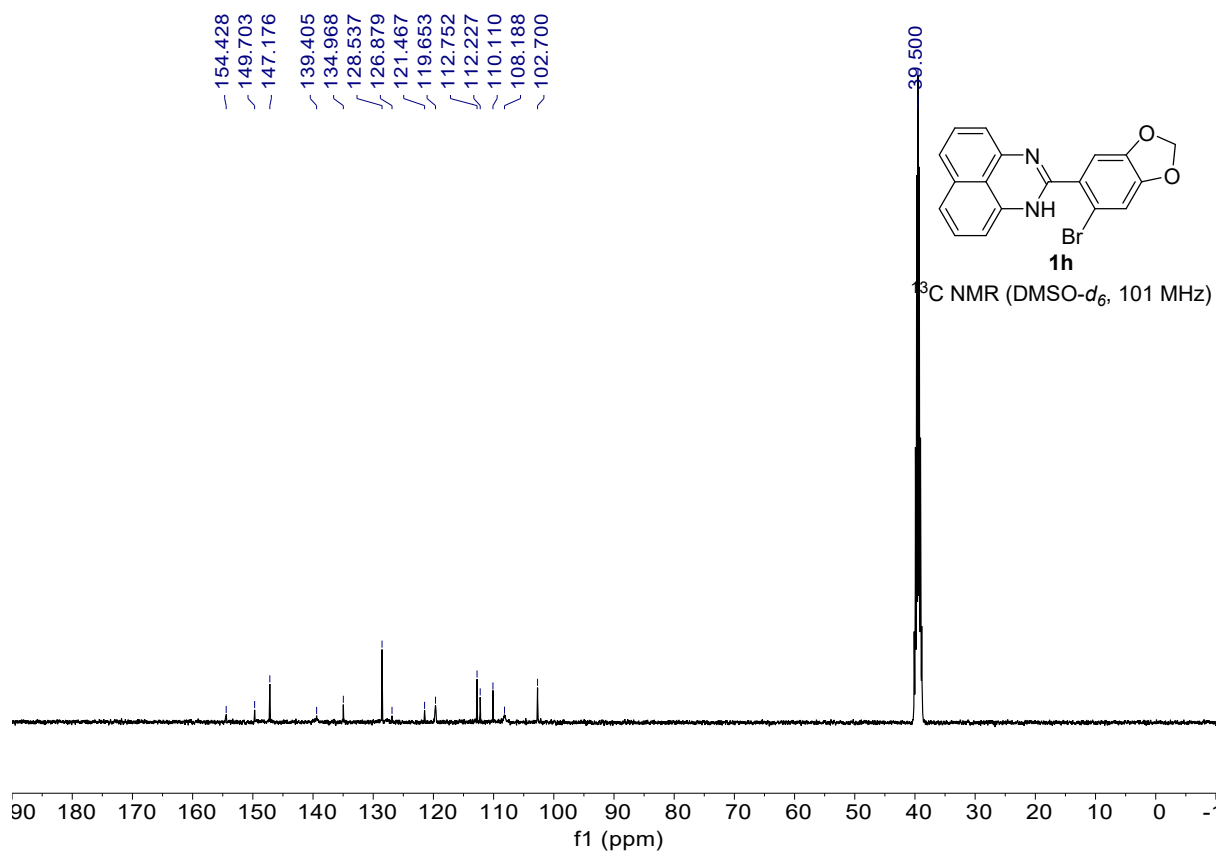
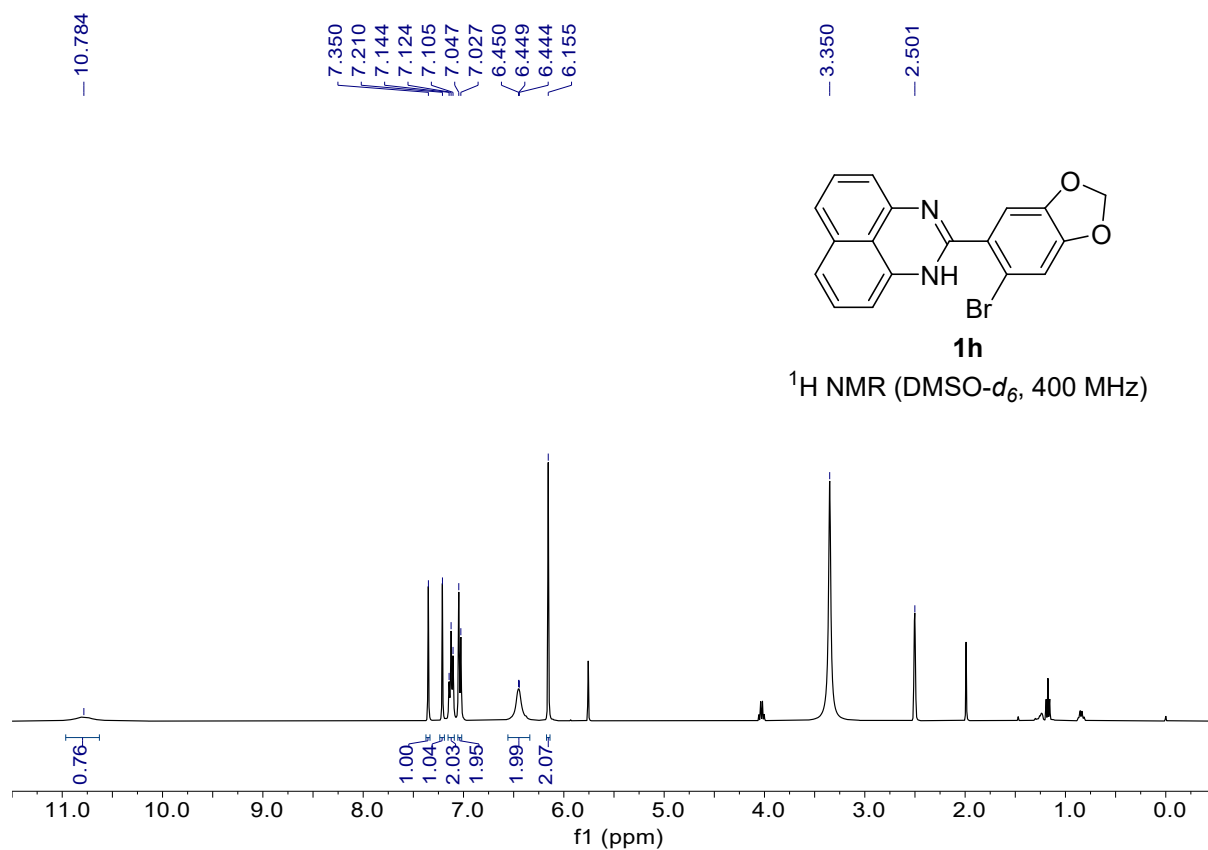
2-(2-bromo-5-fluorophenyl)-1H-perimidine (1d)



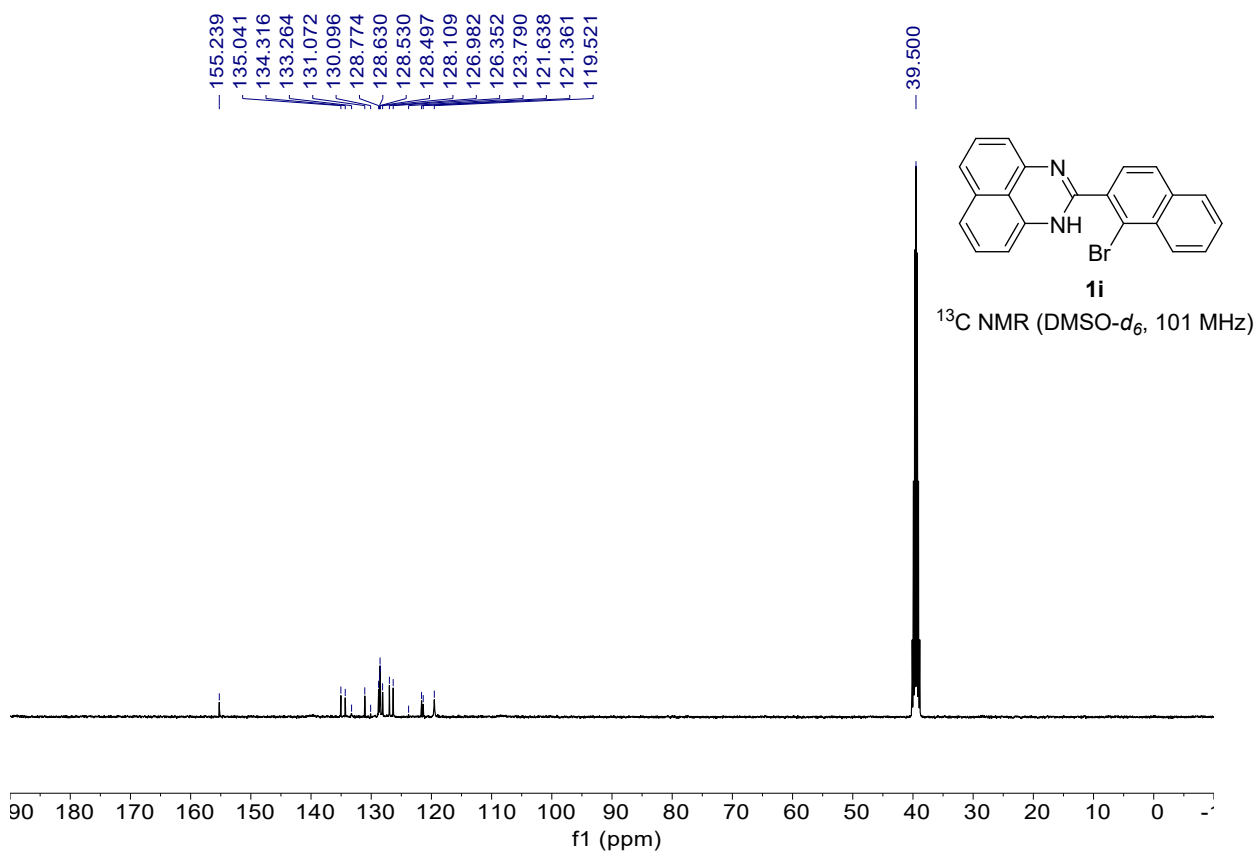
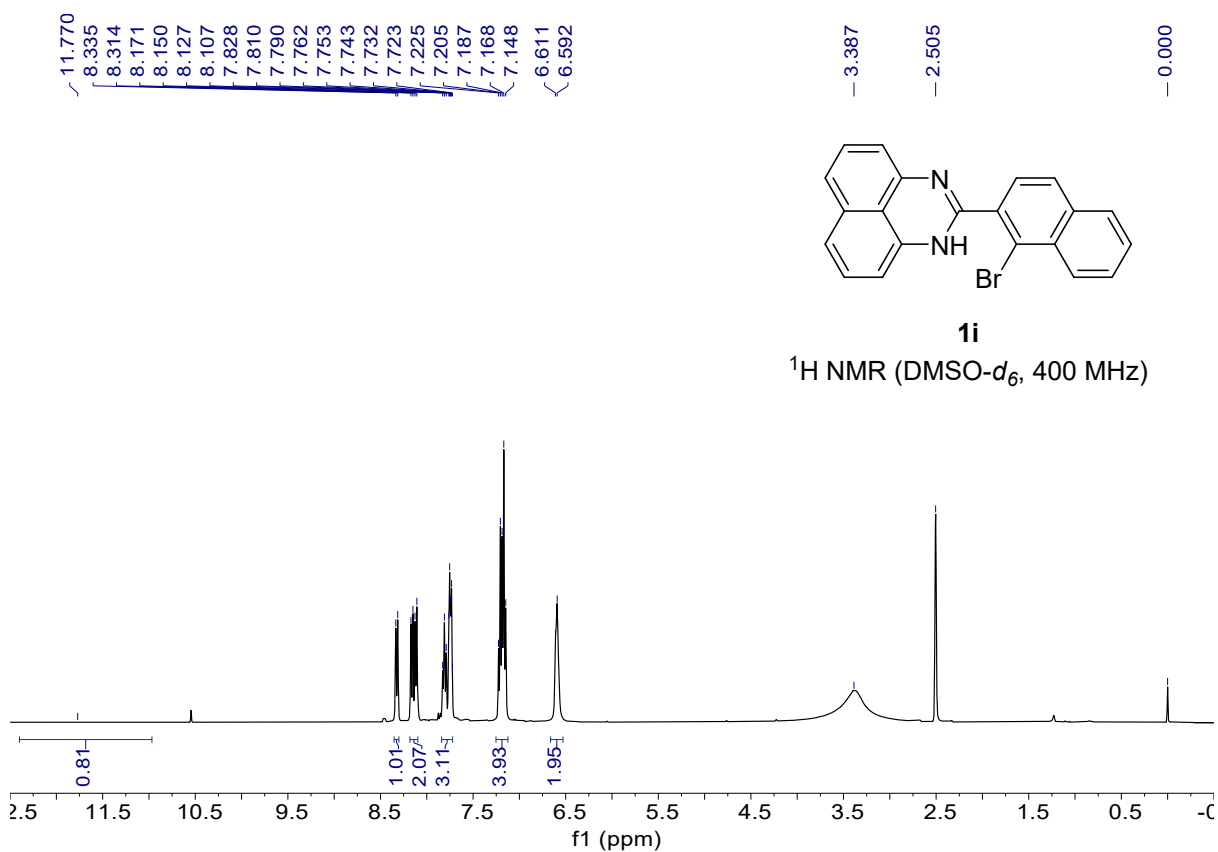
2-(2-bromo-6-fluorophenyl)-1H-perimidine (1g)



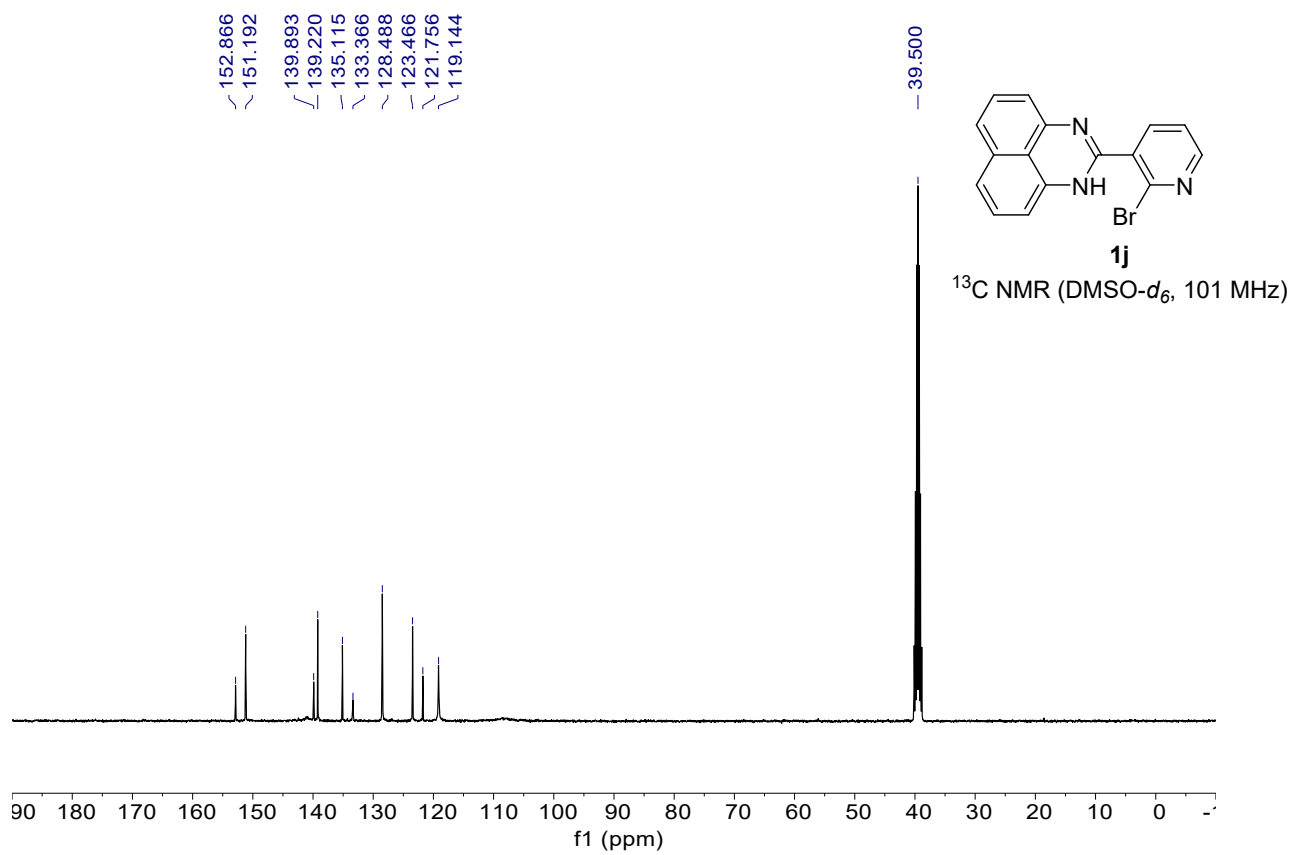
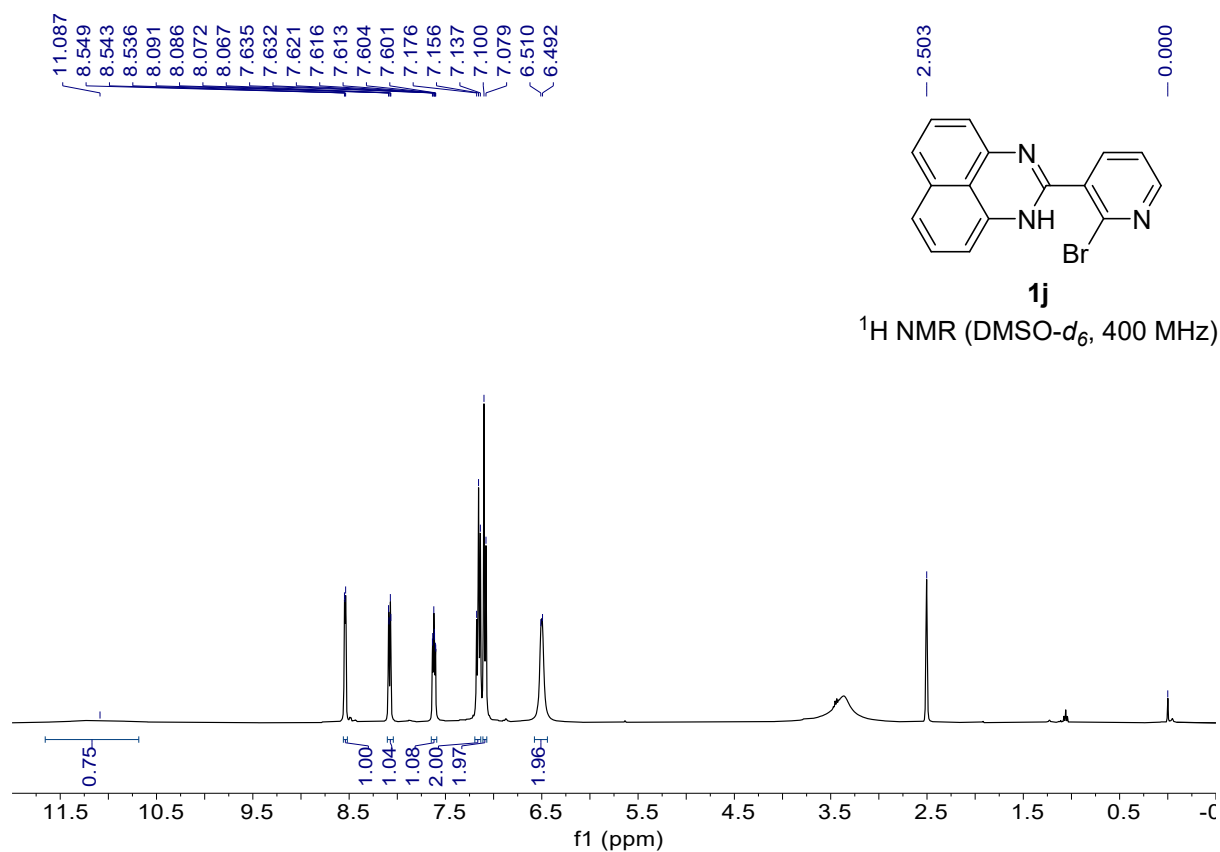
2-(6-bromobenzo[d][1,3]dioxol-5-yl)-1*H*-perimidine (1h)



2-(1-bromonaphthalen-2-yl)-1H-perimidine (1i)

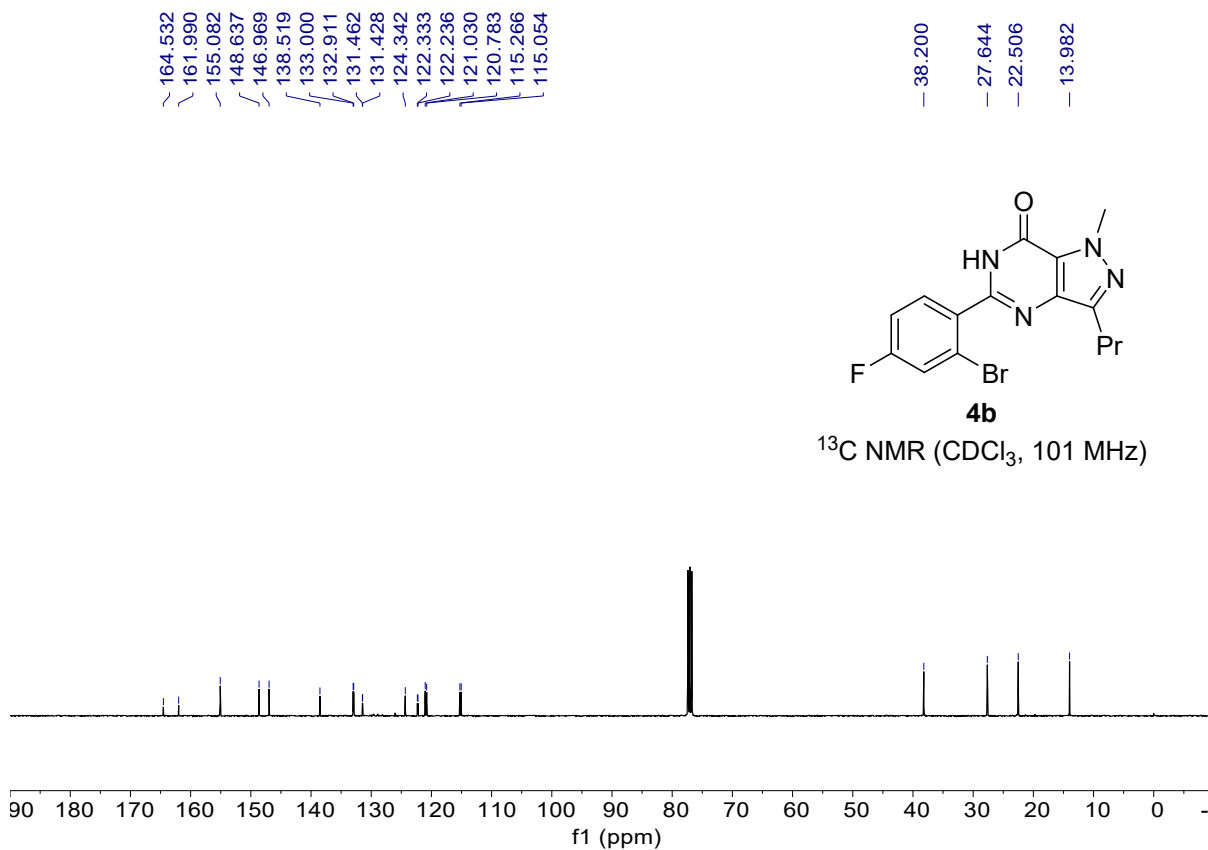
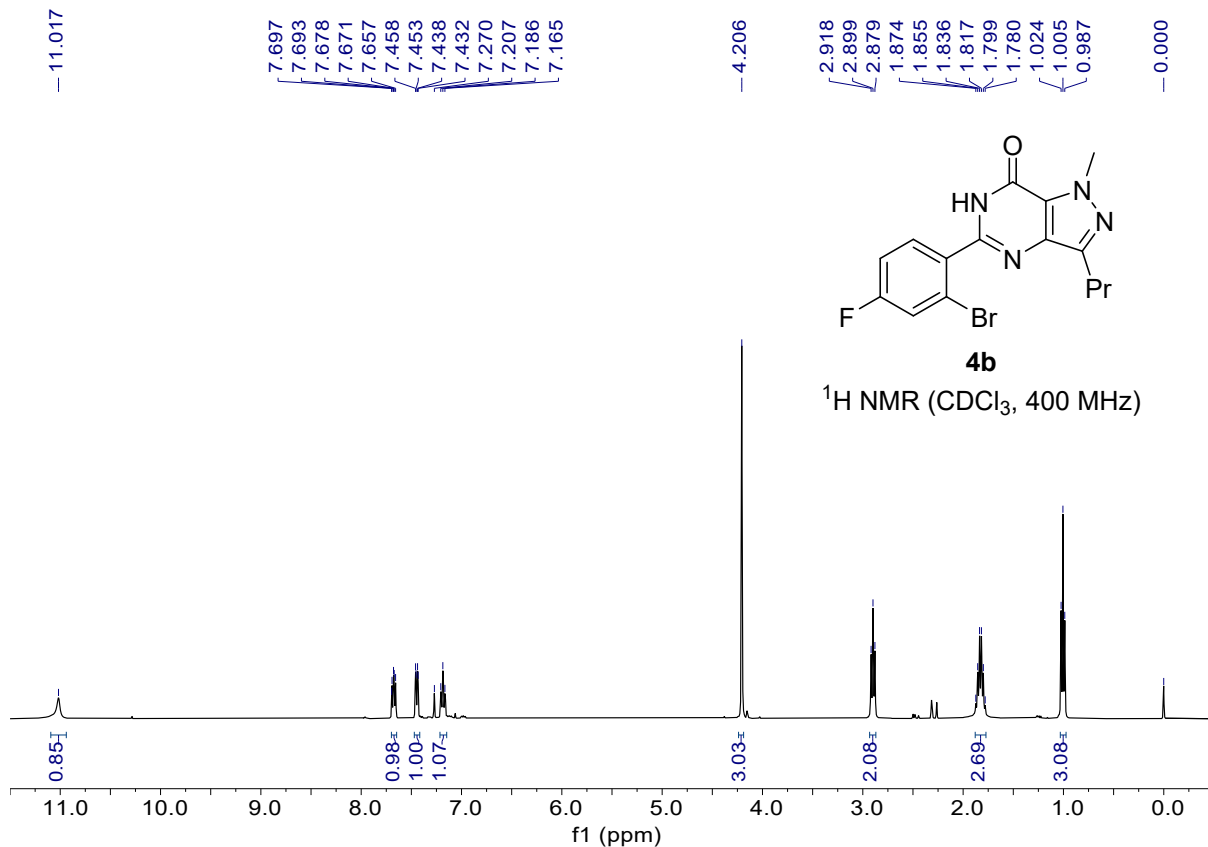


2-(2-bromopyridin-3-yl)-1H-perimidine (1j)

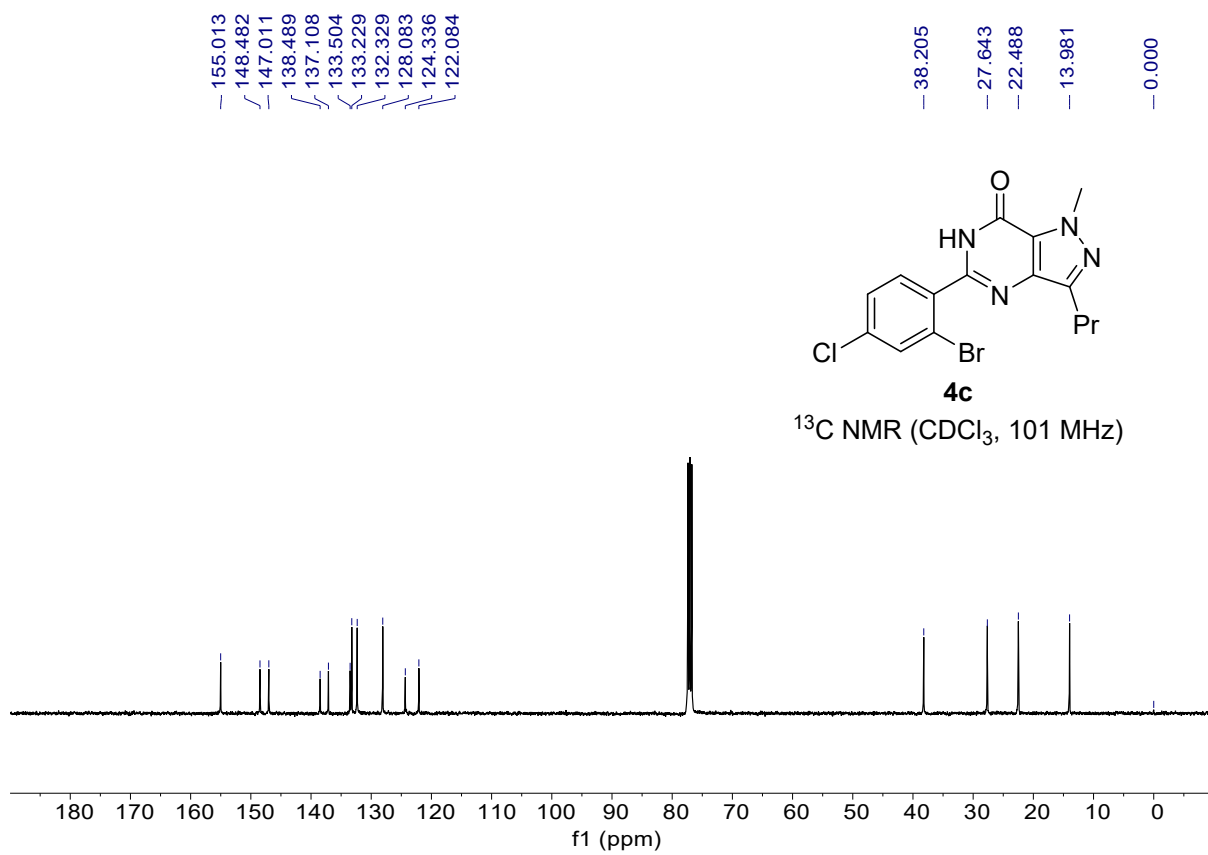
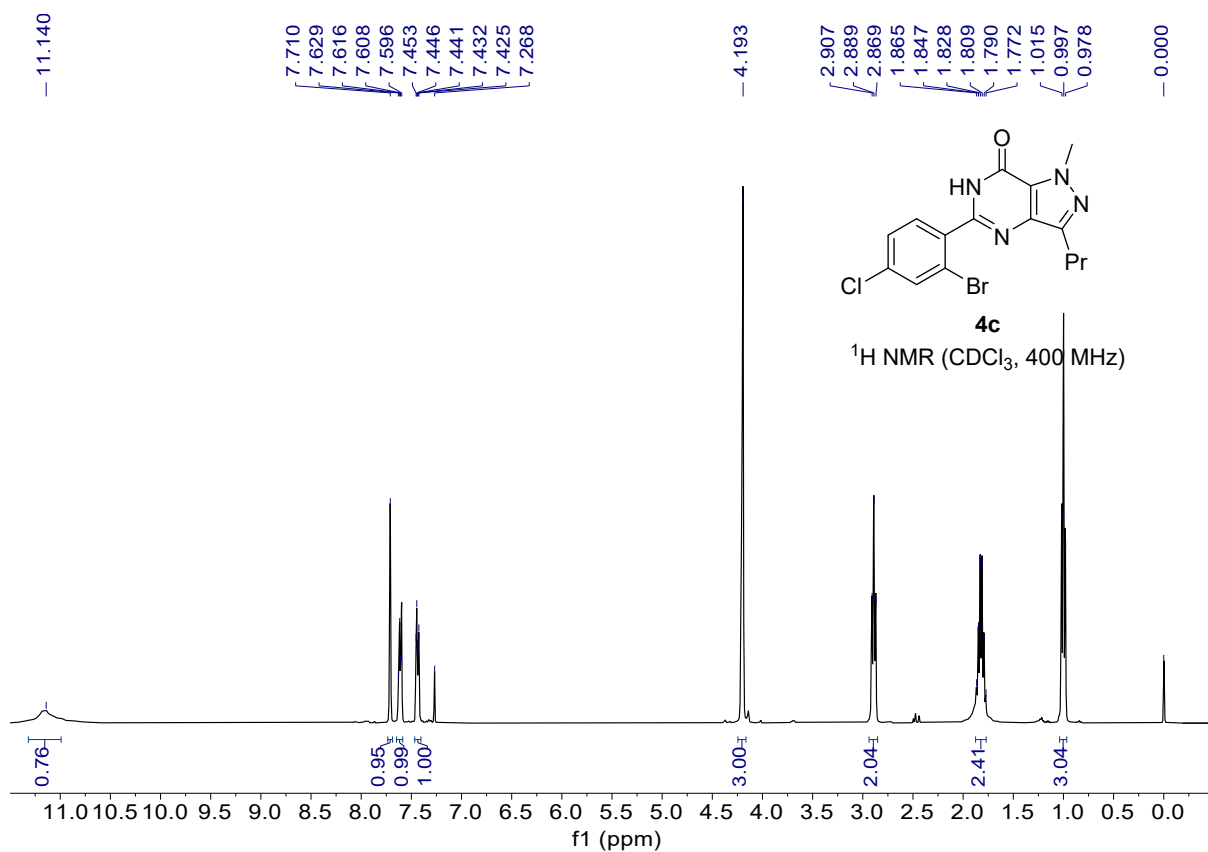


5-(2-bromo-4-fluorophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one

(4b)

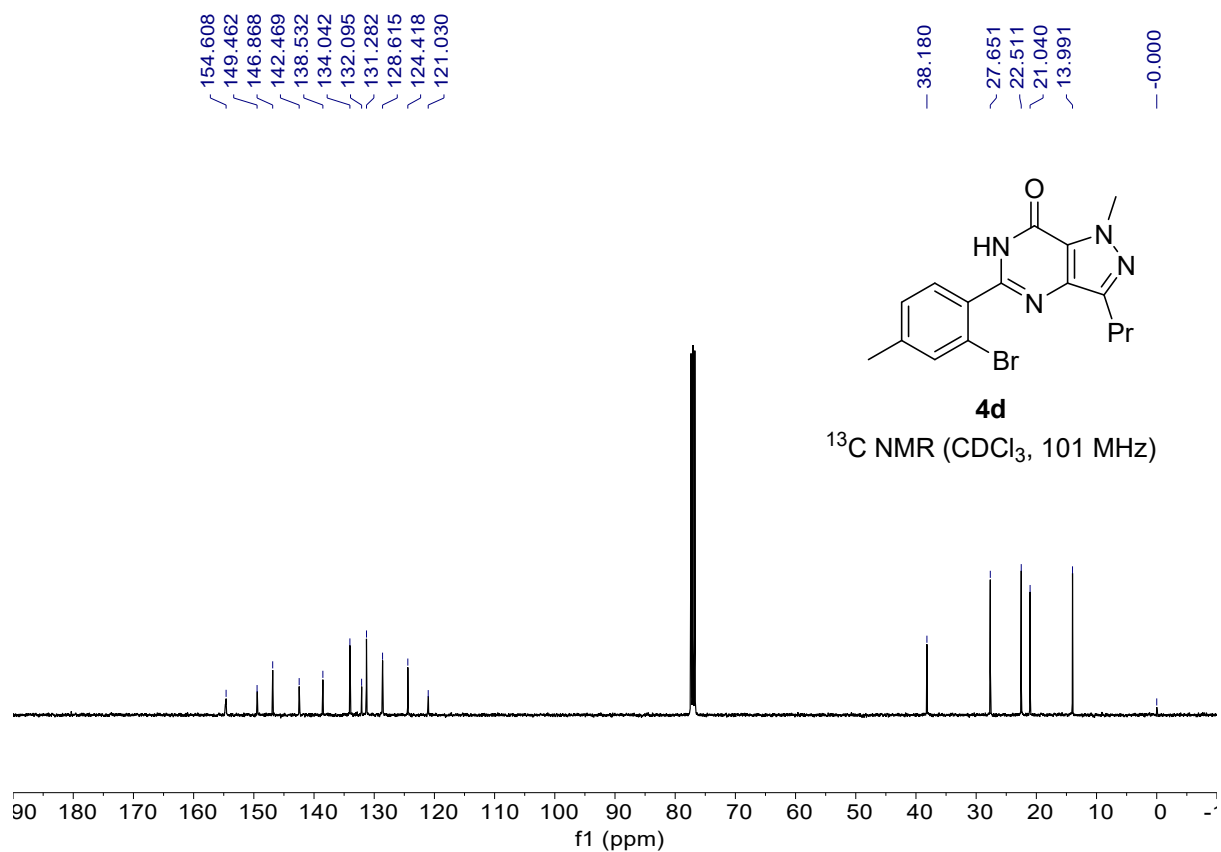
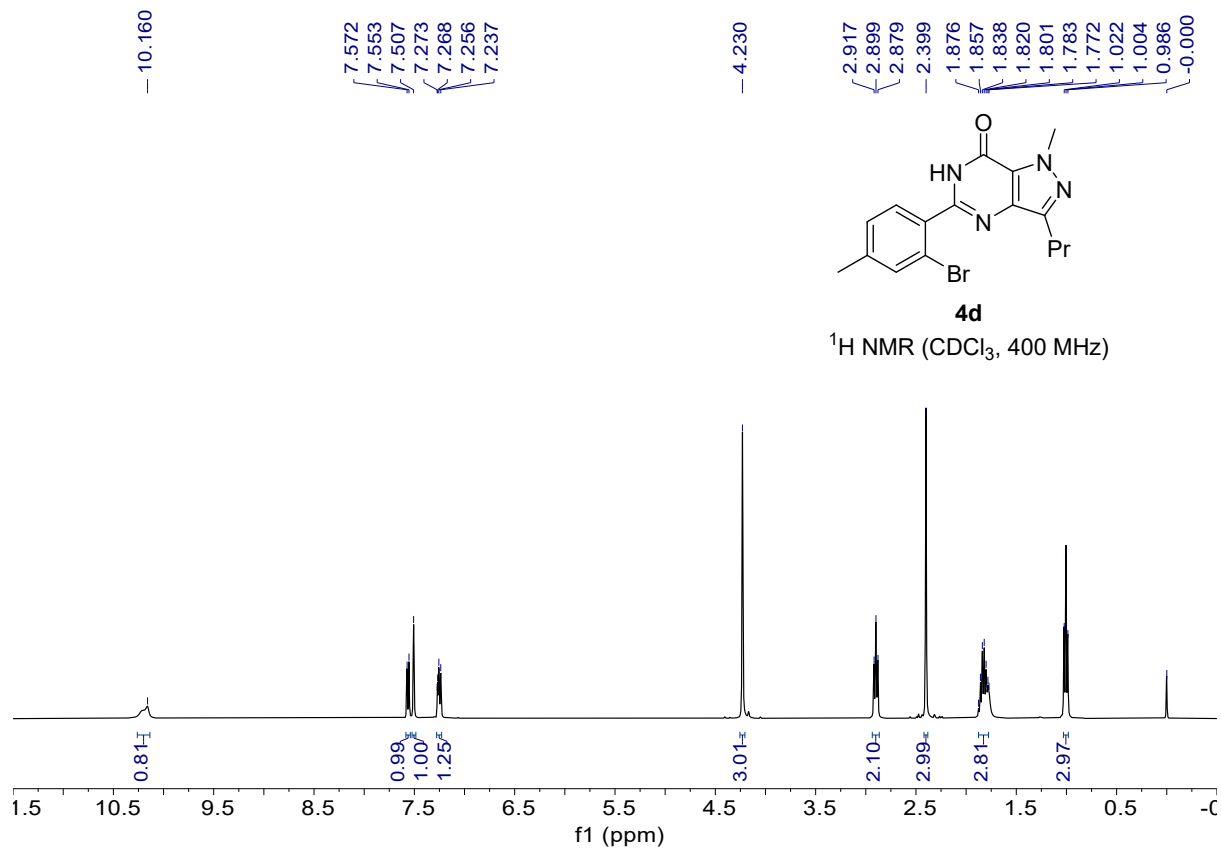


5-(2-bromo-4-chlorophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one (4c)

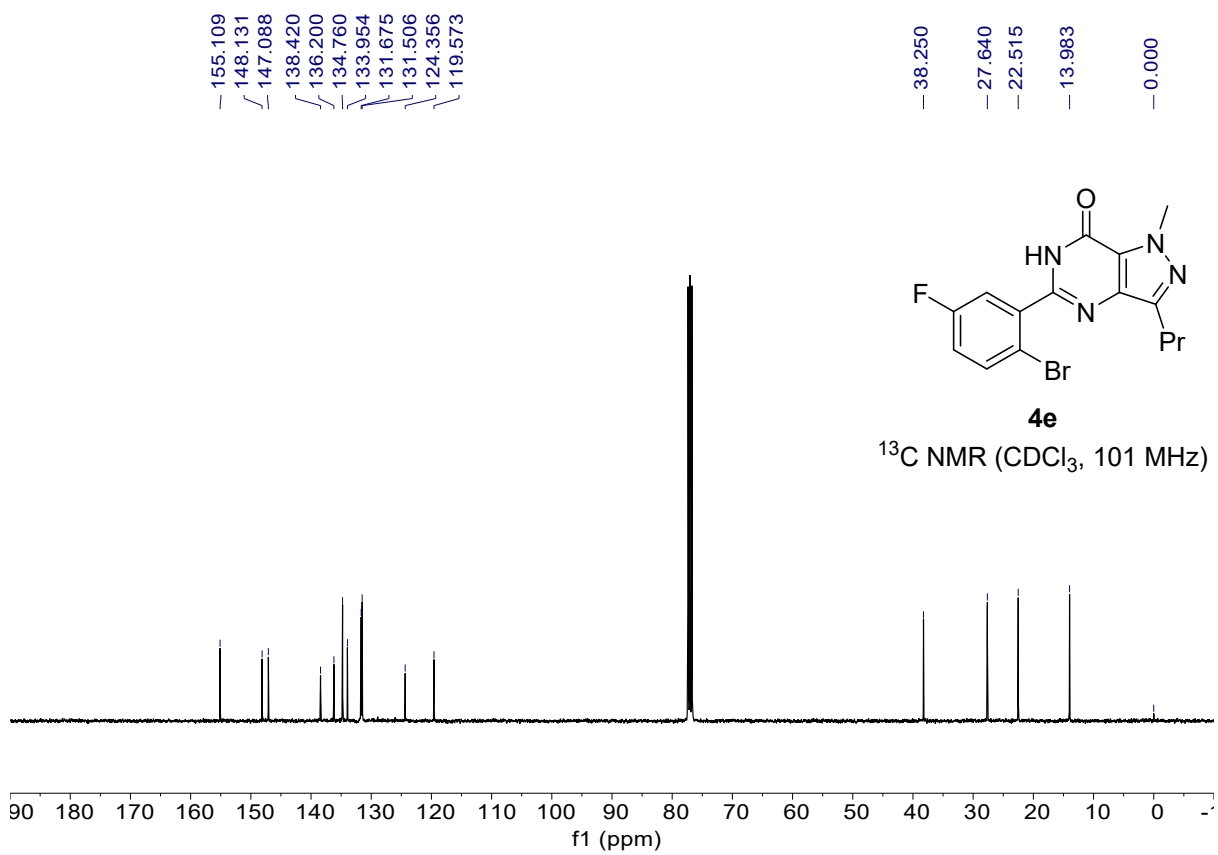
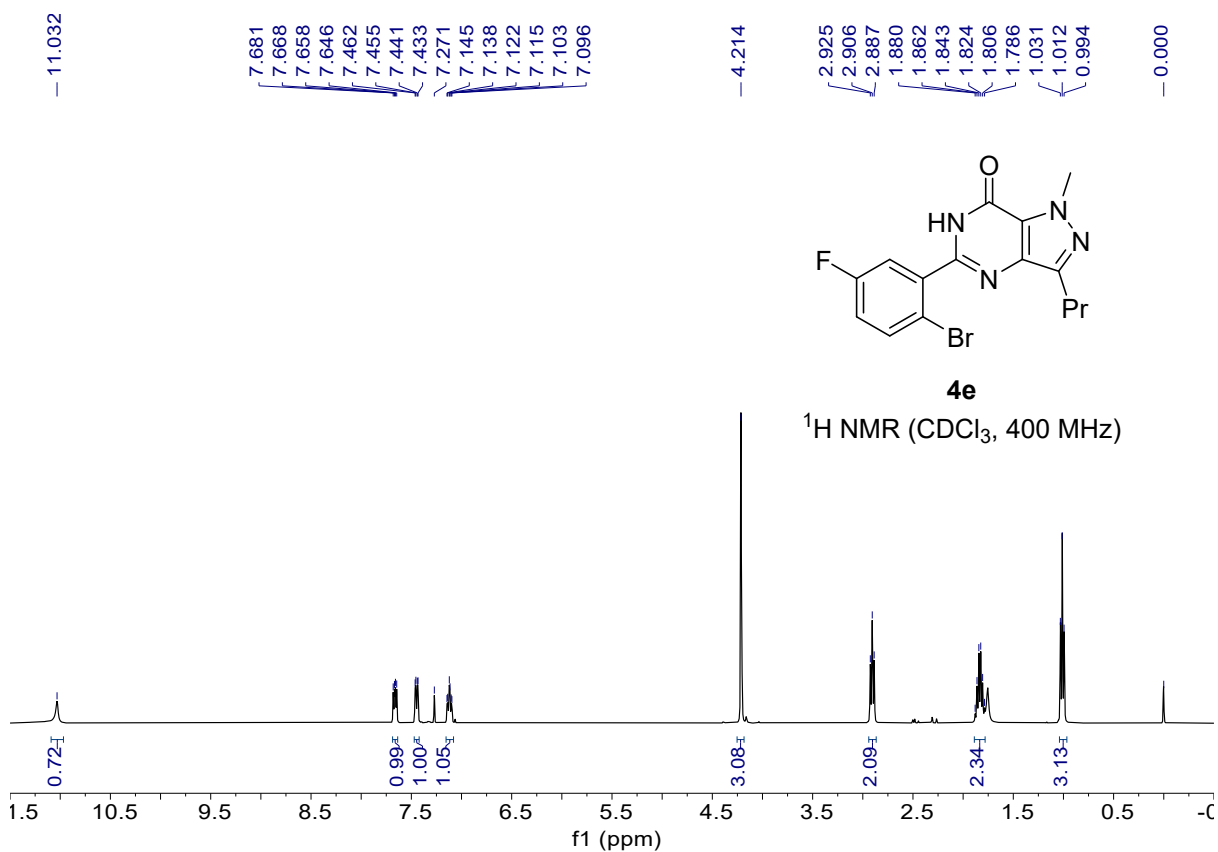


5-(2-bromo-4-methylphenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one

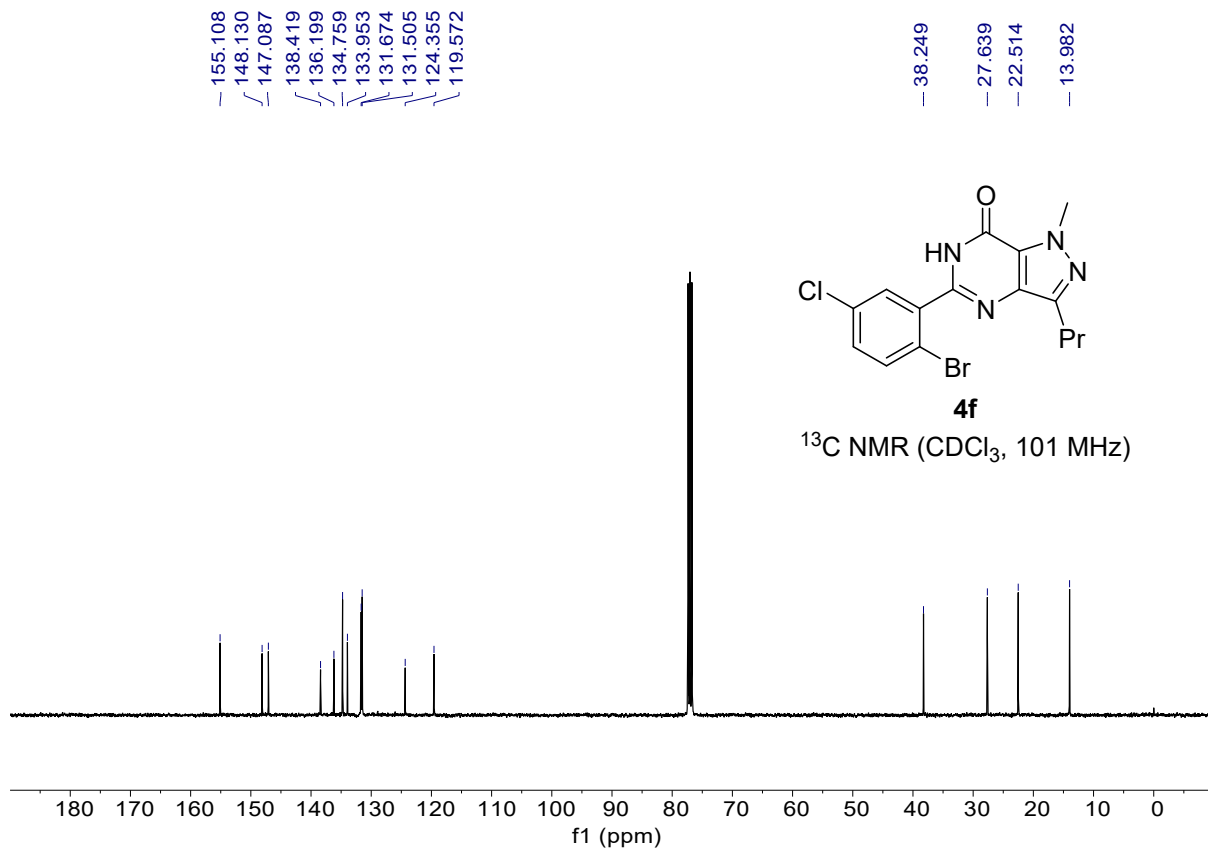
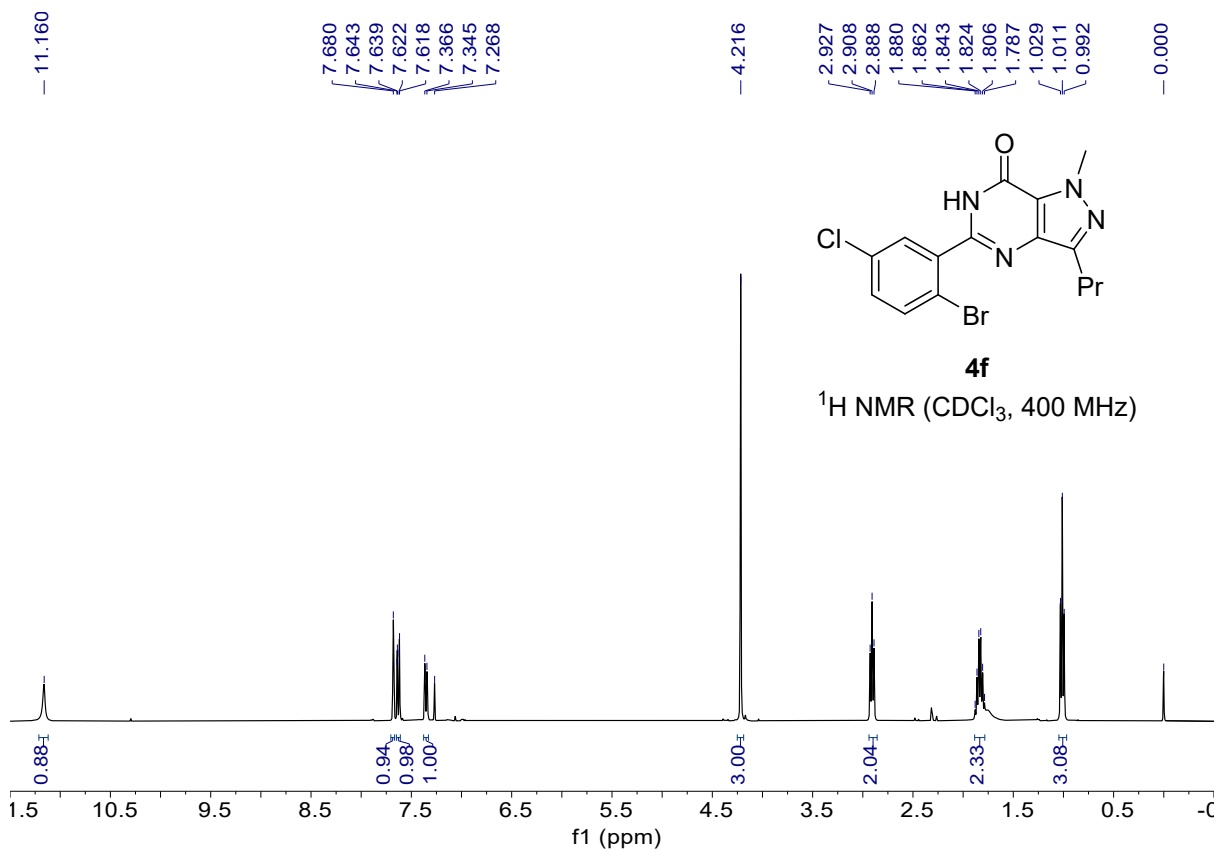
(4d)



5-(2-bromo-5-fluorophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one (4e)

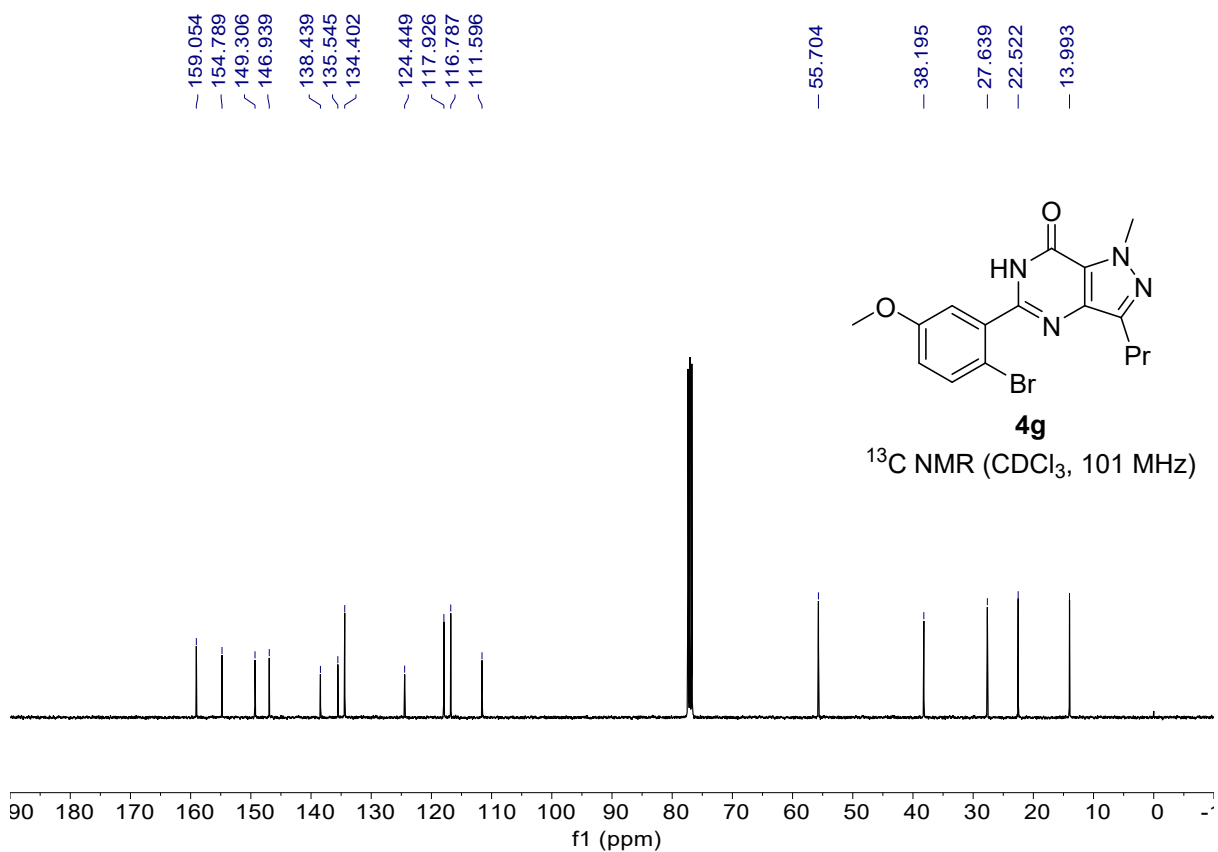
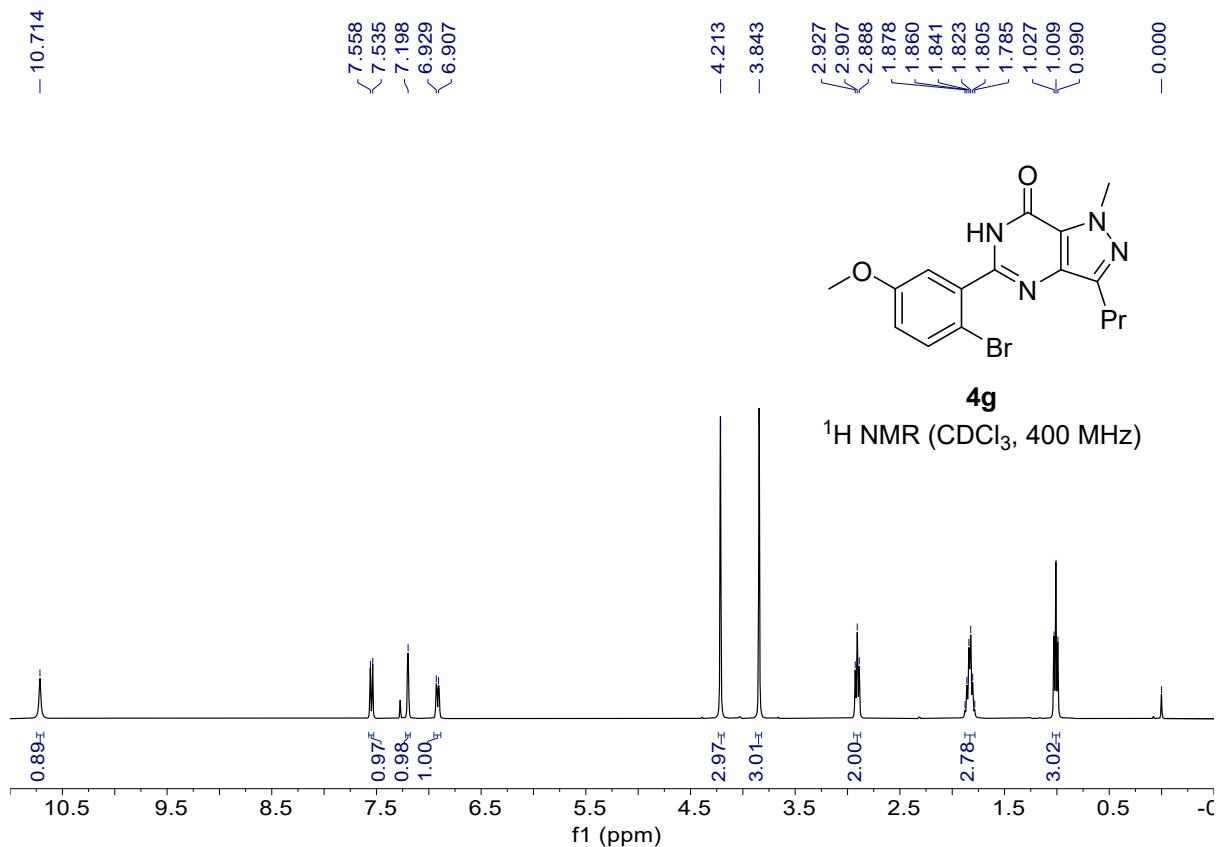


5-(2-bromo-5-chlorophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one (4f)

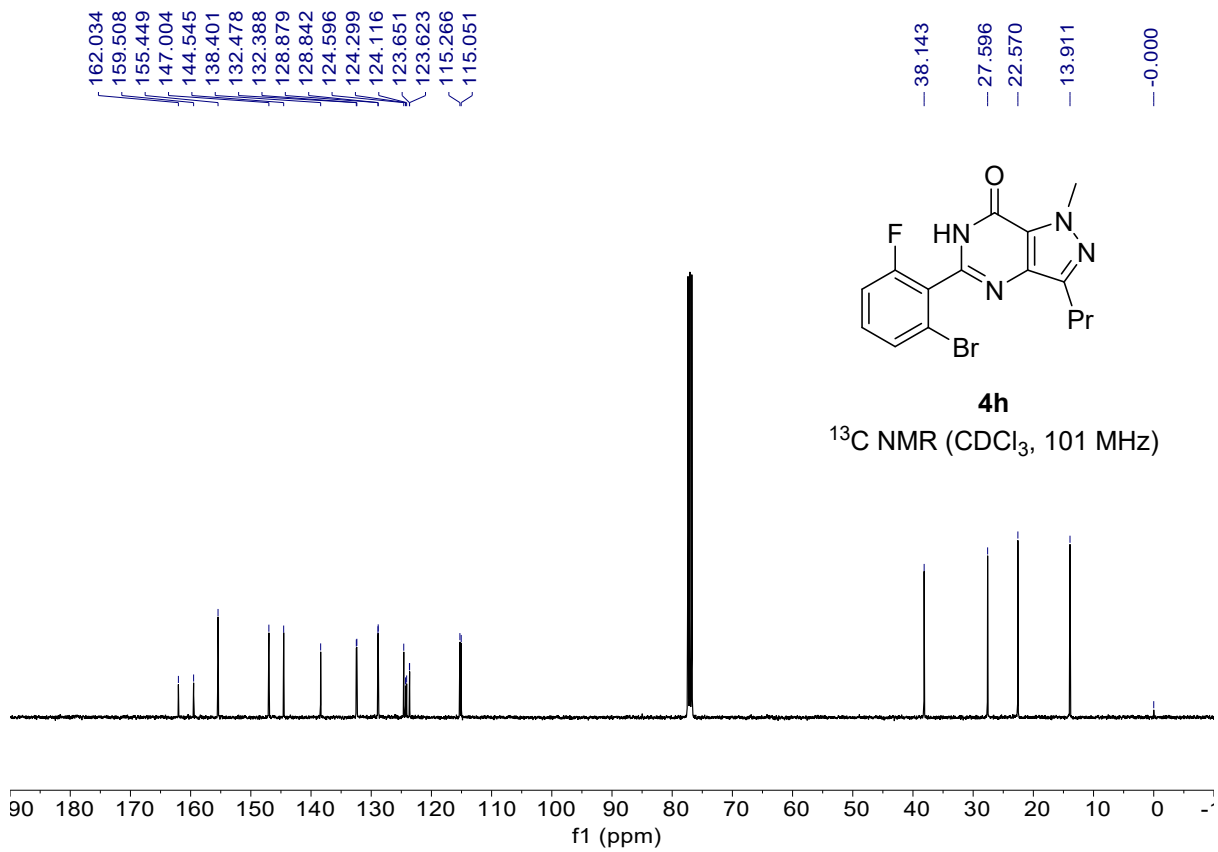
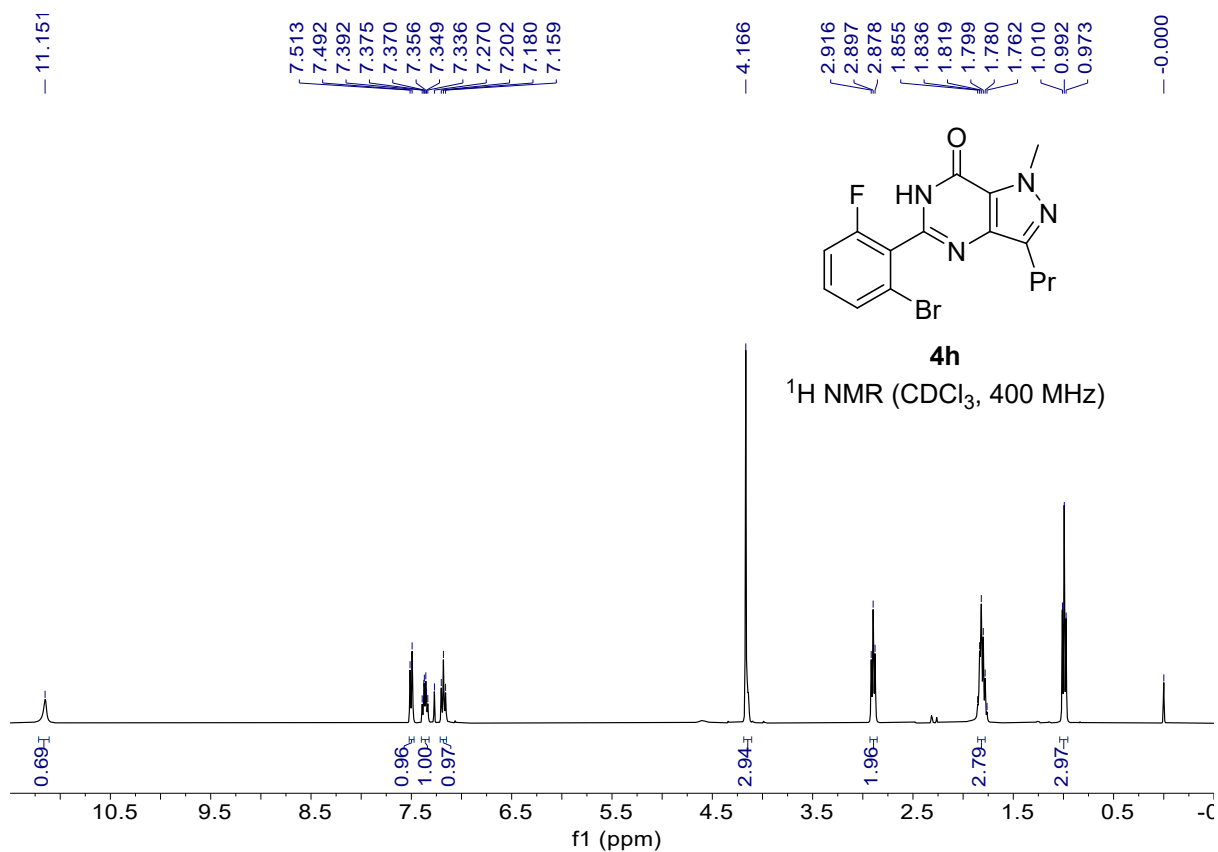


5-(2-bromo-5-methoxyphenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one

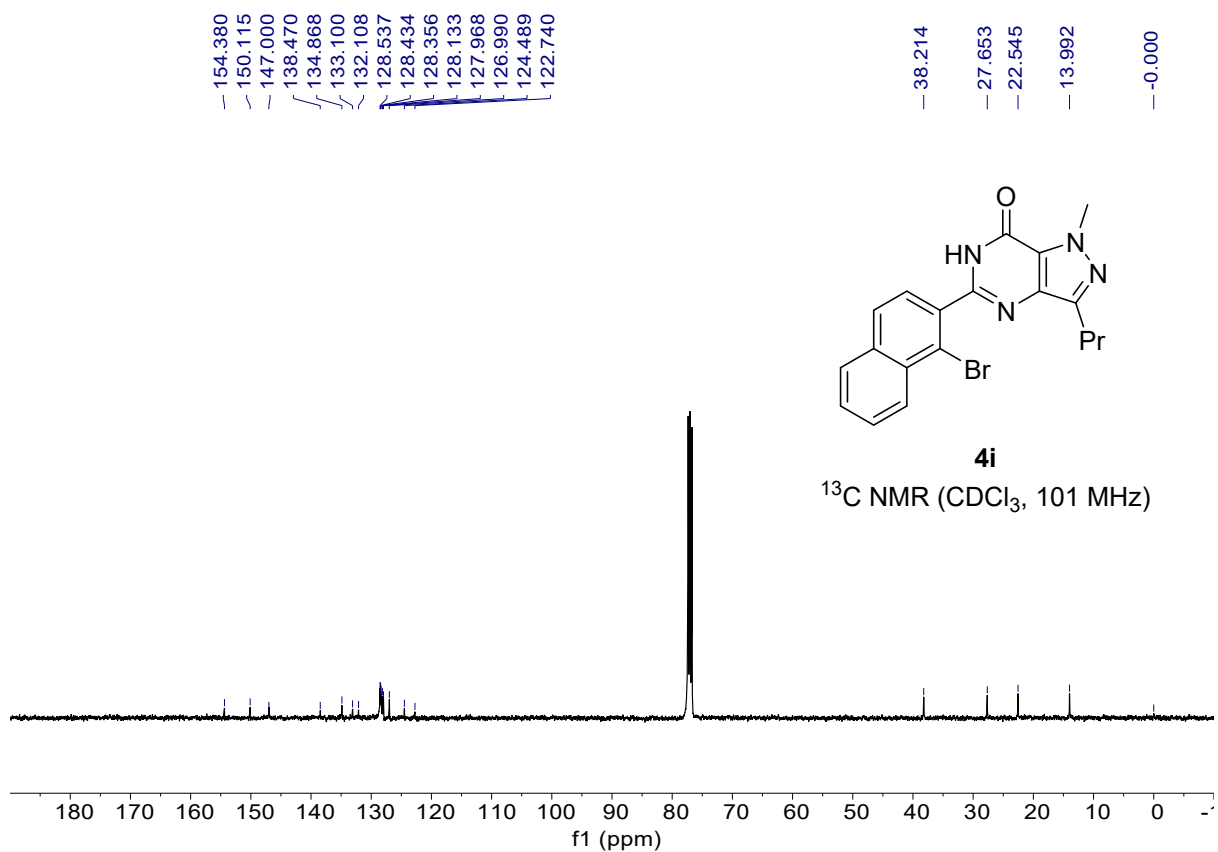
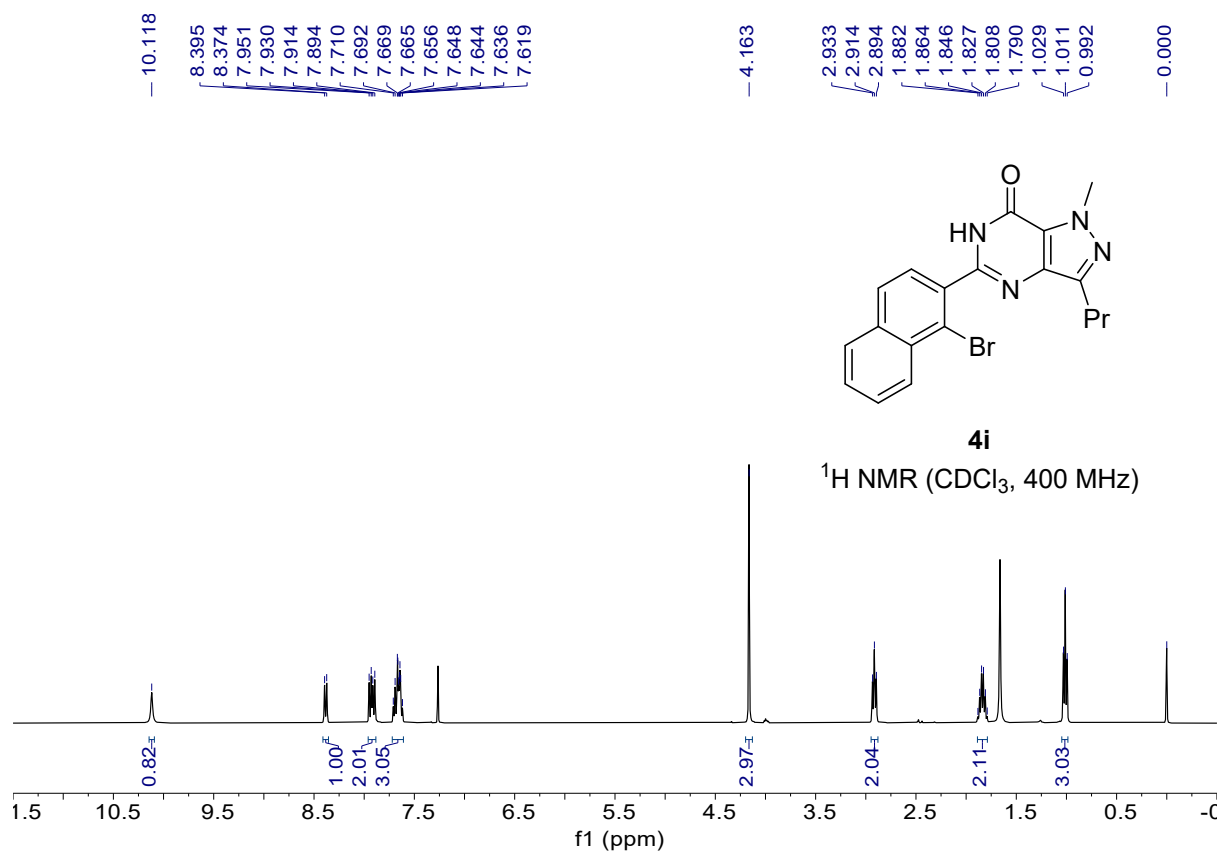
(4g)



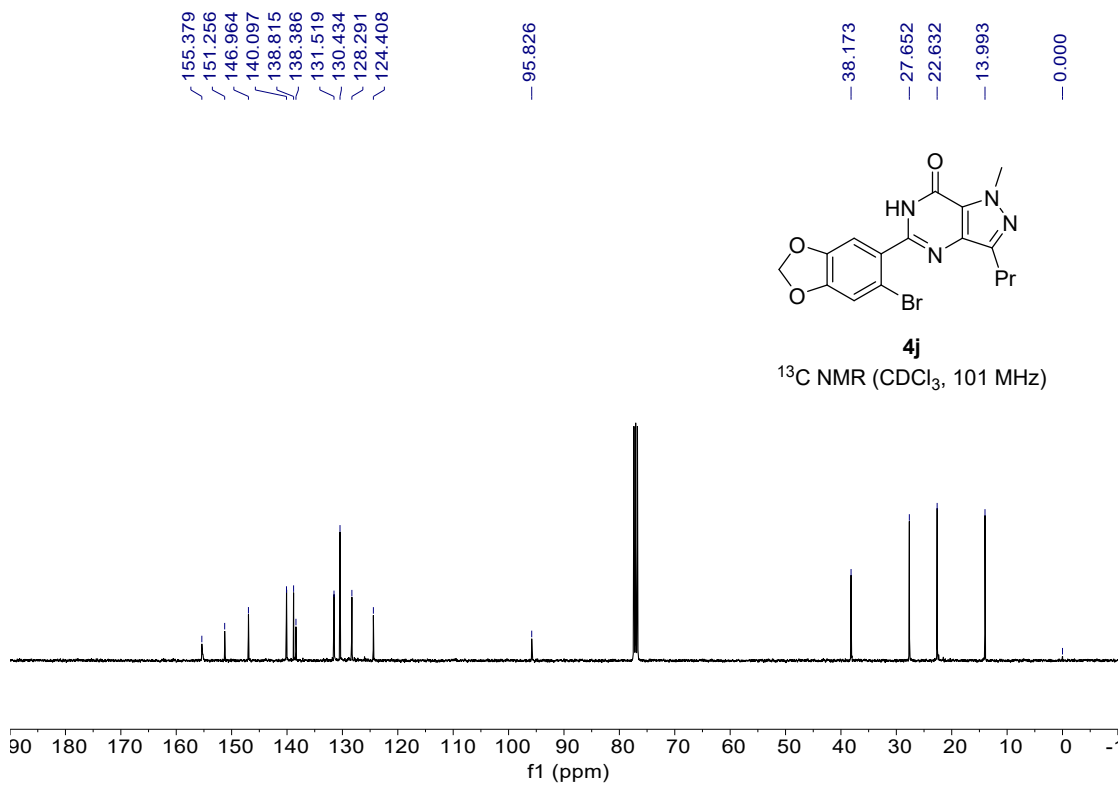
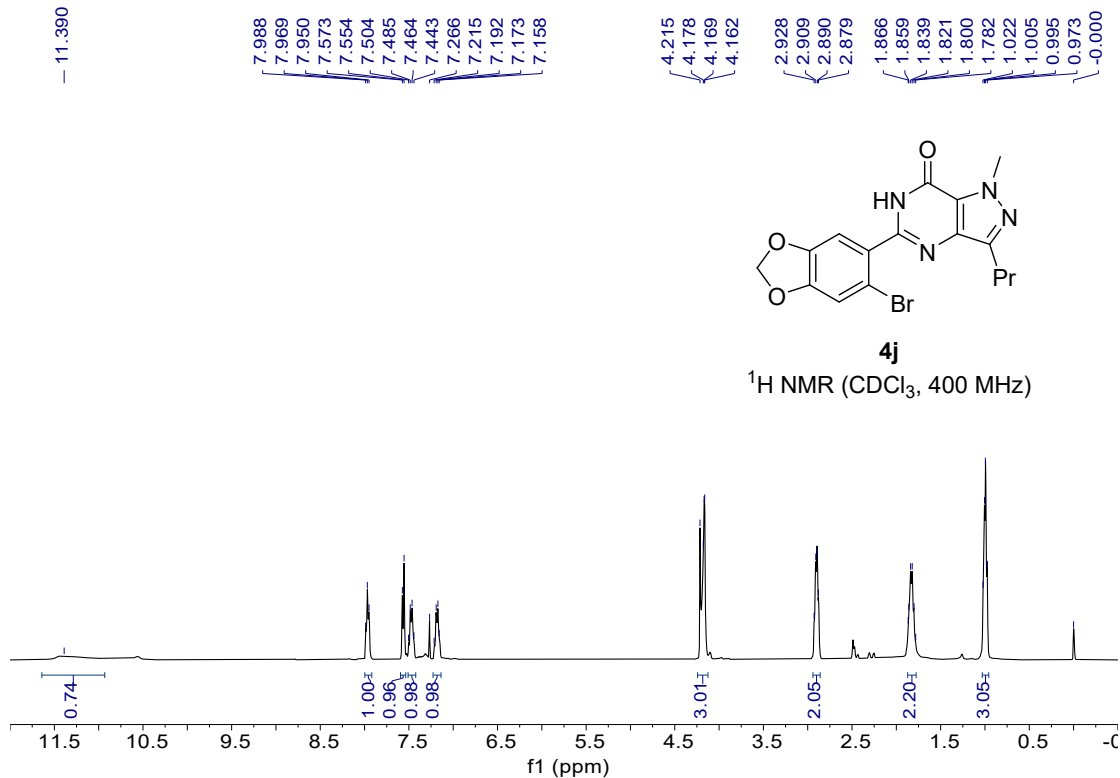
5-(2-bromo-6-fluorophenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one (4h)



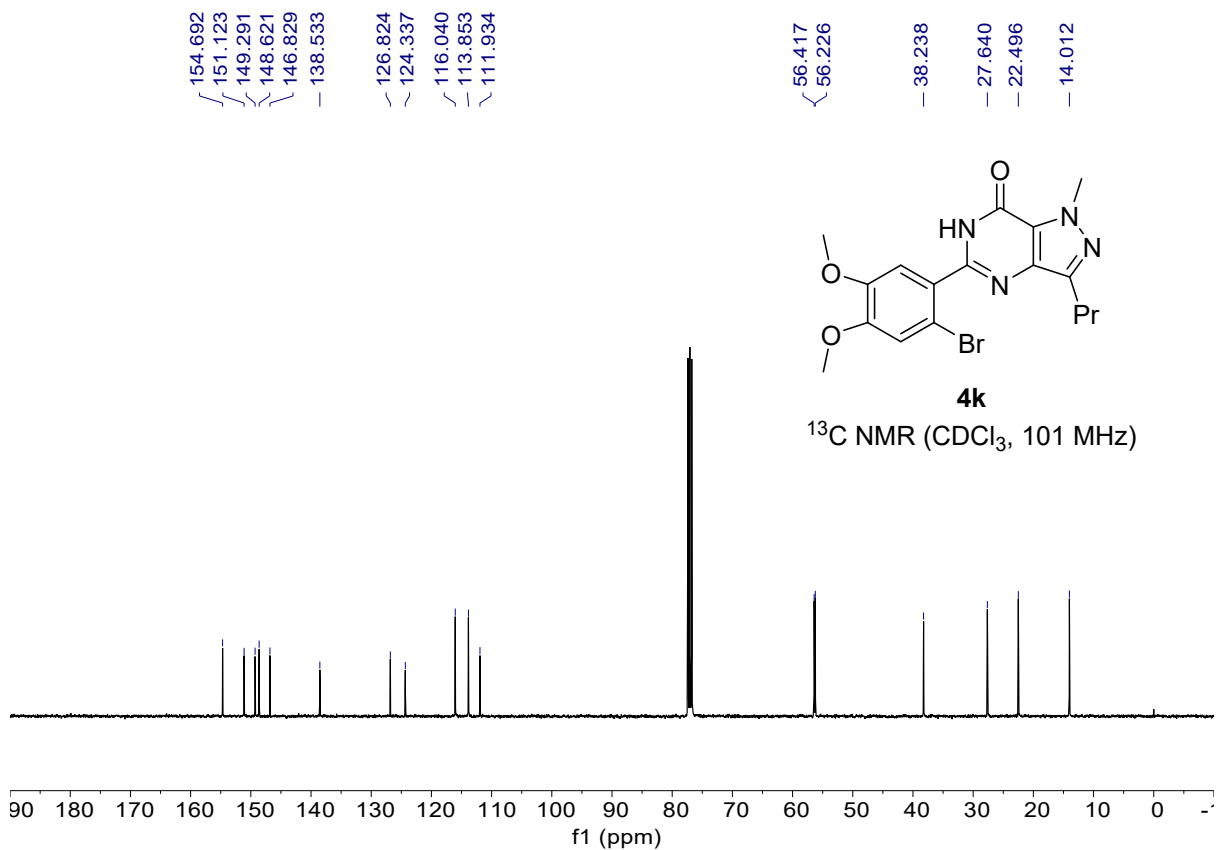
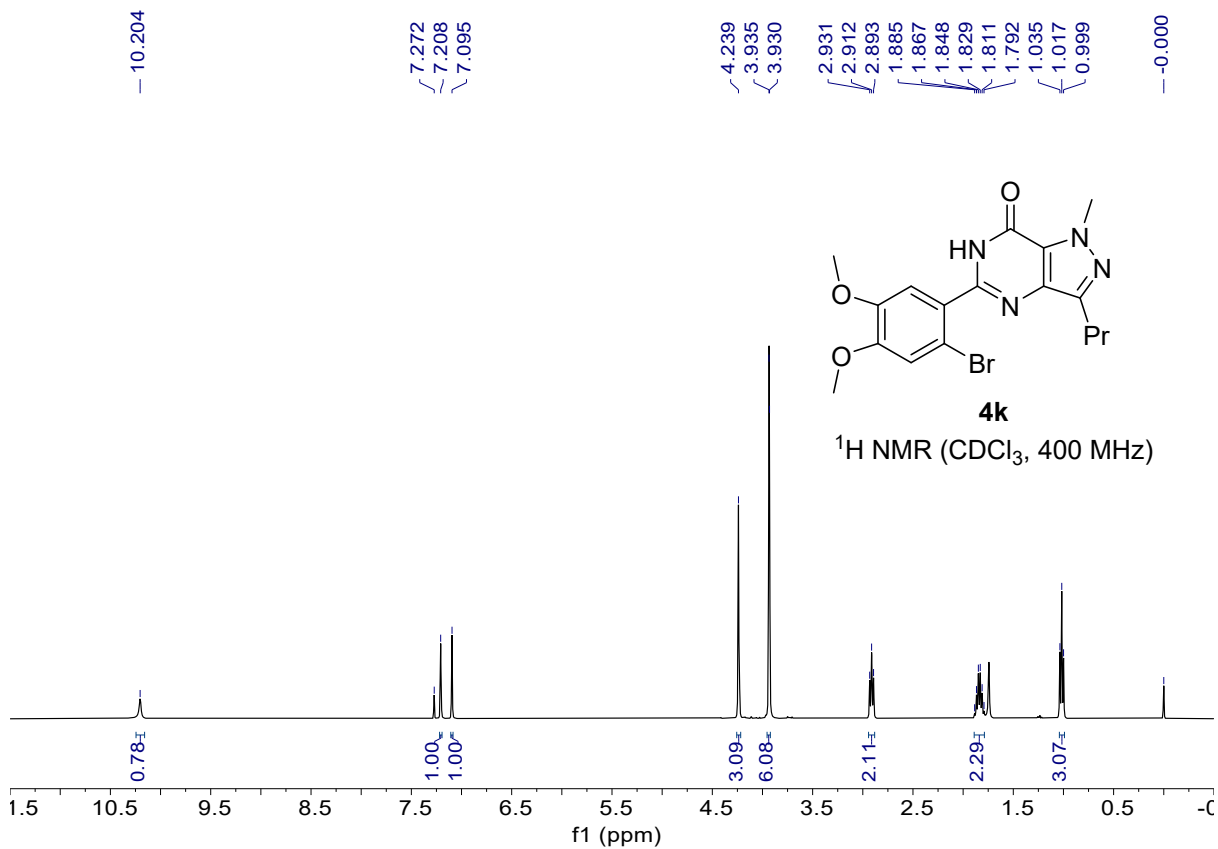
5-(1-bromonaphthalen-2-yl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one (4i)



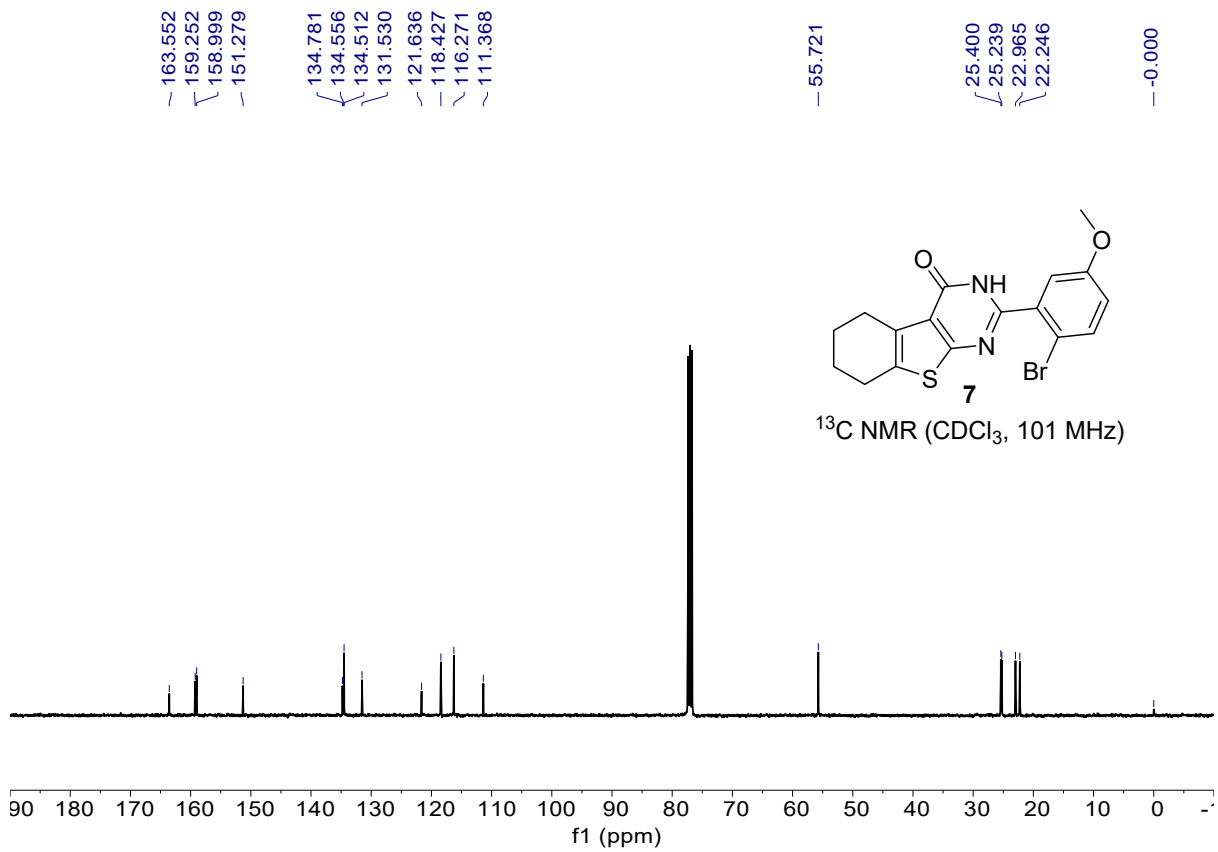
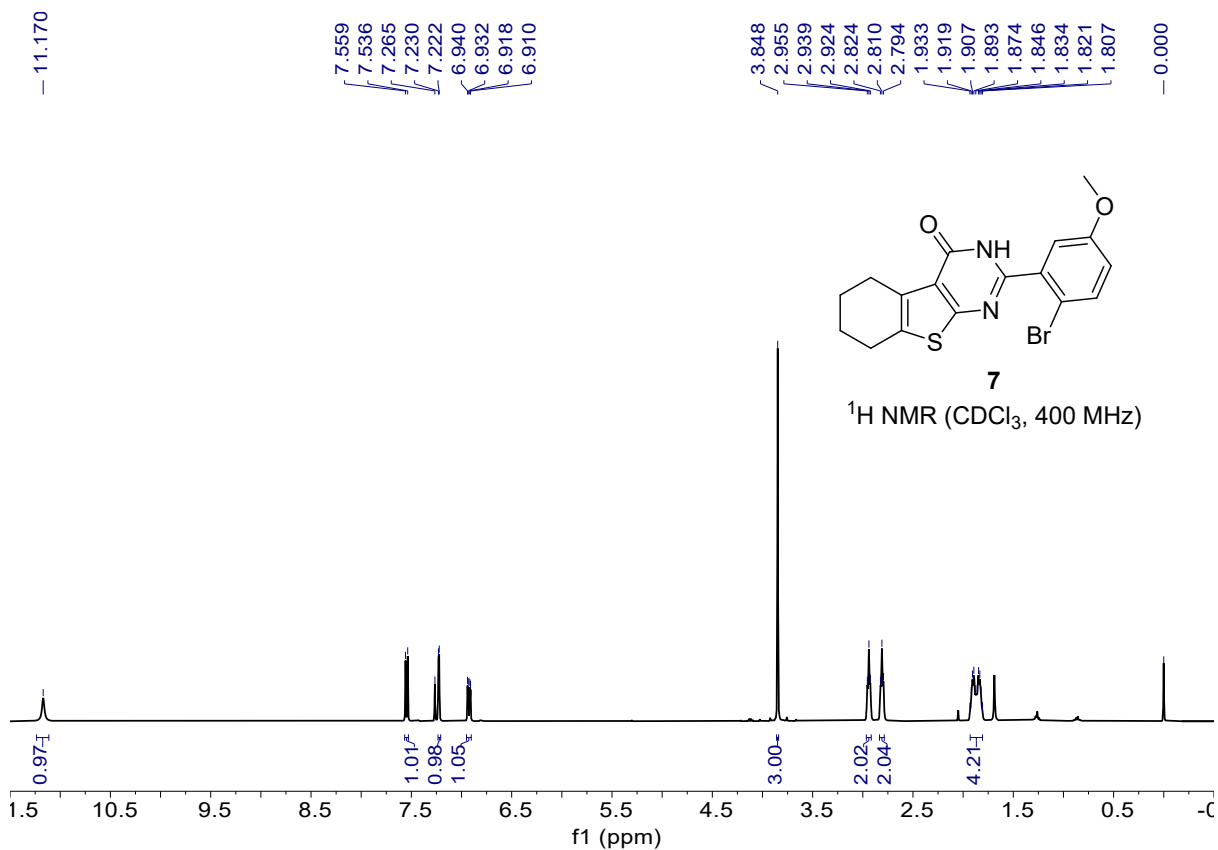
5-(6-bromobenzo[d][1,3]dioxol-5-yl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one (4j)



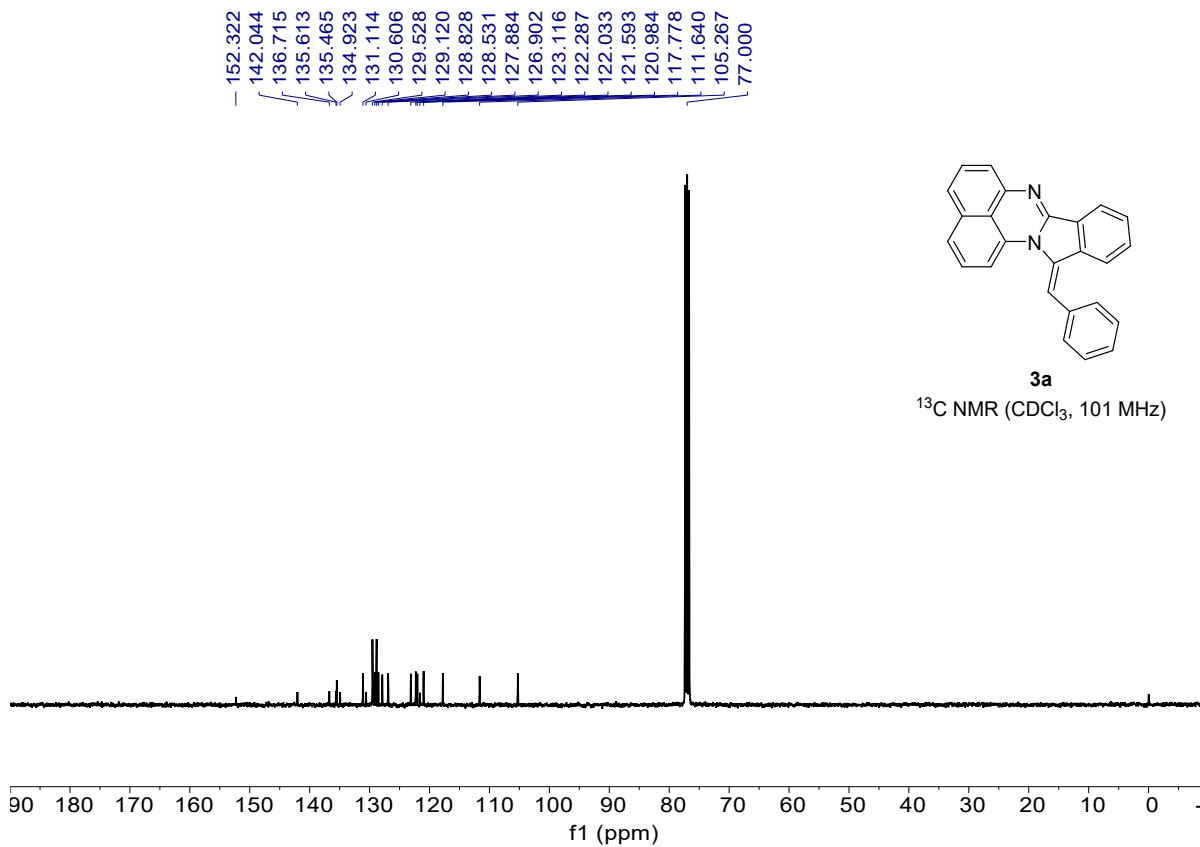
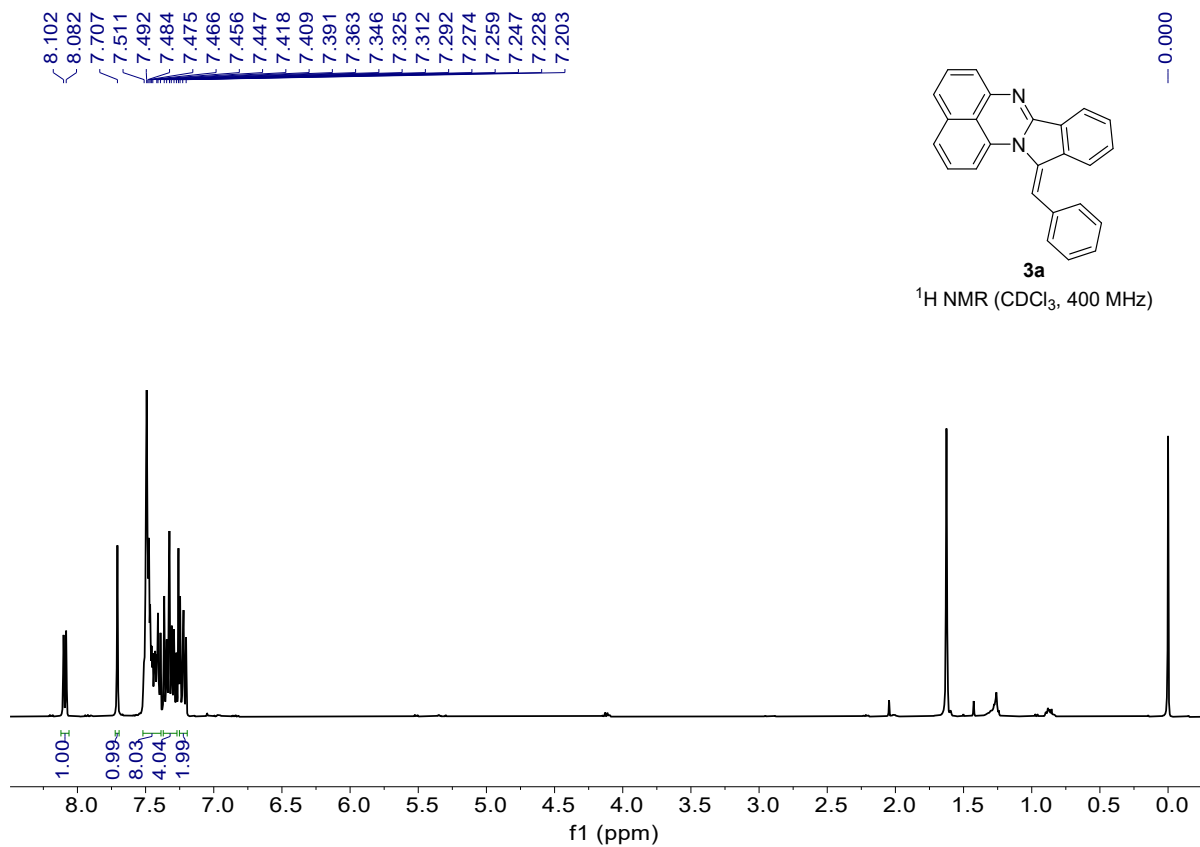
5-(2-bromo-4,5-dimethoxyphenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one (4k)



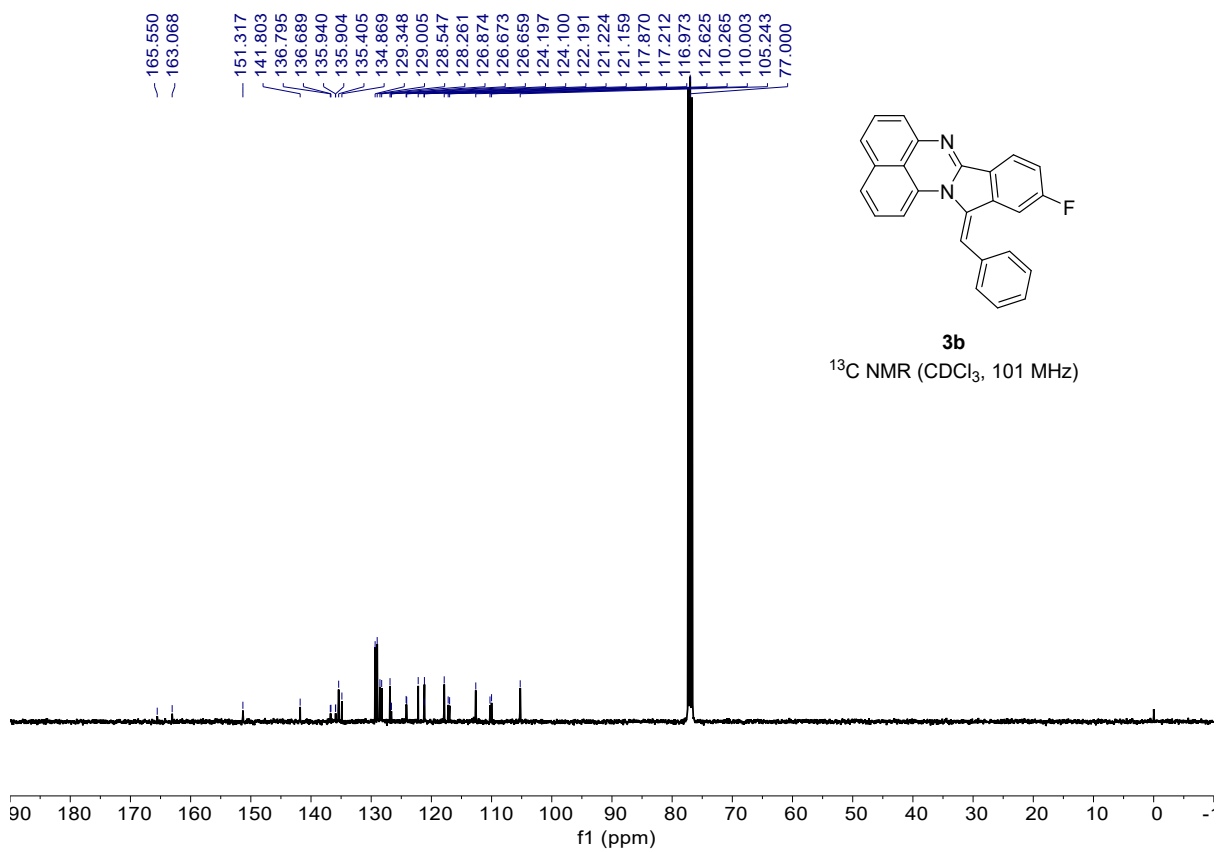
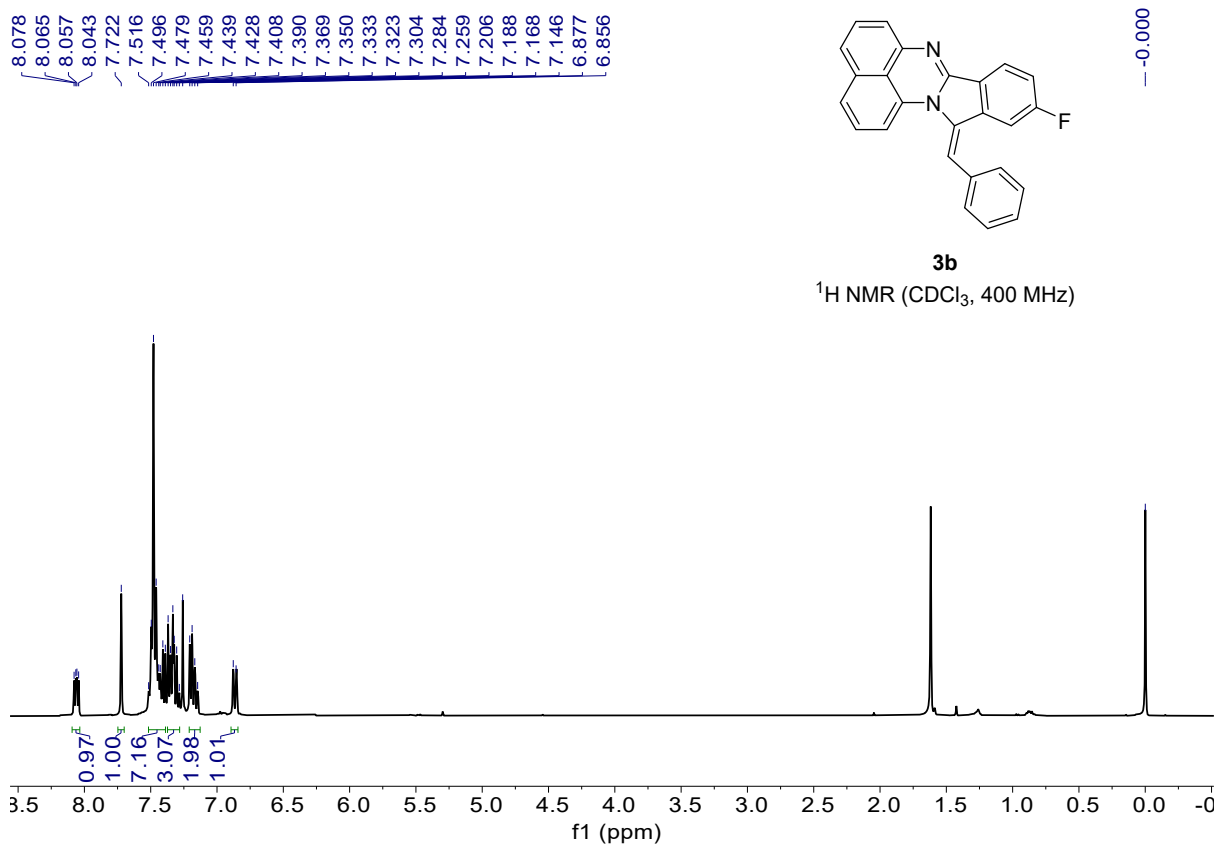
2-(2-bromo-5-methoxyphenyl)-5,6,7,8-tetrahydrobenzo[4,5]thieno[2,3-d]pyrimidin-4(3H)-one (7)



(E)-12-benzylidene-12H-isoindolo[2,1-a]perimidine (3a)

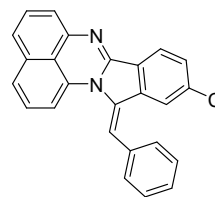


(E)-12-benzylidene-10-fluoro-12H-isoindolo[2,1-a]perimidine (3b)



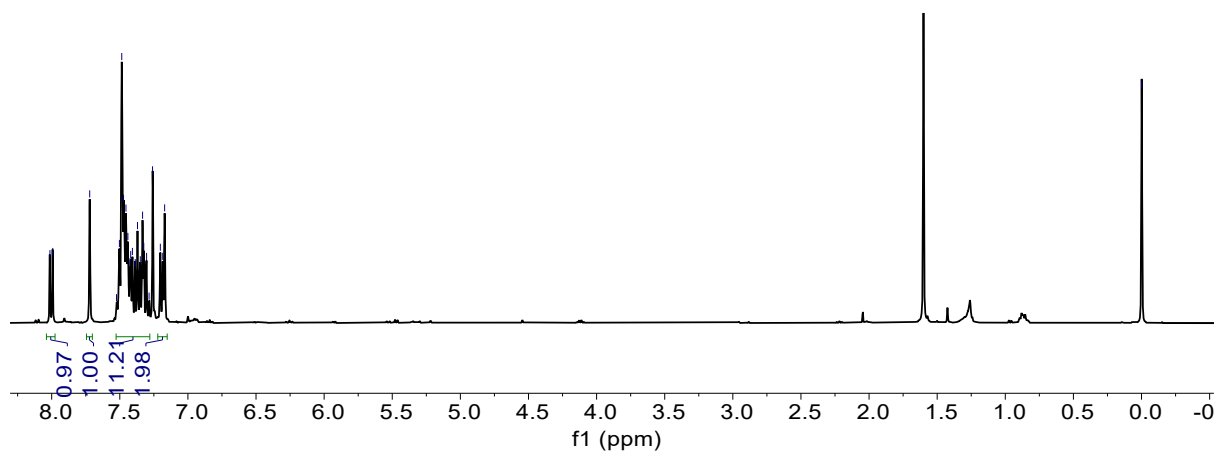
(E)-12-benzylidene-10-chloro-12H-isoindolo[2,1-a]perimidine (3c)

8.013
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7.503
7.486
7.472
7.455
7.441
7.425
7.420
7.407
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7.202
7.185
7.171

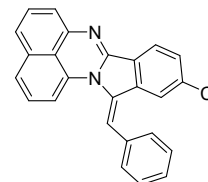


3c

¹H NMR (CDCl₃, 400 MHz)

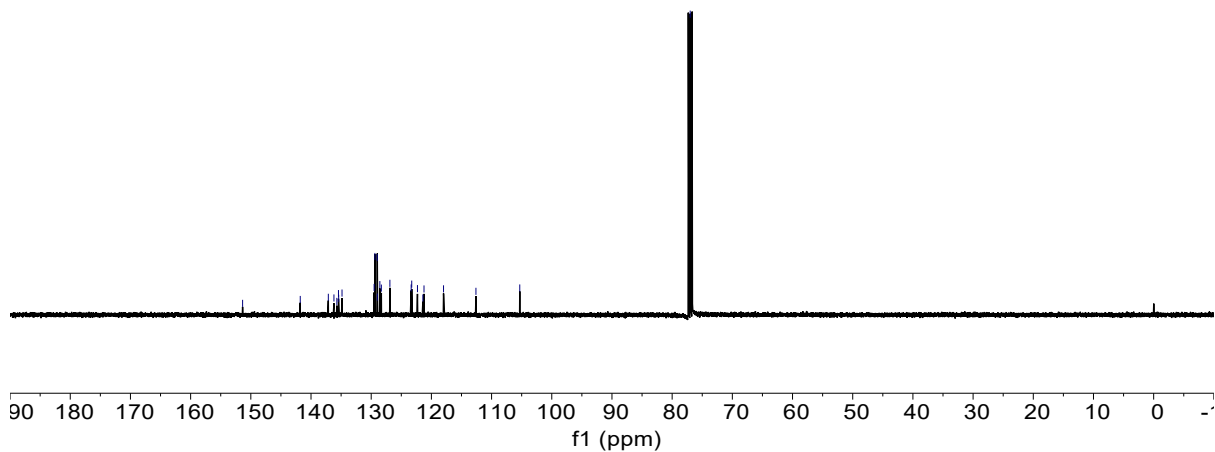


151.365
141.788
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136.190
135.708
135.437
135.404
134.848
129.516
129.385
128.987
128.975
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121.227
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112.599
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77.000

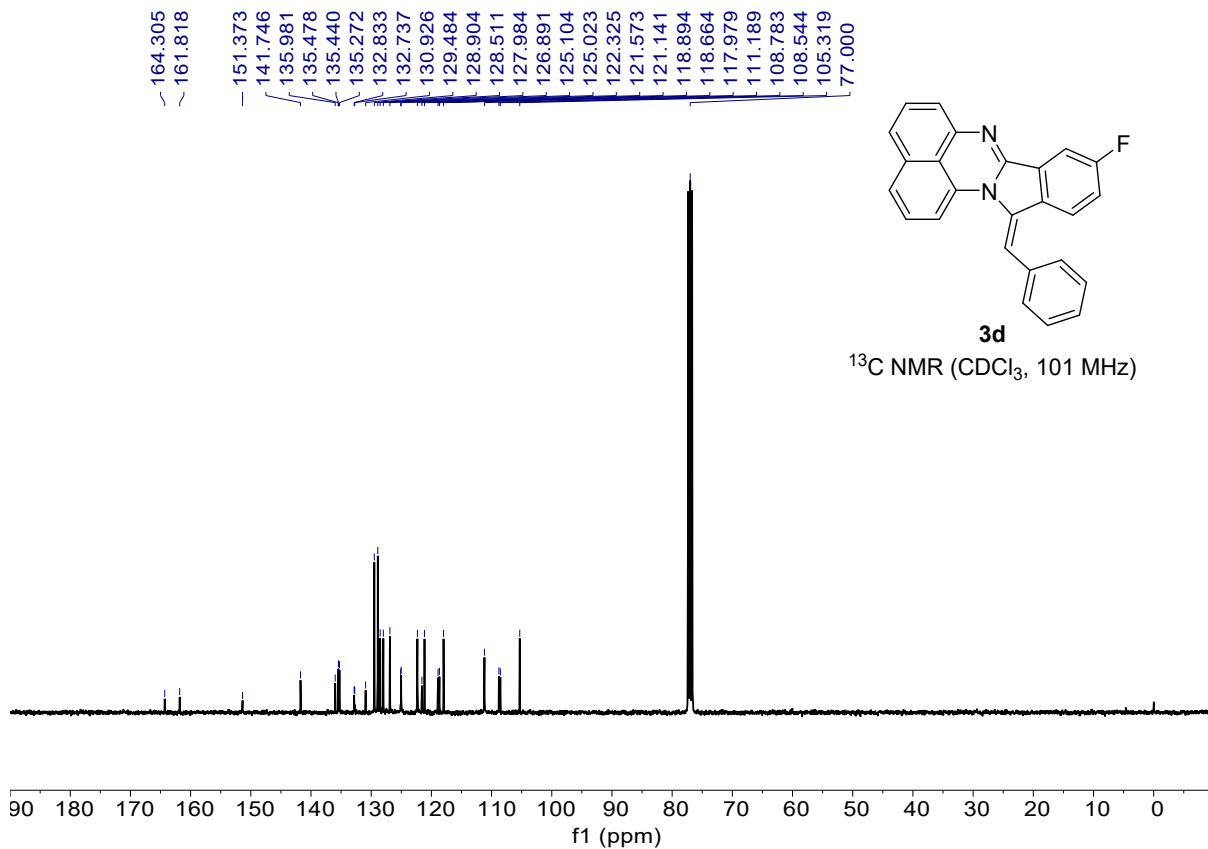
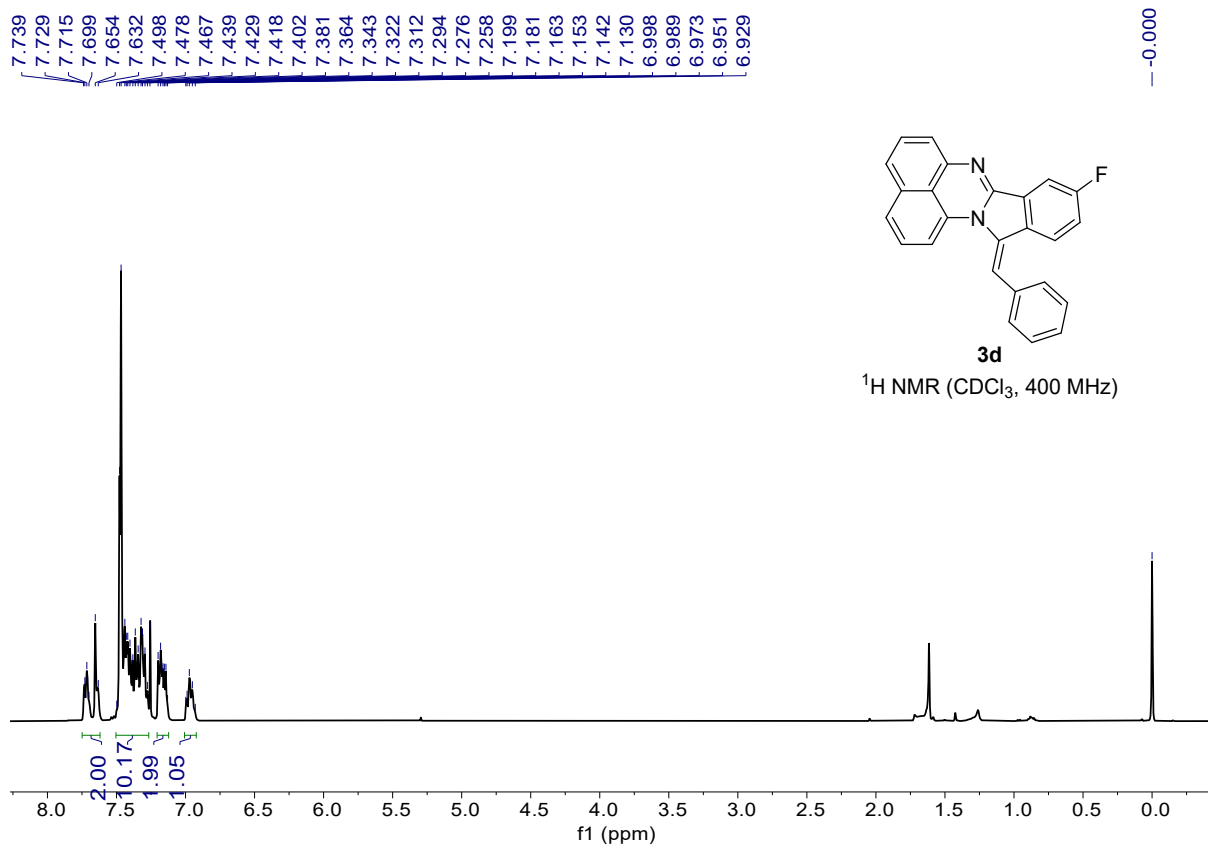


3c

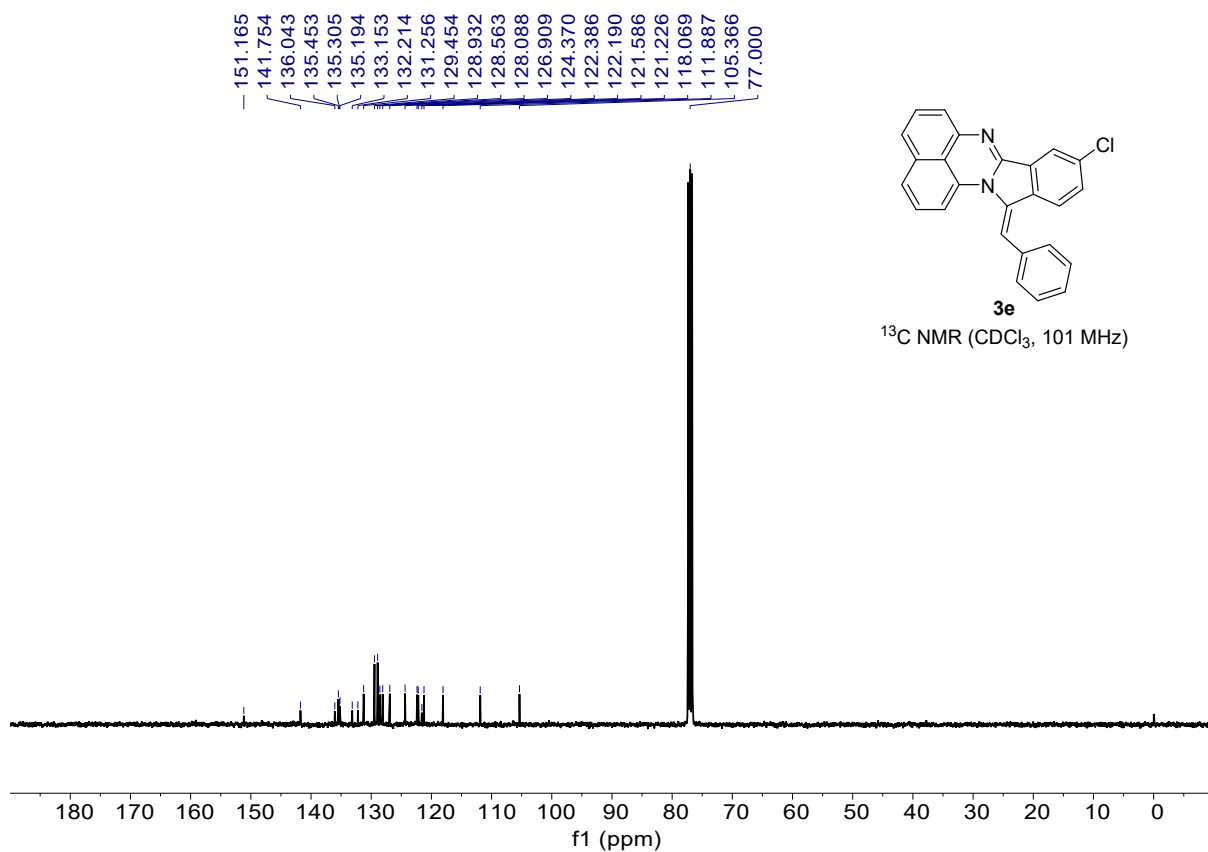
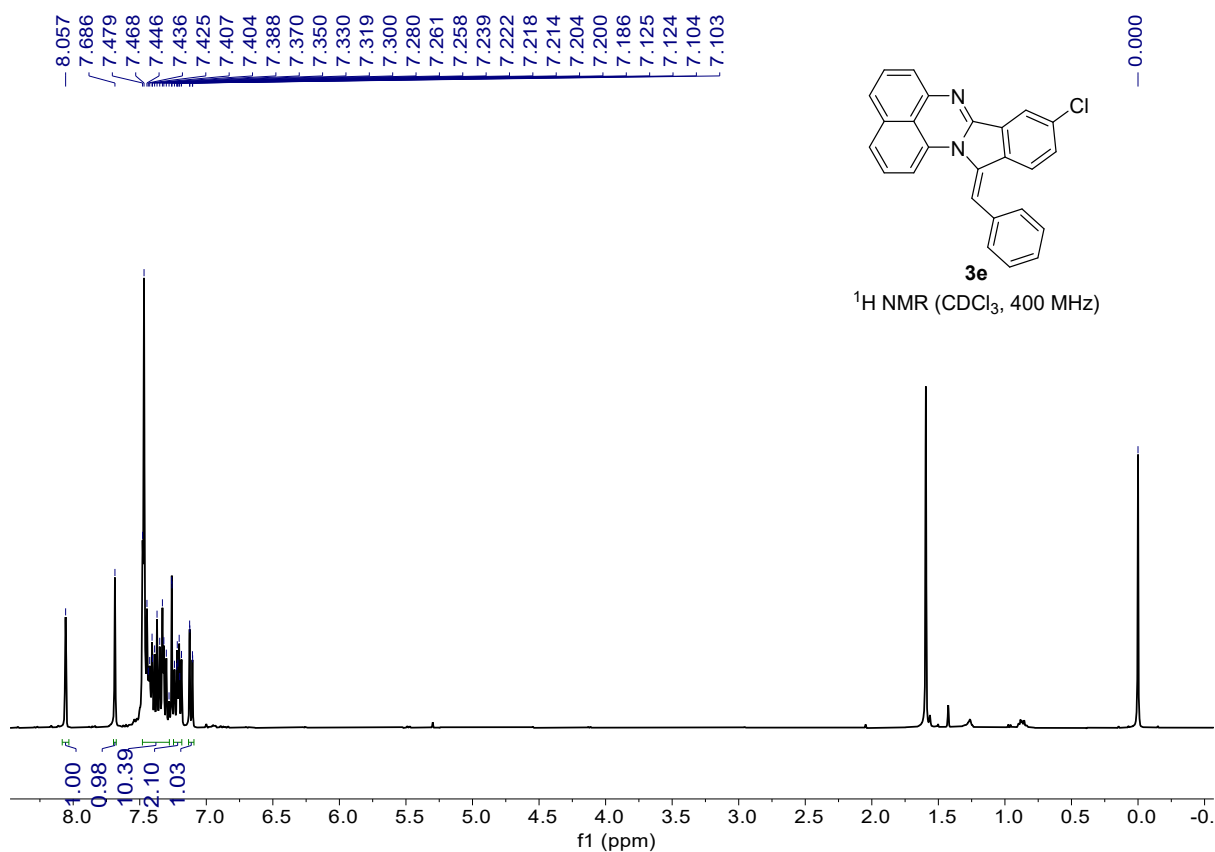
¹³C NMR (CDCl₃, 101 MHz)



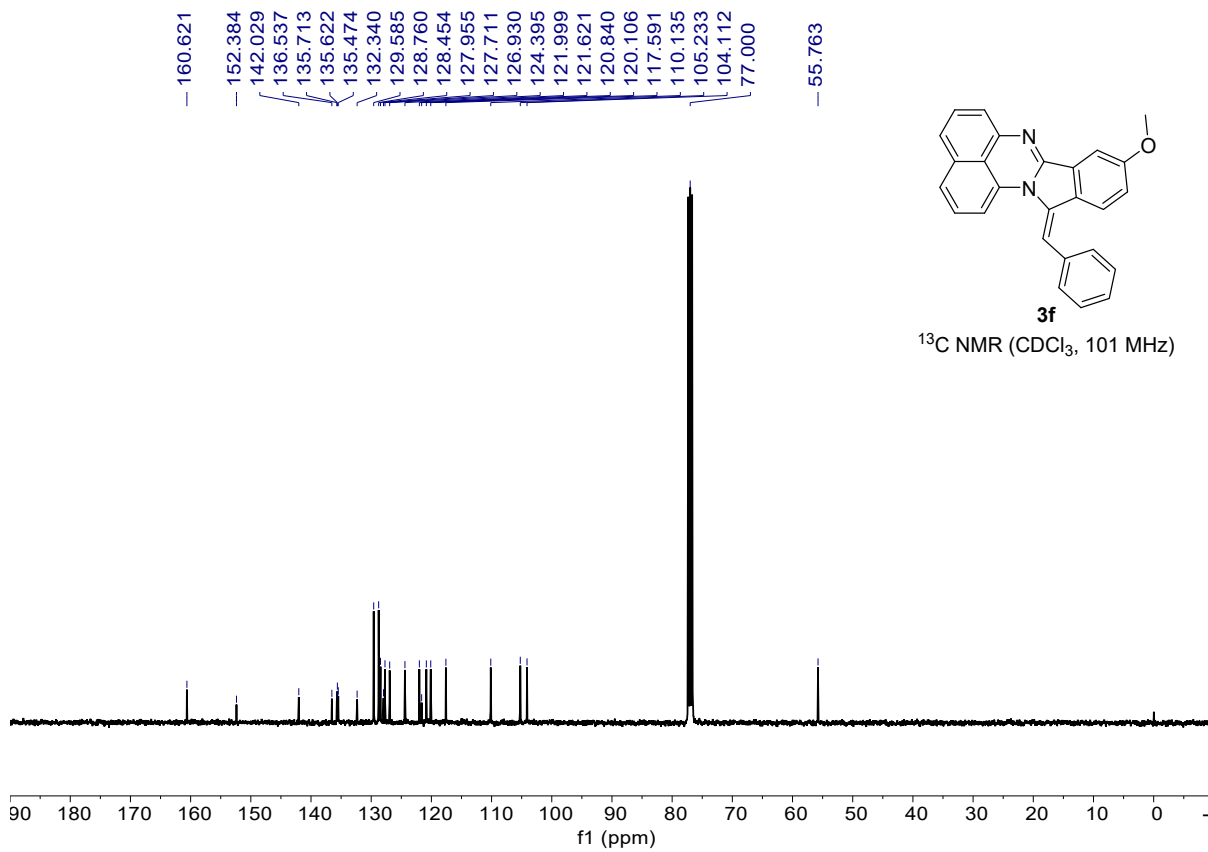
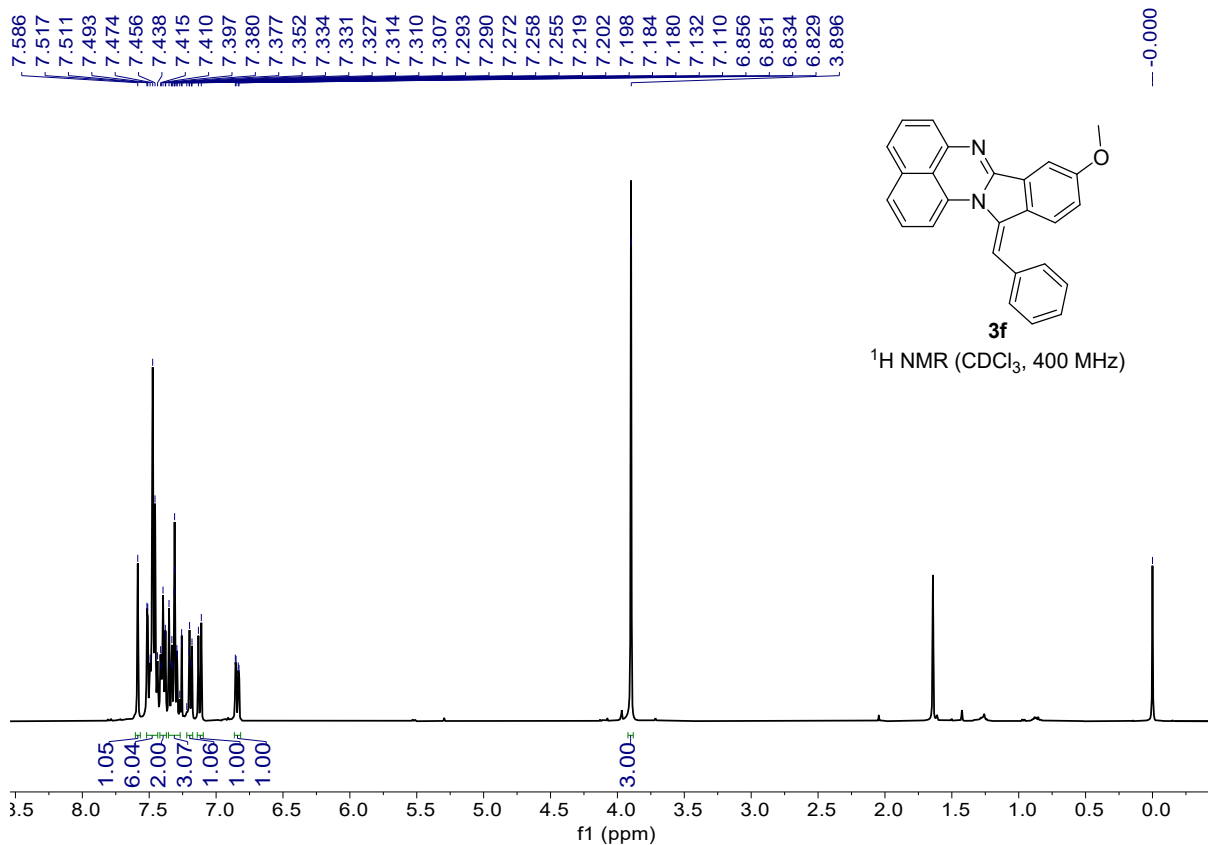
(E)-12-benzylidene-9-fluoro-12H-isoindolo[2,1-a]perimidine (3d)



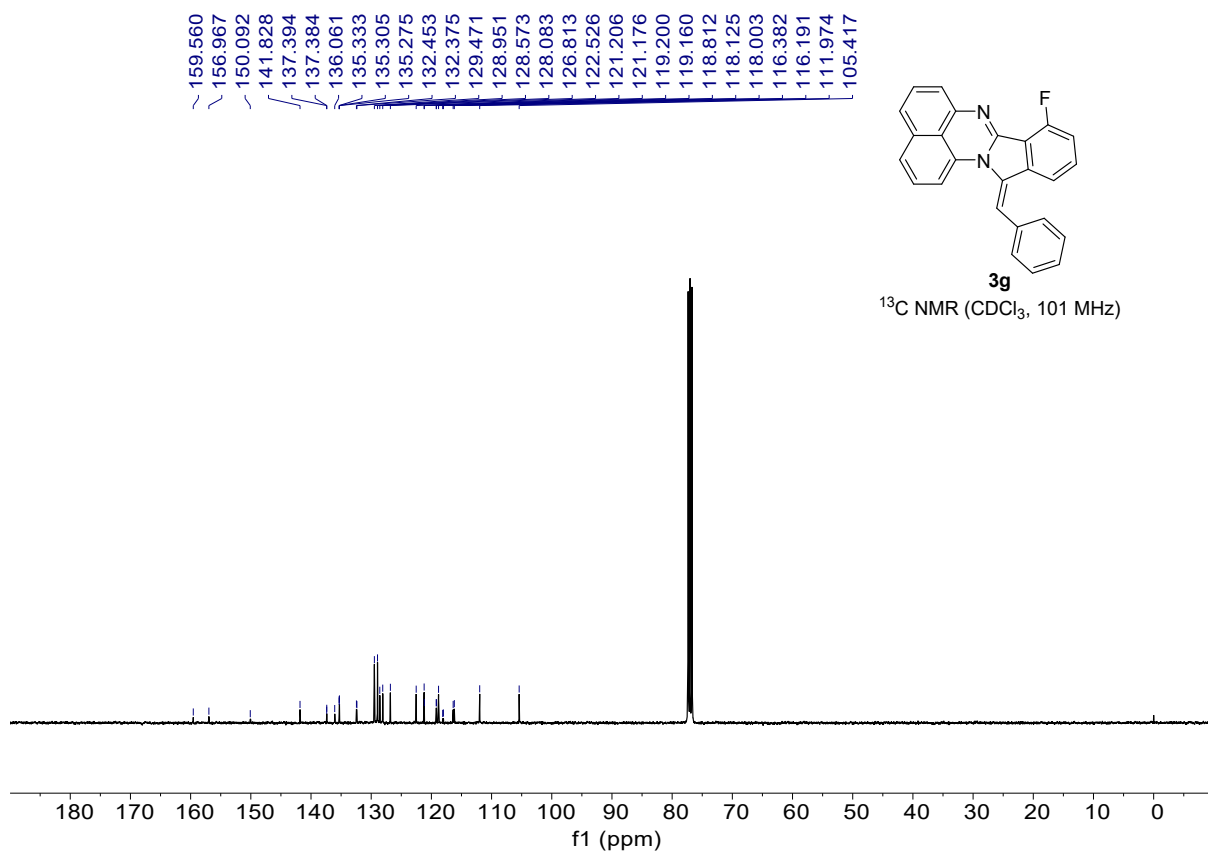
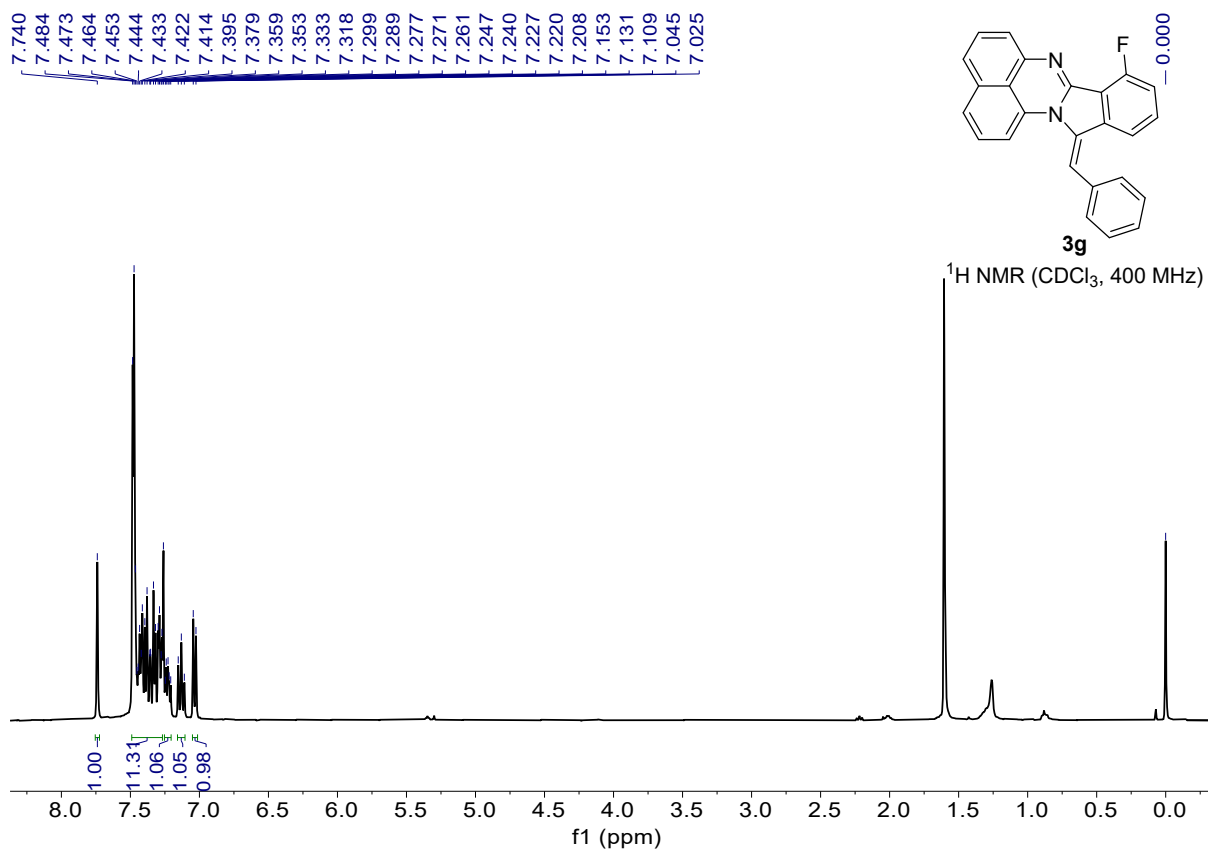
(E)-12-benzylidene-9-chloro-12H-isoindolo[2,1-a]perimidine (3e)



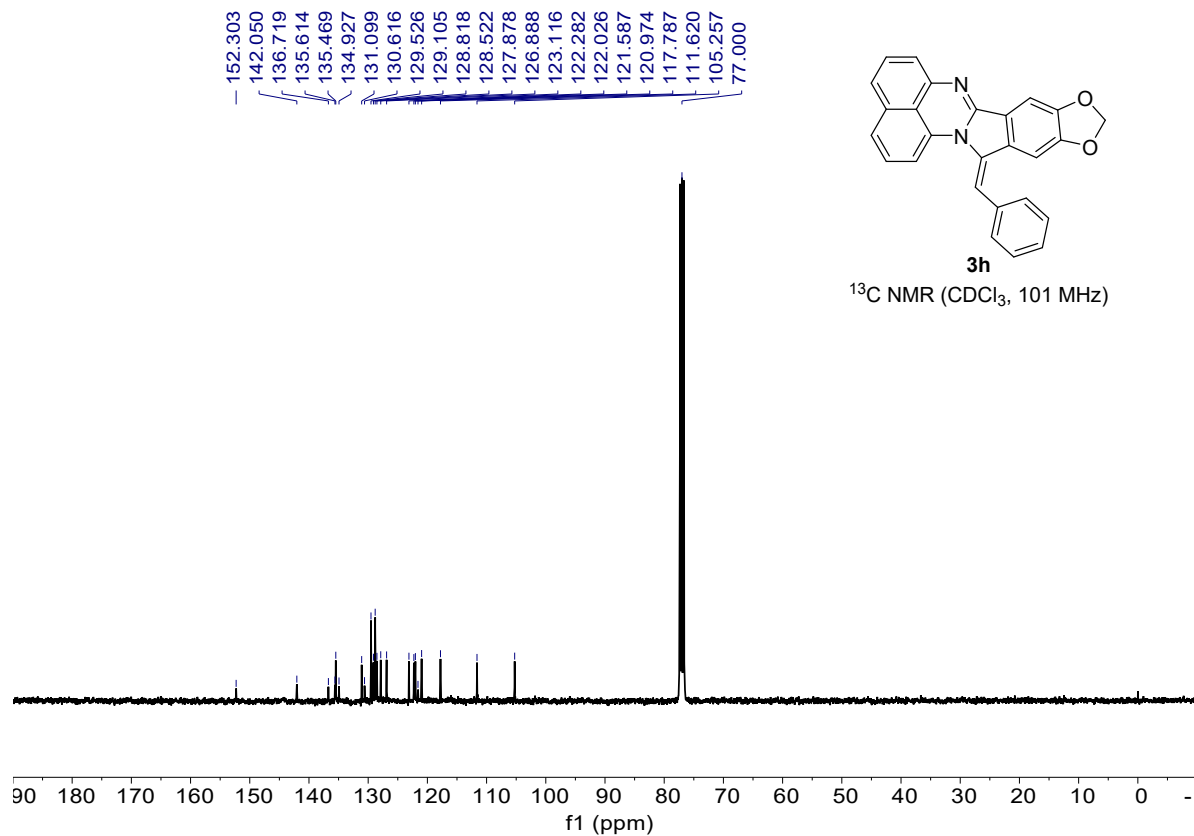
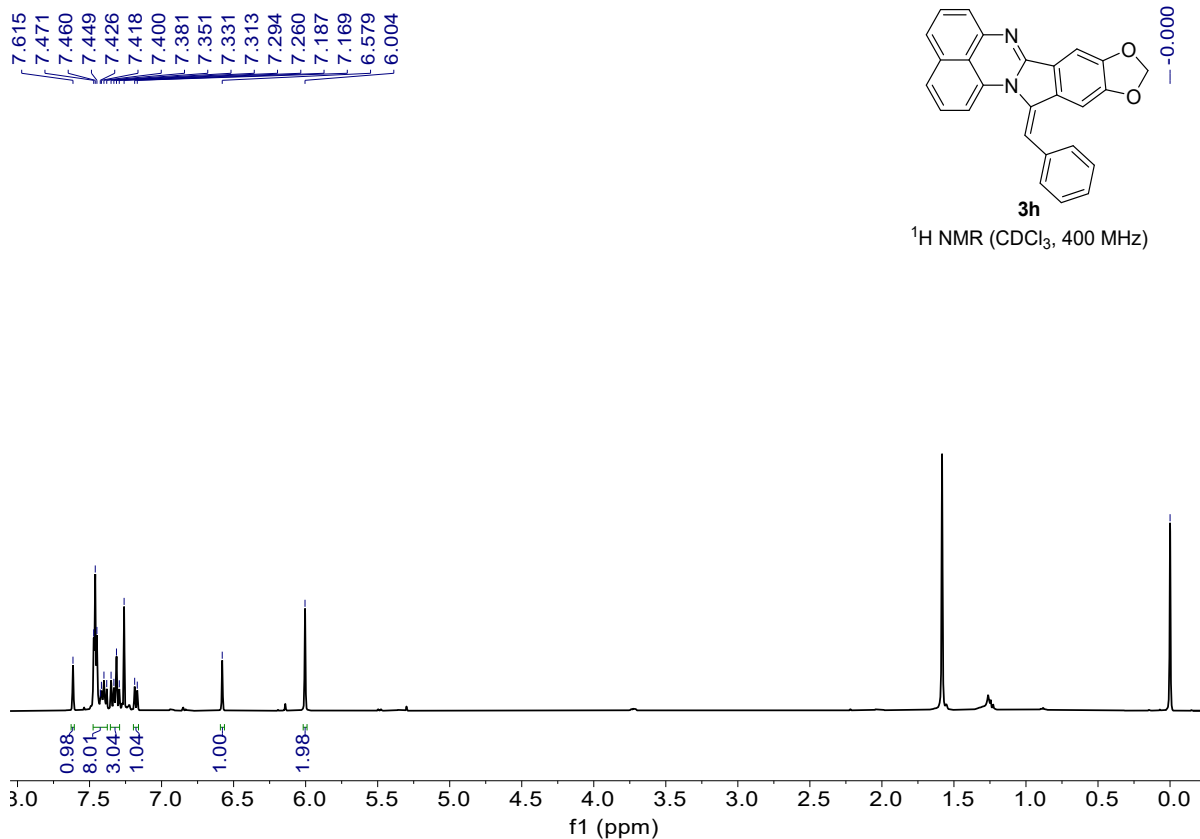
(E)-12-benzylidene-9-methoxy-12H-isoindolo[2,1-a]perimidine (3f)



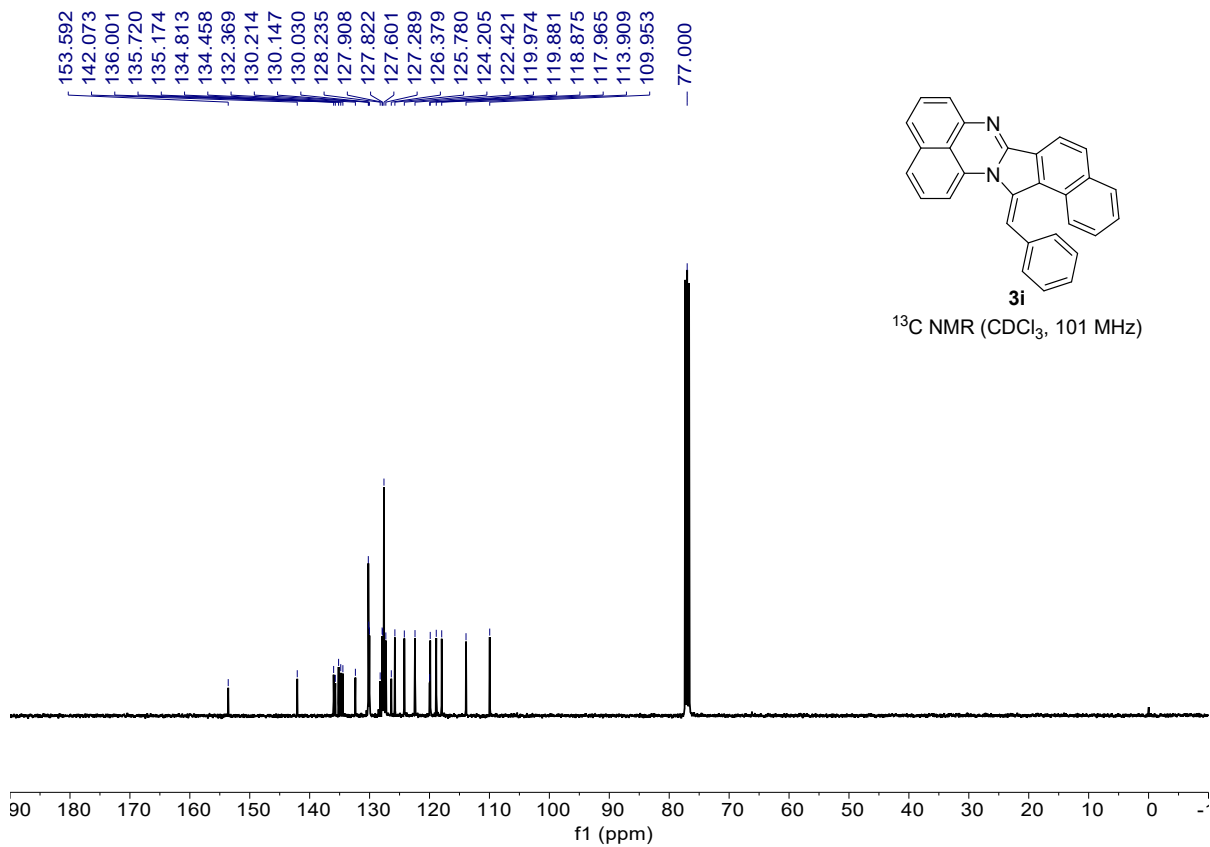
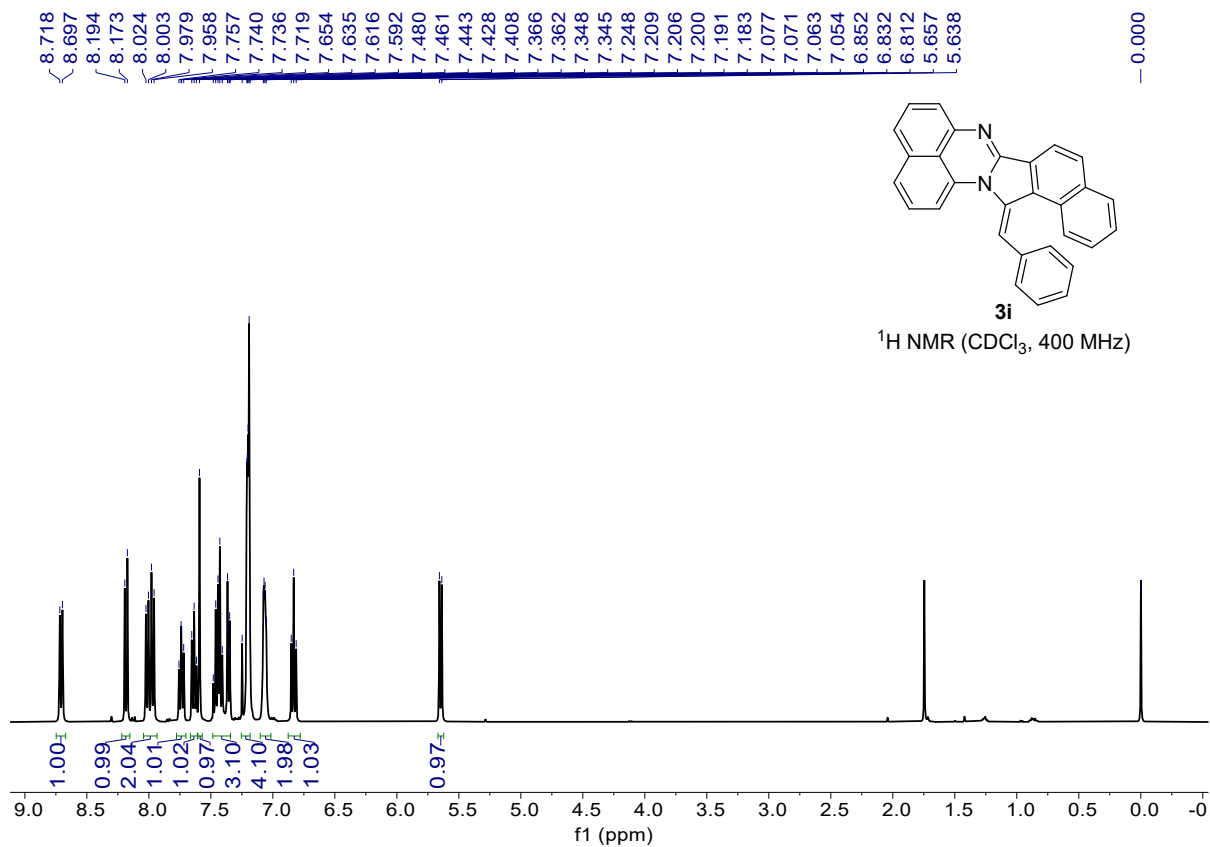
(E)-12-benzylidene-8-fluoro-12H-isoindolo[2,1-a]perimidine (3g)



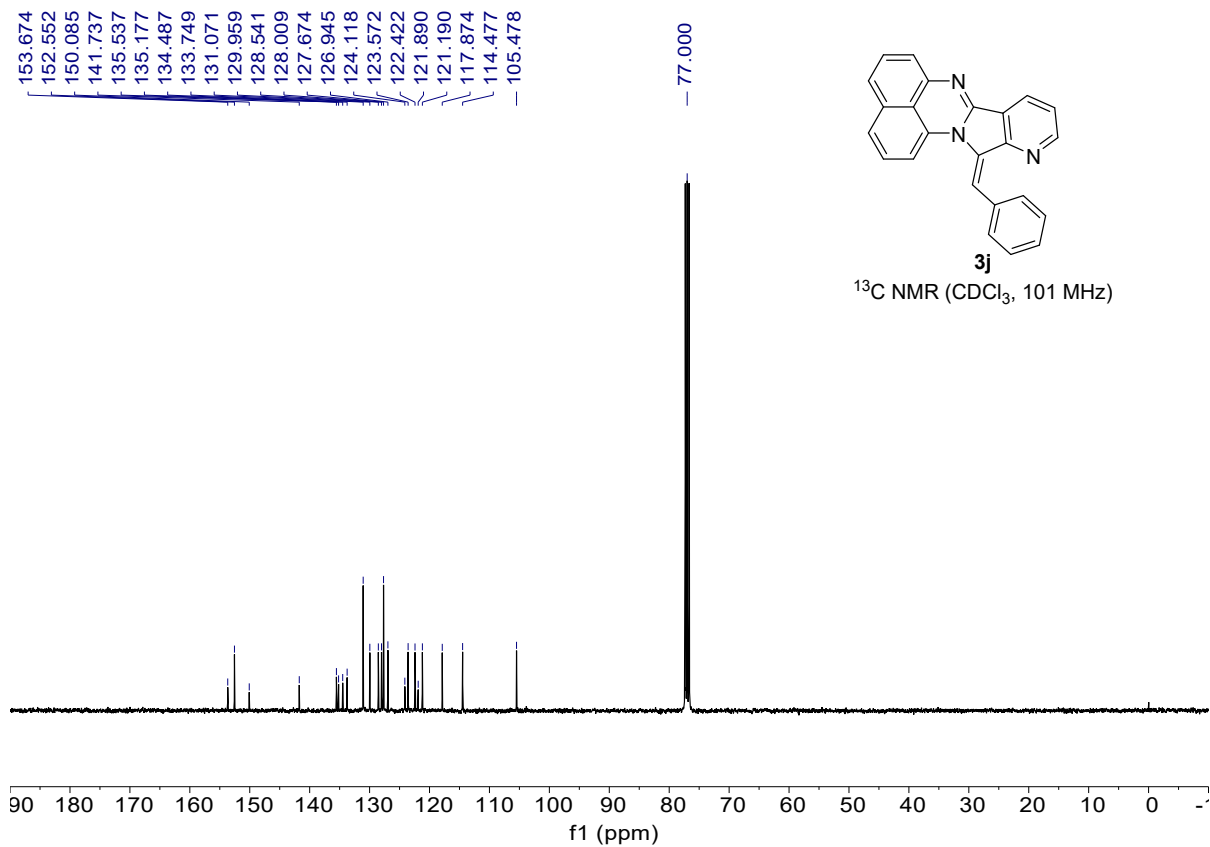
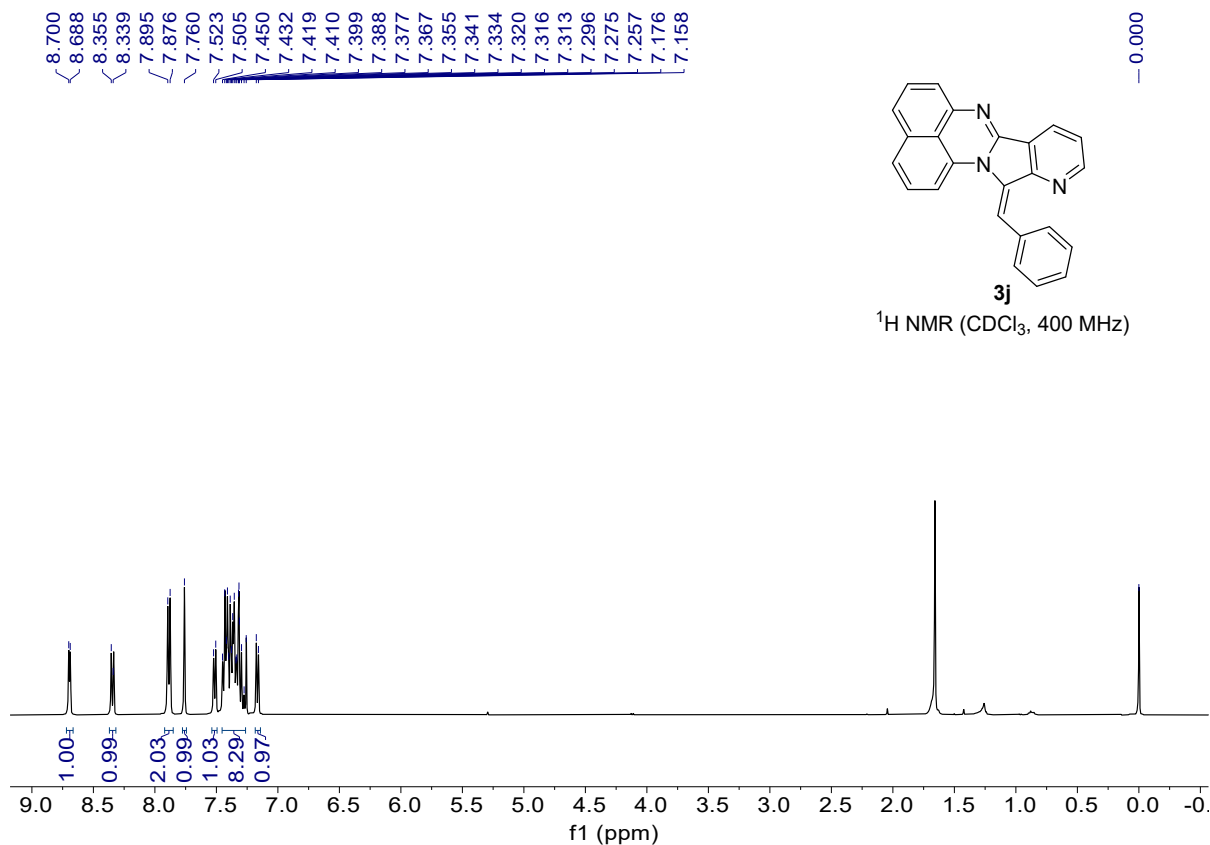
(E)-13-benzylidene-13H-[1,3]dioxolo[4',5':5,6]isoindolo[2,1- σ]perimidin (3h)



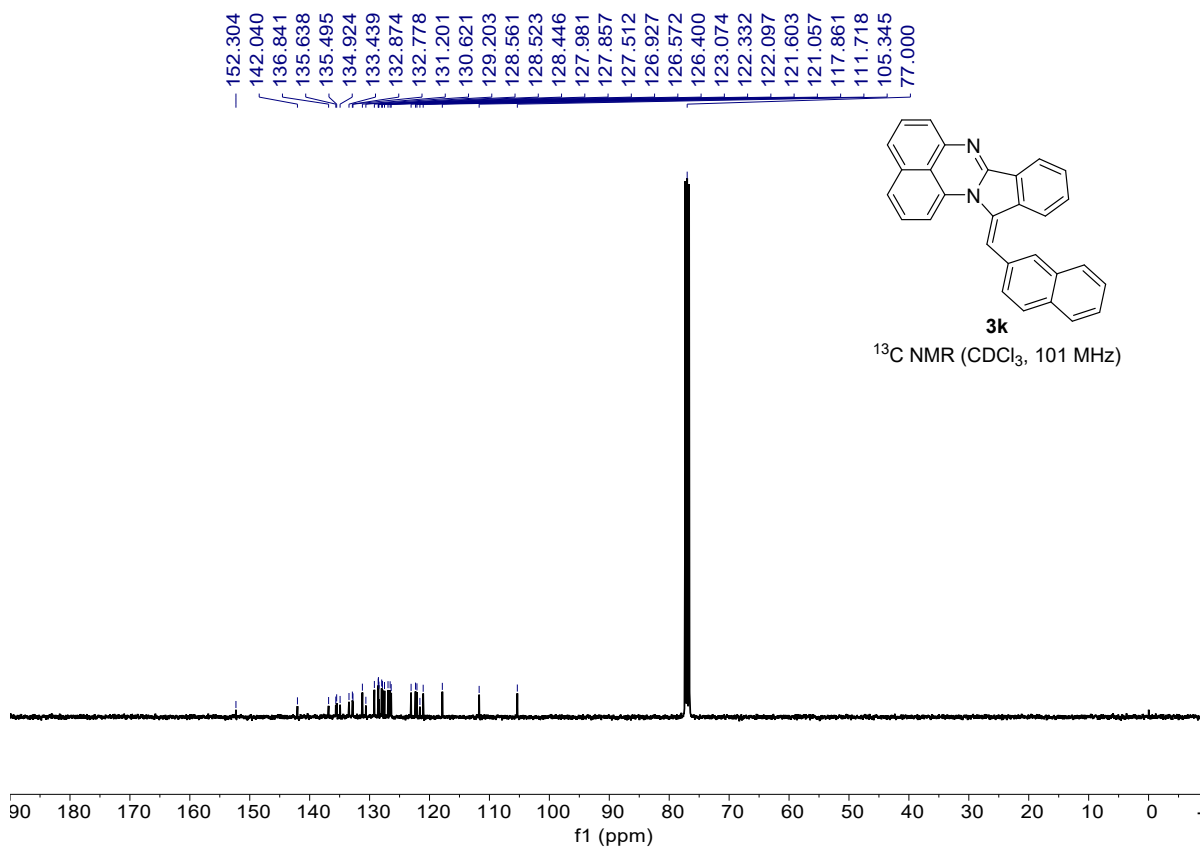
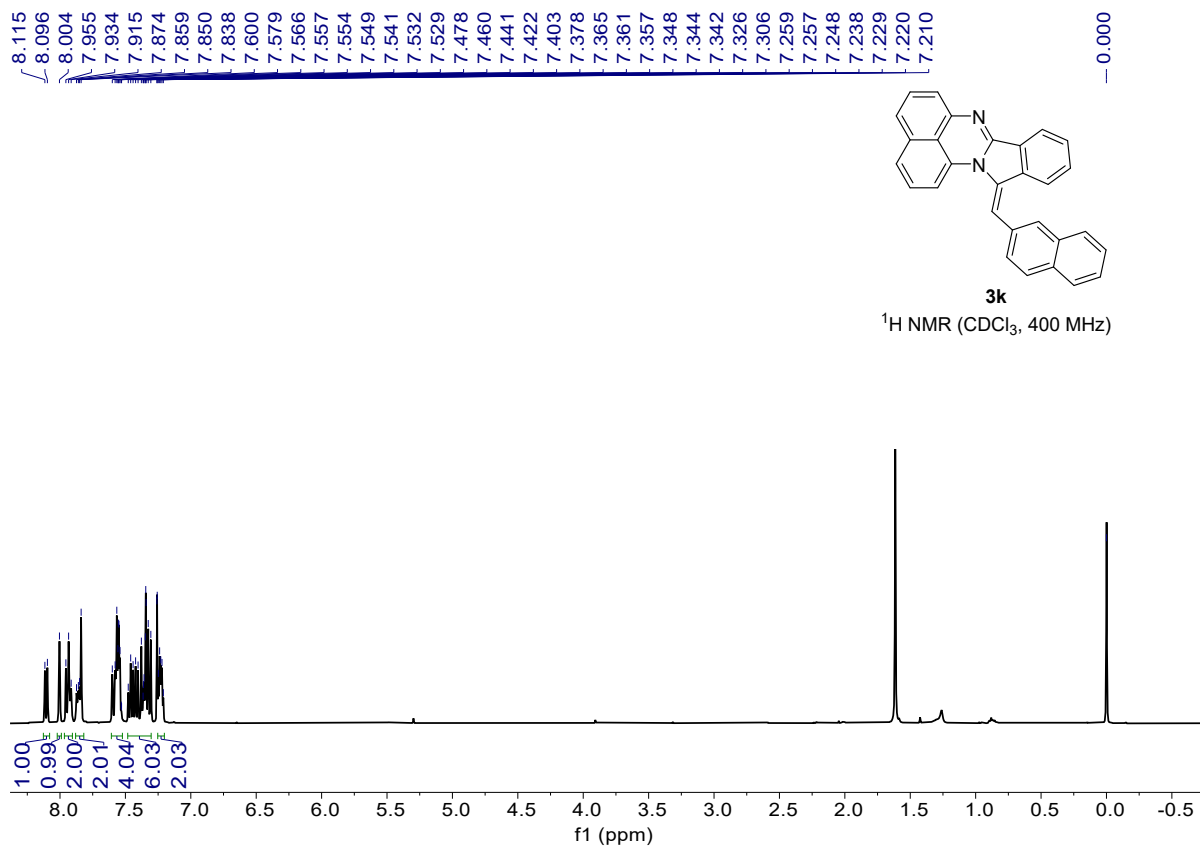
(E)-14-benzylidene-14H-benzo[5,6]isoindolo[2,1-a]perimidine (3i)



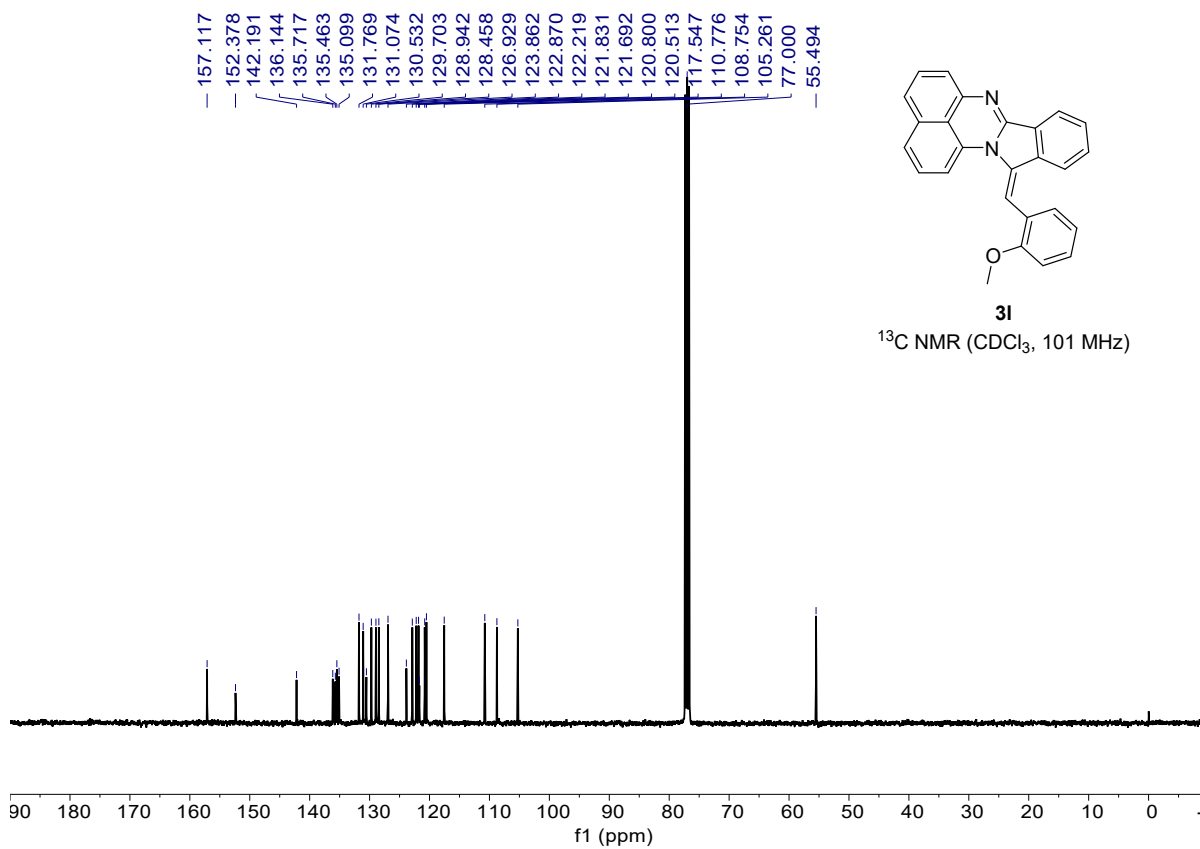
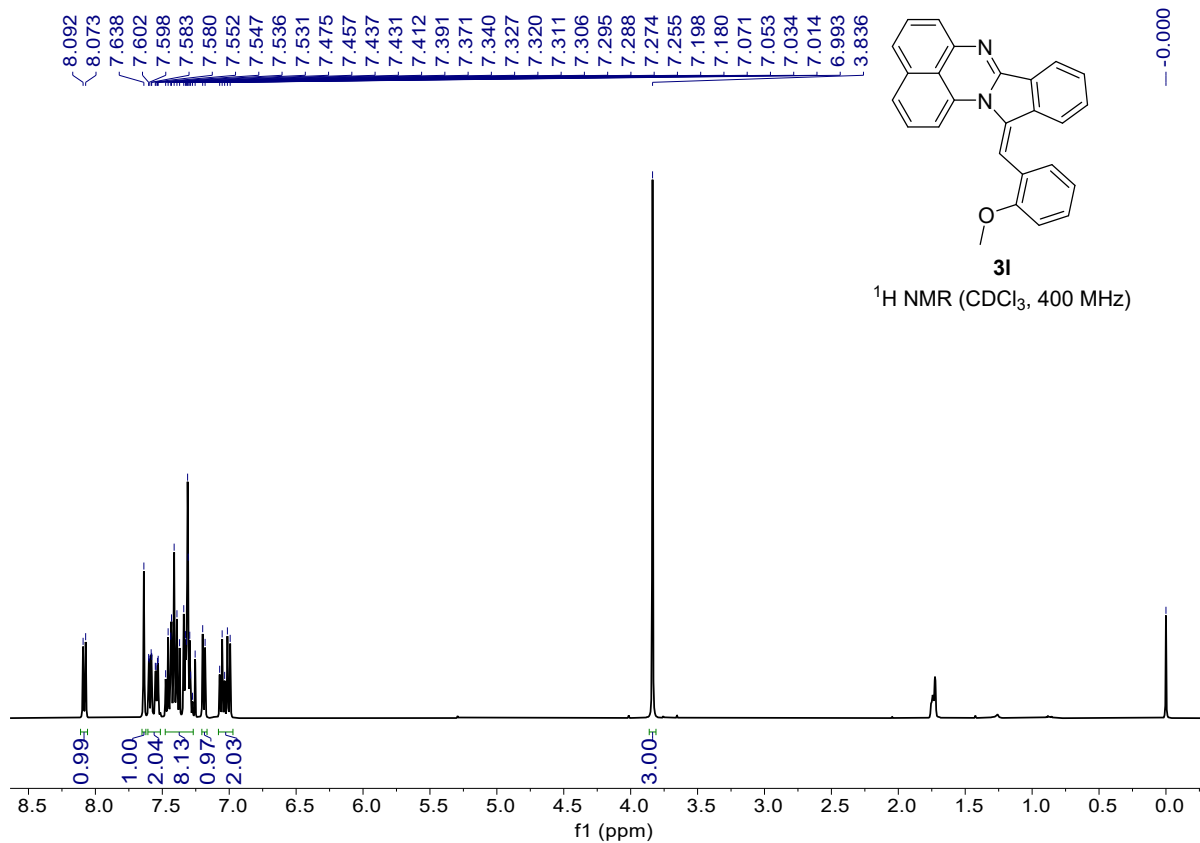
(E)-12-benzylidene-12H-pyrido[3',2':3,4]pyrrolo[1,2-a]perimidine (3j)



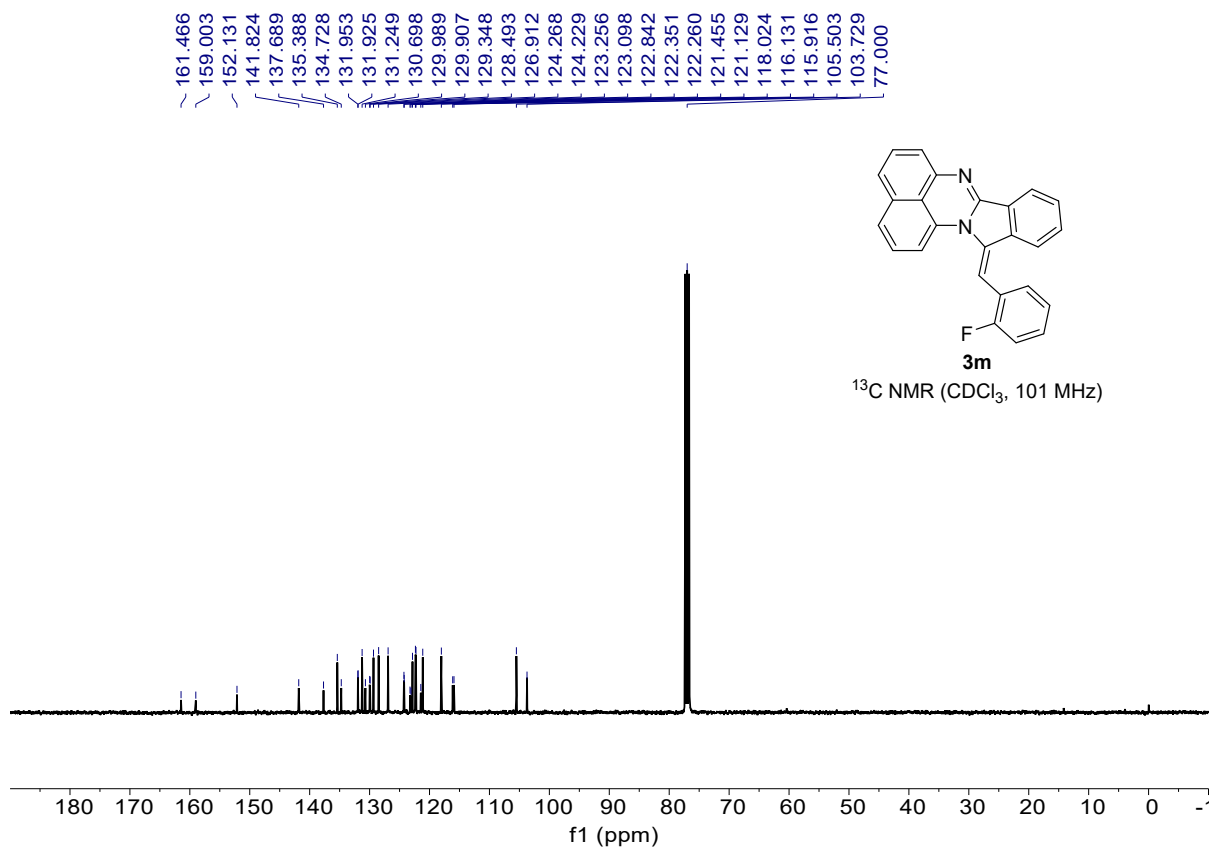
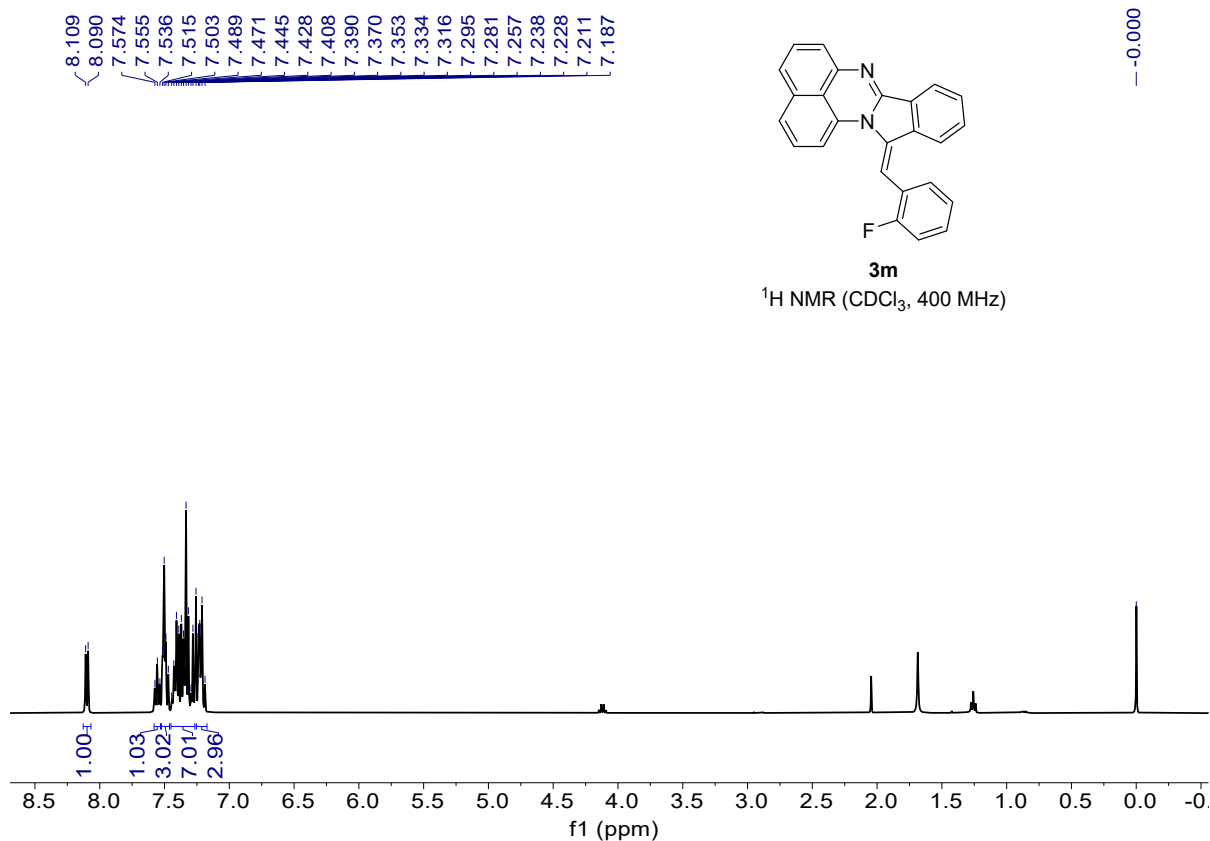
(E)-12-(naphthalen-1-ylmethylene)-12H-isoindolo[2,1-a]perimidin (3k)



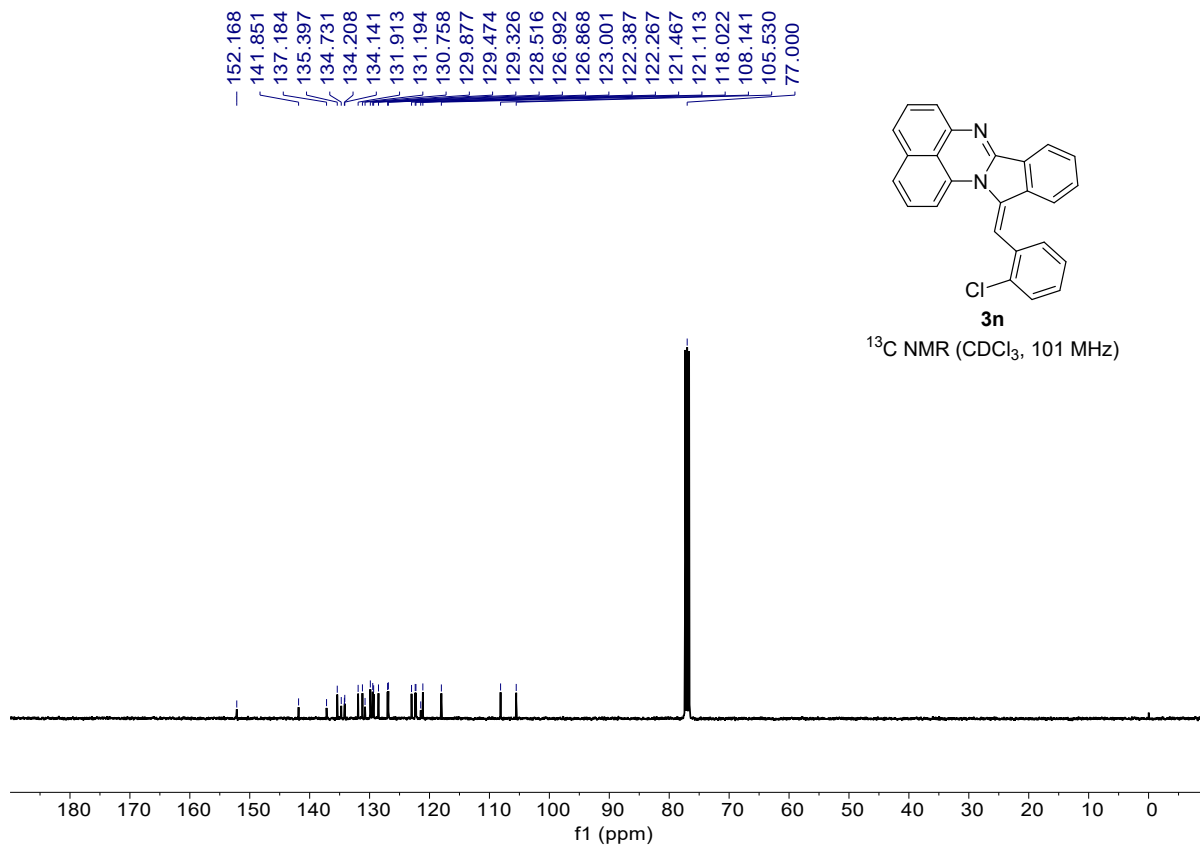
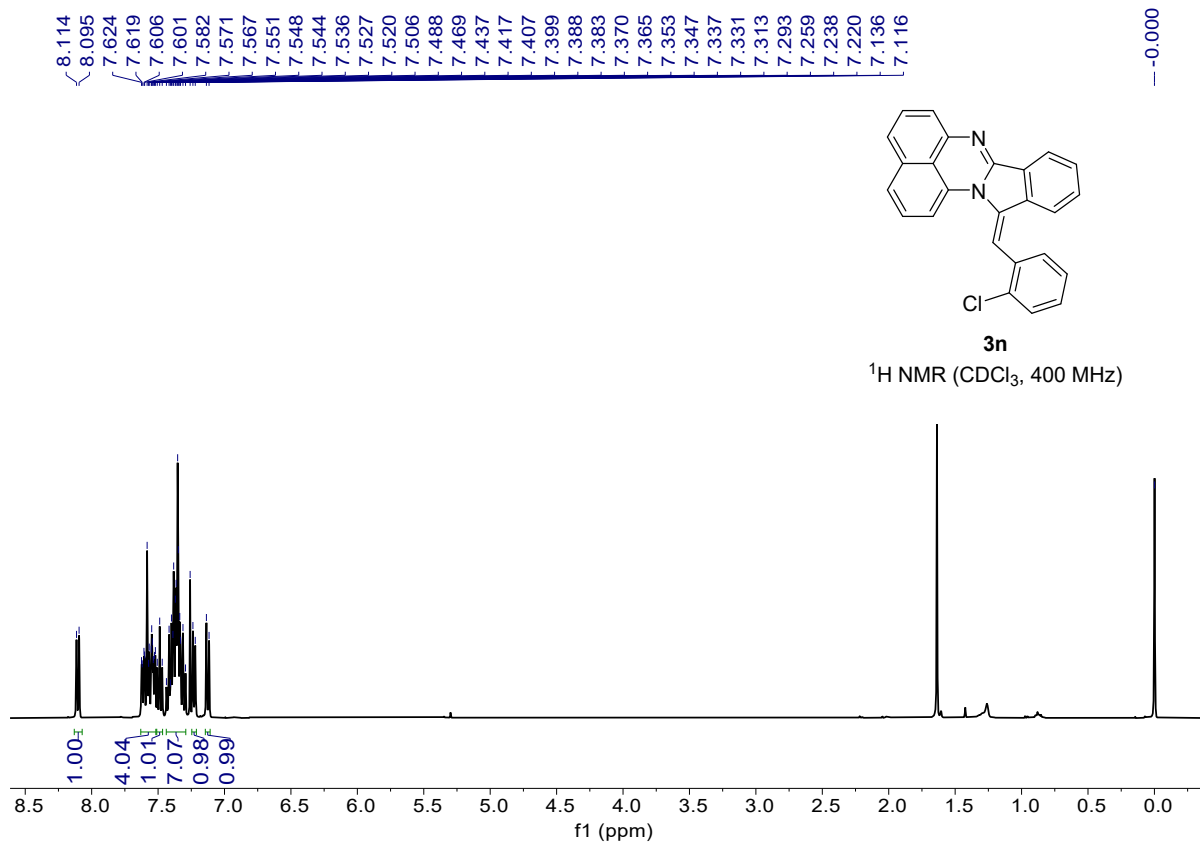
(E)-12-(2-methoxybenzylidene)-12H-isoindolo[2,1-a]perimidine (31)



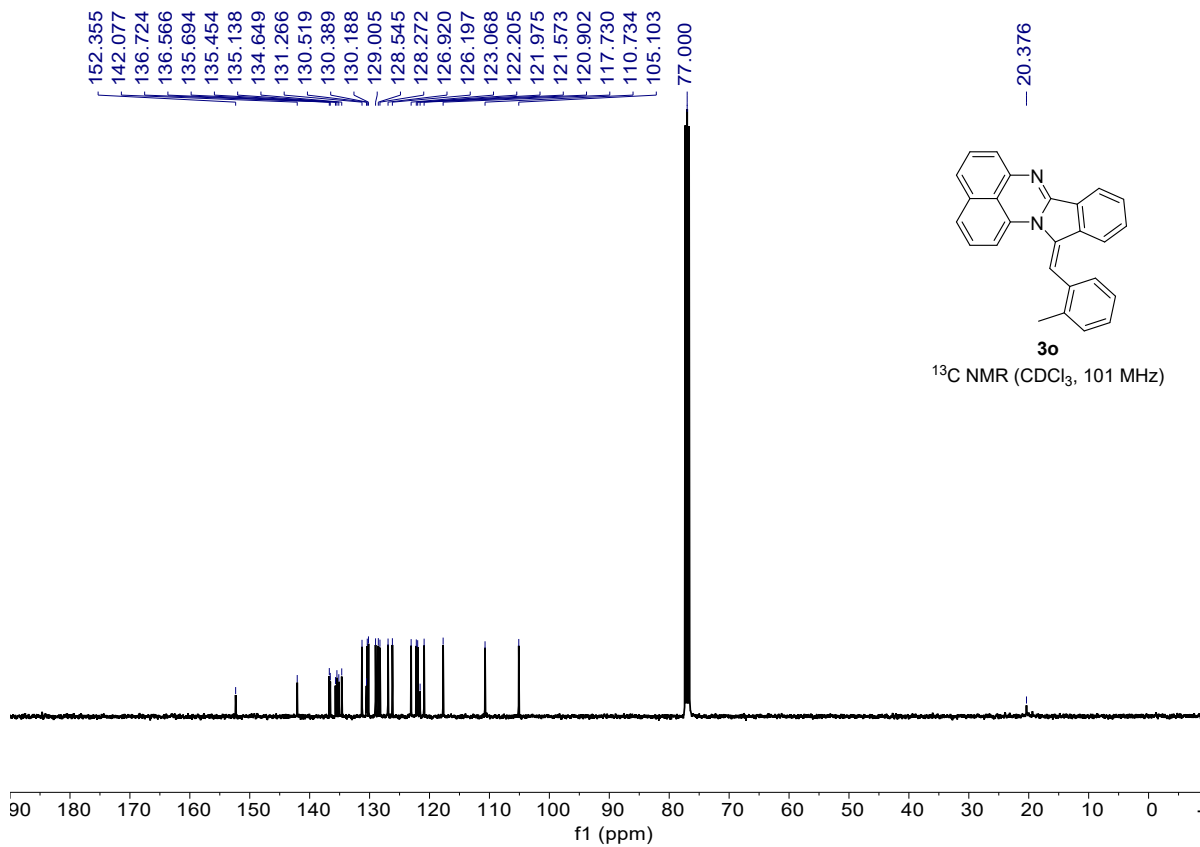
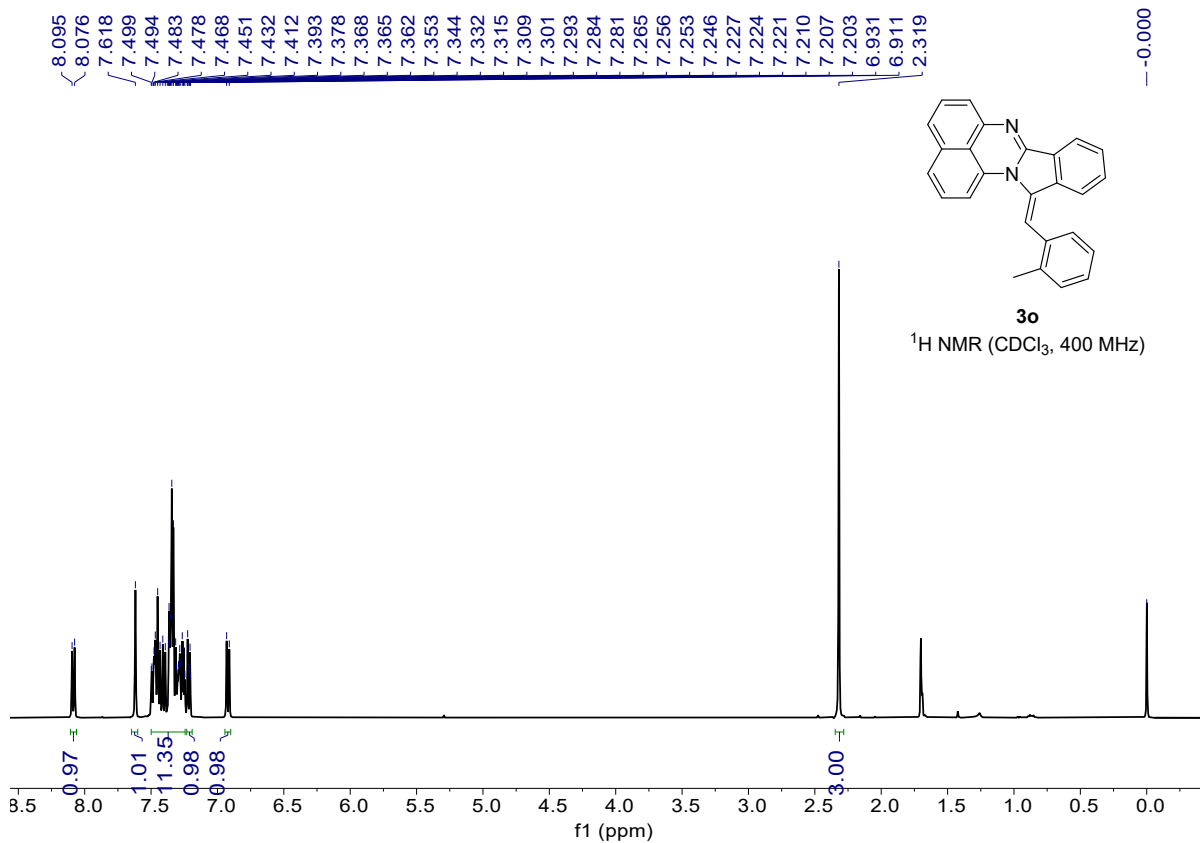
(E)-12-(2-fluorobenzylidene)-12H-isoindolo[2,1-a]perimidine (3m)



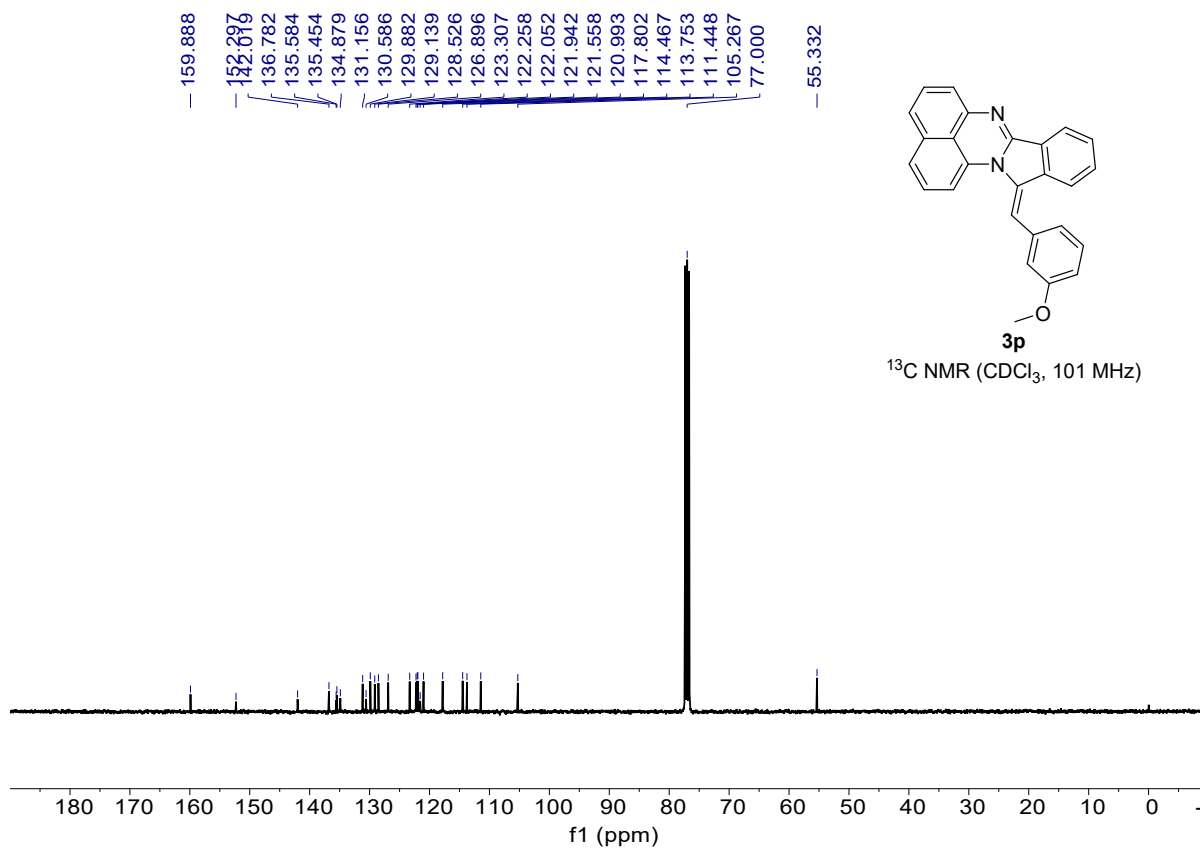
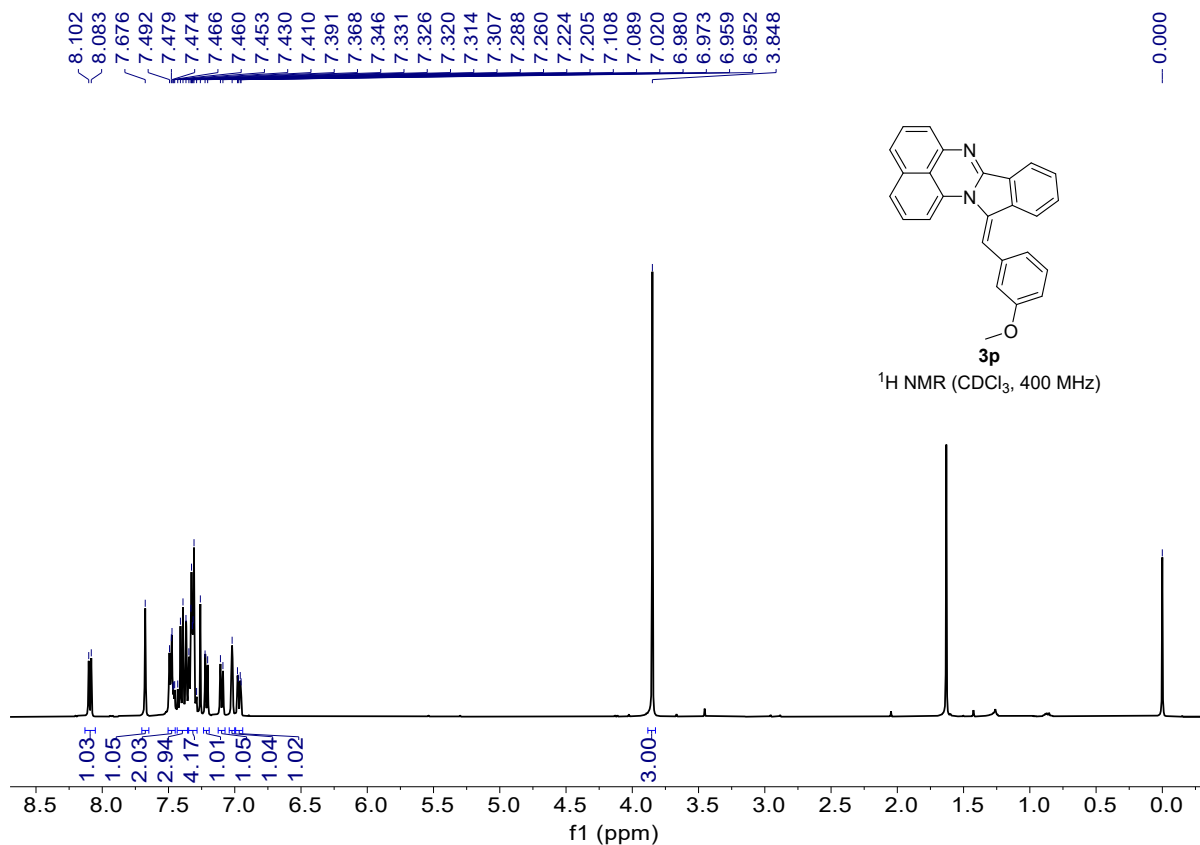
(E)-12-(2-chlorobenzylidene)-12H-isoindolo[2,1-a]perimidine (3n)



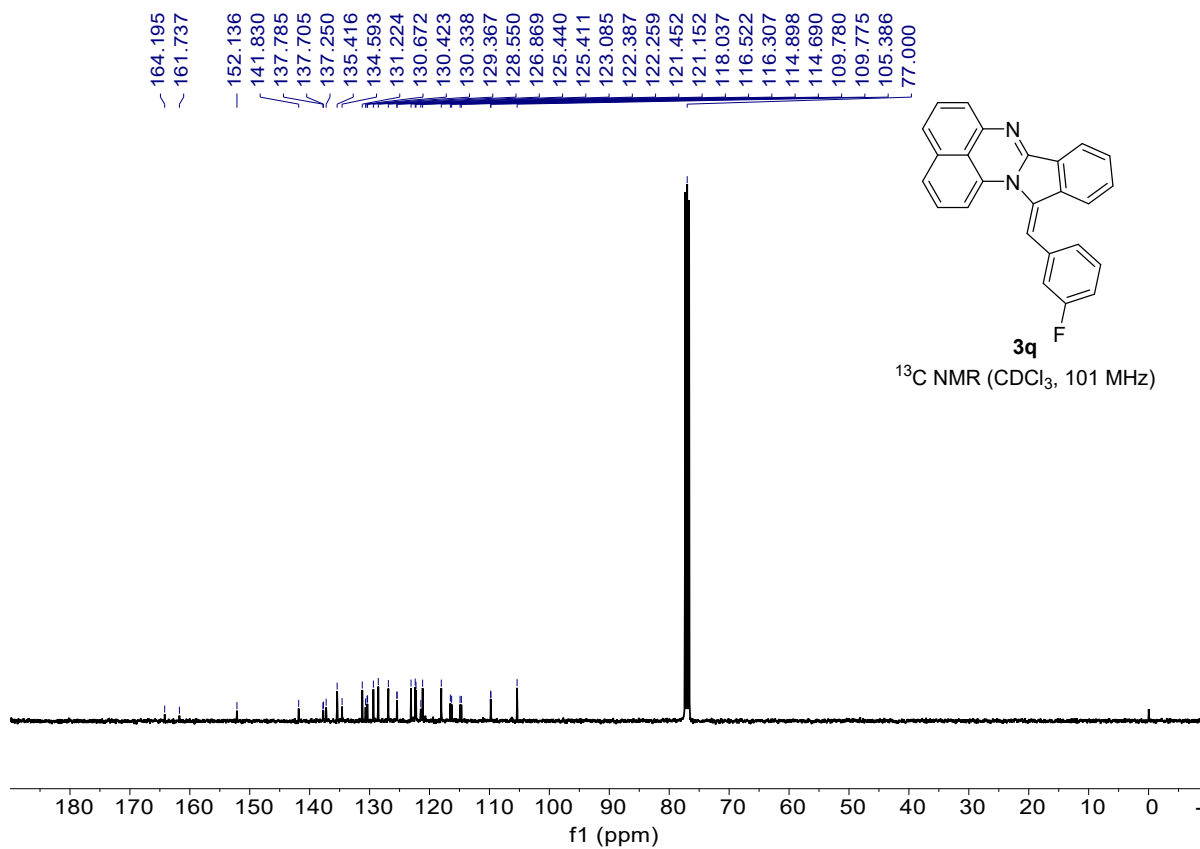
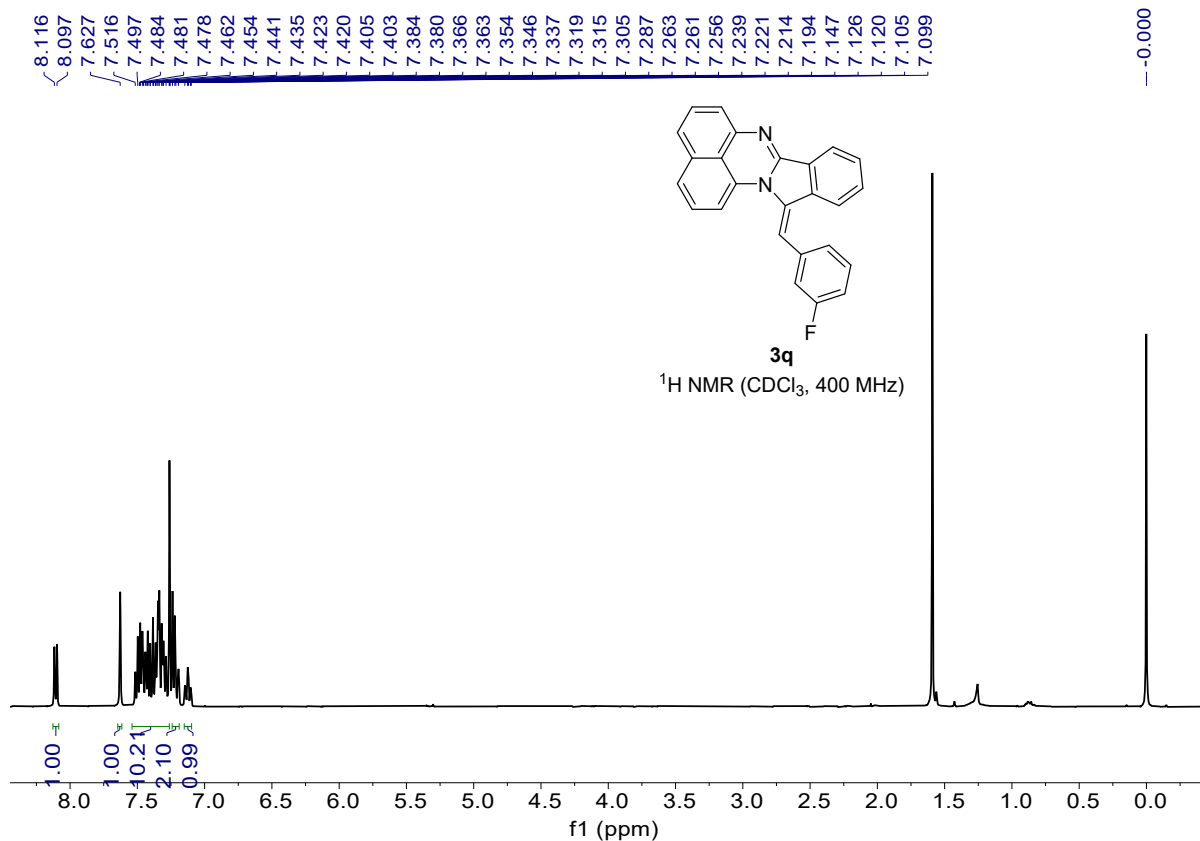
(E)-12-(2-methylbenzylidene)-12H-isoindolo[2,1-a]perimidine (3o)



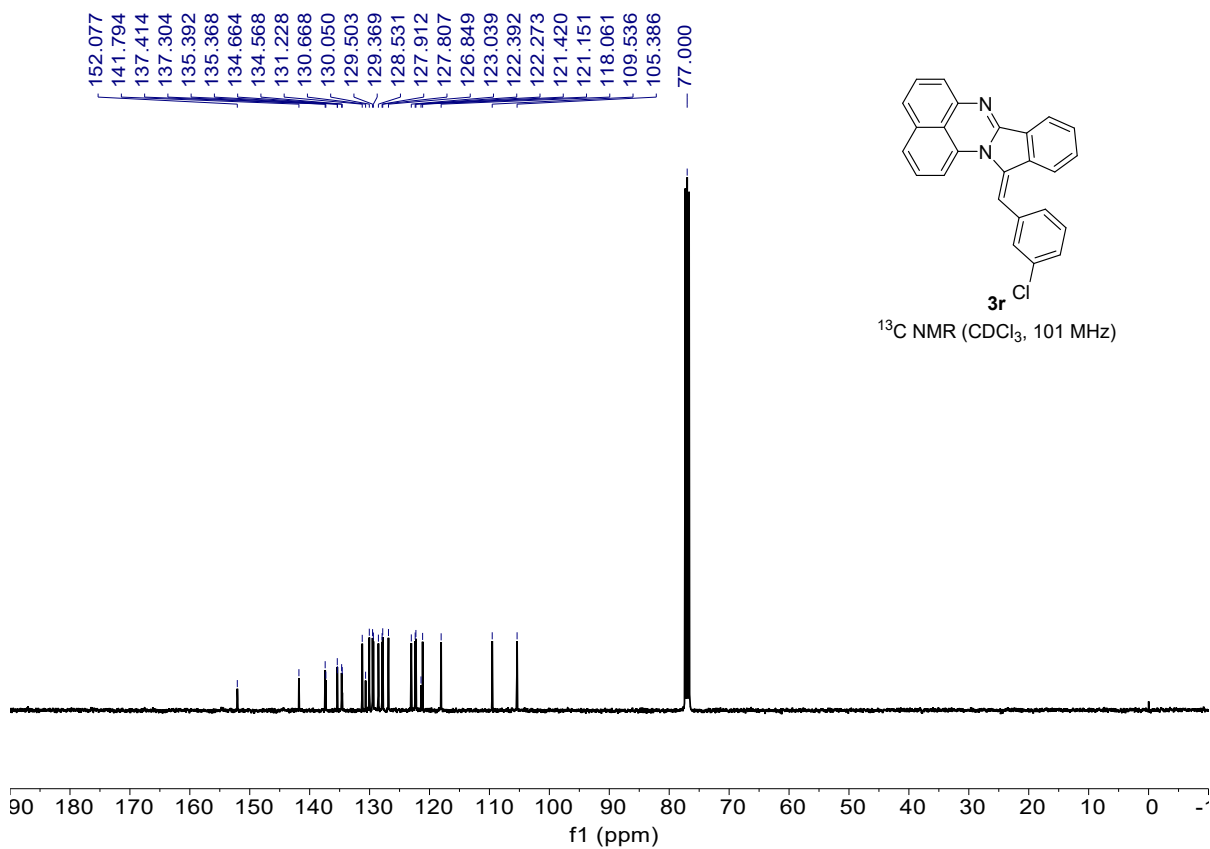
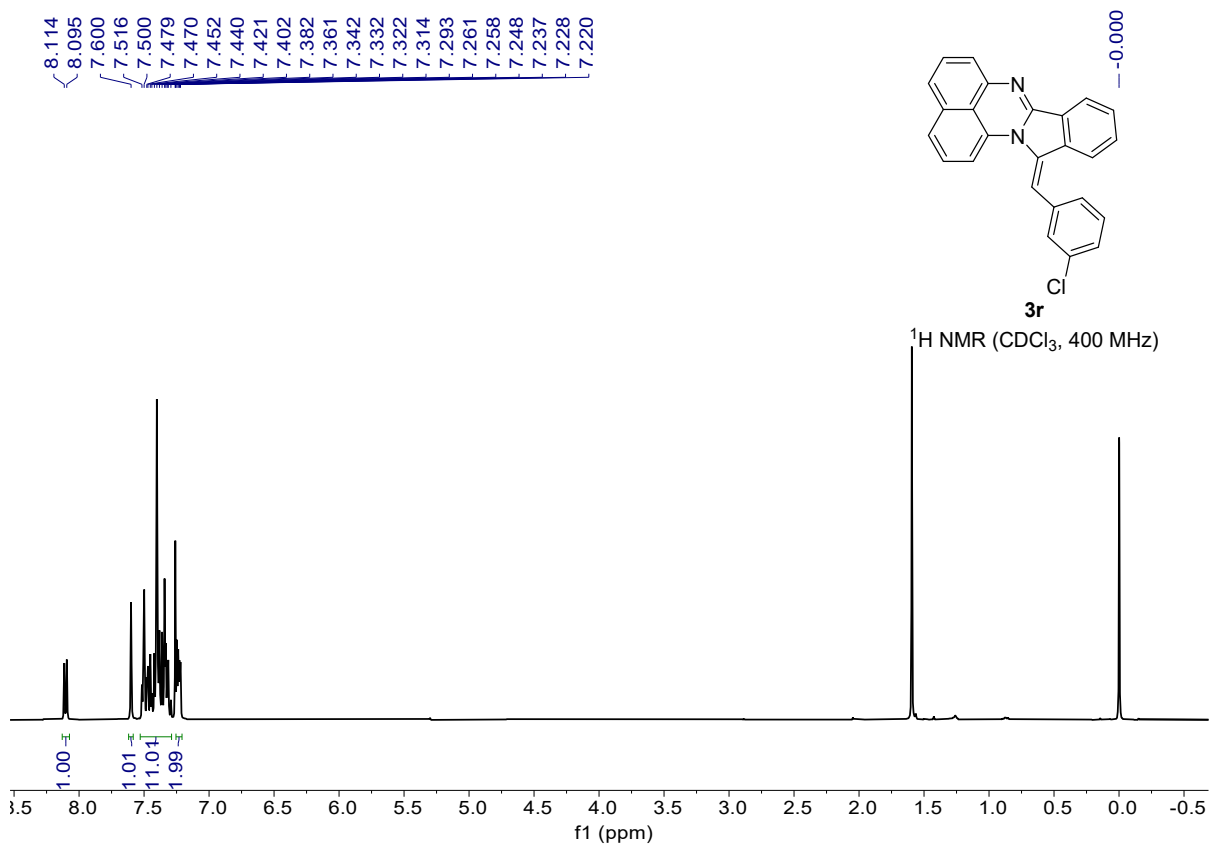
(E)-12-(3-methoxybenzylidene)-12H-isoindolo[2,1-a]perimidine (3p)



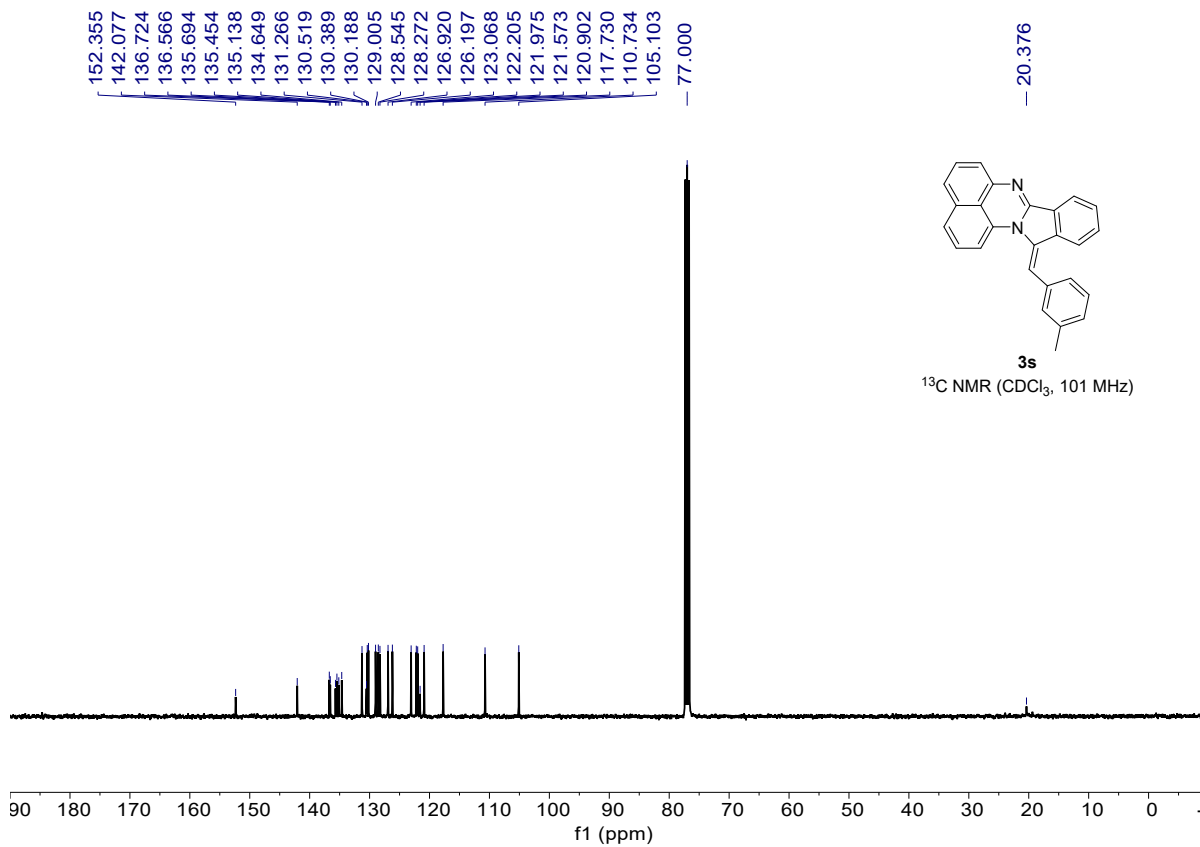
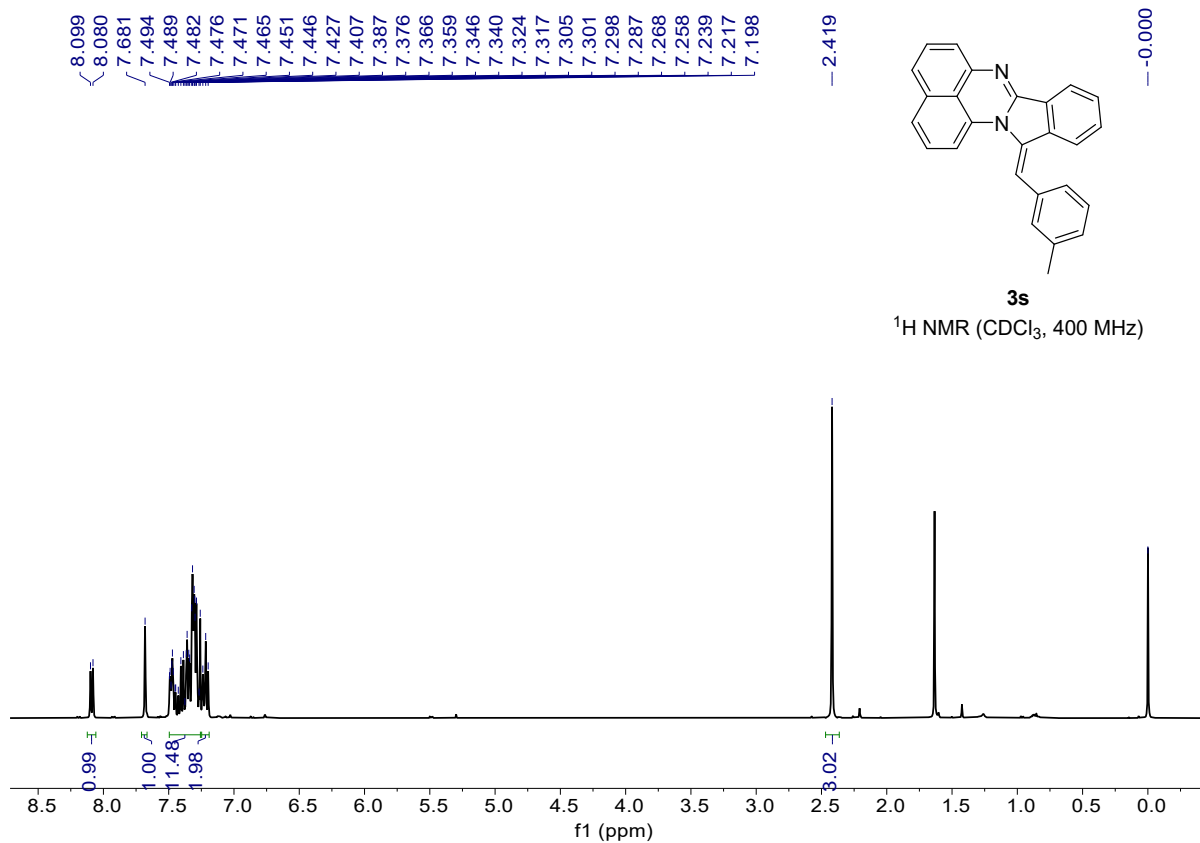
(E)-12-(3-fluorobenzylidene)-12H-isoindolo[2,1-a]perimidine (3q)



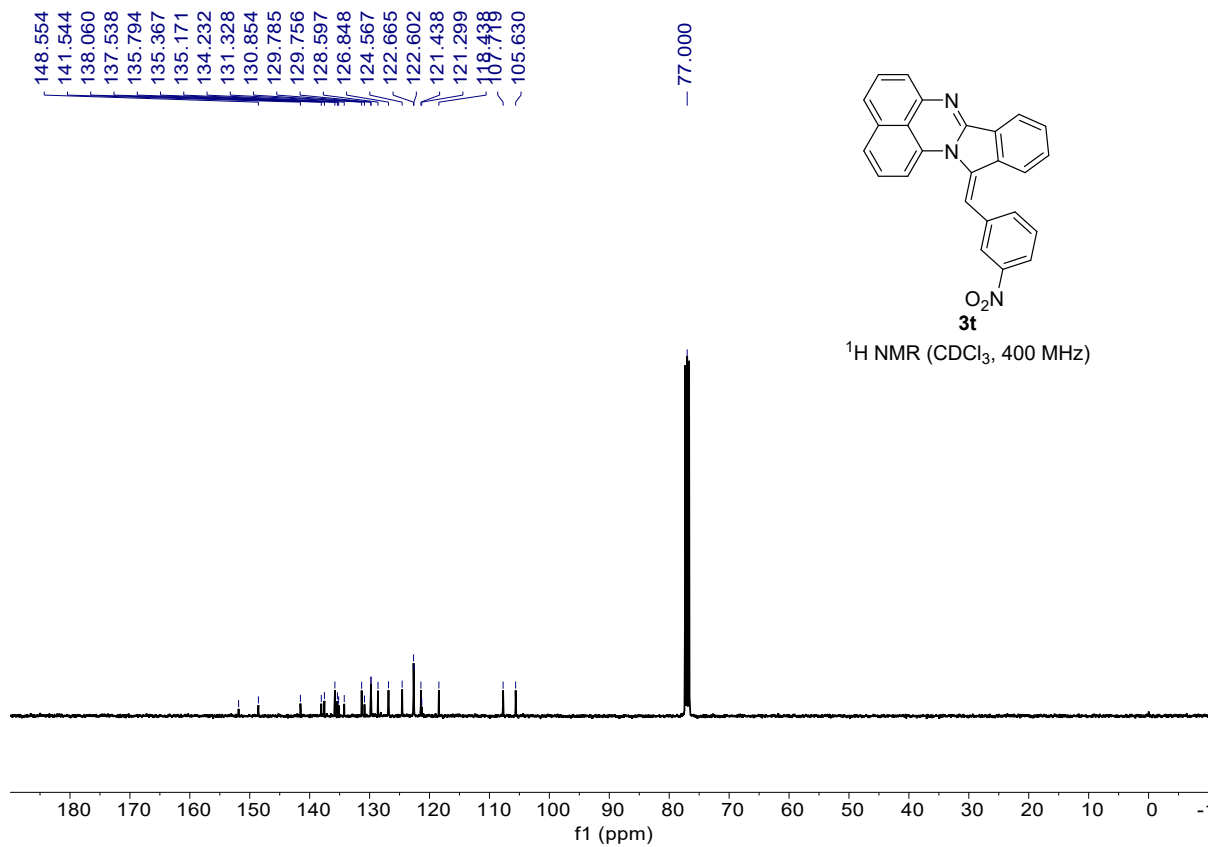
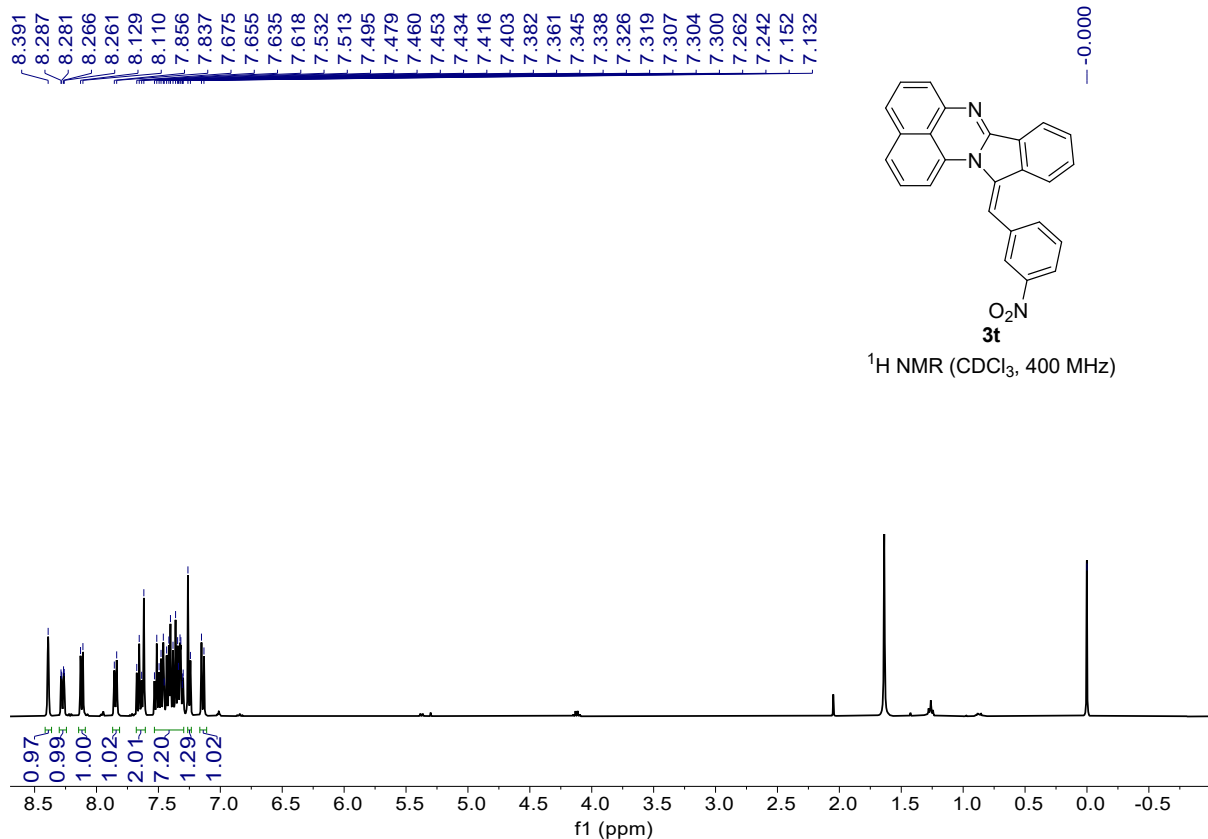
(E)-12-(3-chlorobenzylidene)-12H-isoindolo[2,1-a]perimidine (3r)



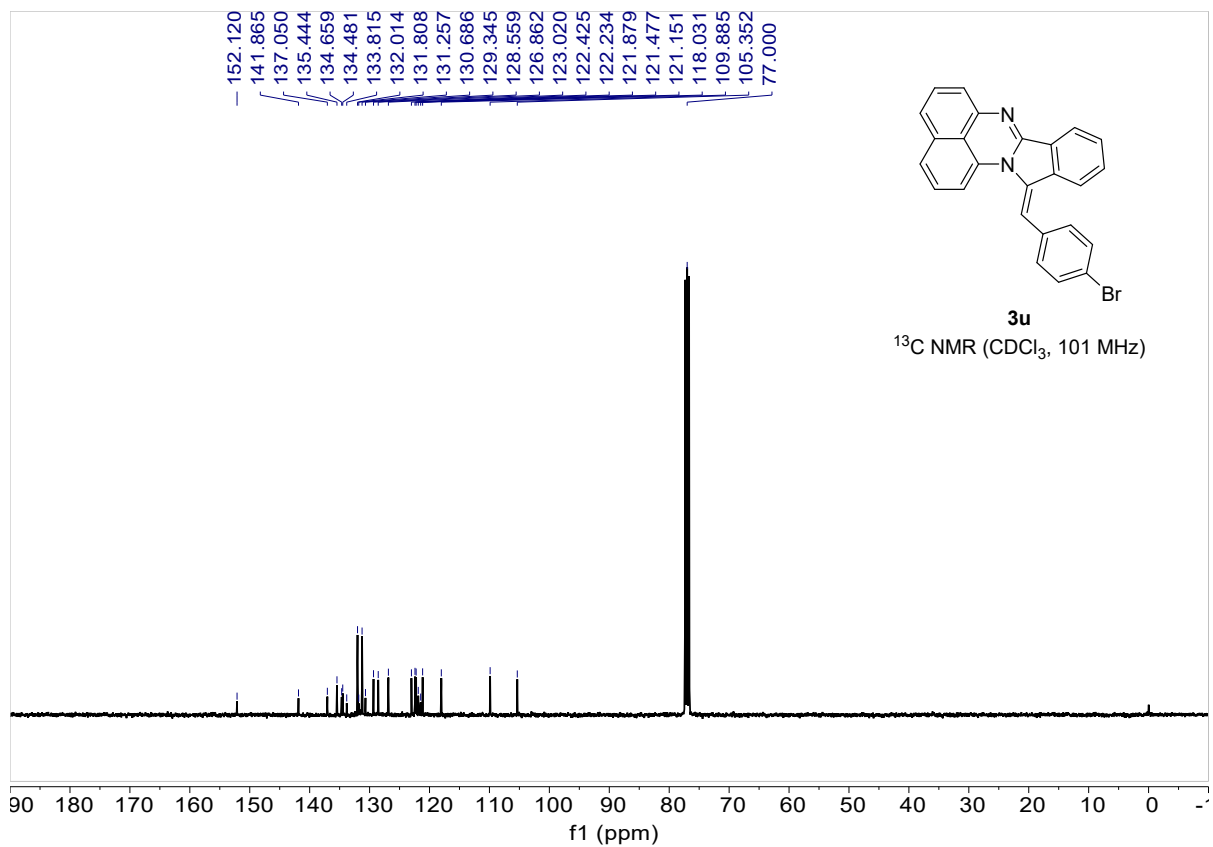
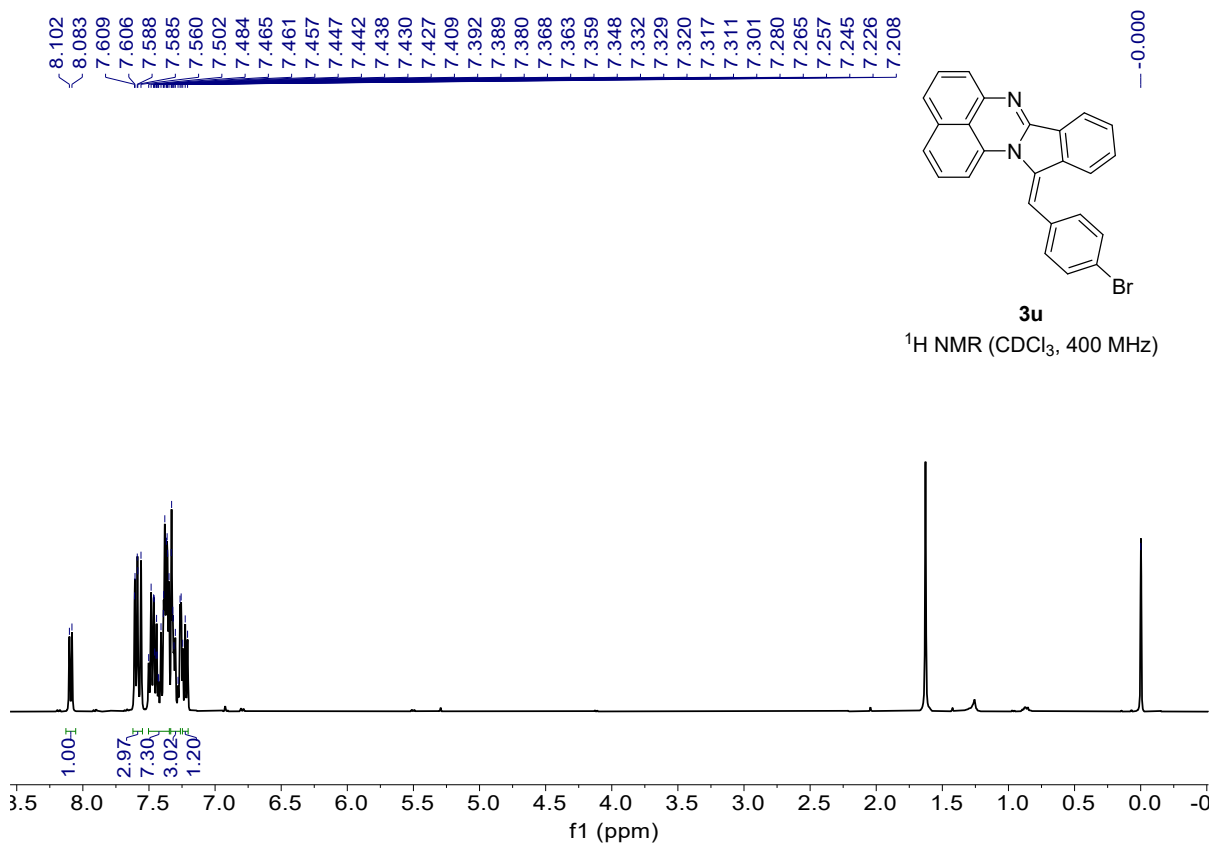
(E)-12-(3-methylbenzylidene)-12H-isoindolo[2,1-a]perimidine (3s)



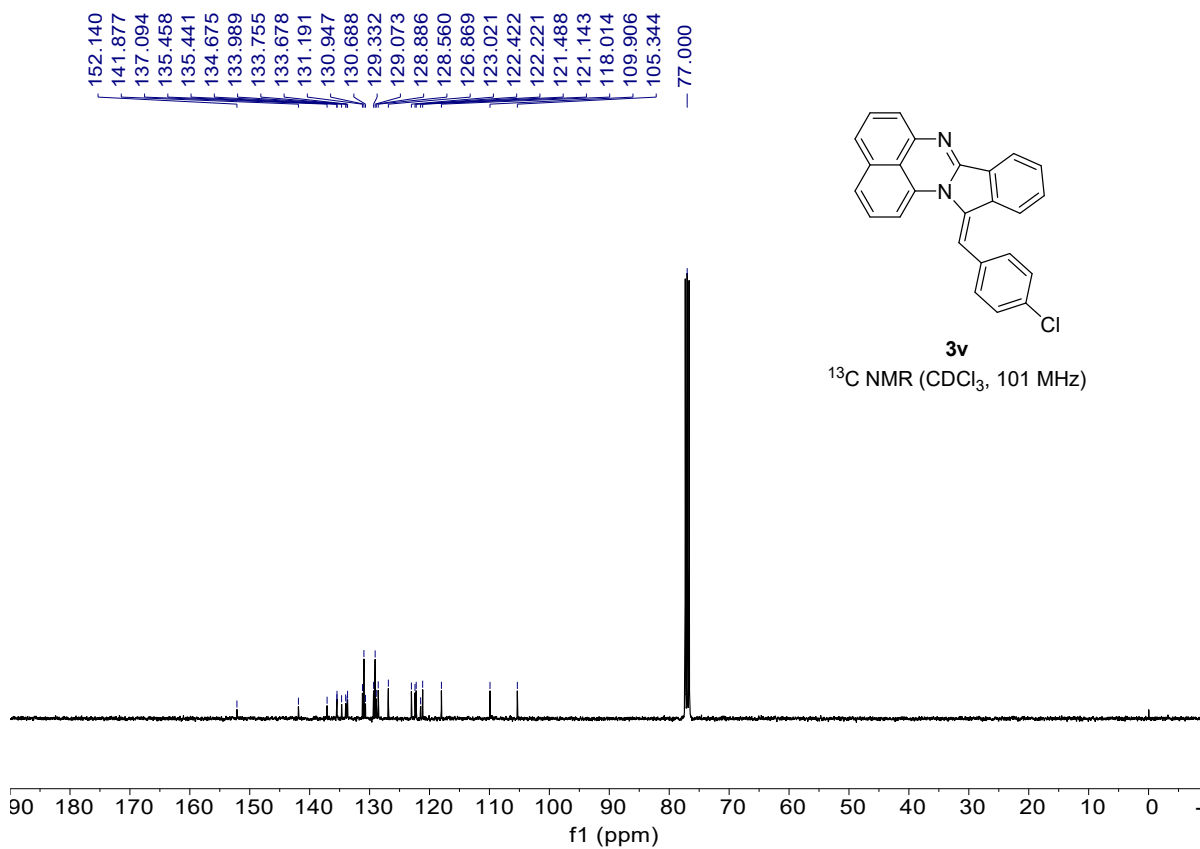
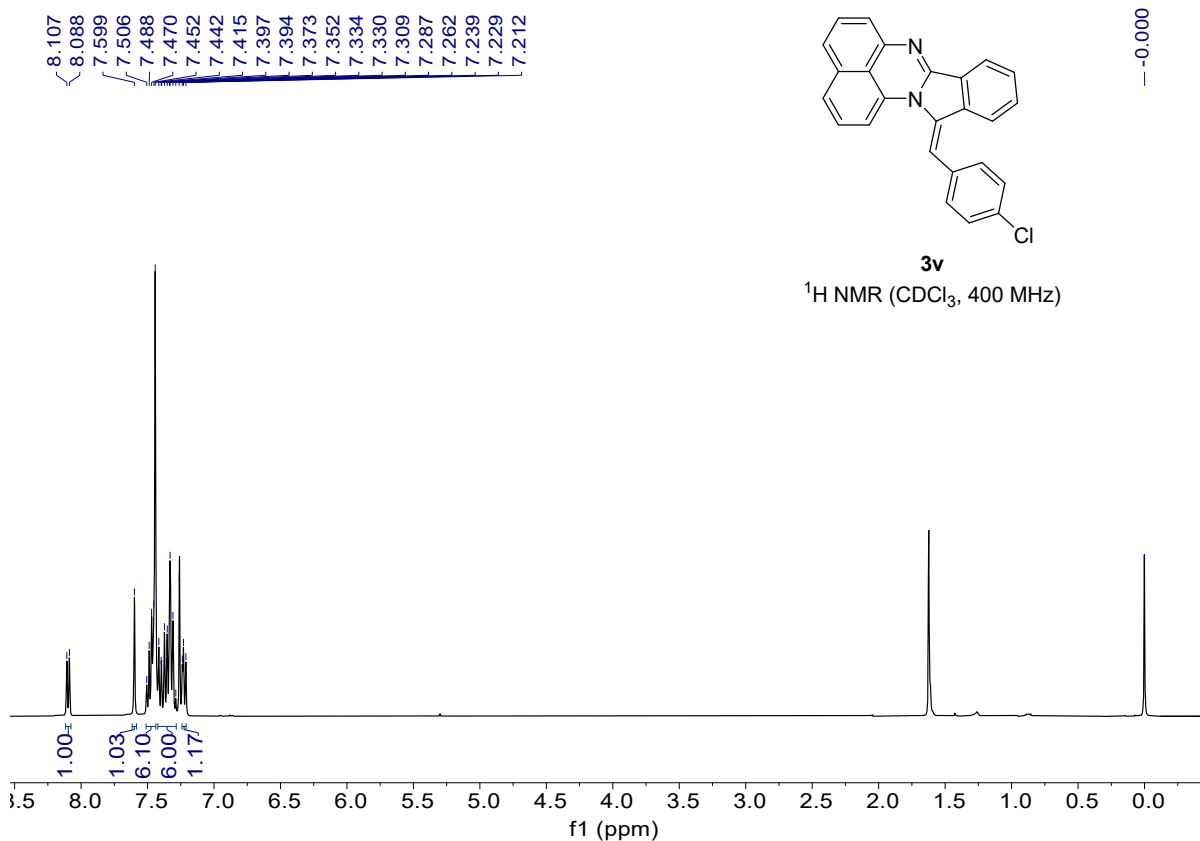
(E)-12-(3-nitrobenzylidene)-12H-isoindolo[2,1-a]perimidine (3t)



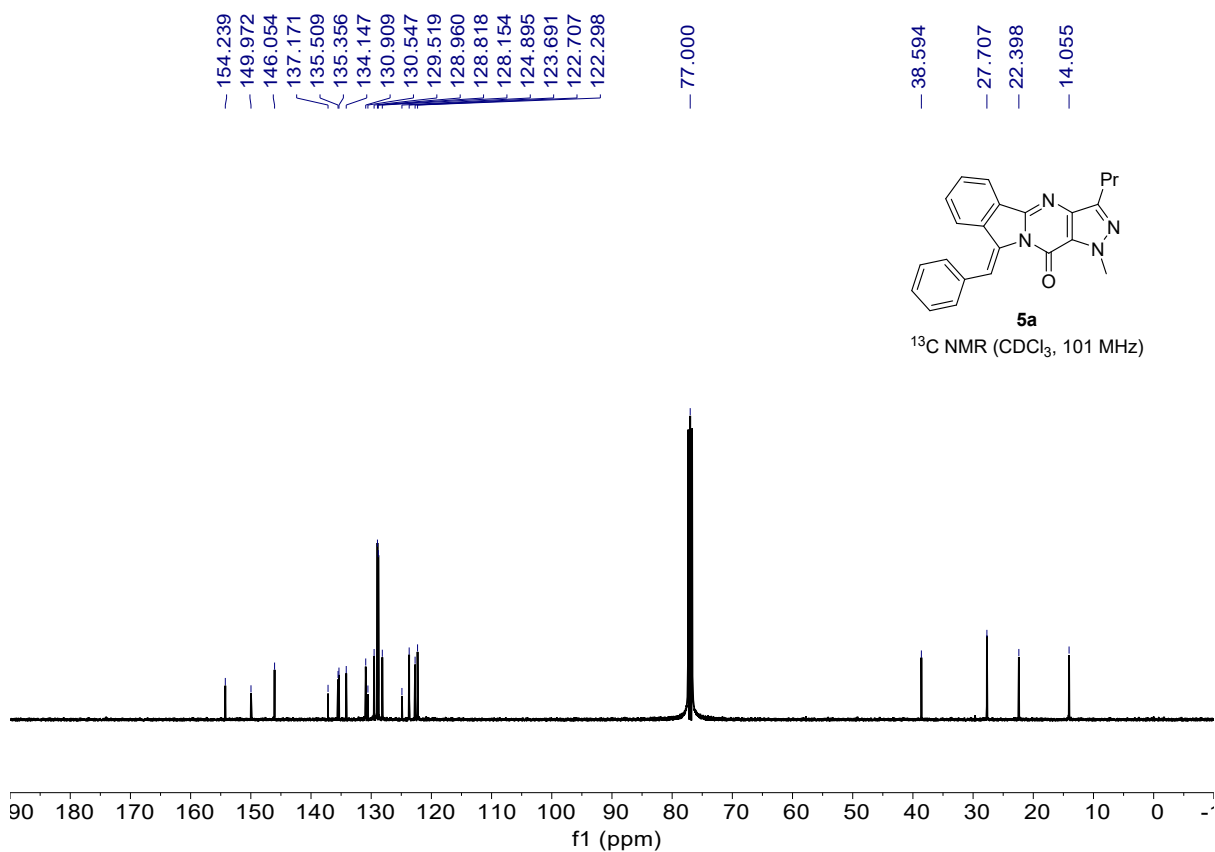
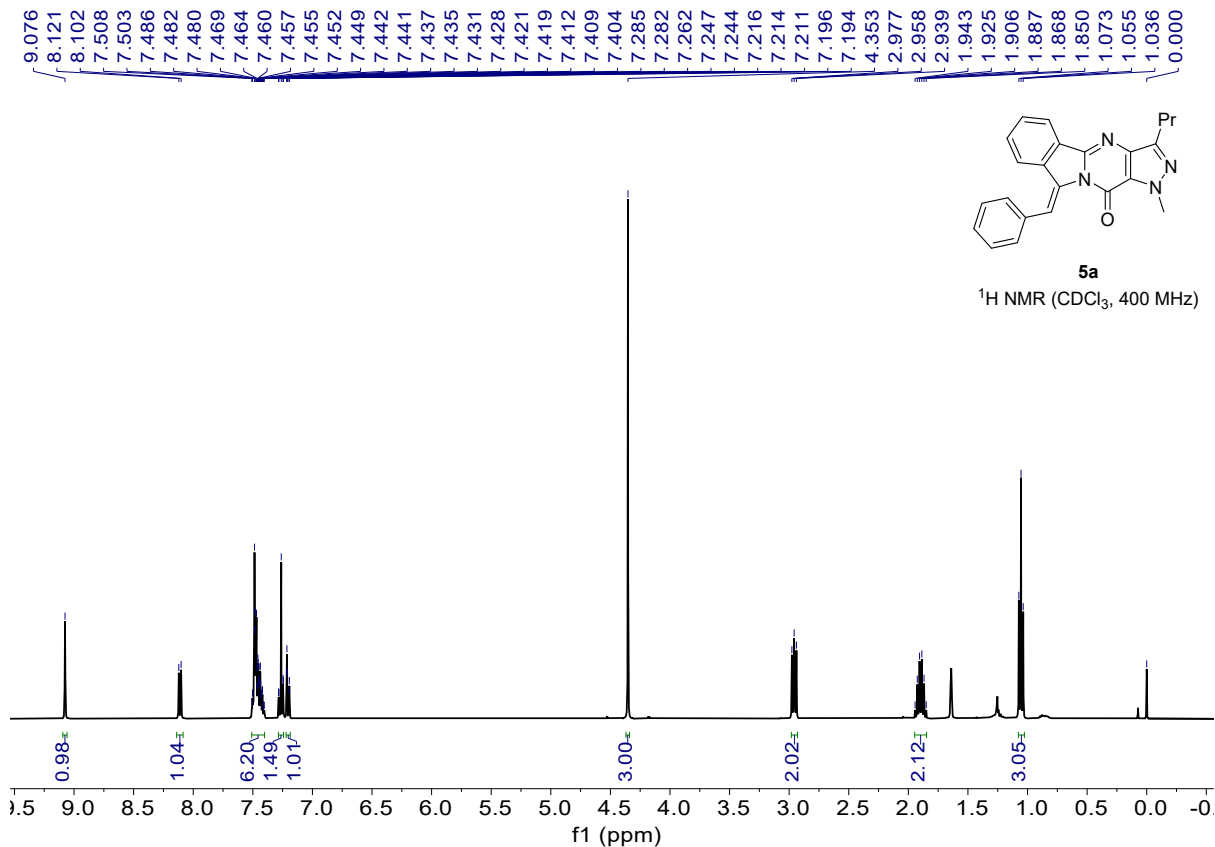
(E)-12-(4-bromobenzylidene)-12H-isoindolo[2,1-a]perimidine (3u)



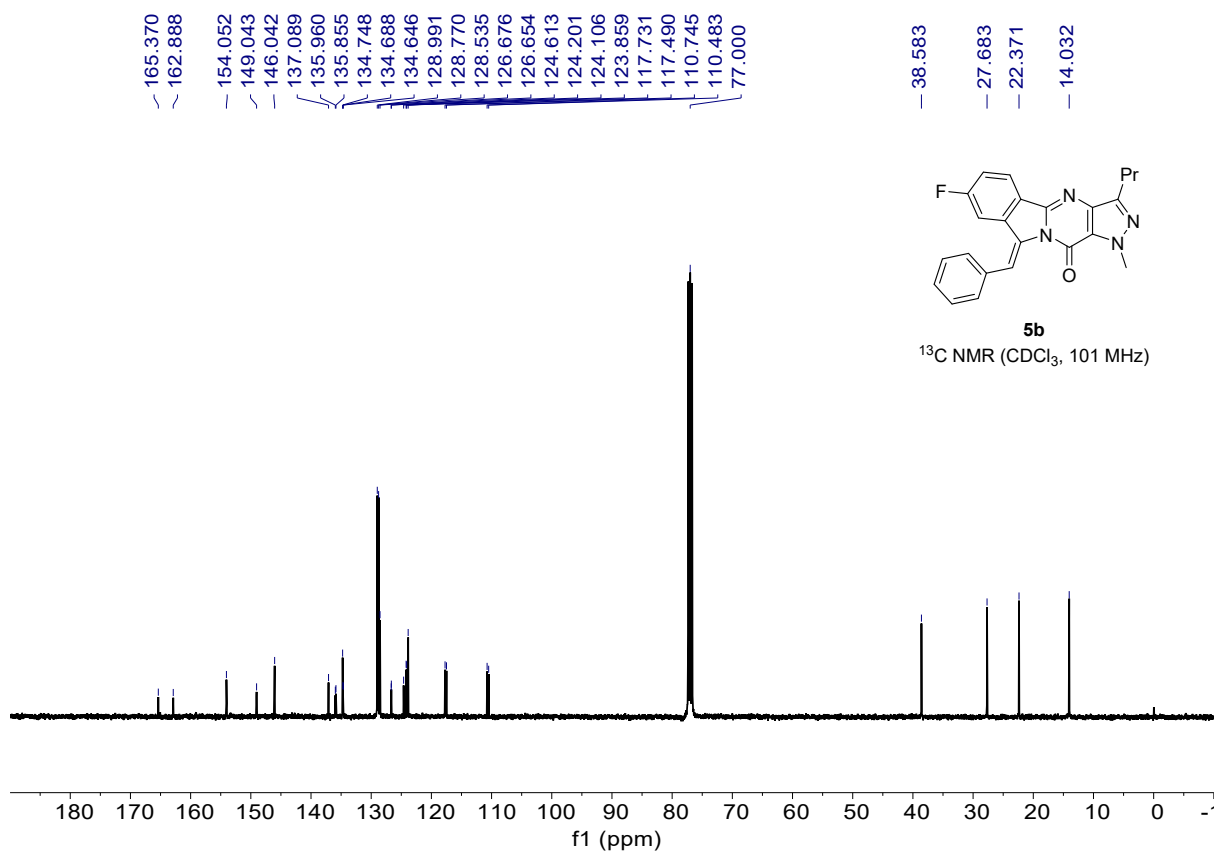
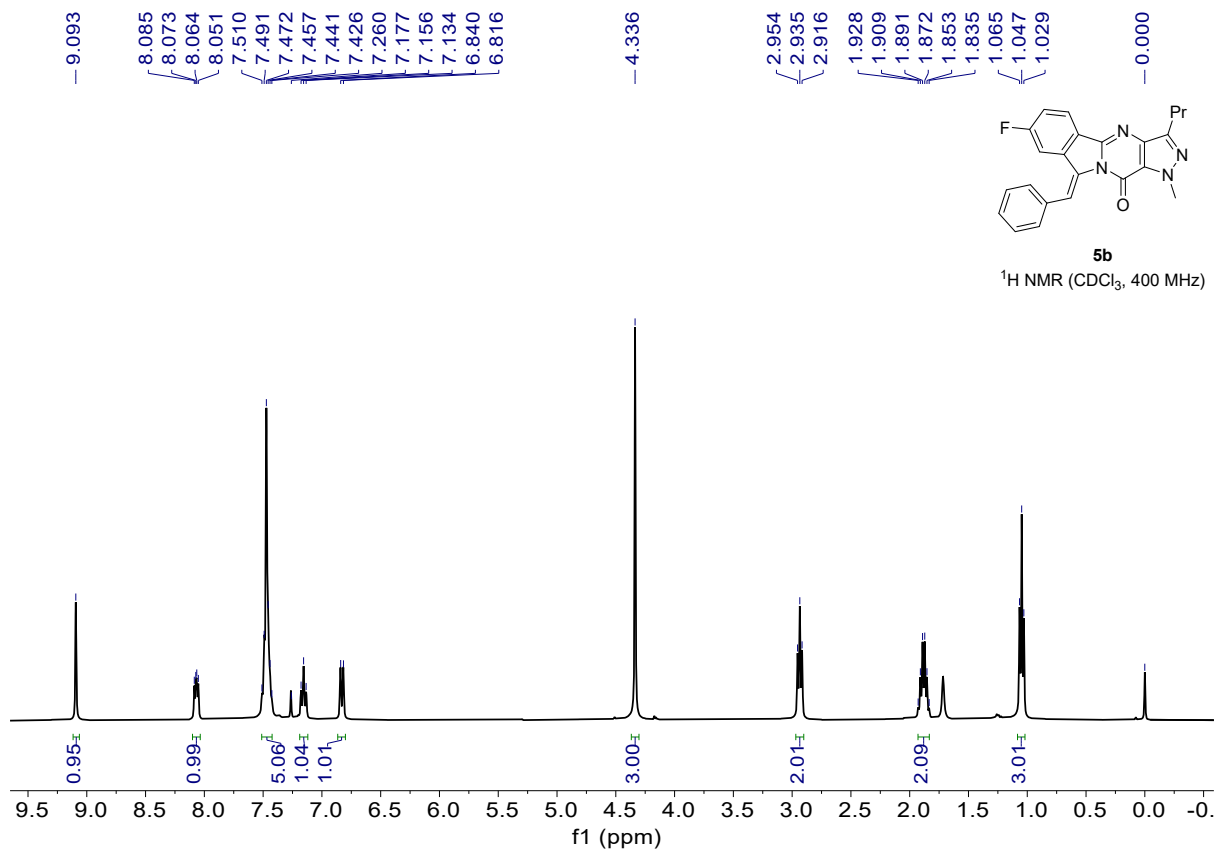
(E)-12-(4-chlorobenzylidene)-12H-isoindolo[2,1-a]perimidine (3v)



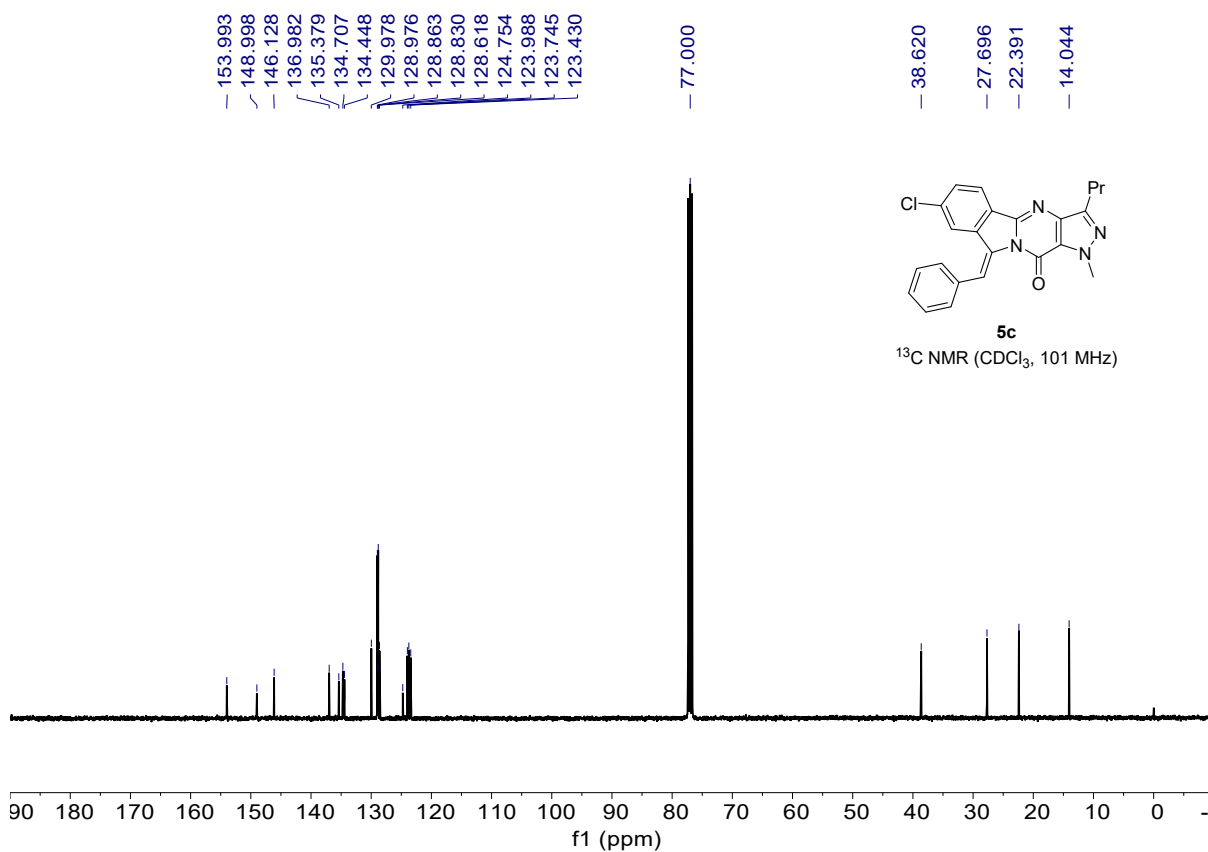
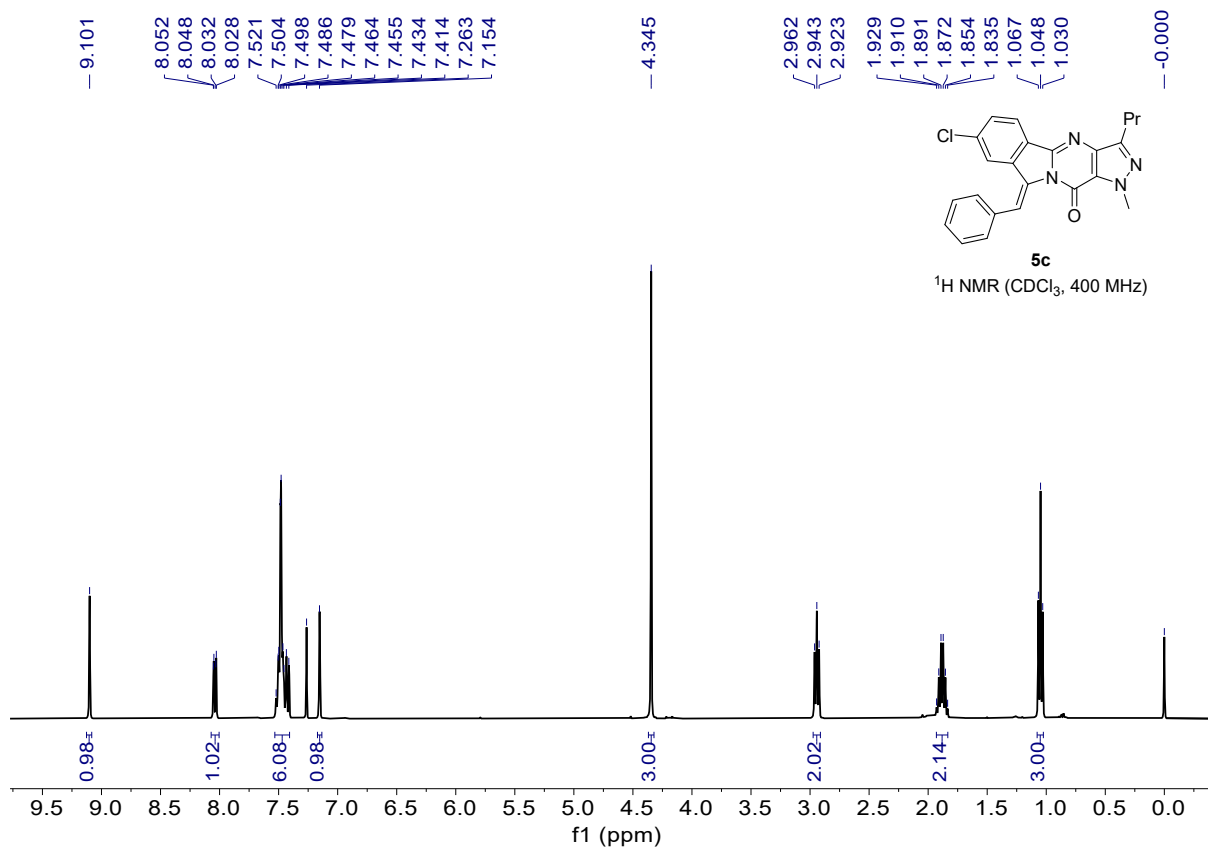
(E)-9-benzylidene-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (5a)



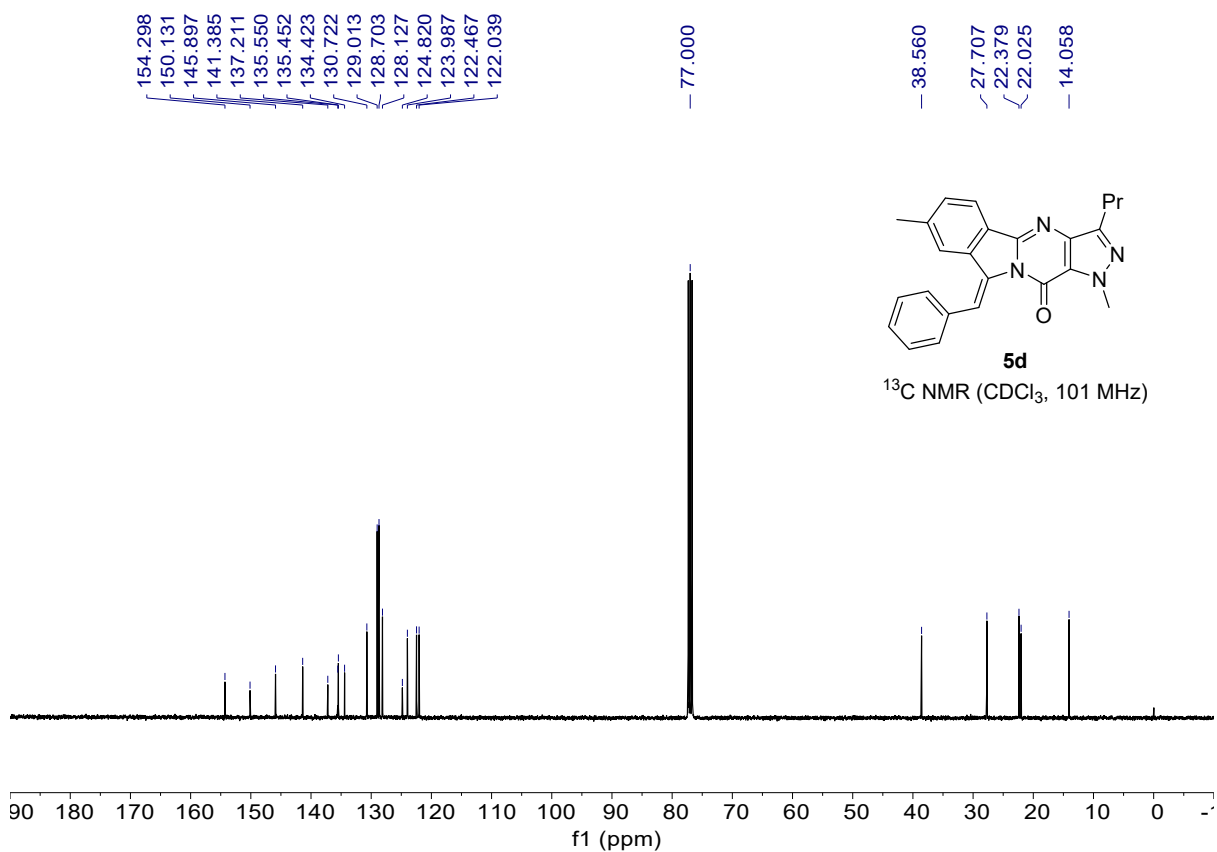
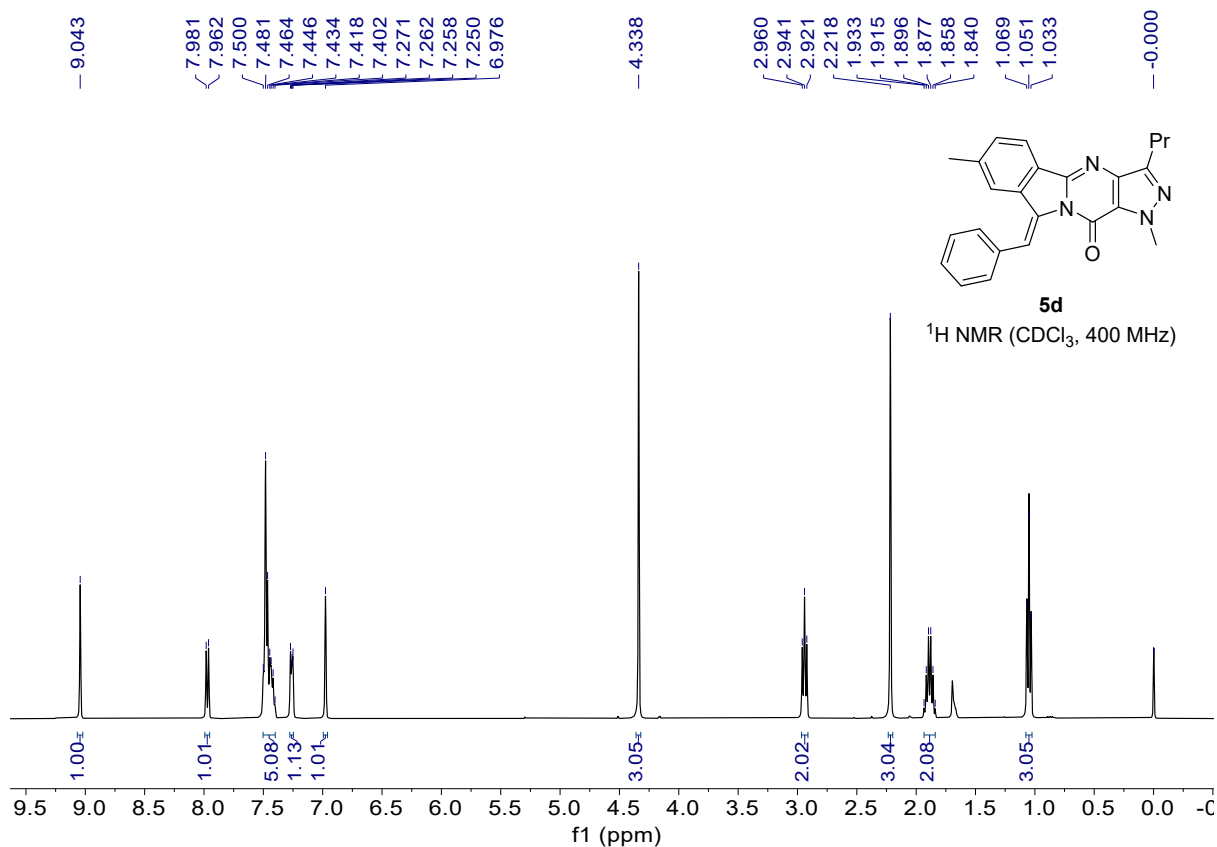
(E)-9-benzylidene-7-fluoro-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (5b)



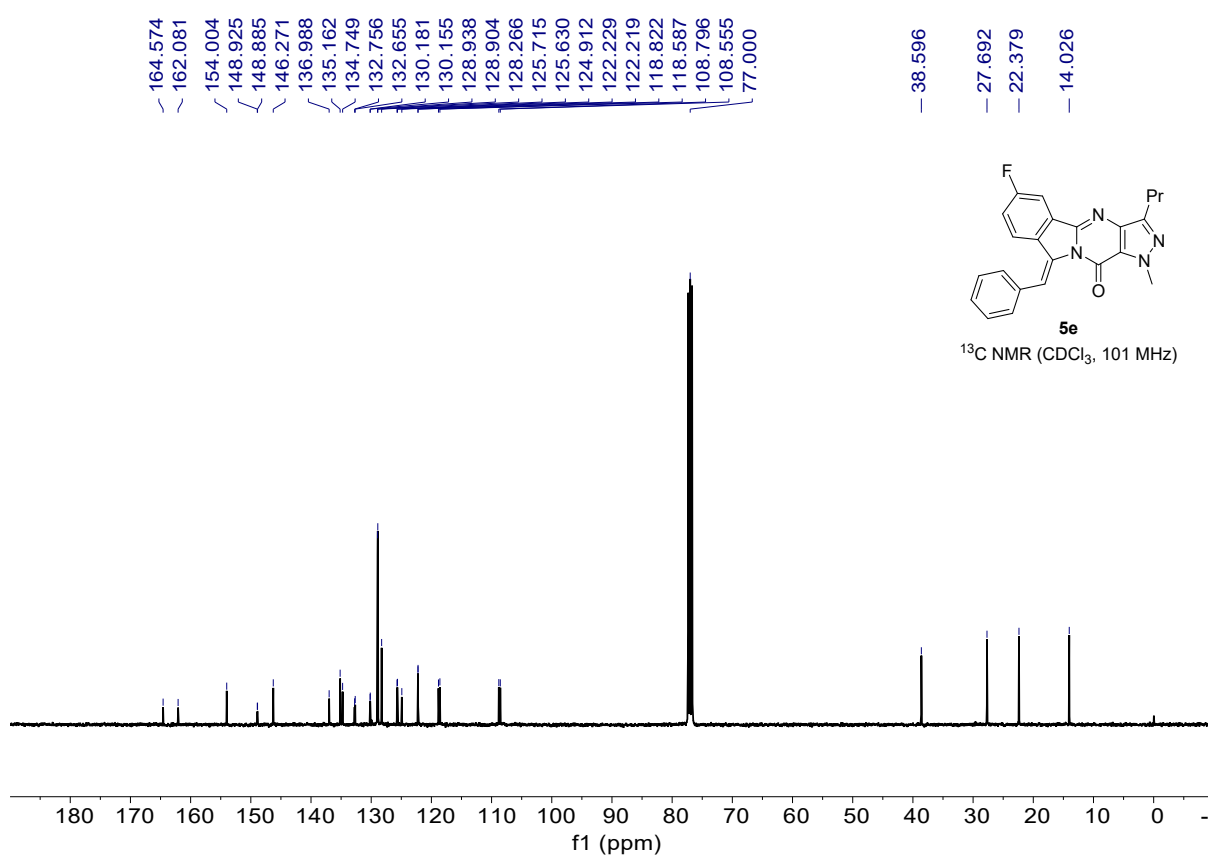
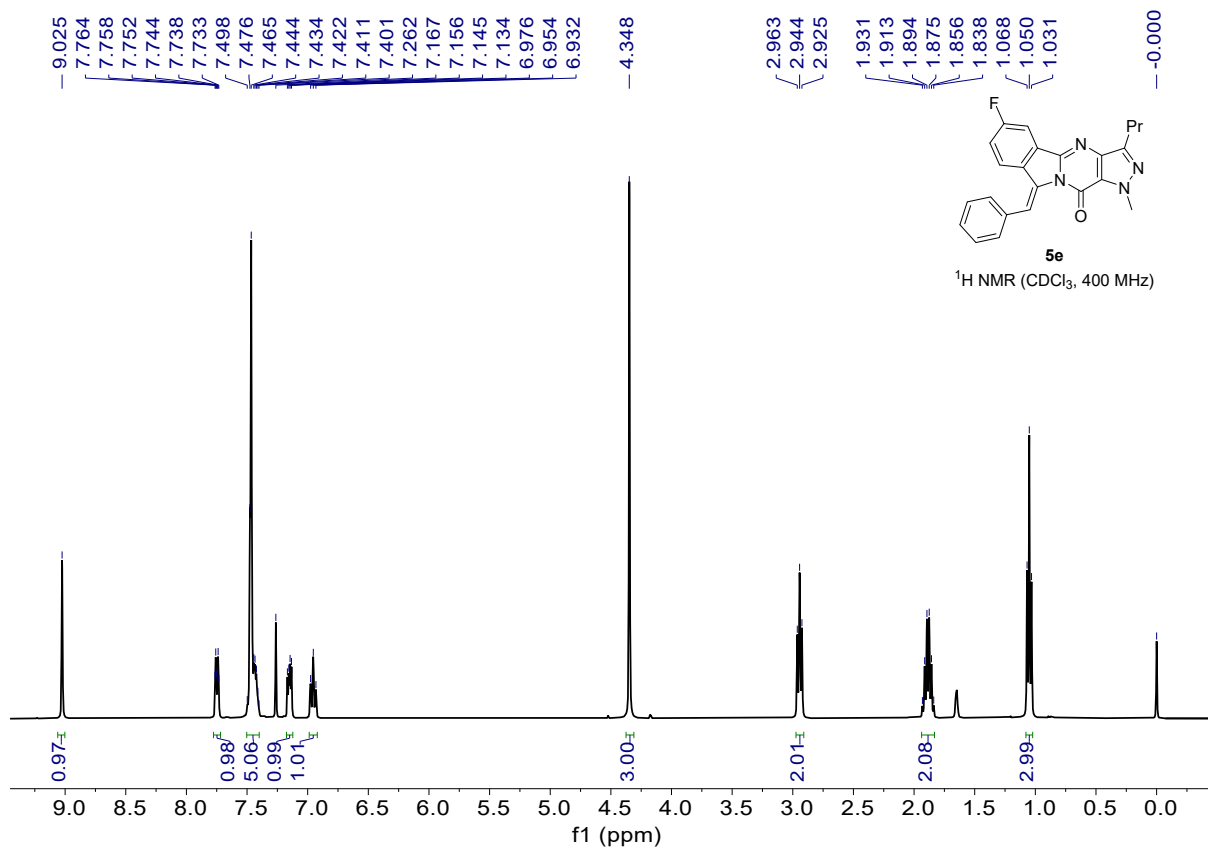
(E)-9-benzylidene-7-chloro-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (5c)



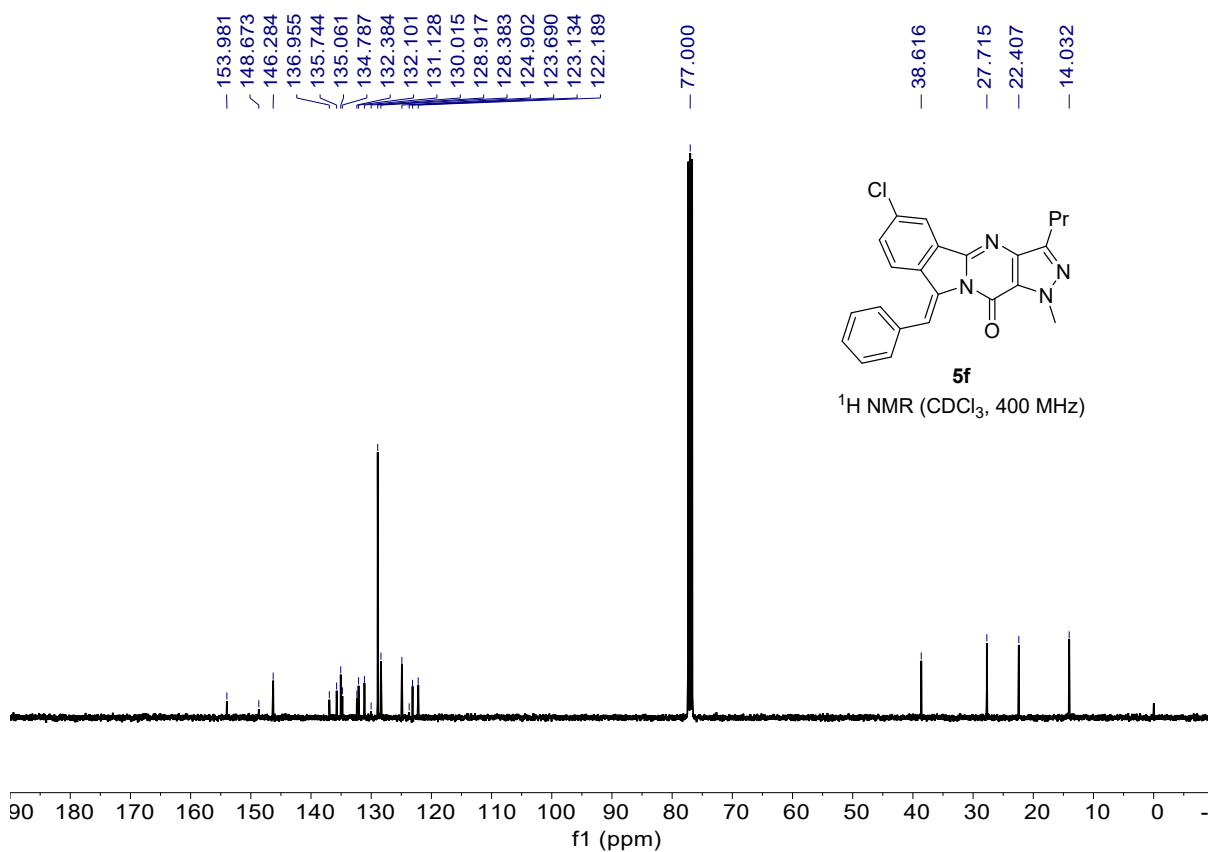
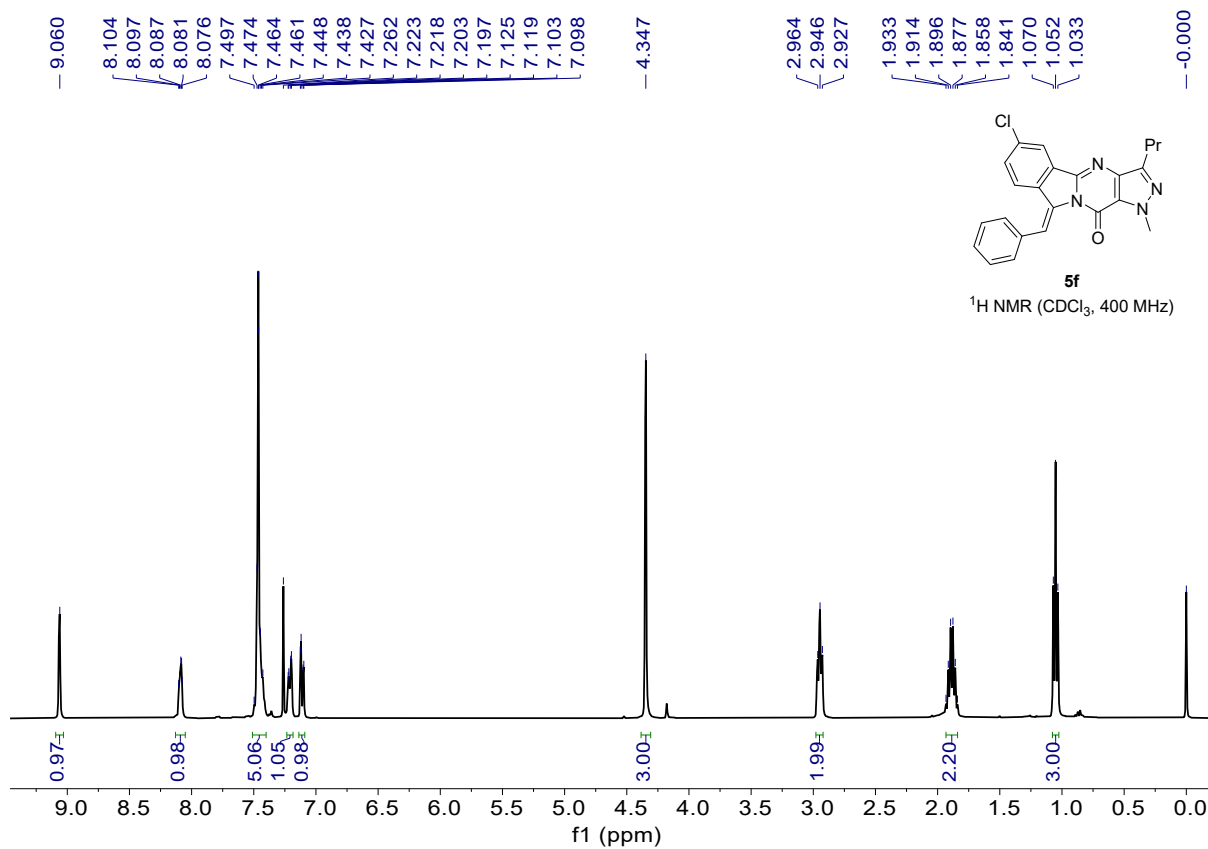
(E)-9-benzylidene-1,7-dimethyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (5d)



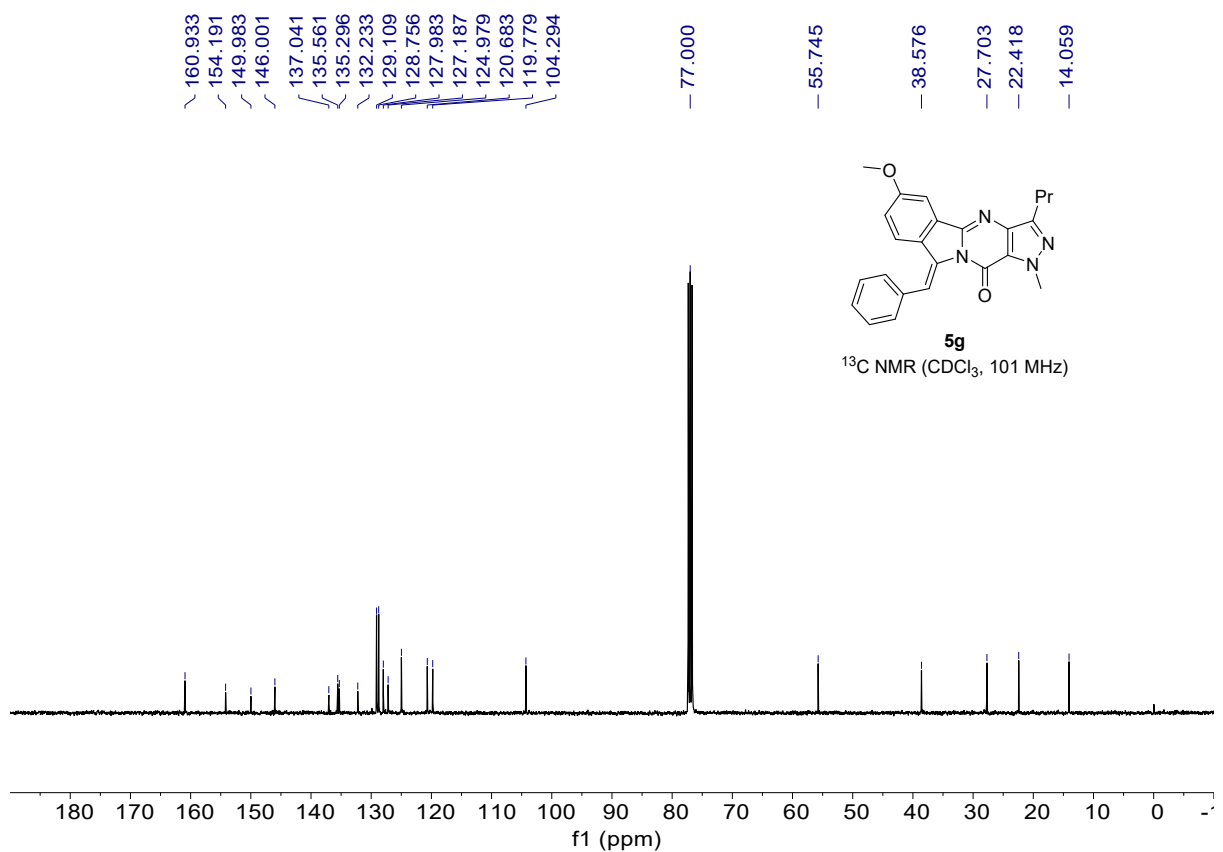
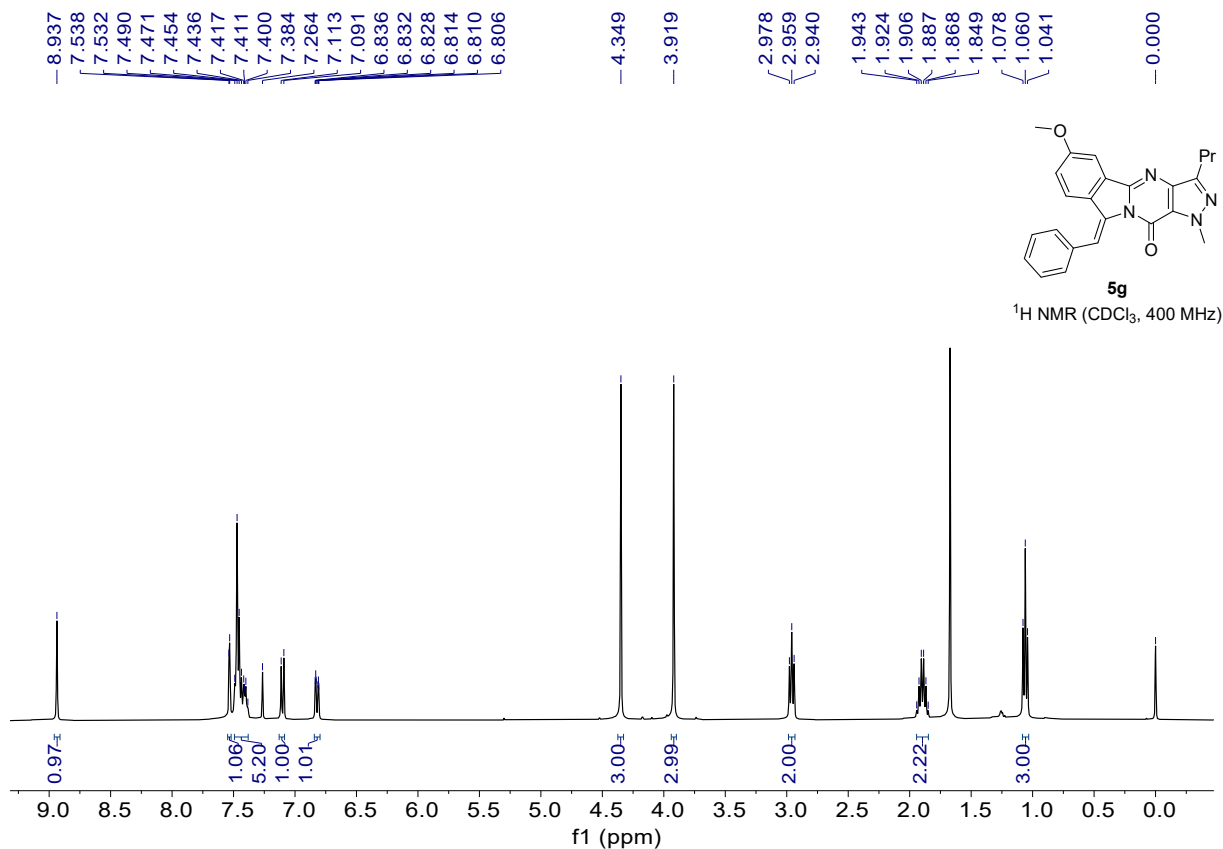
(E)-9-benzylidene-6-fluoro-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (5e)



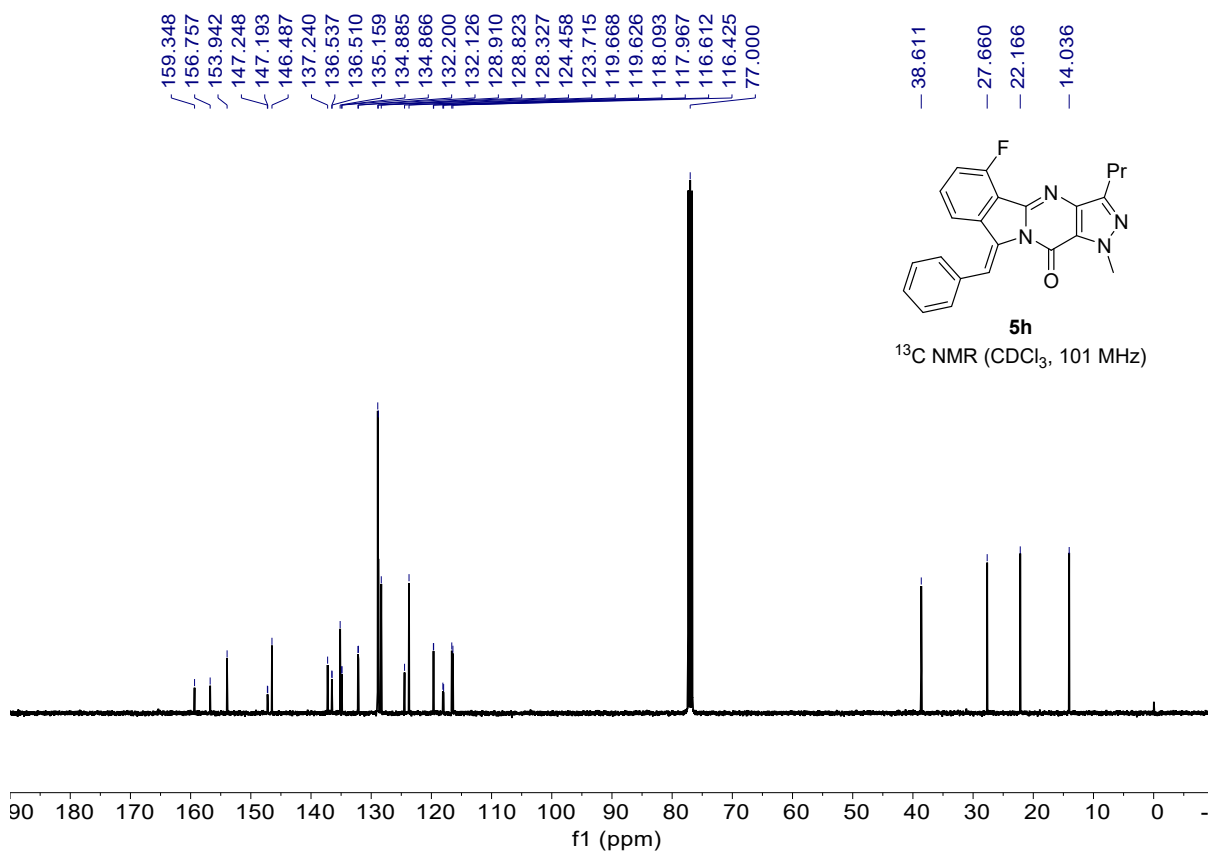
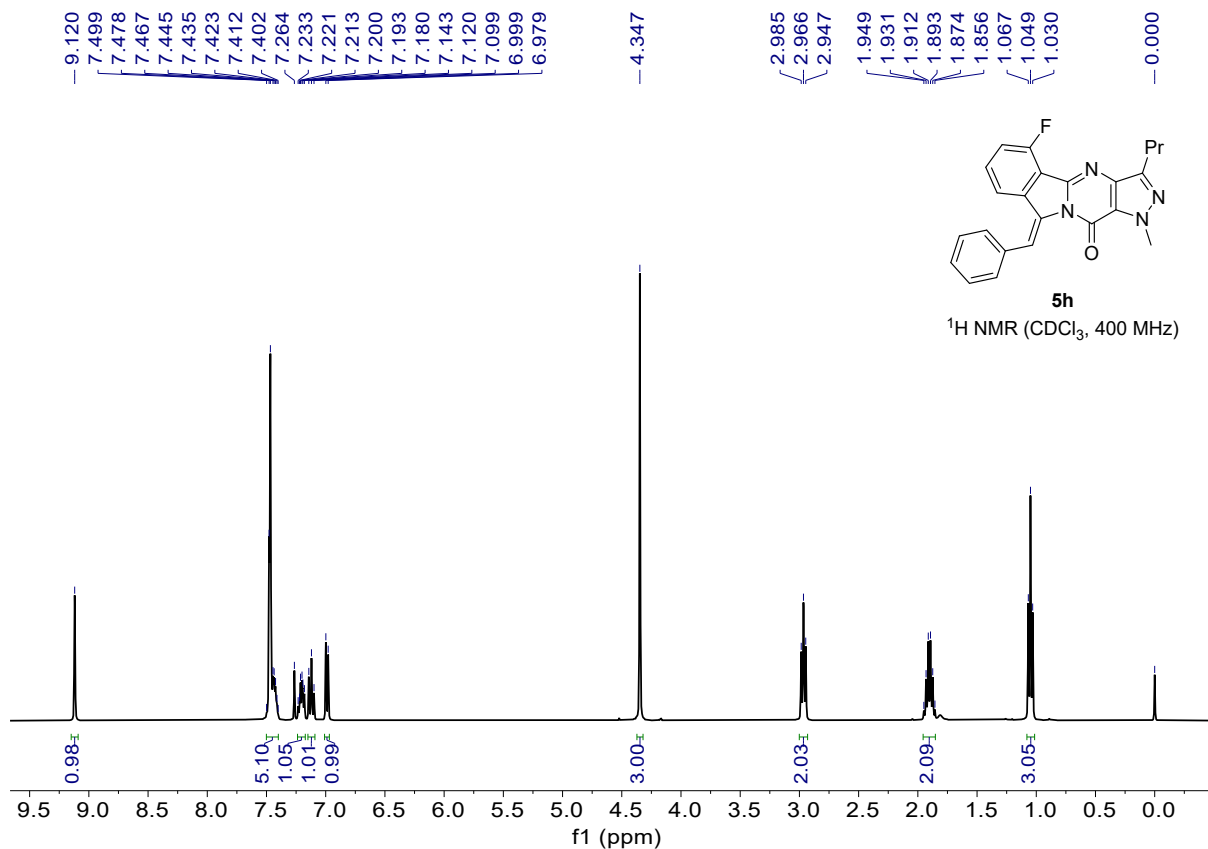
(E)-9-benzylidene-6-chloro-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (5f)



(E)-9-benzylidene-6-methoxy-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (5g)

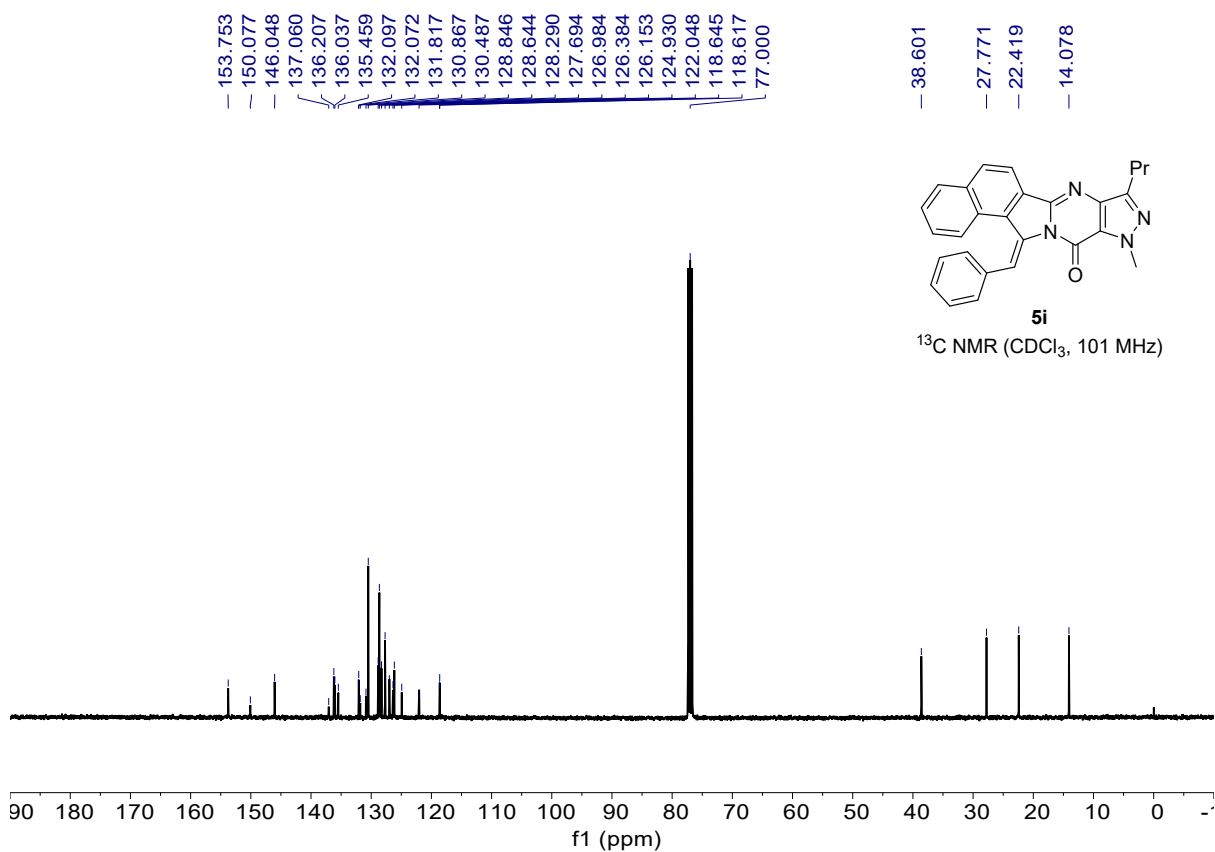
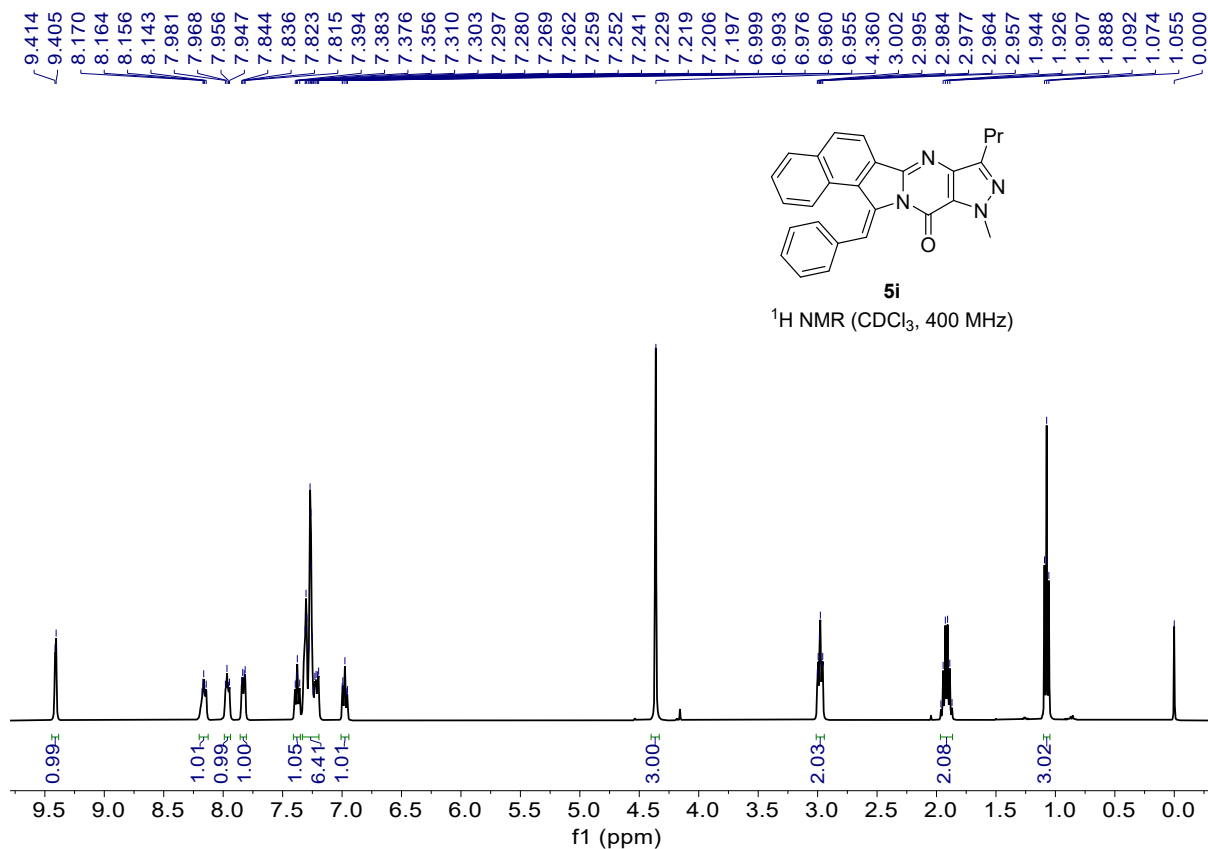


(E)-9-benzylidene-6-fluoro-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (5h)

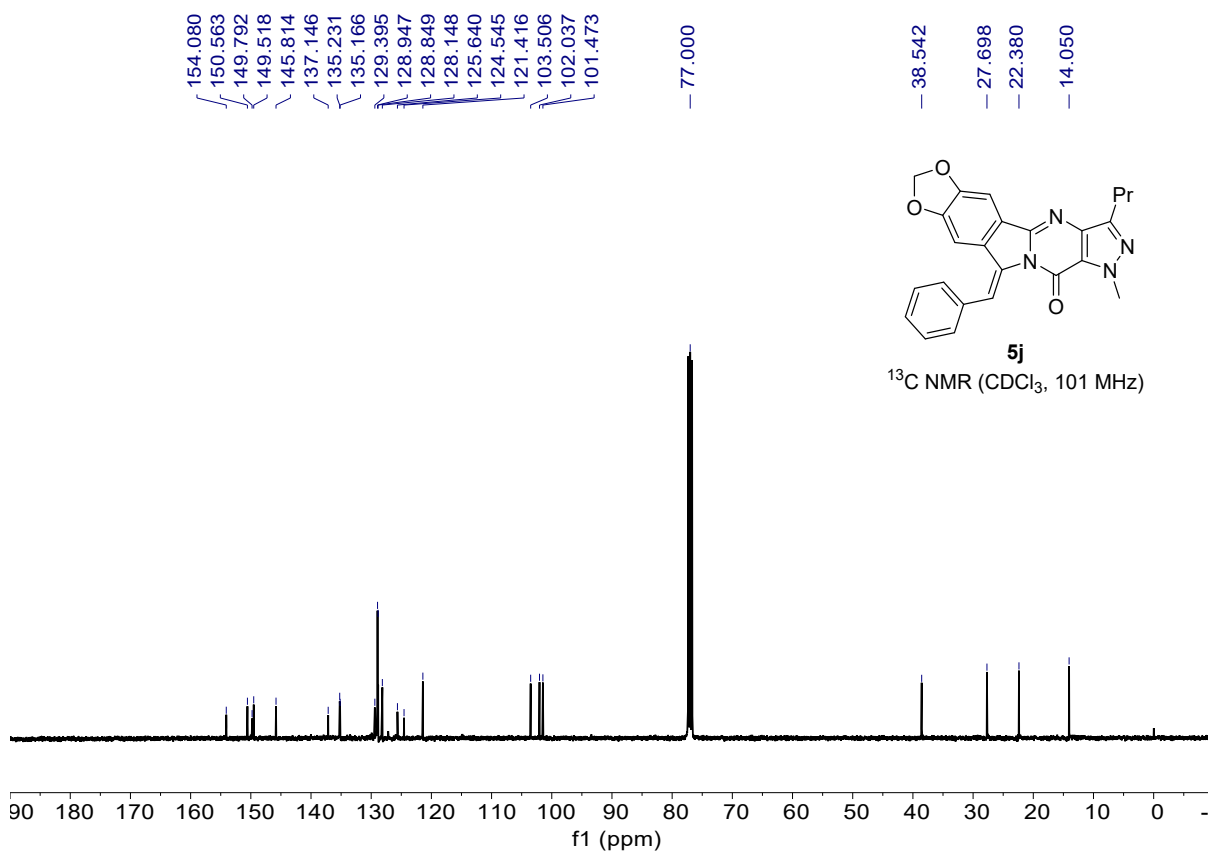
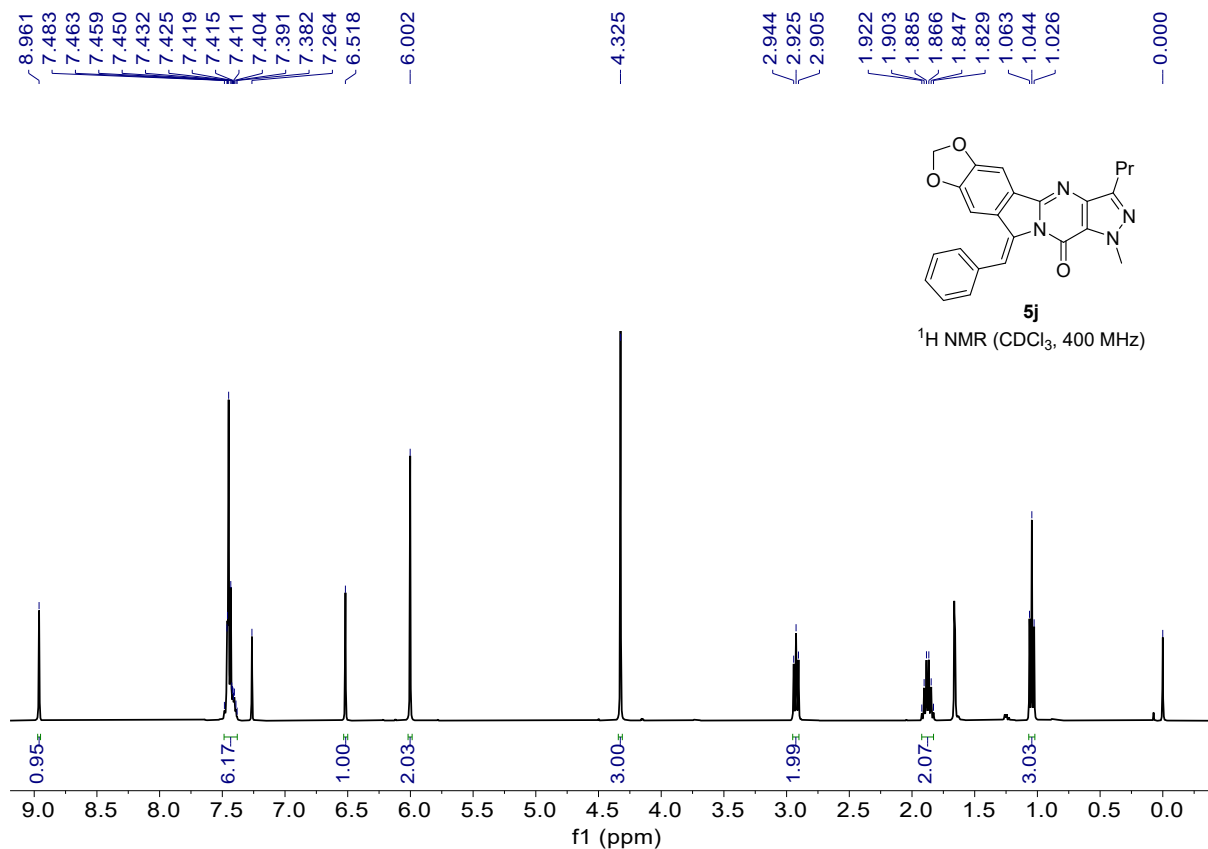


(E)-13-benzylidene-10-methyl-8-propyl-10,13-dihydro-11H-

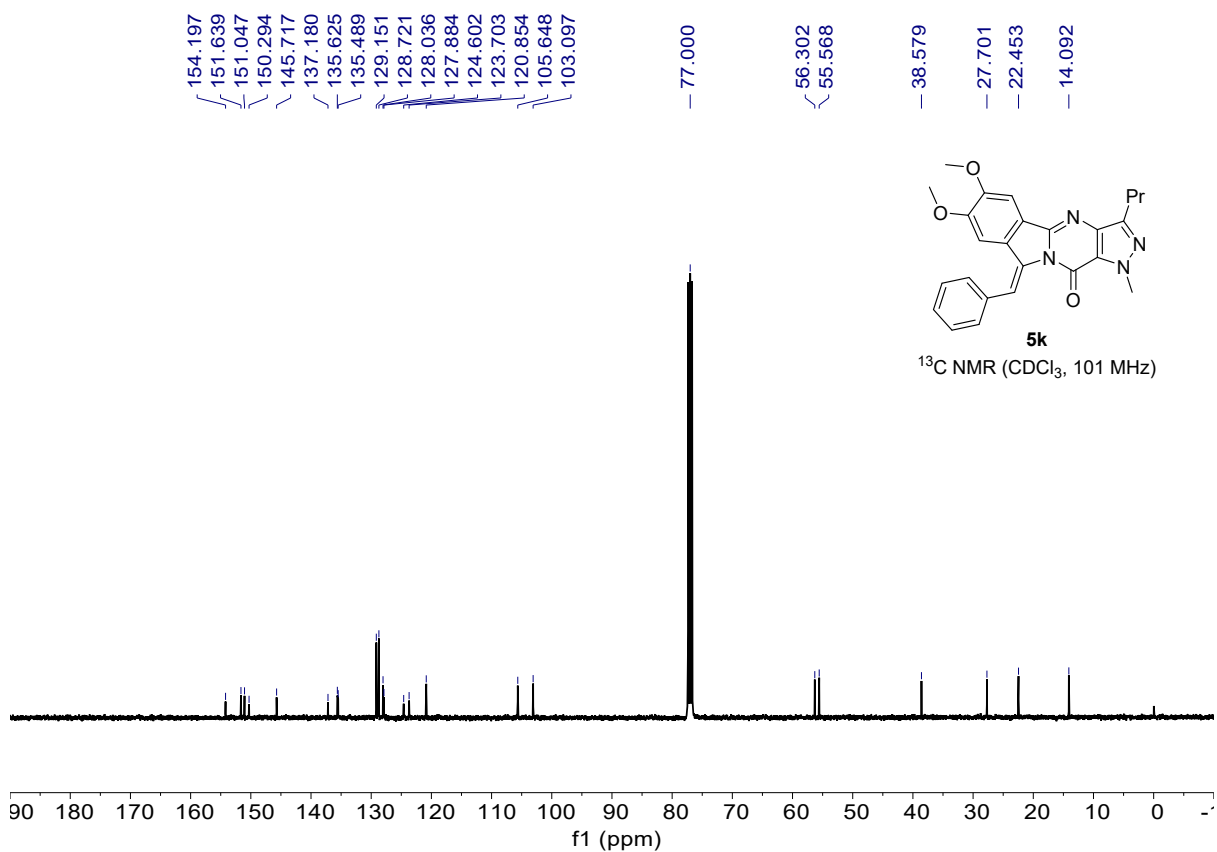
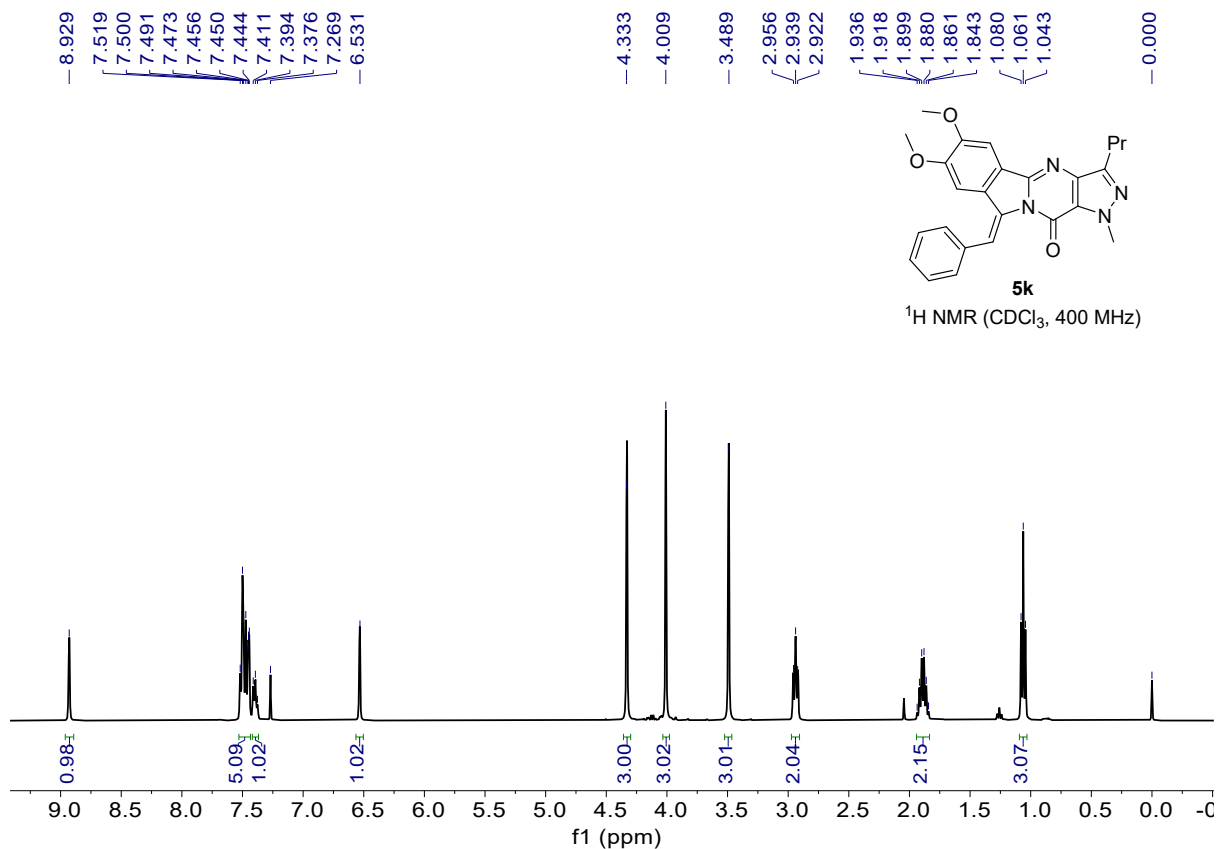
benzo[e]pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (5i)



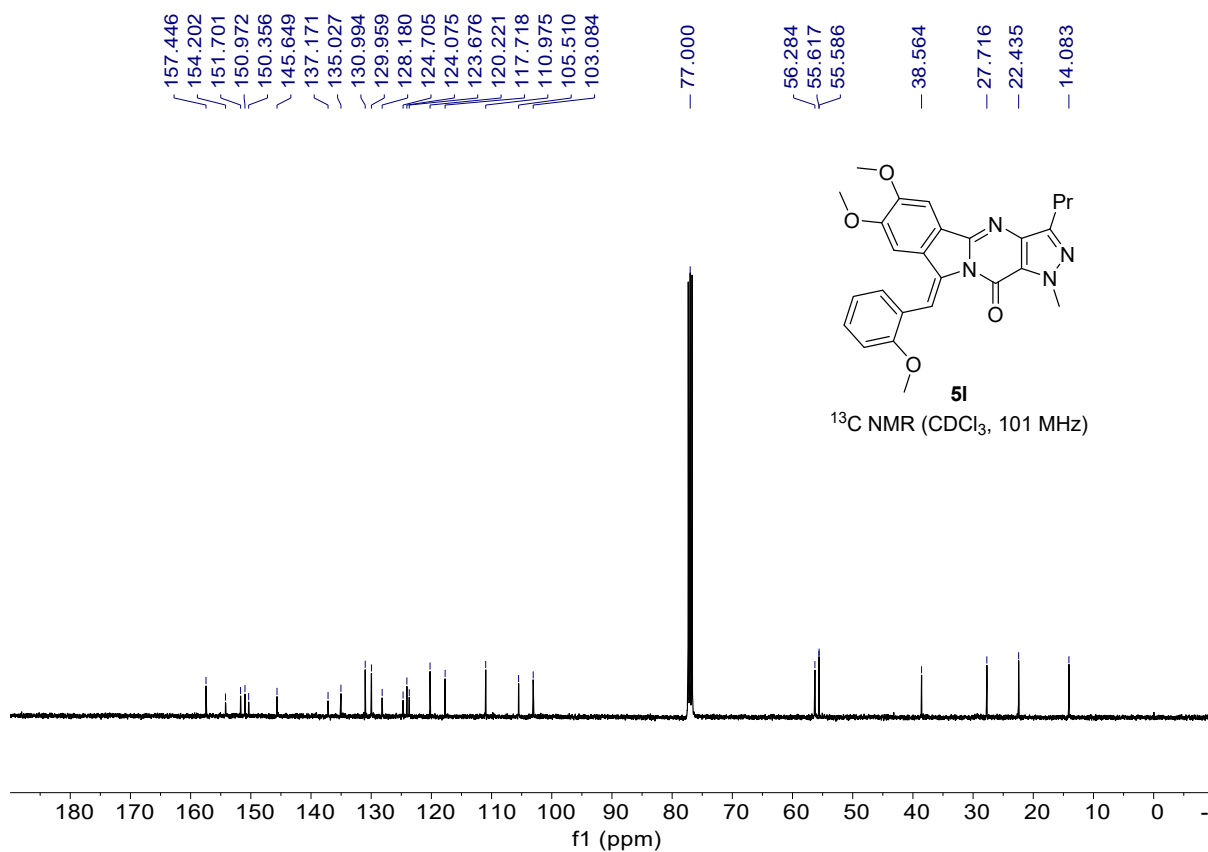
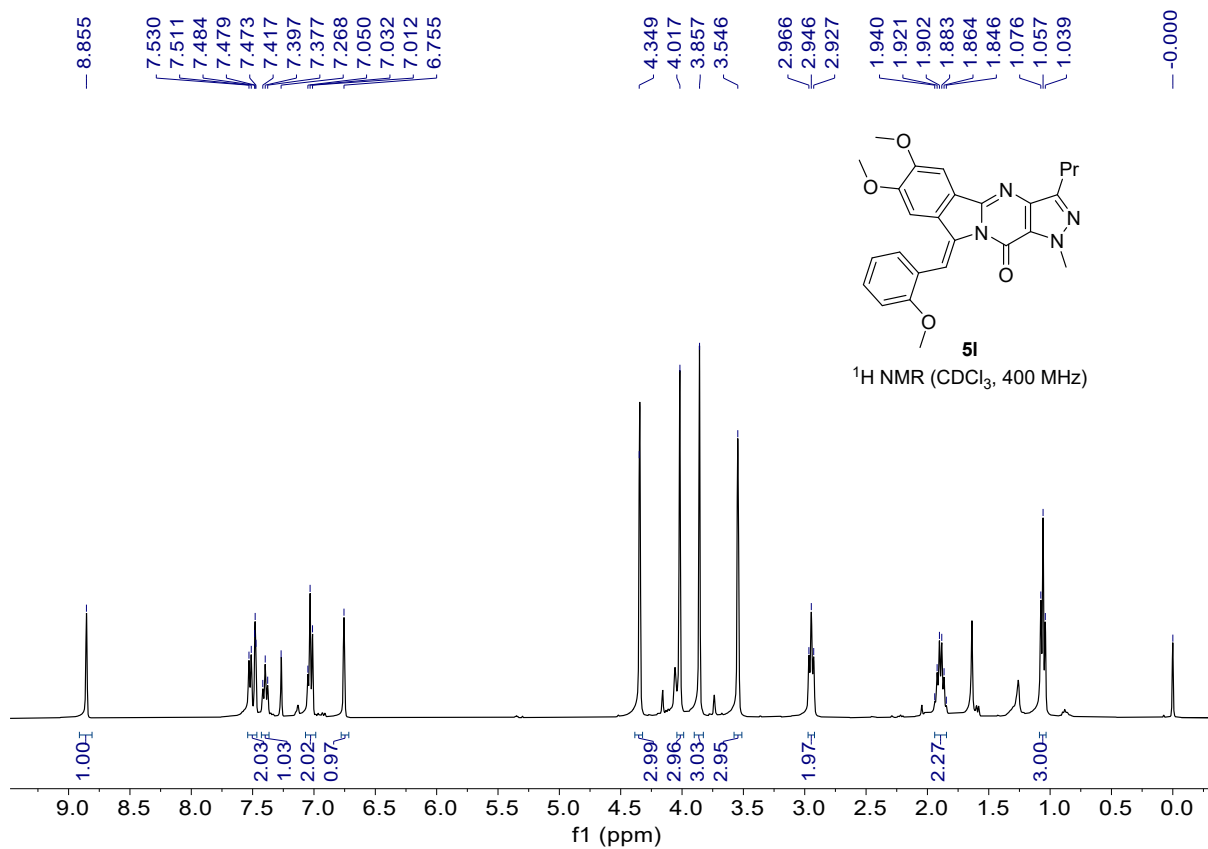
(E)-10-benzylidene-1-methyl-3-propyl-1,10-dihydro-12H-[1,3]dioxolo[4,5-f]pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-12-one (5j)



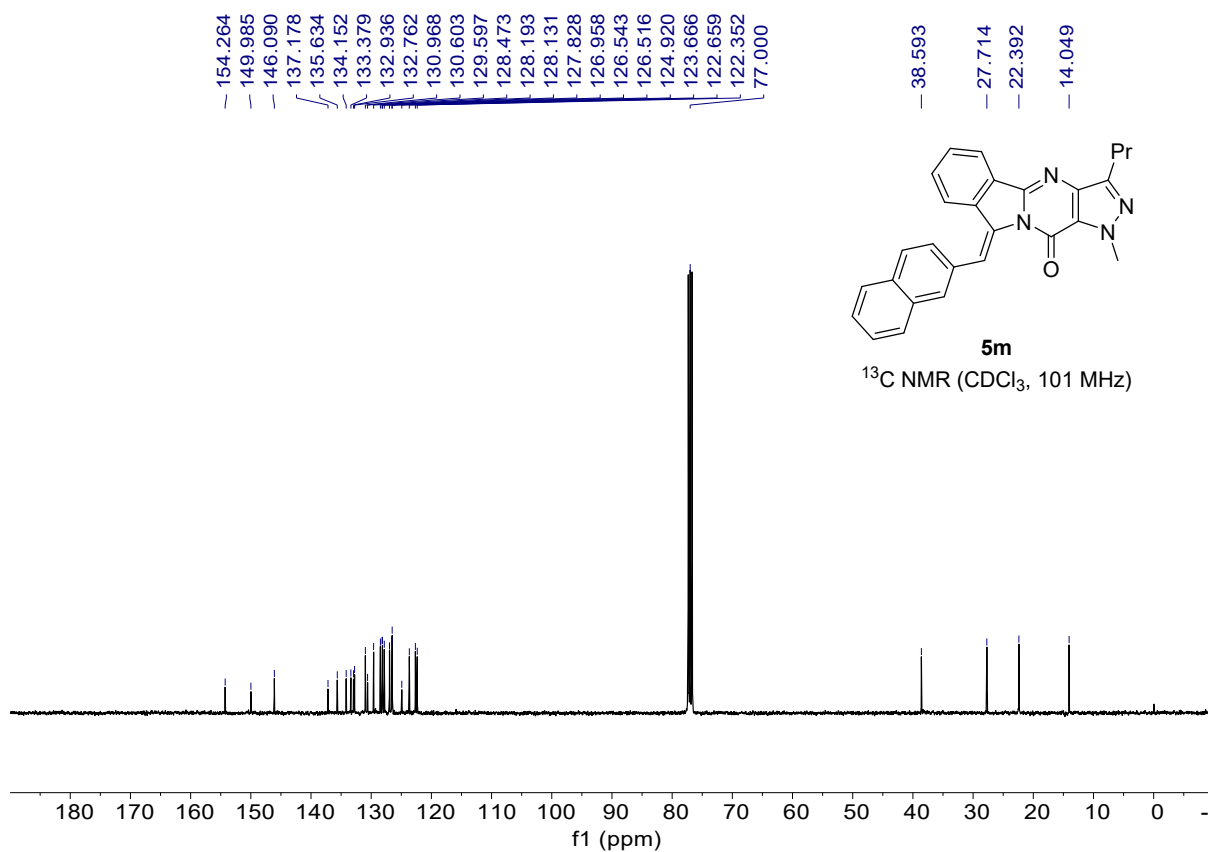
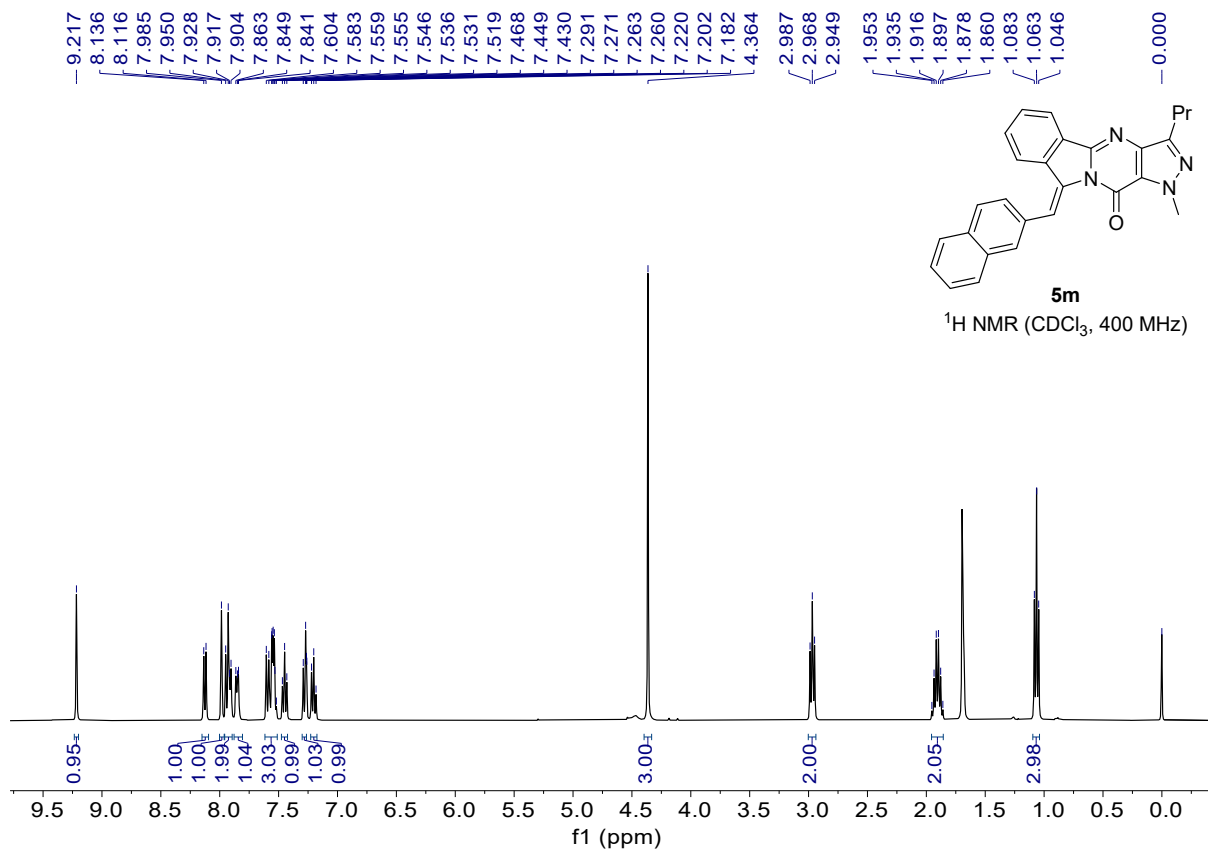
(E)-9-benzylidene-6,7-dimethoxy-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (5k)



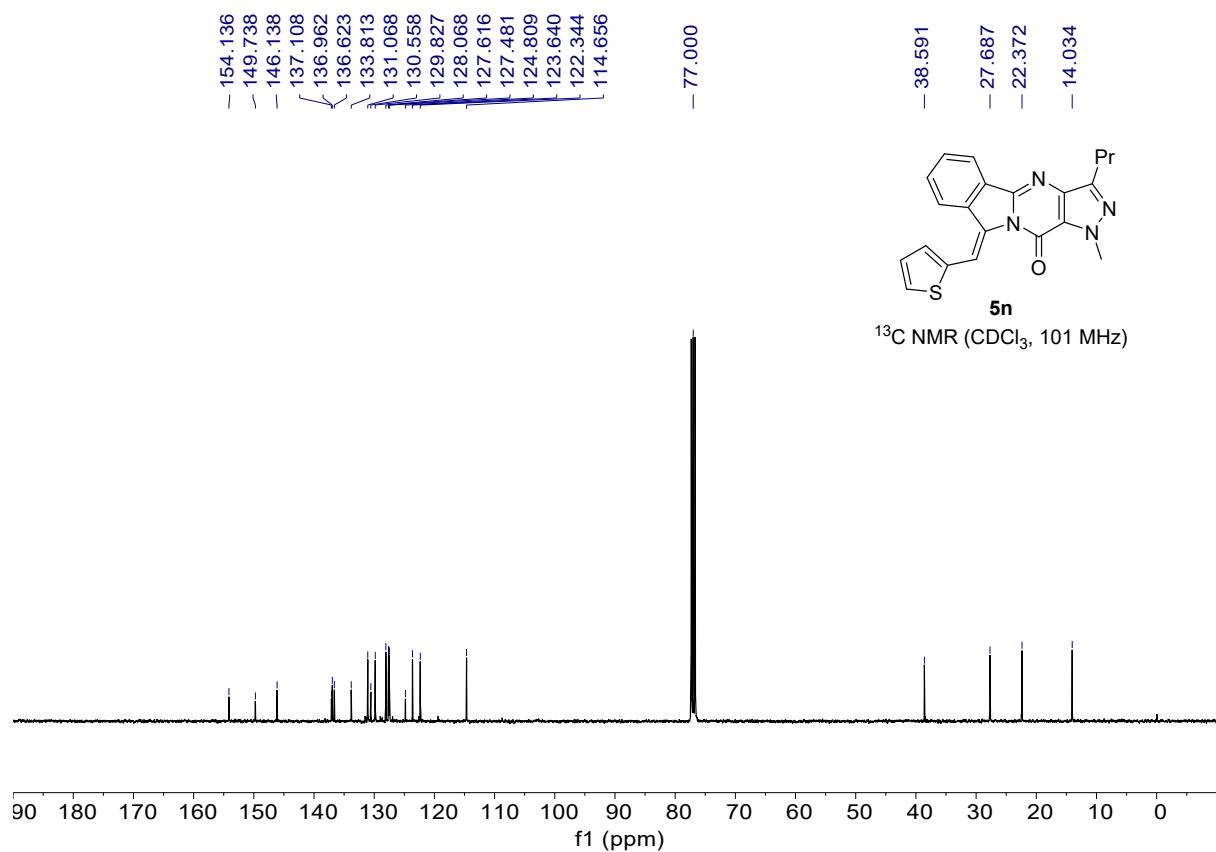
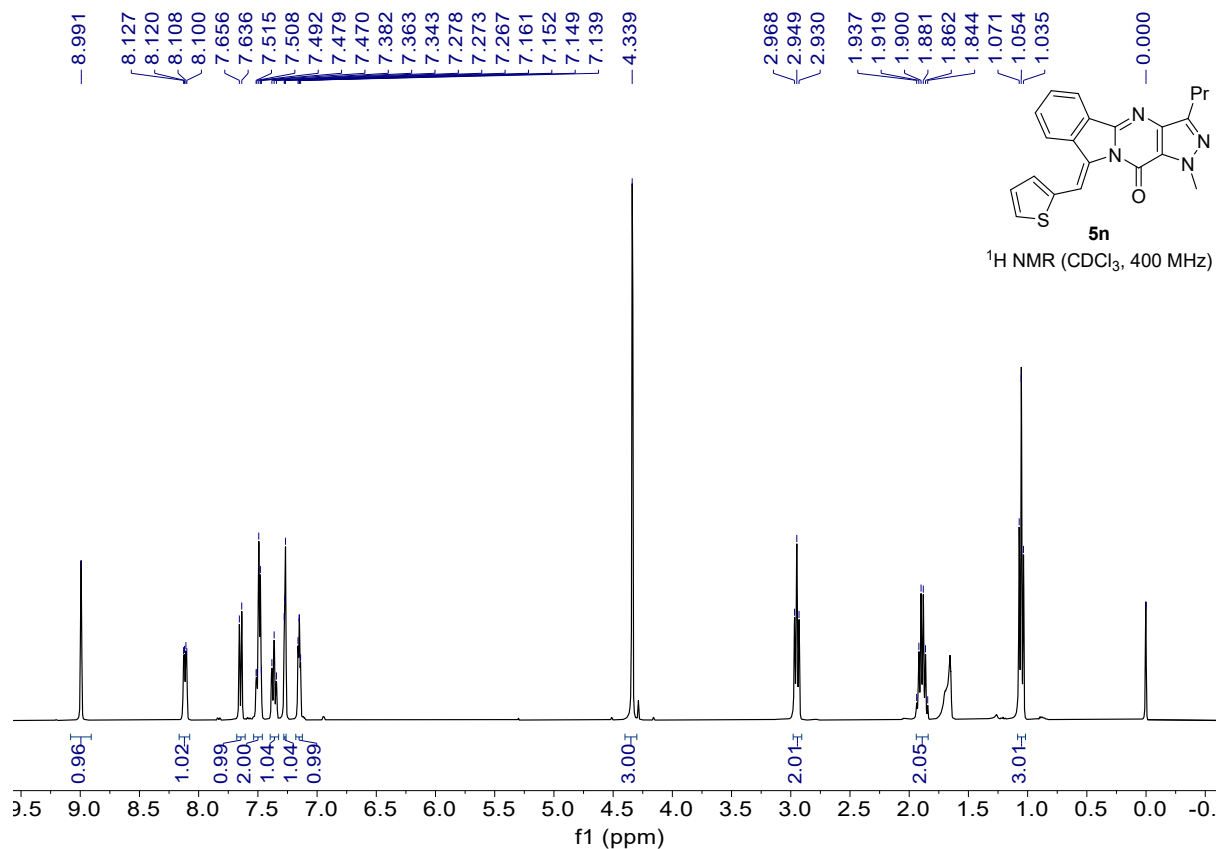
(E)-6,7-dimethoxy-9-(2-methoxybenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (5I)



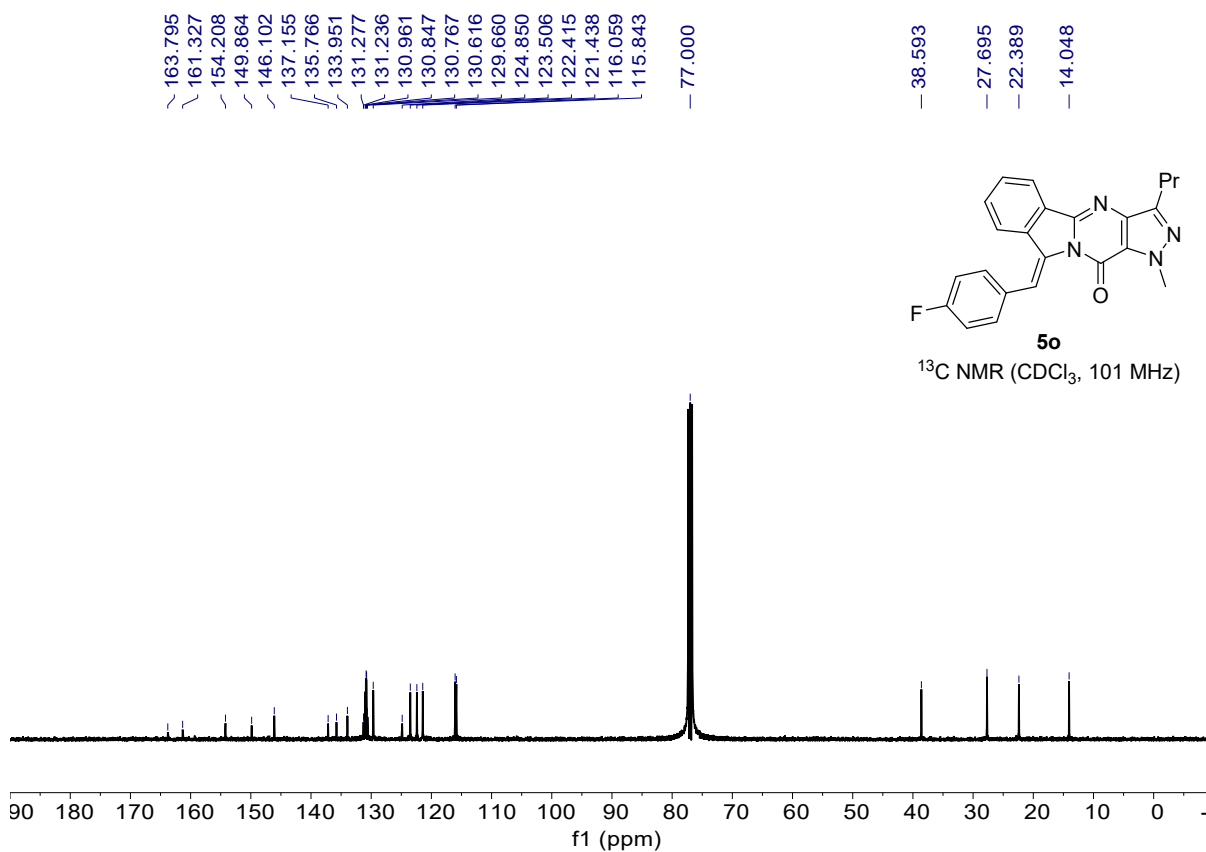
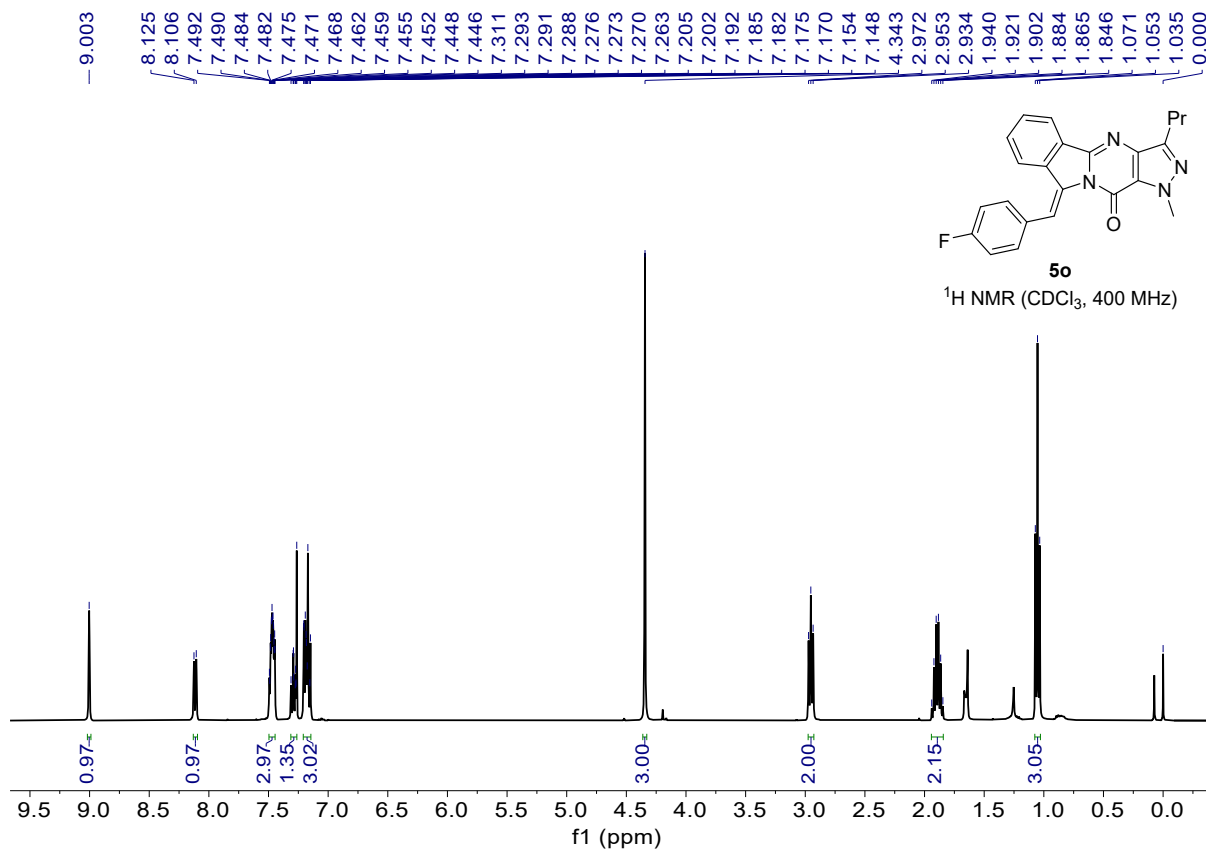
(E)-1-methyl-9-(naphthalen-2-ylmethylene)-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (5m)



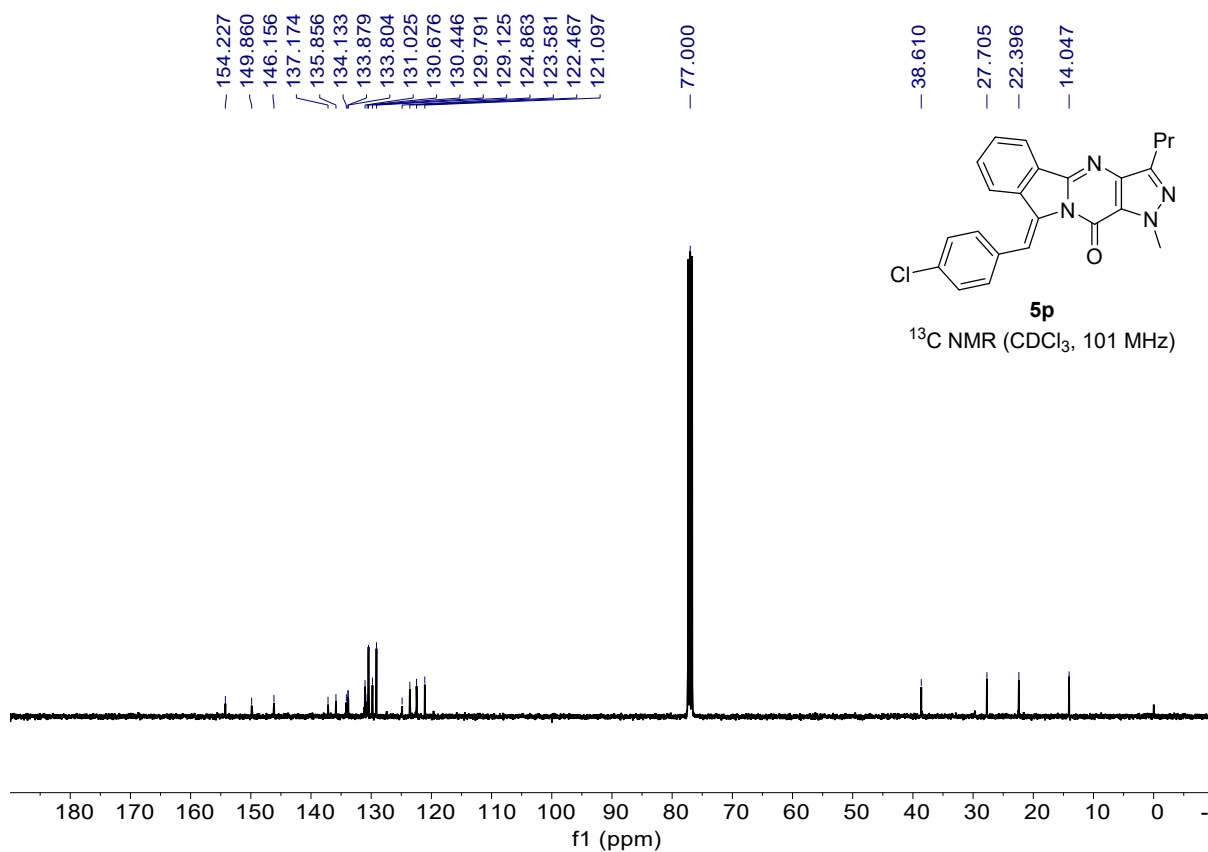
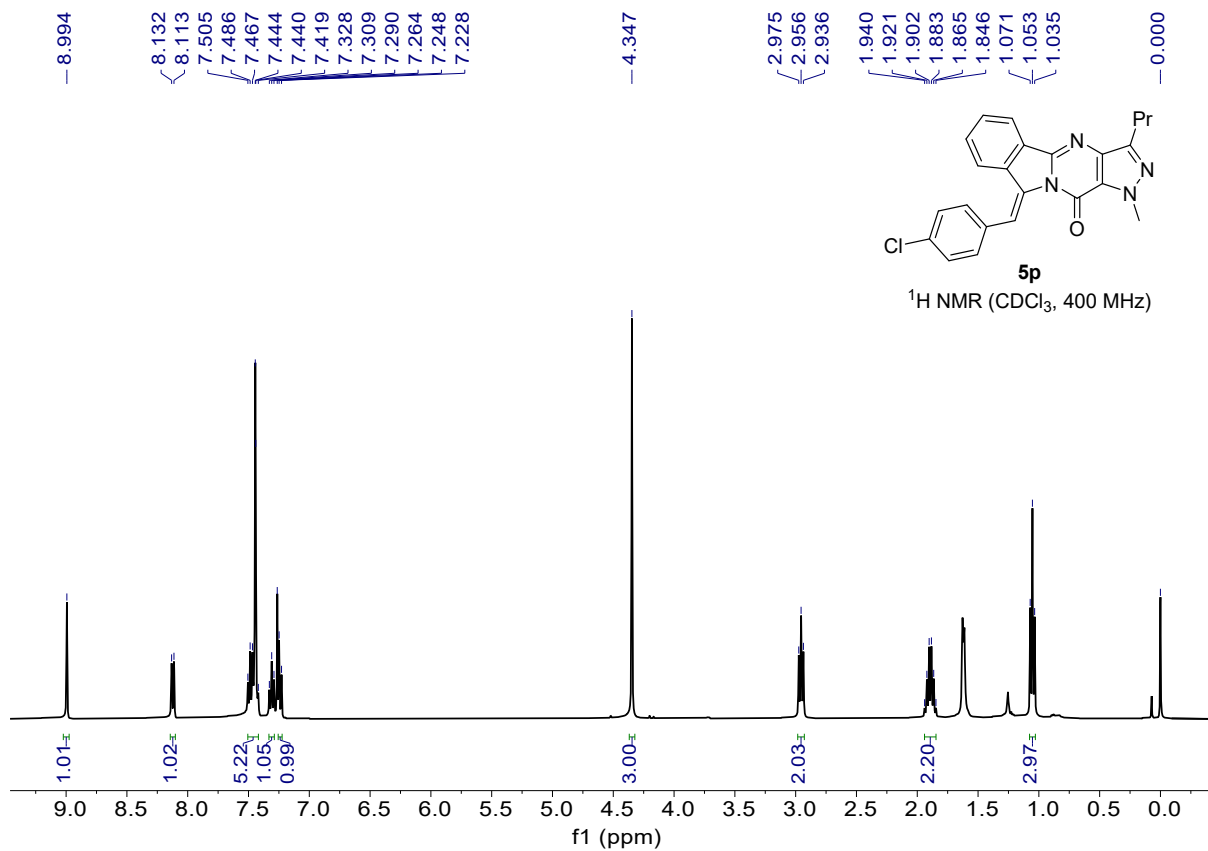
(E)-1-methyl-3-propyl-9-(thiophen-2-ylmethylene)-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (5n)



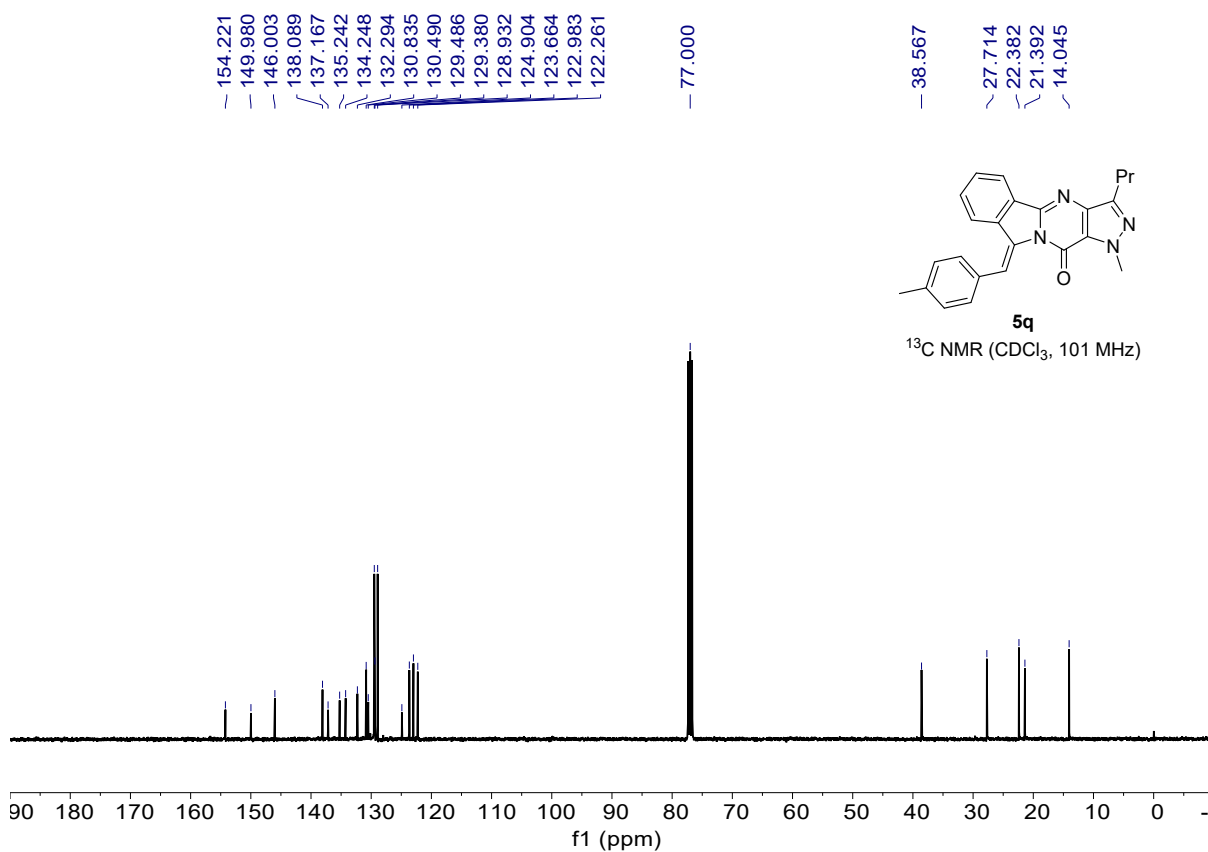
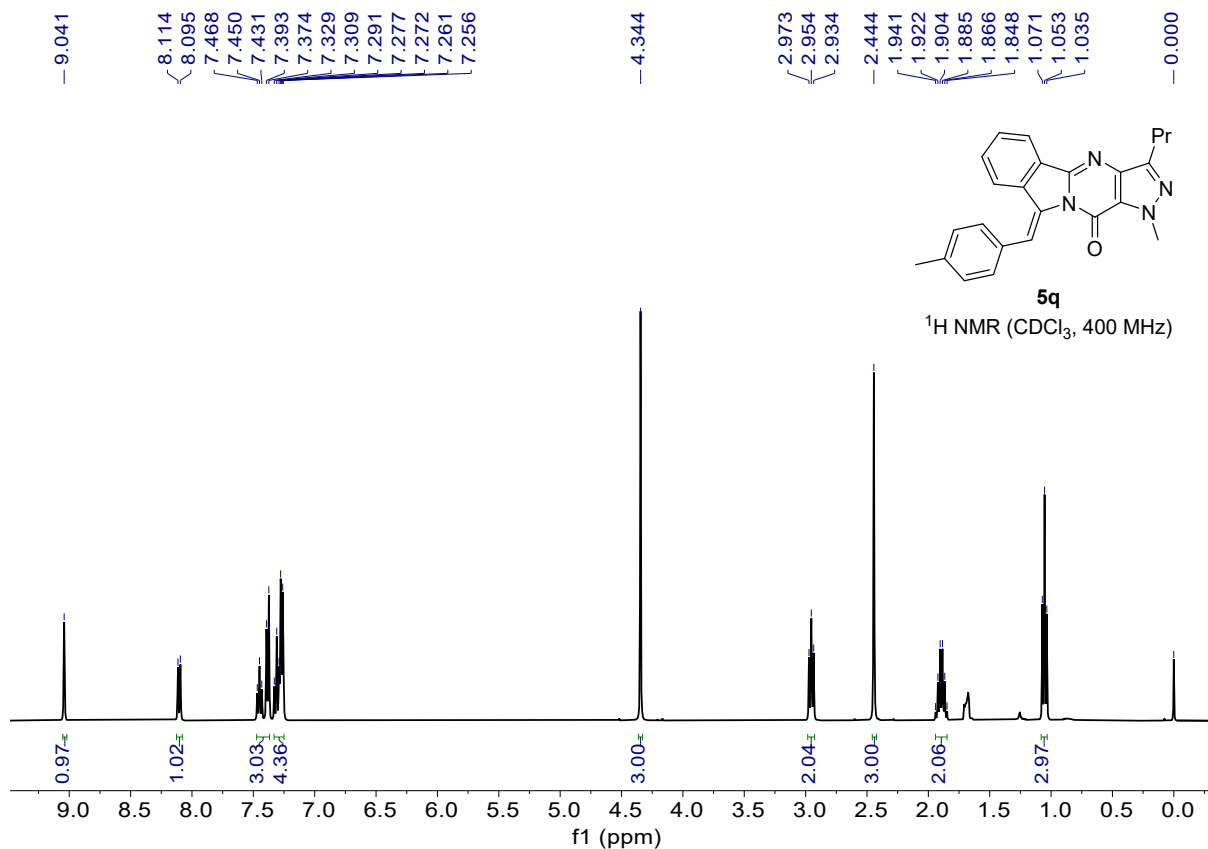
(E)-9-(4-fluorobenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-*a*]isoindol-11-one (5o)



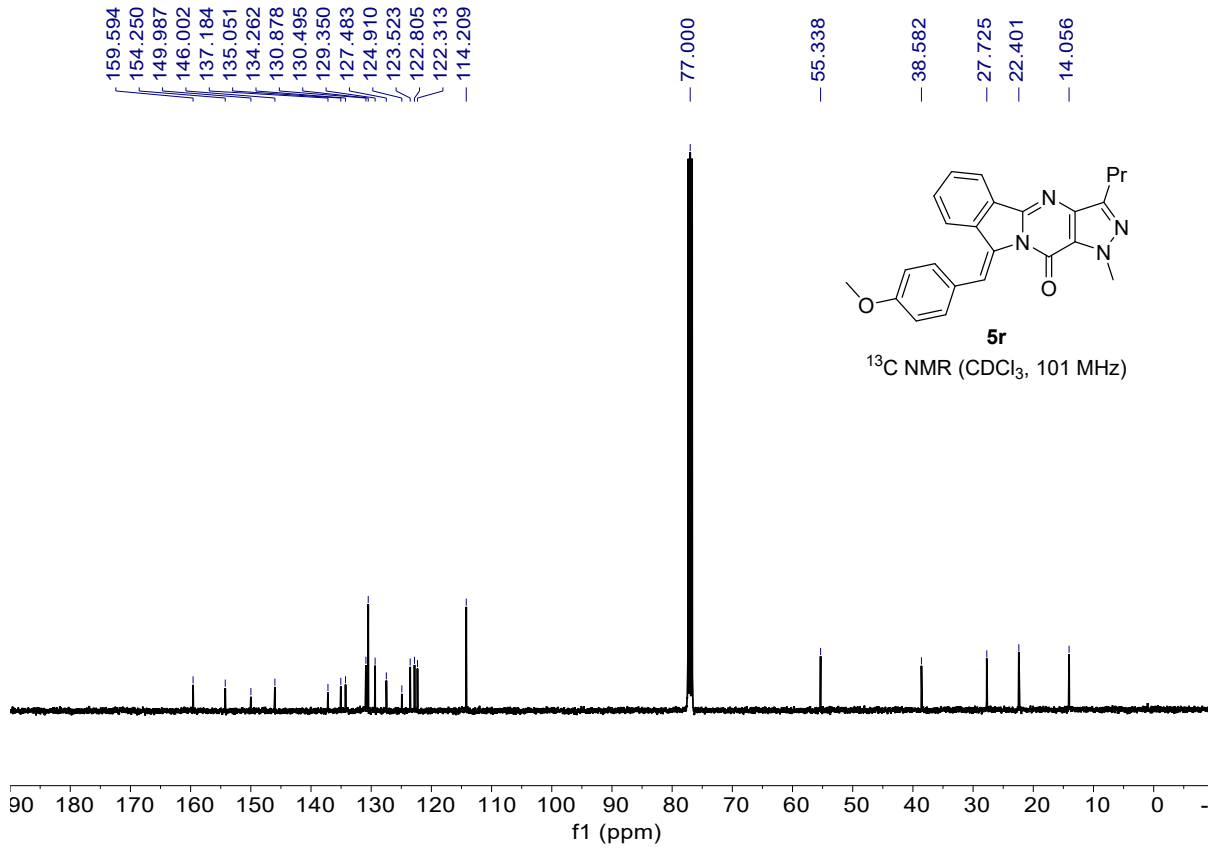
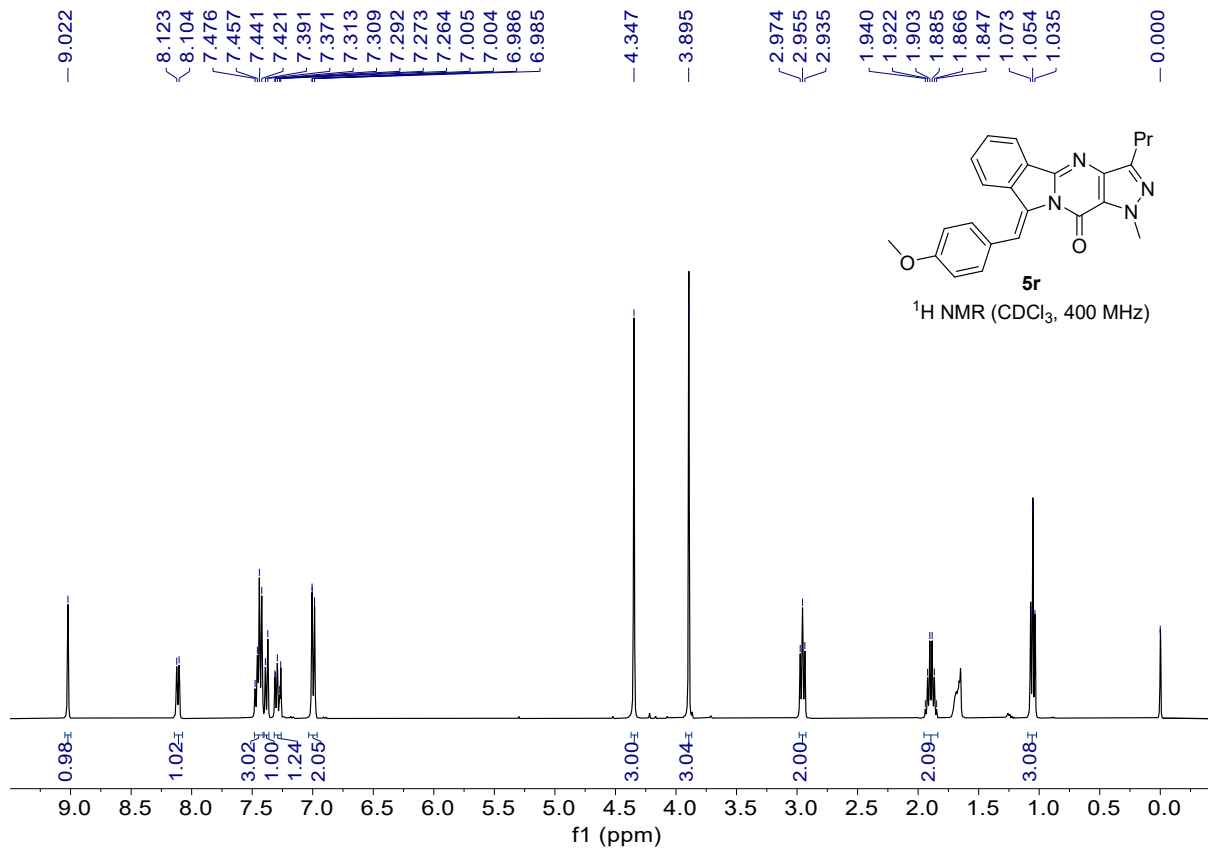
(E)-9-(4-chlorobenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (5p)



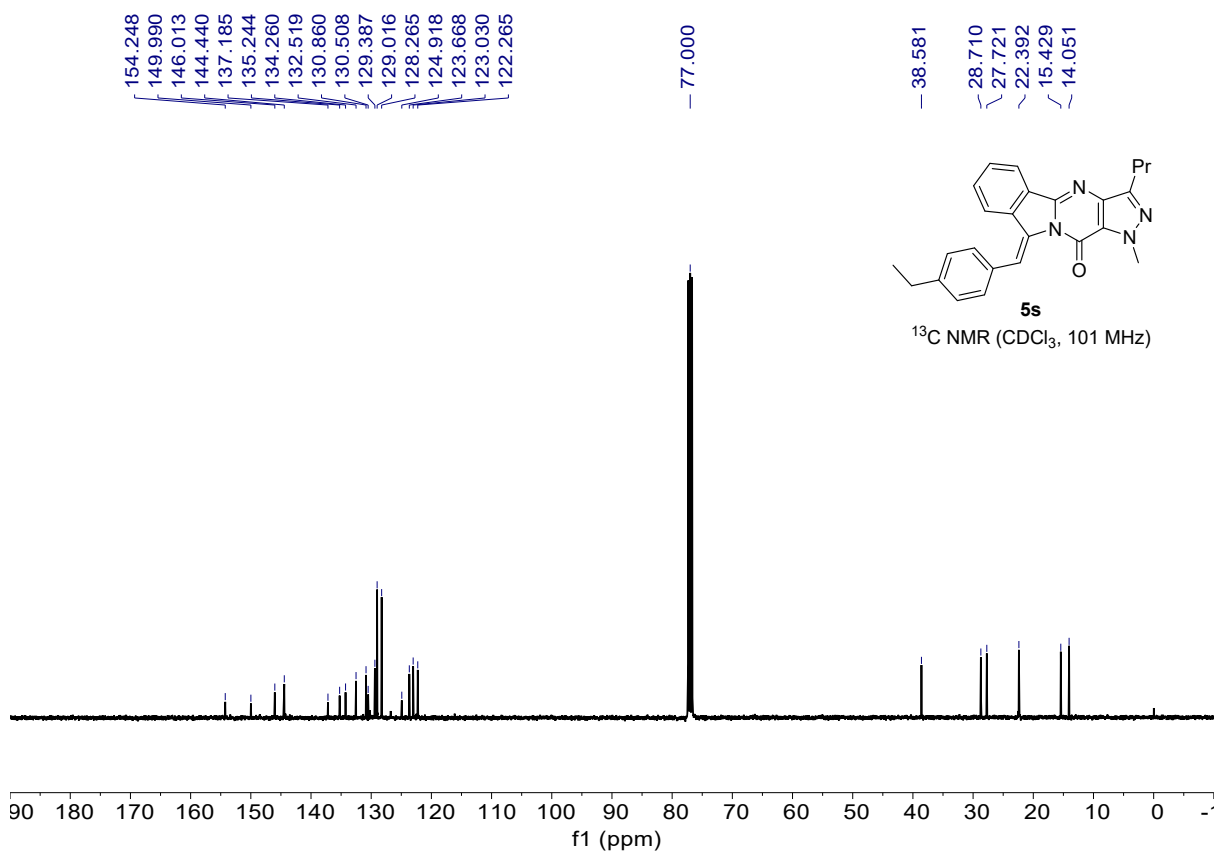
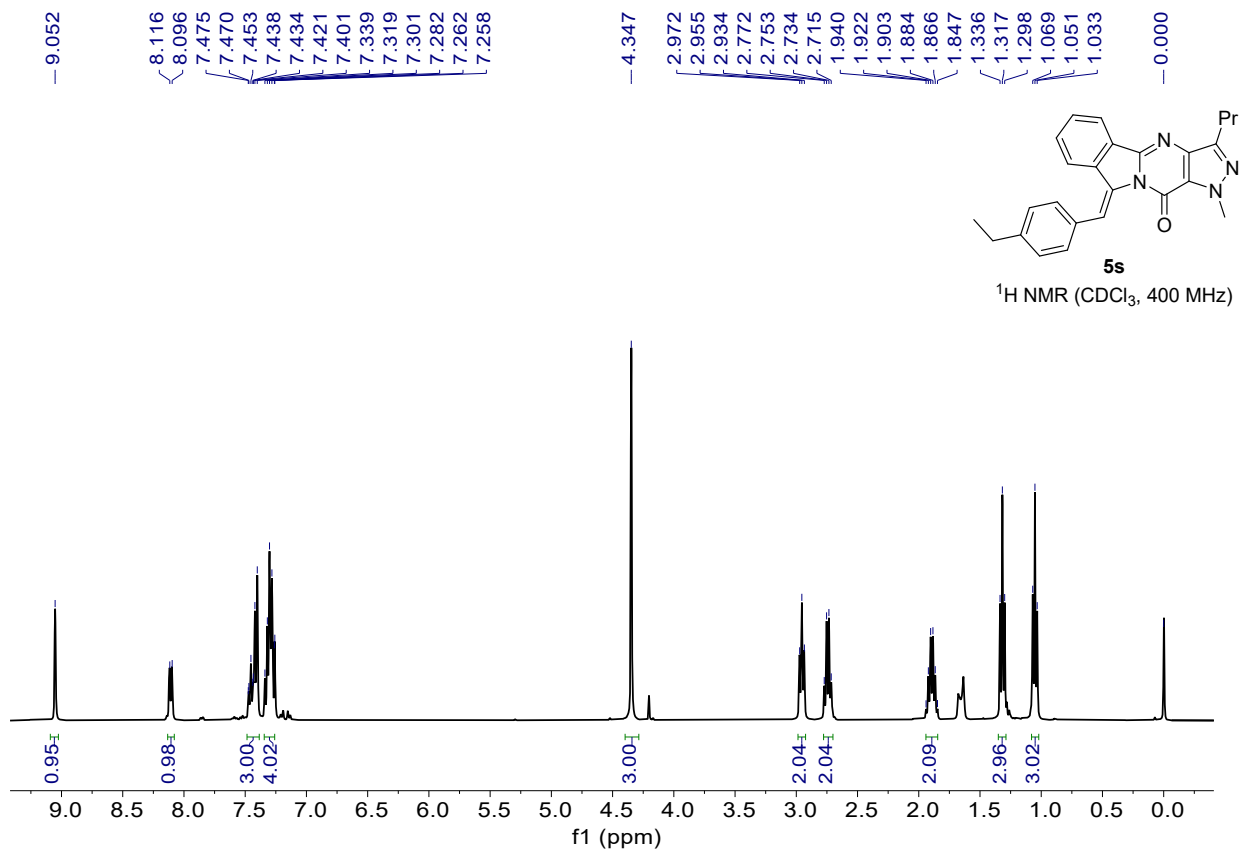
(E)-1-methyl-9-(4-methylbenzylidene)-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-*a*]isoindol-11-one (5q)



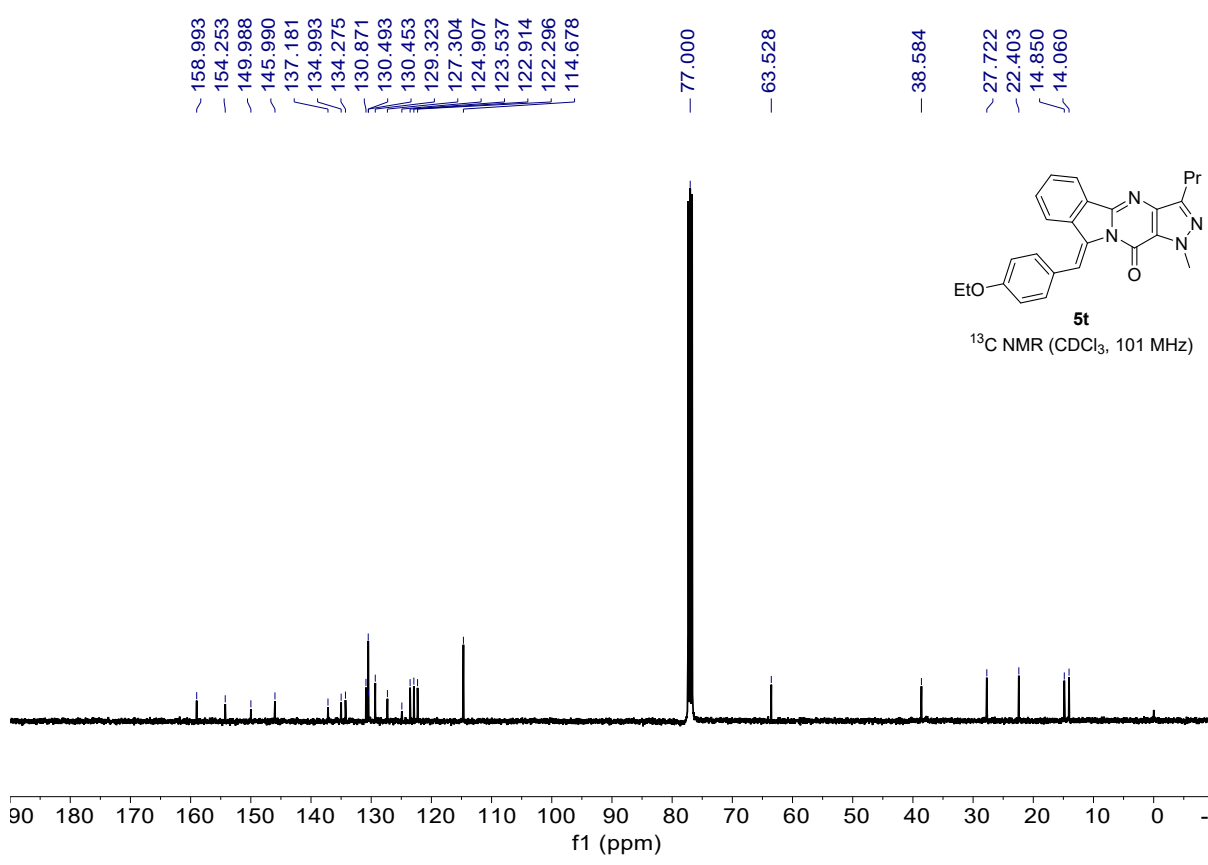
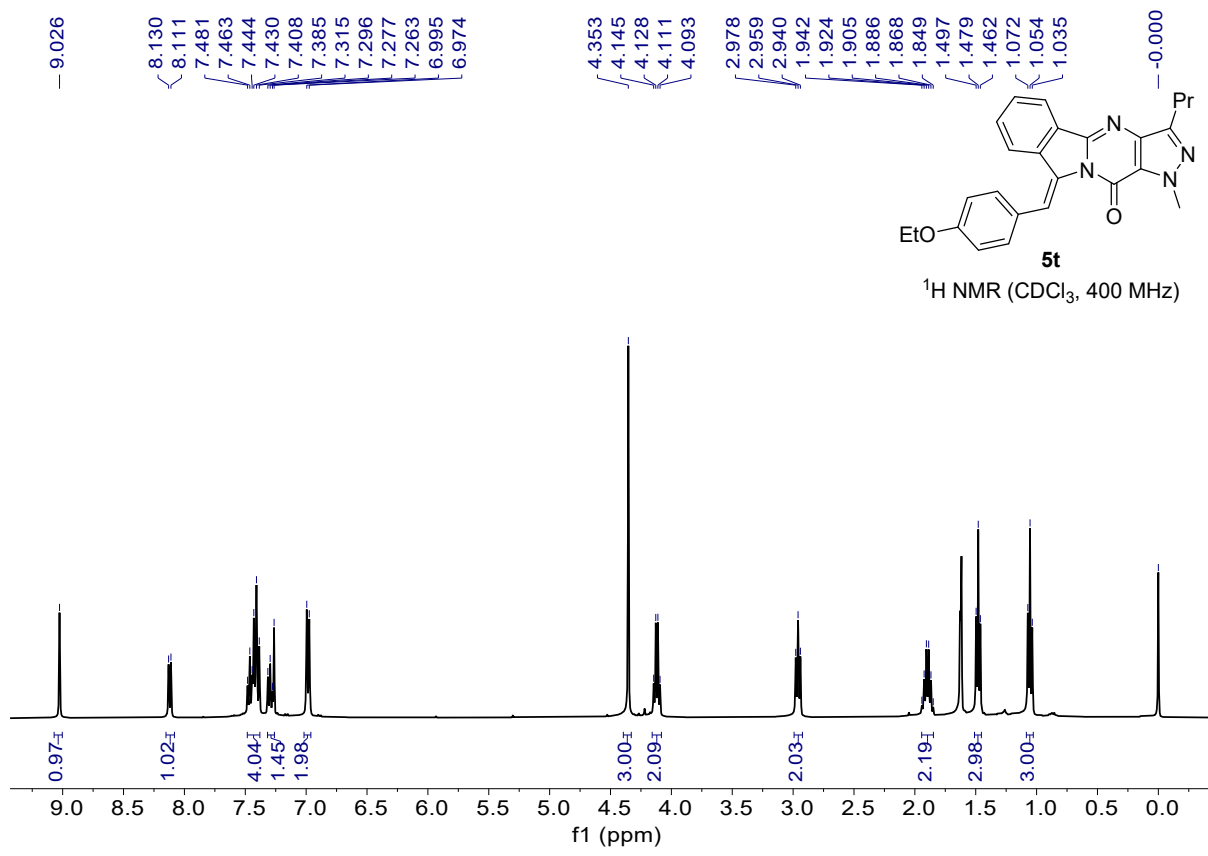
(E)-9-(4-methoxybenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (5r)



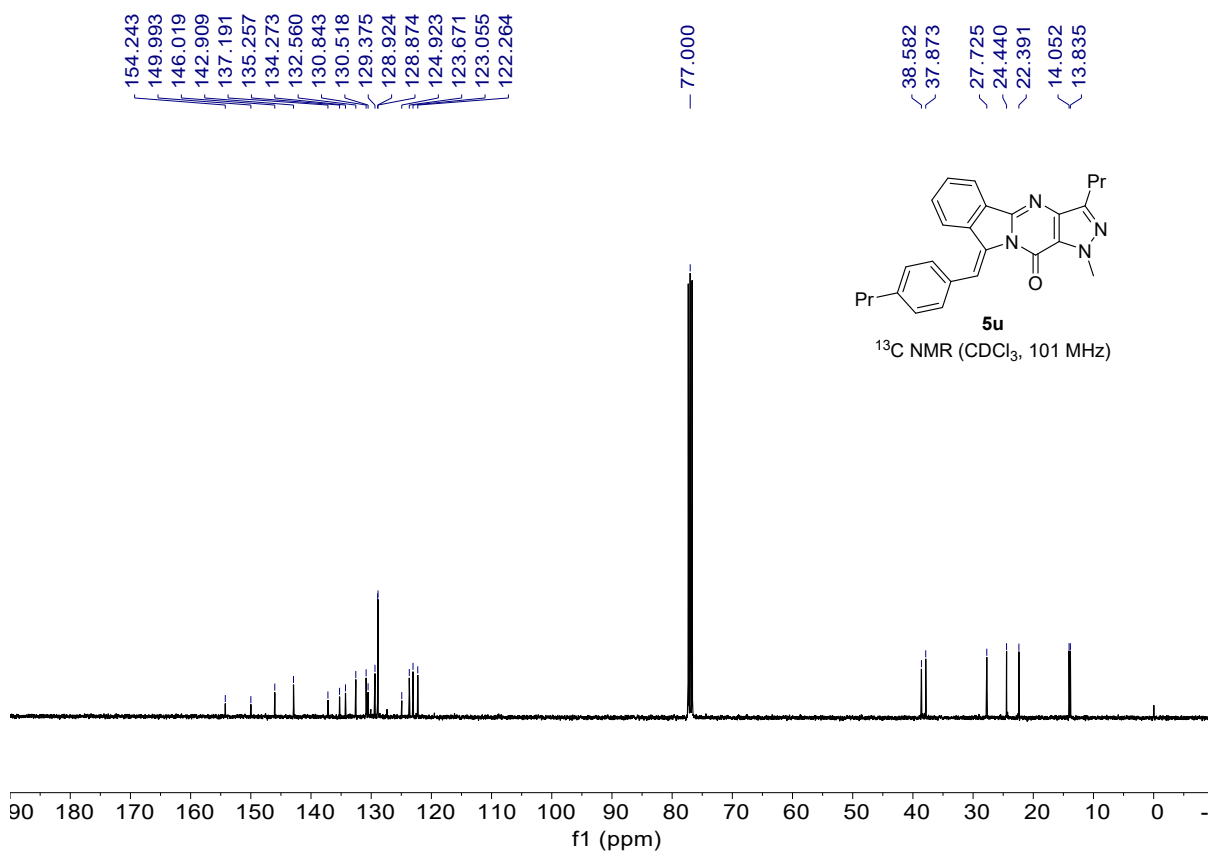
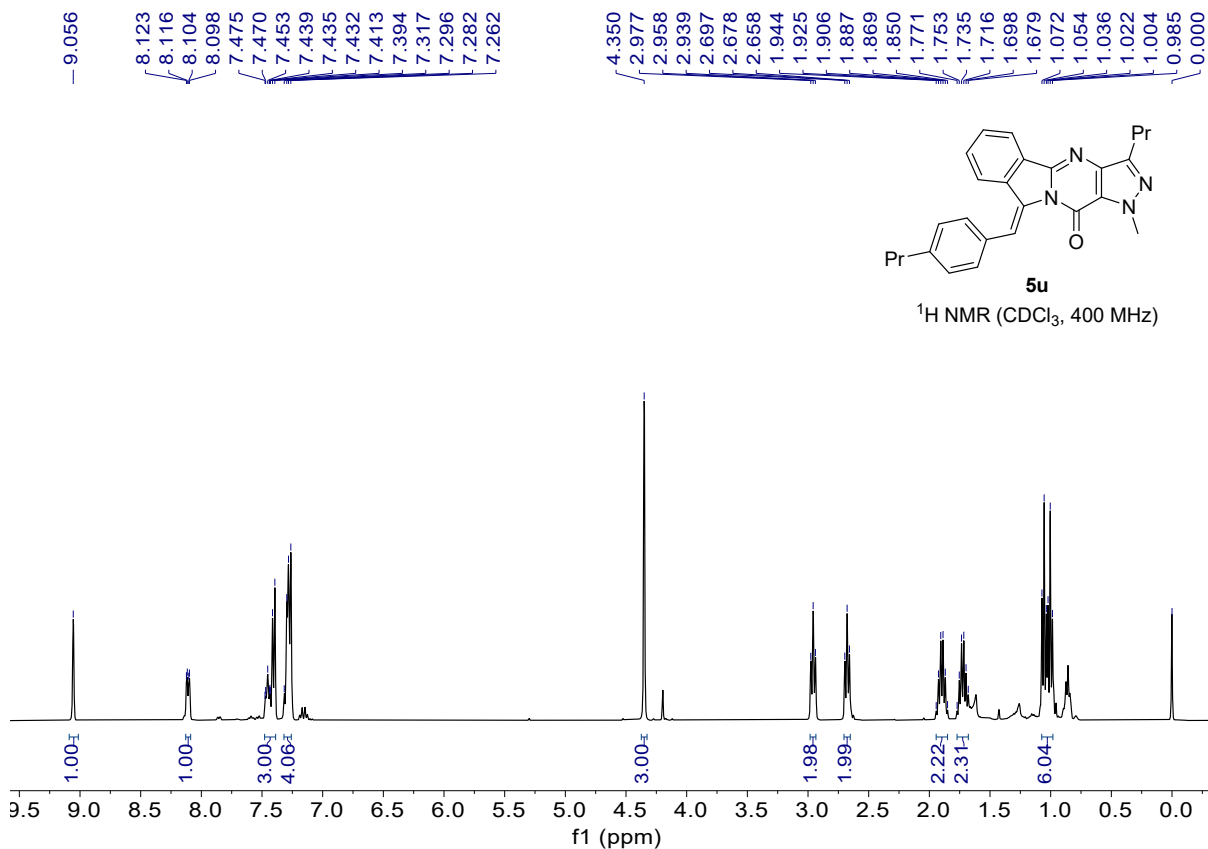
(E)-9-(4-ethylbenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (5s)



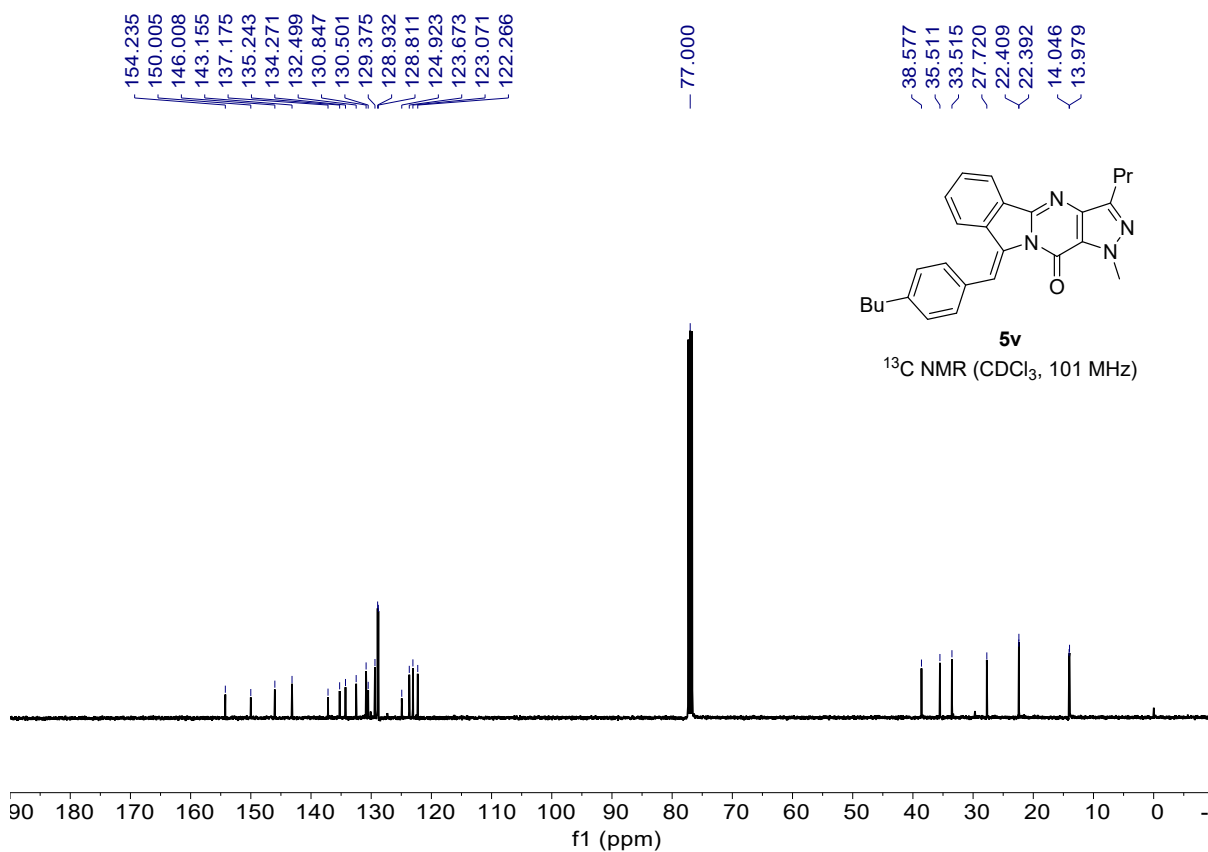
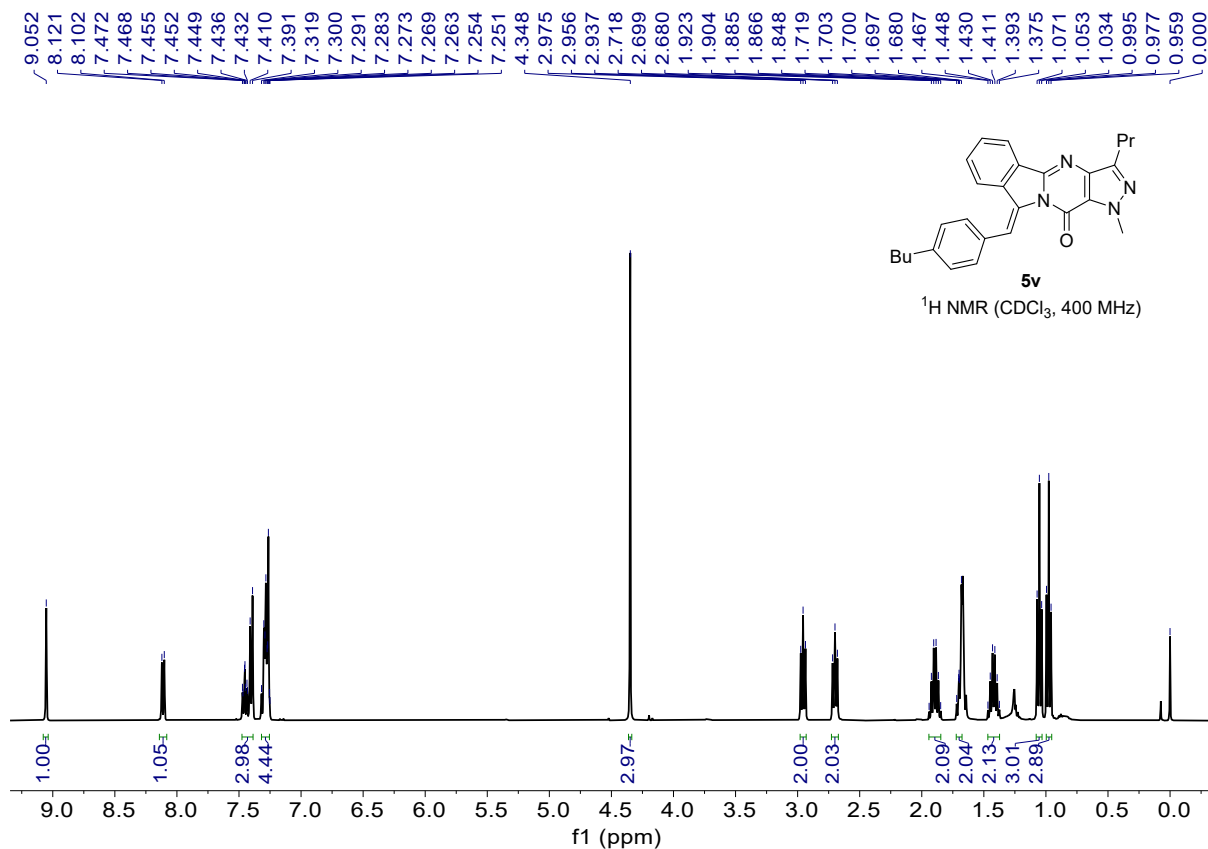
(E)-9-(4-ethoxybenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (5t)



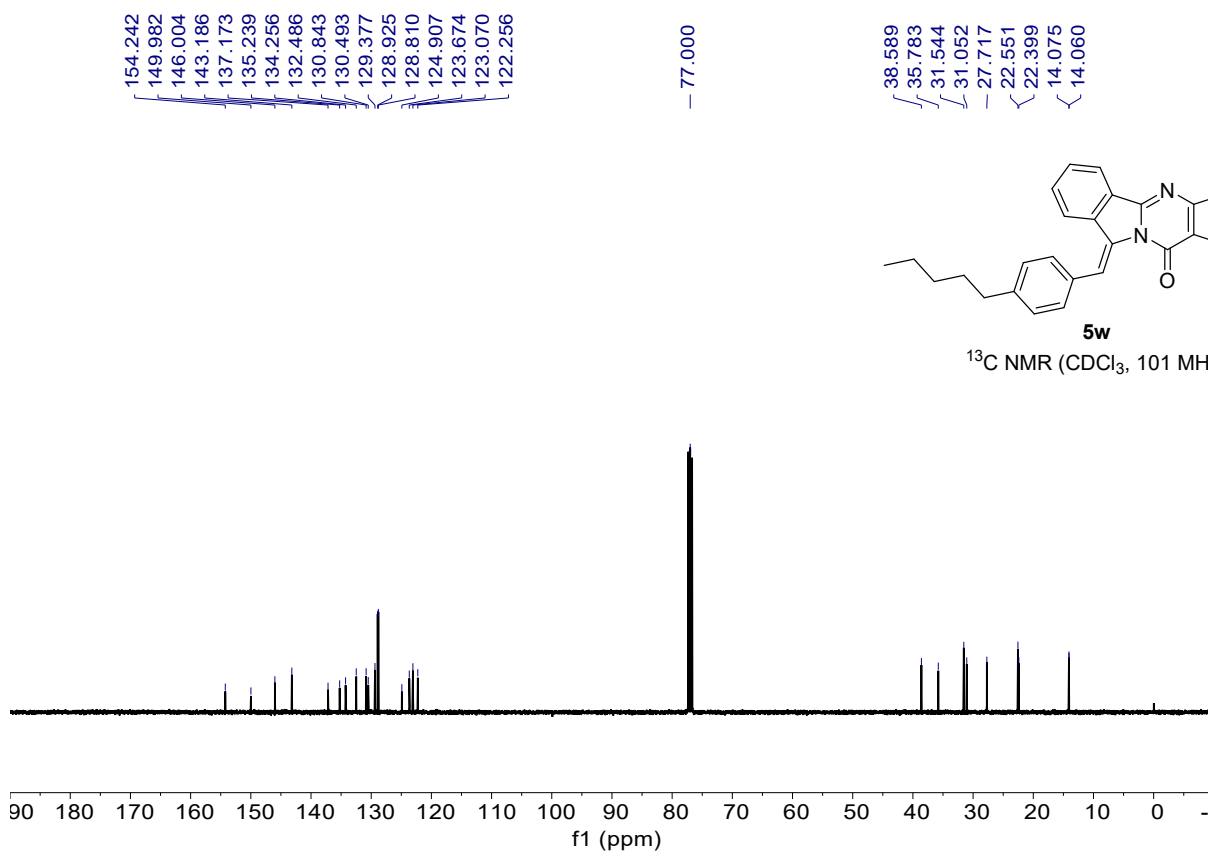
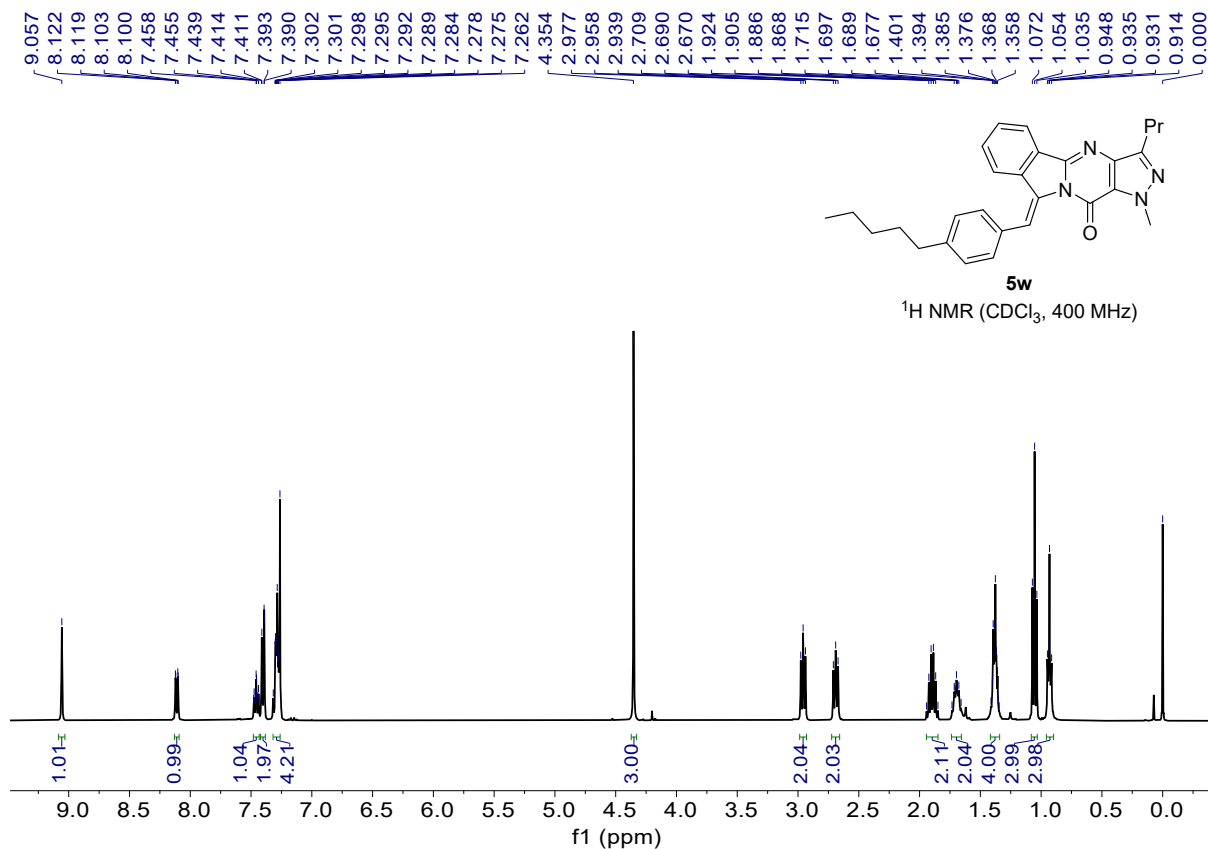
(E)-1-methyl-3-propyl-9-(4-propylbenzylidene)-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-*a*]isoindol-11-one (5u)



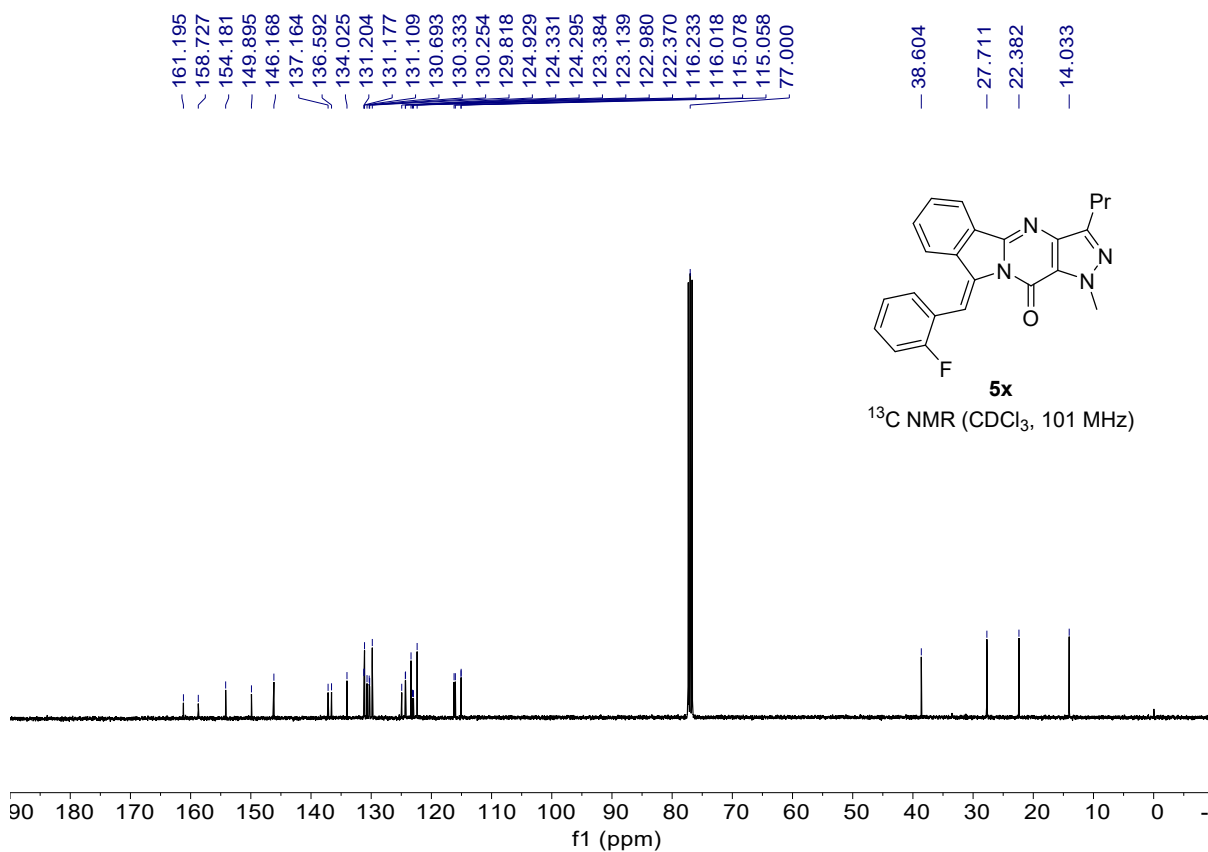
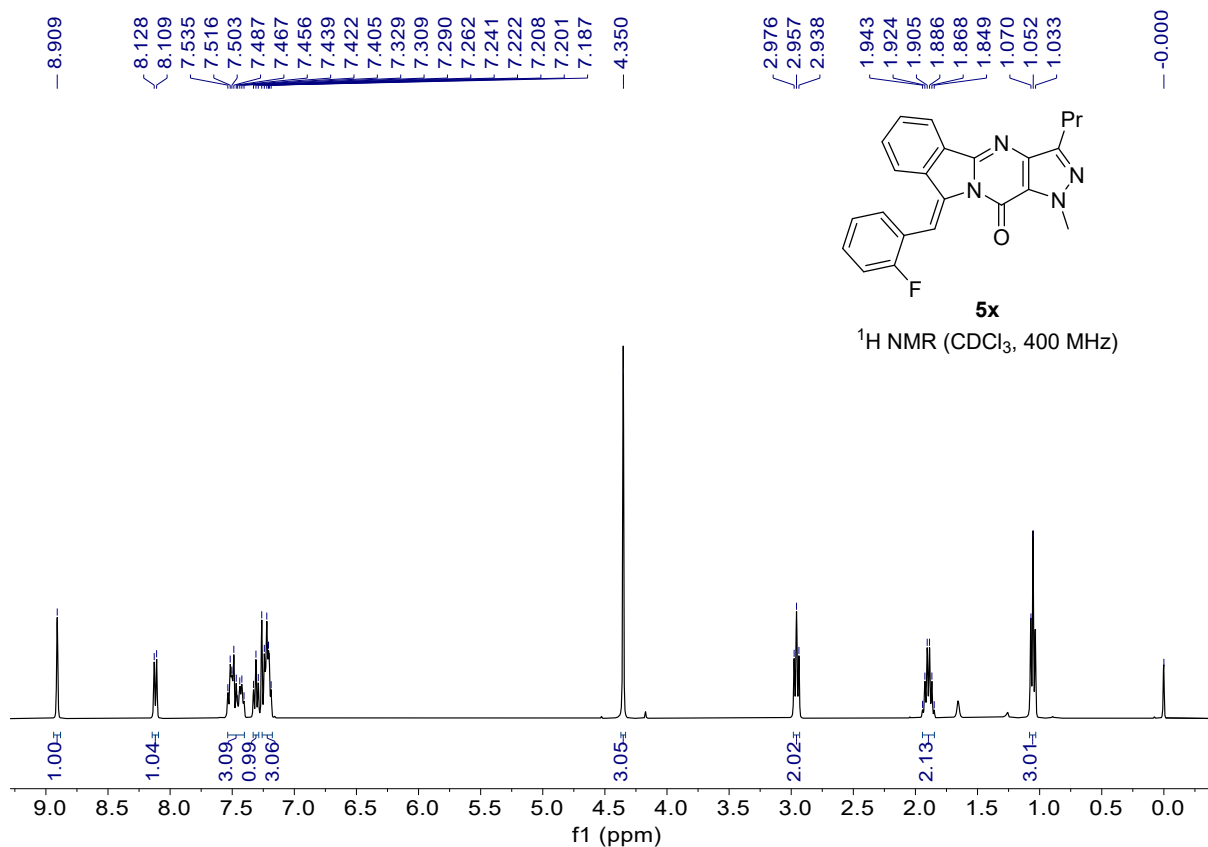
(E)-9-(4-butylbenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (5v)



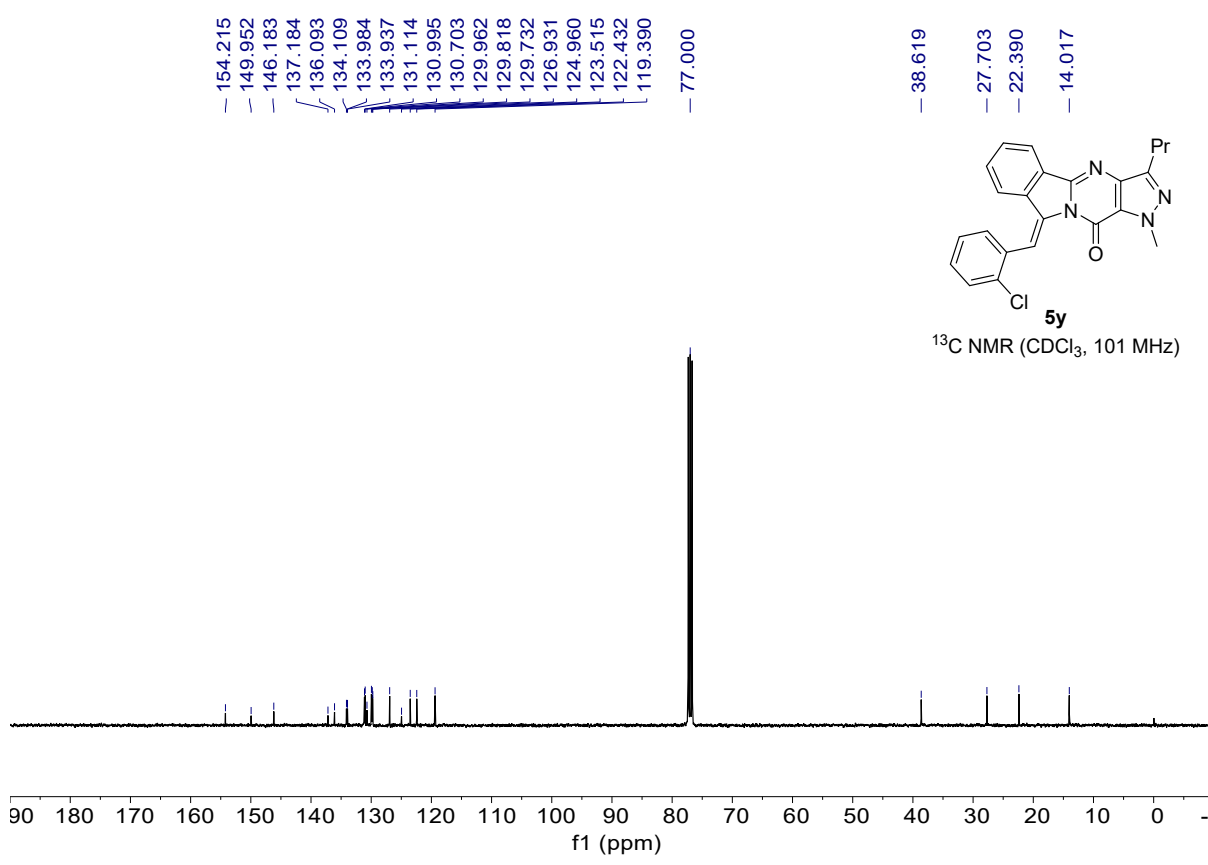
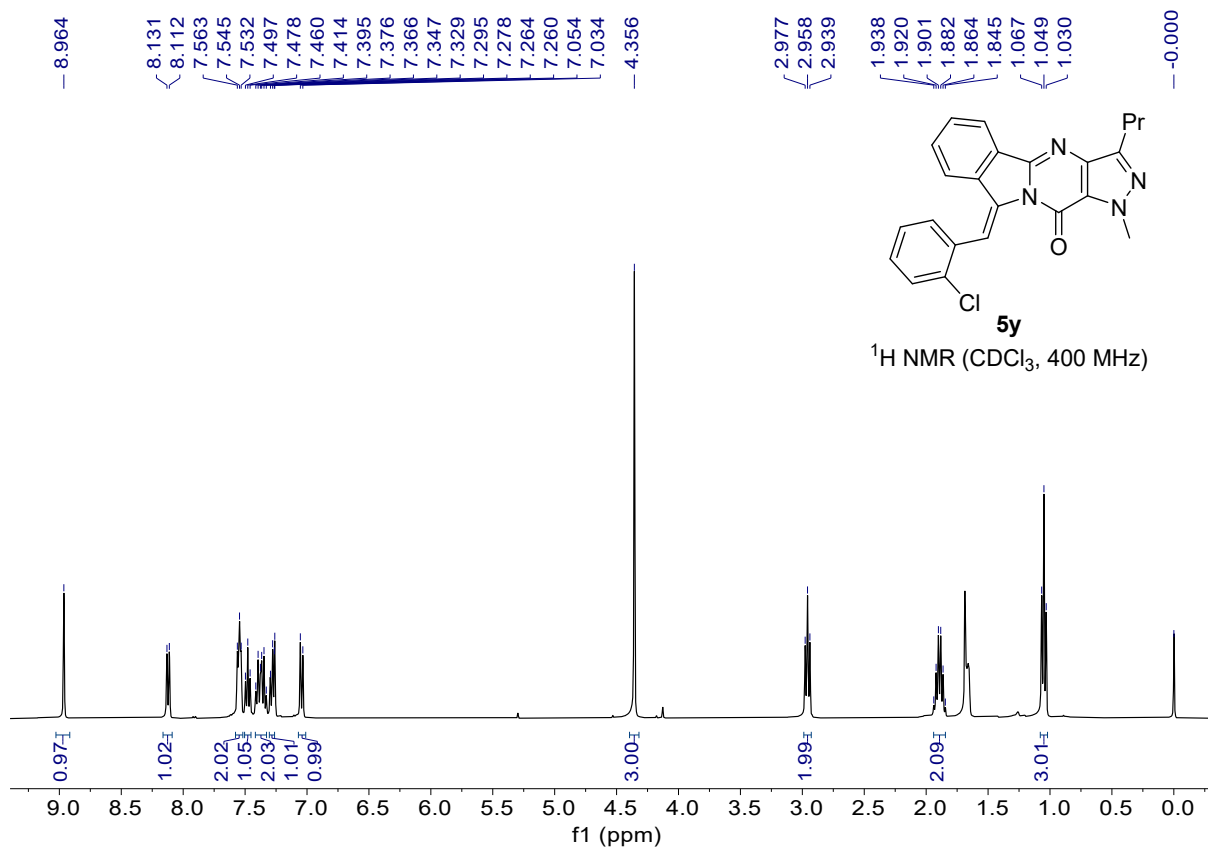
(E)-1-methyl-9-(4-pentylbenzylidene)-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-*a*]isoindol-11-one (5w)



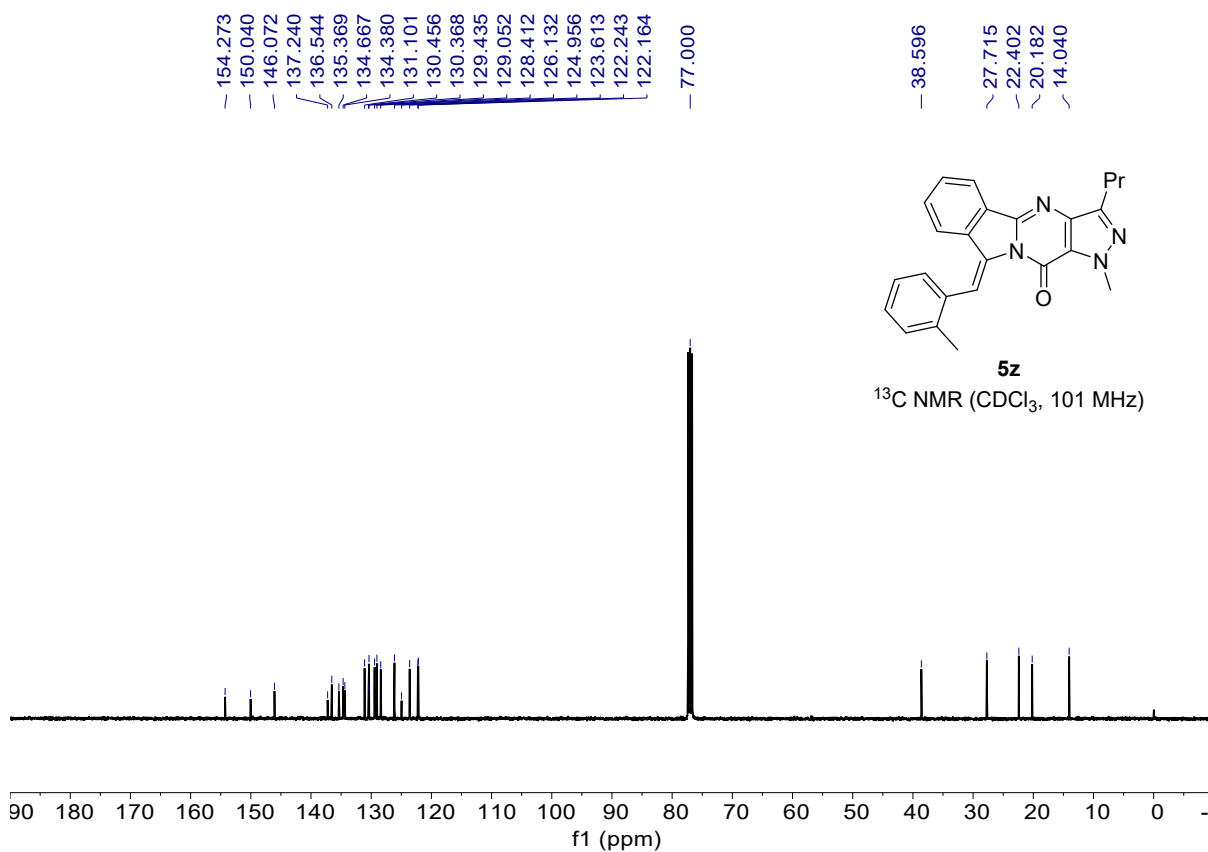
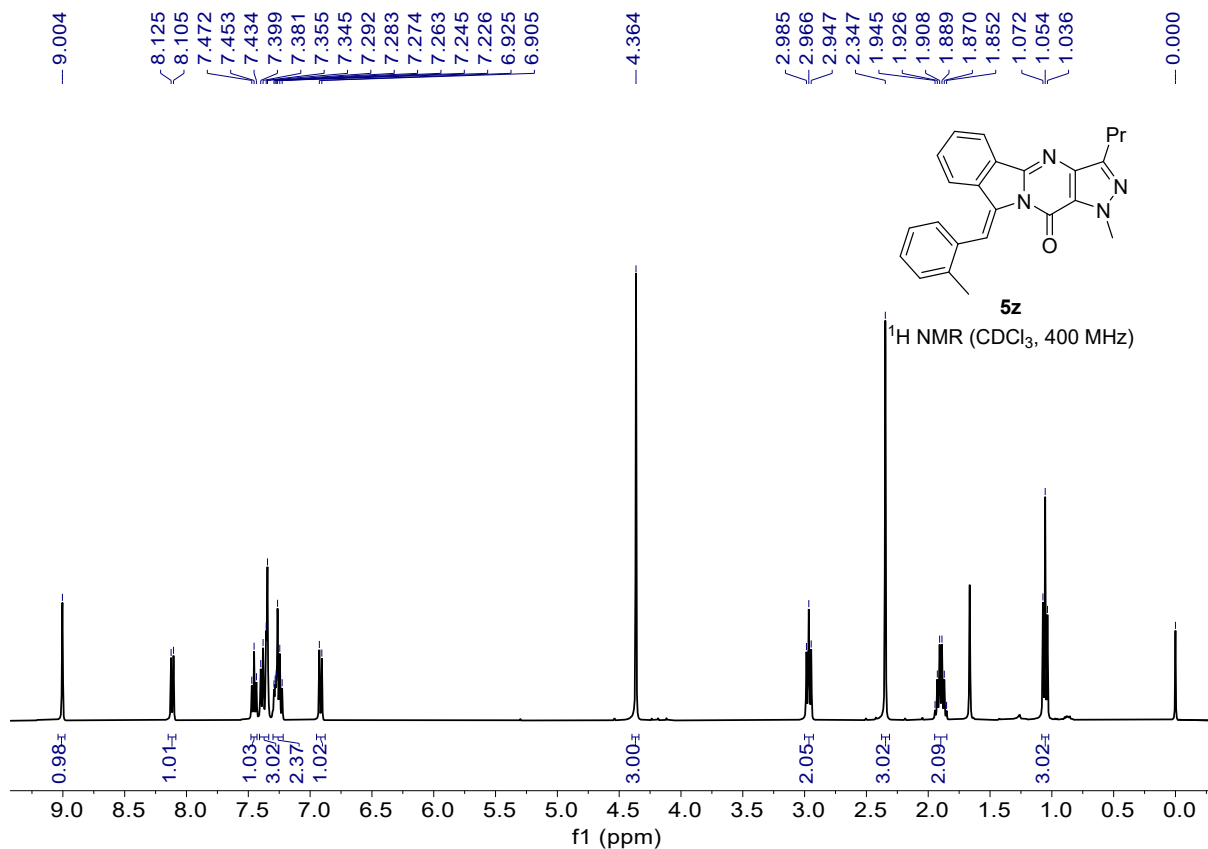
(E)-9-(2-fluorobenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (5x)



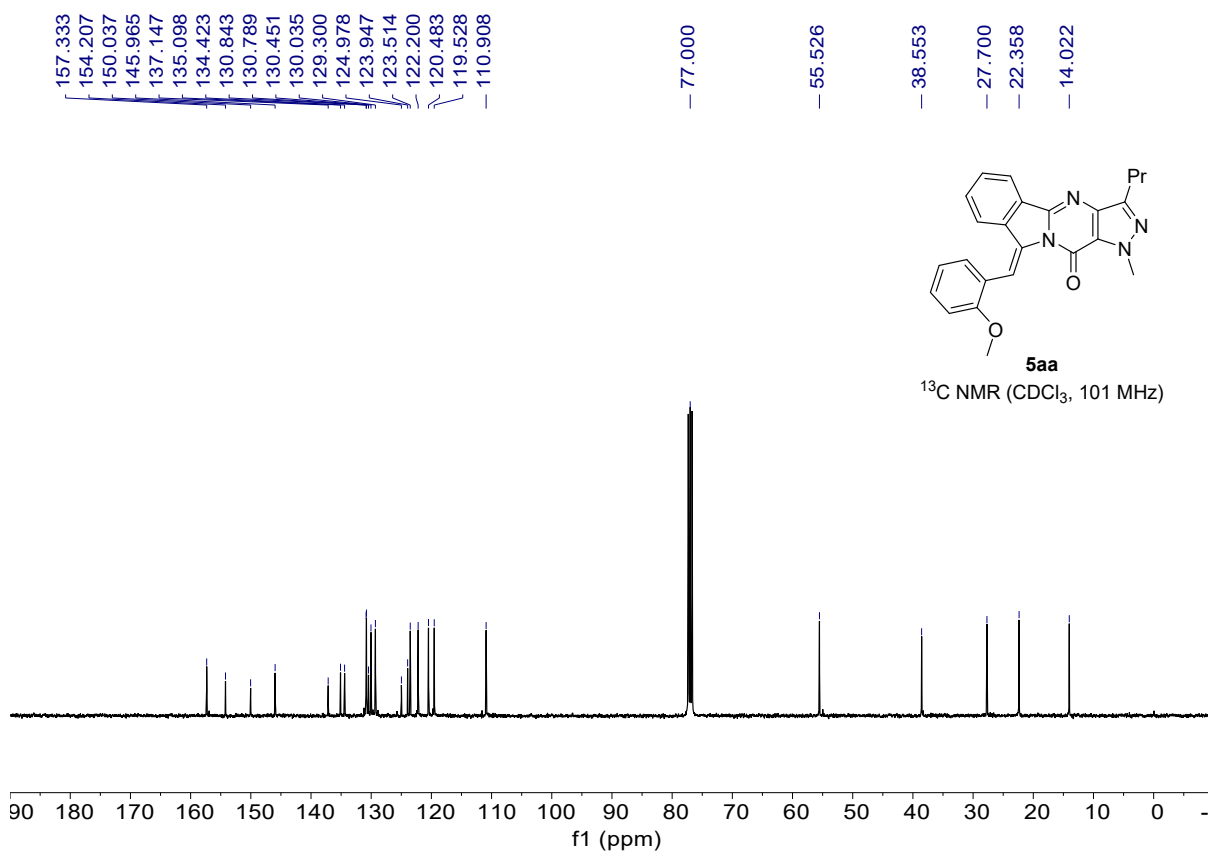
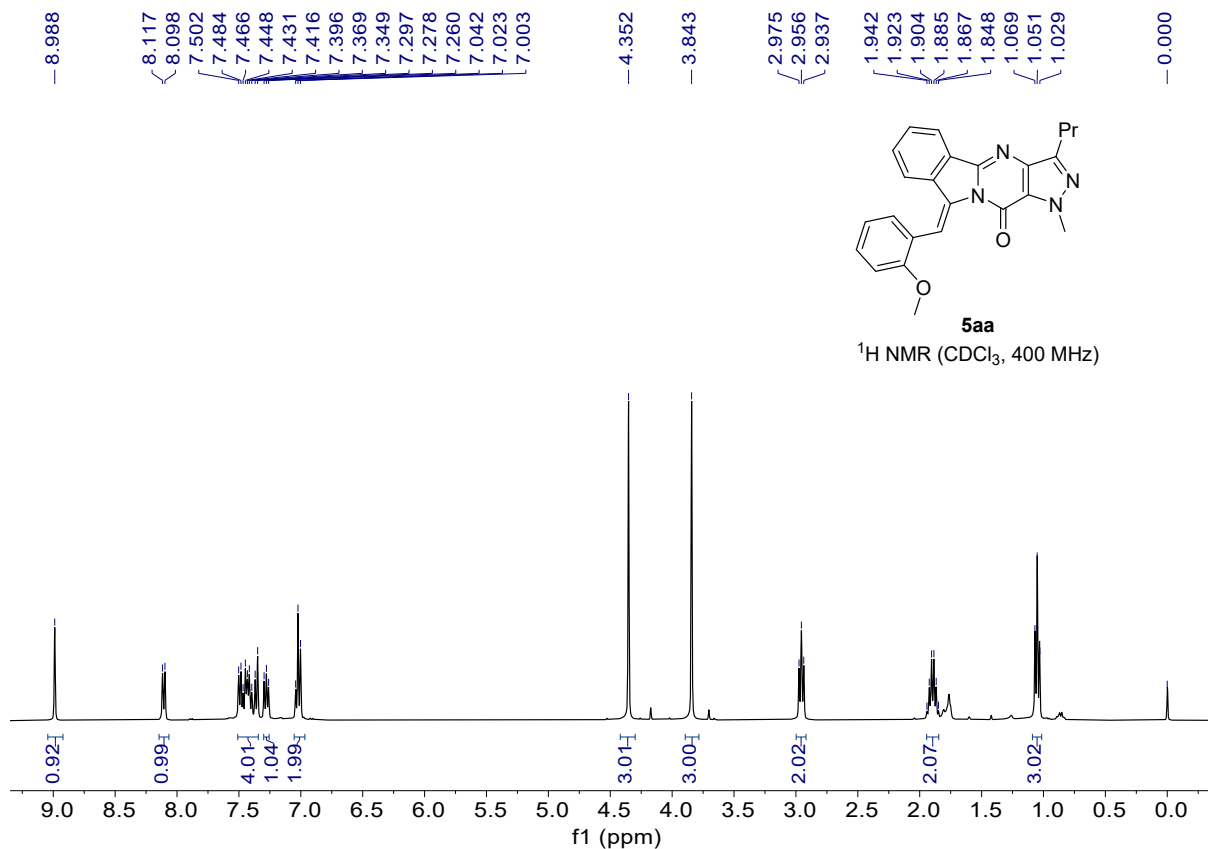
(E)-9-(2-chlorobenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (5y)



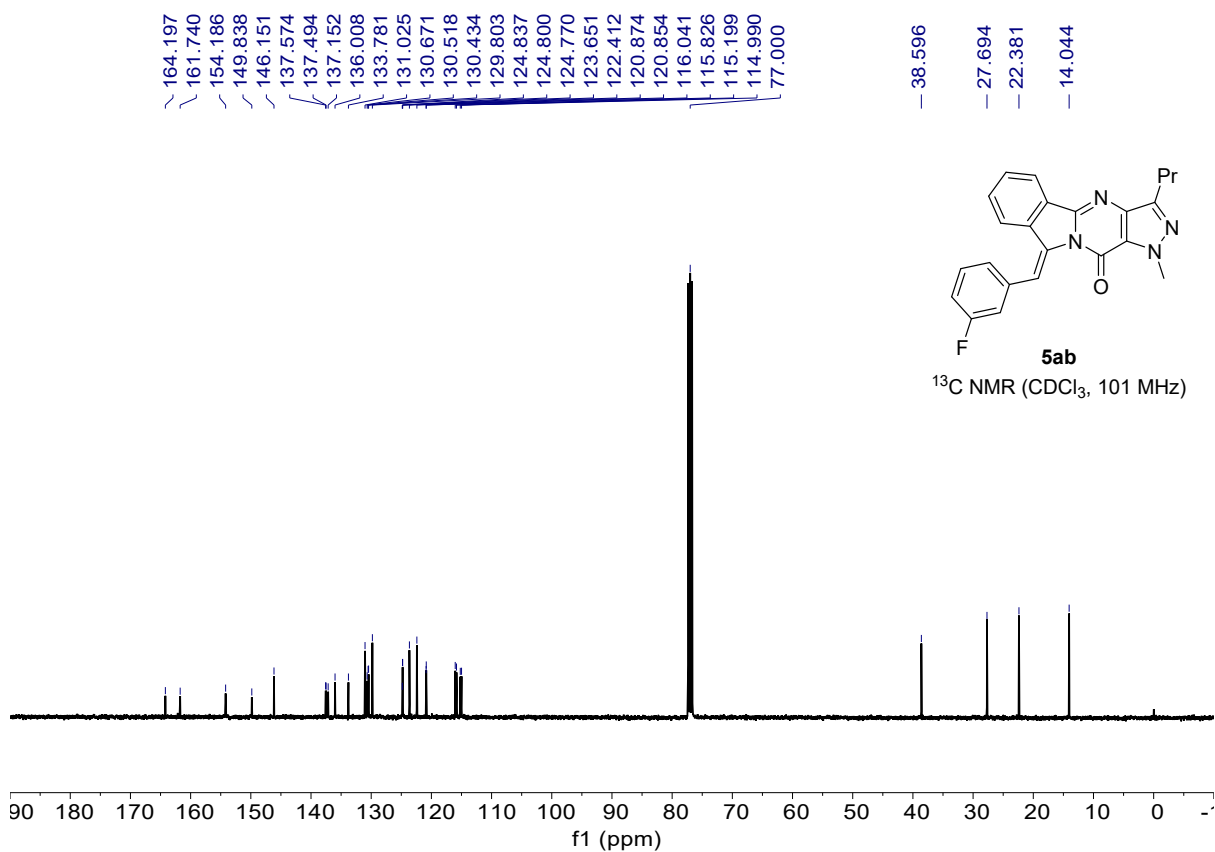
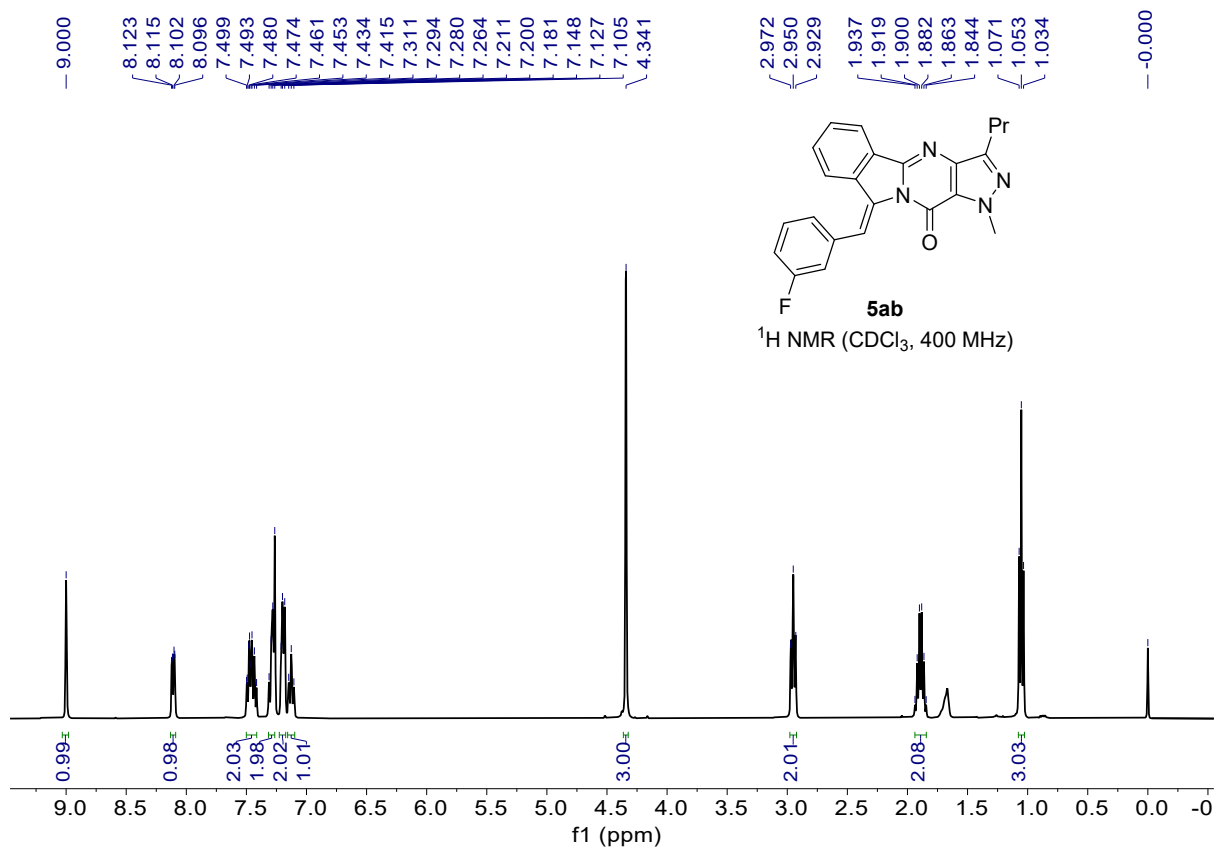
(E)-1-methyl-9-(2-methylbenzylidene)-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (5z)



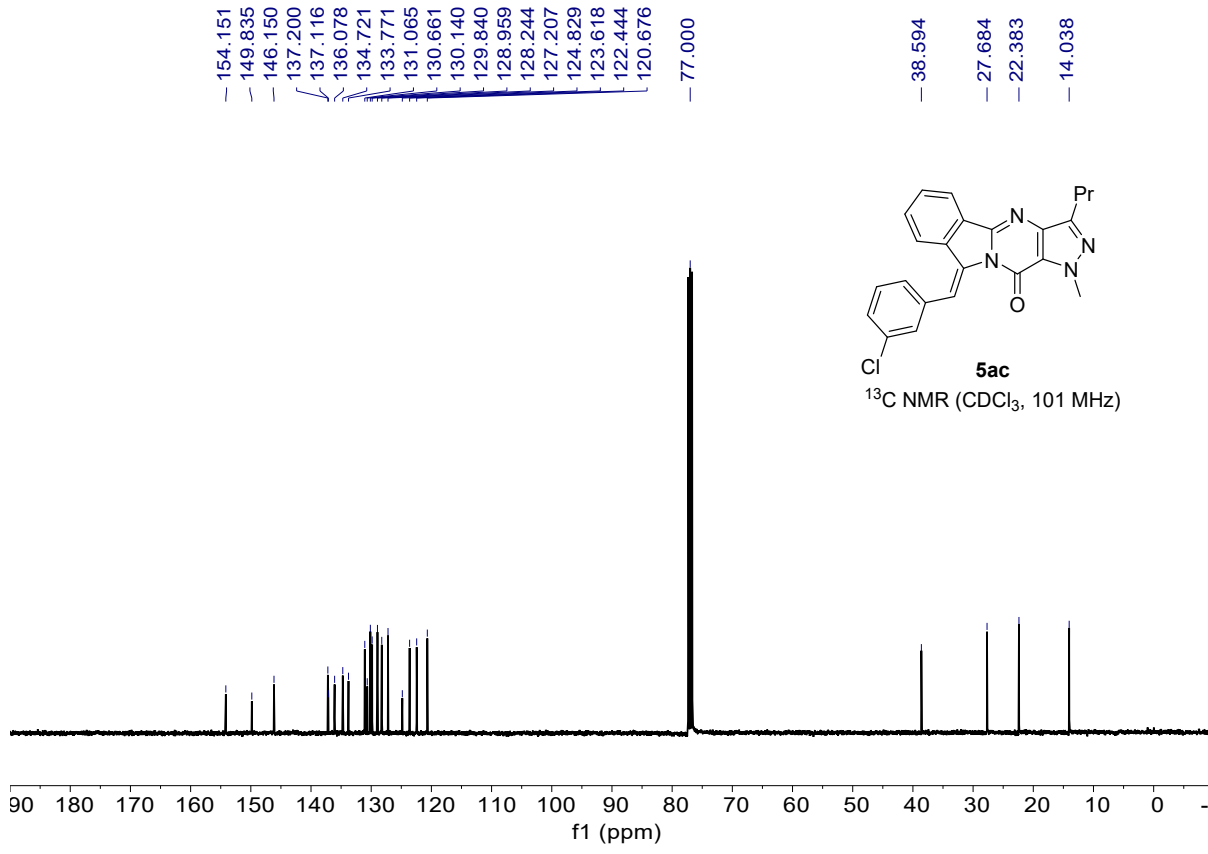
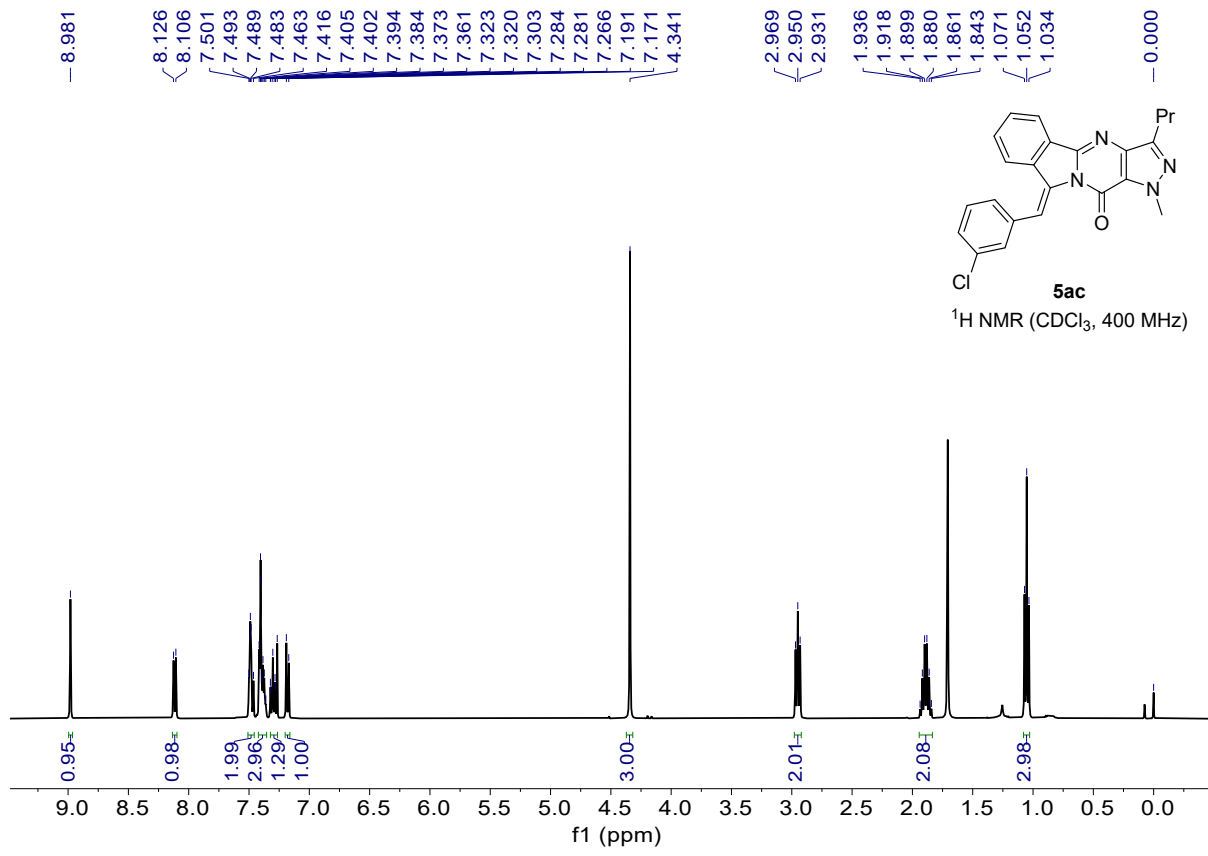
(E)-9-(2-methoxybenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (5aa)



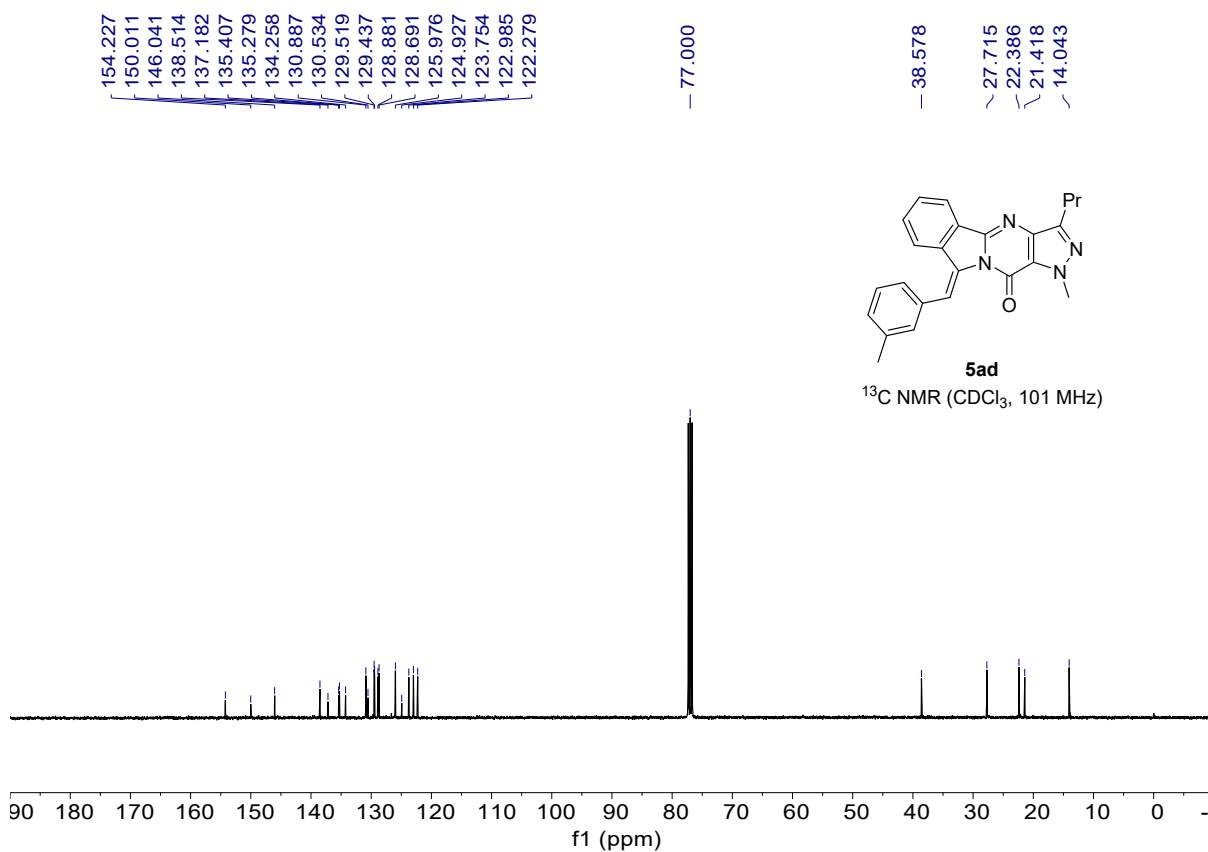
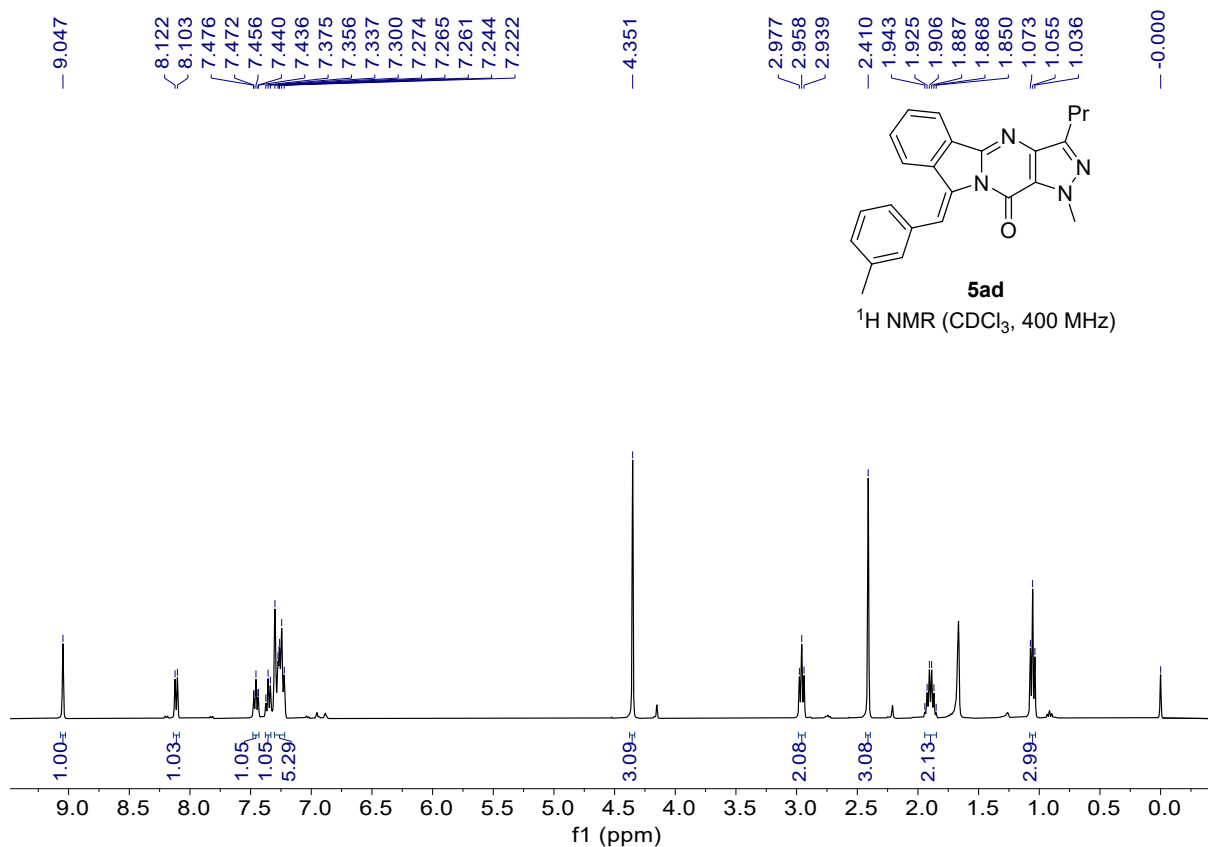
(E)-9-(3-fluorobenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (5ab)



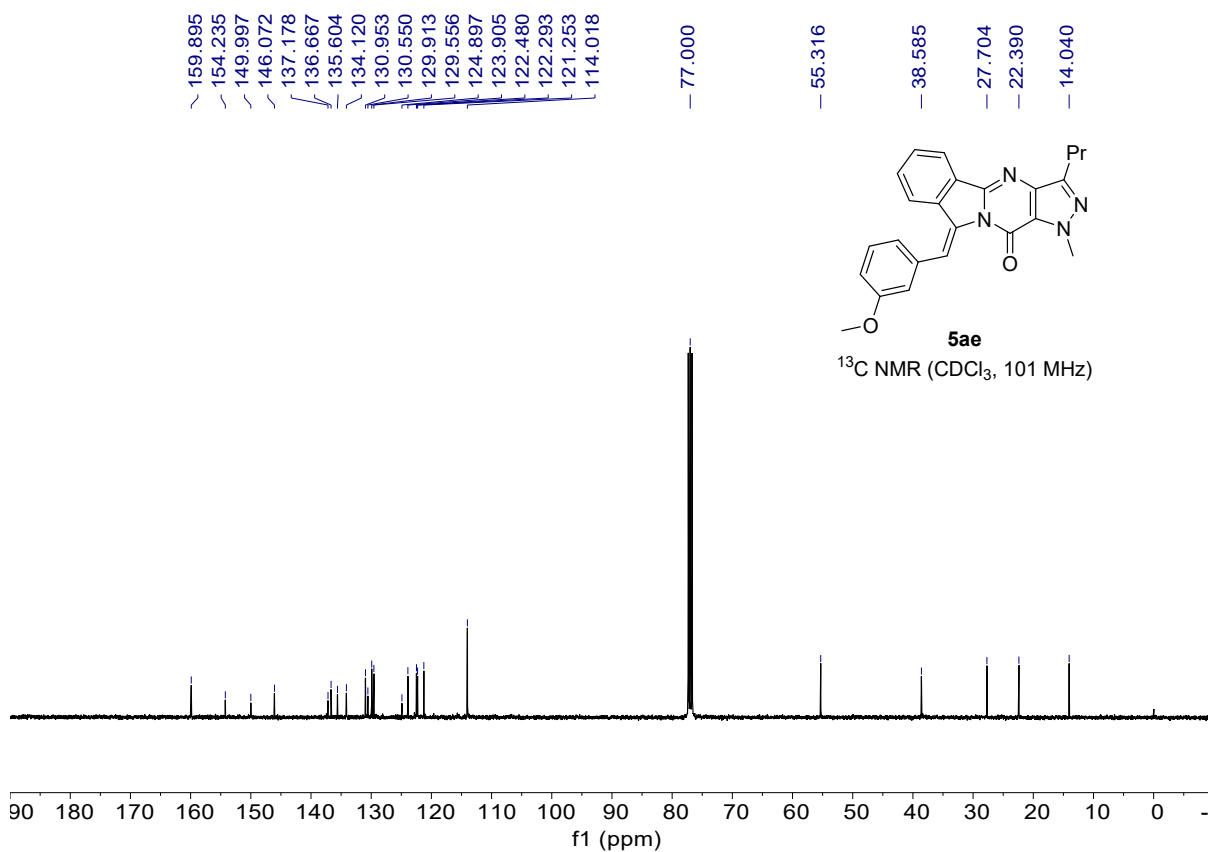
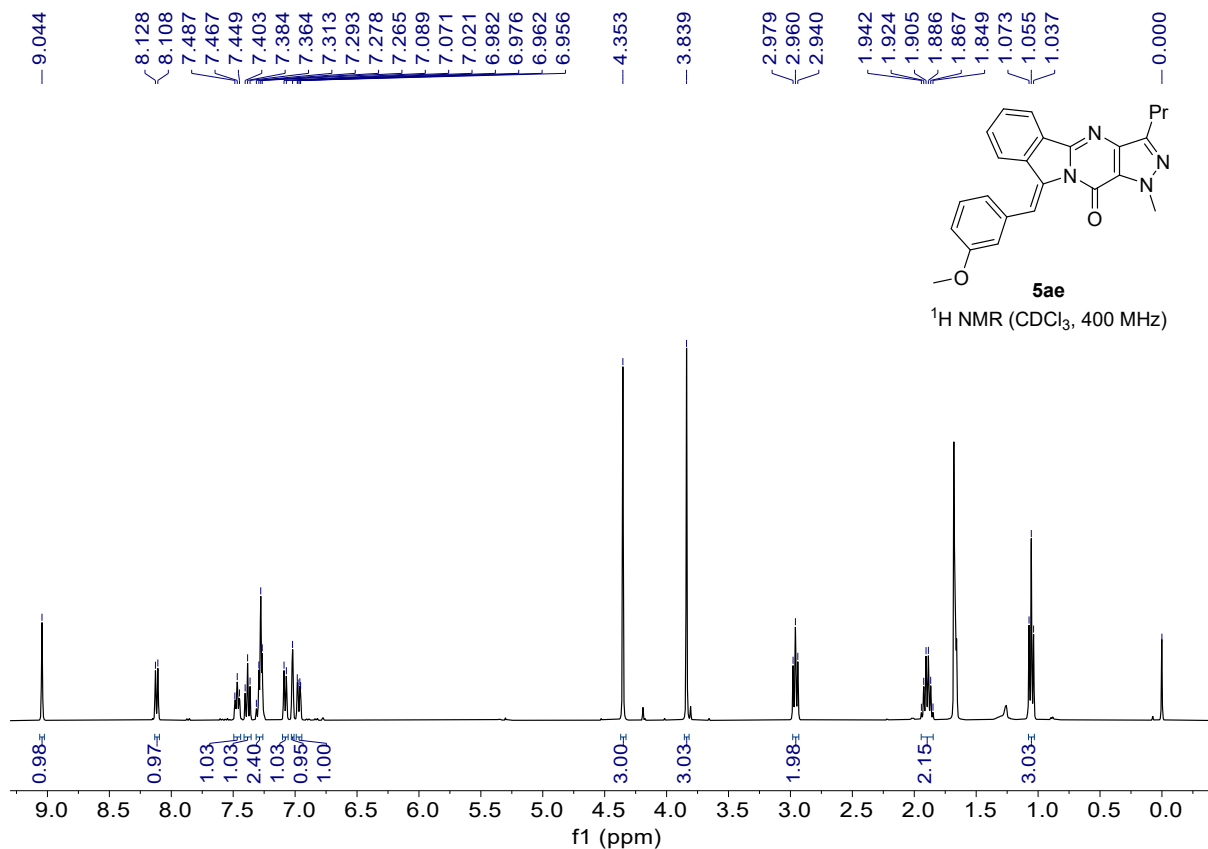
(E)-9-(3-chlorobenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (5ac)



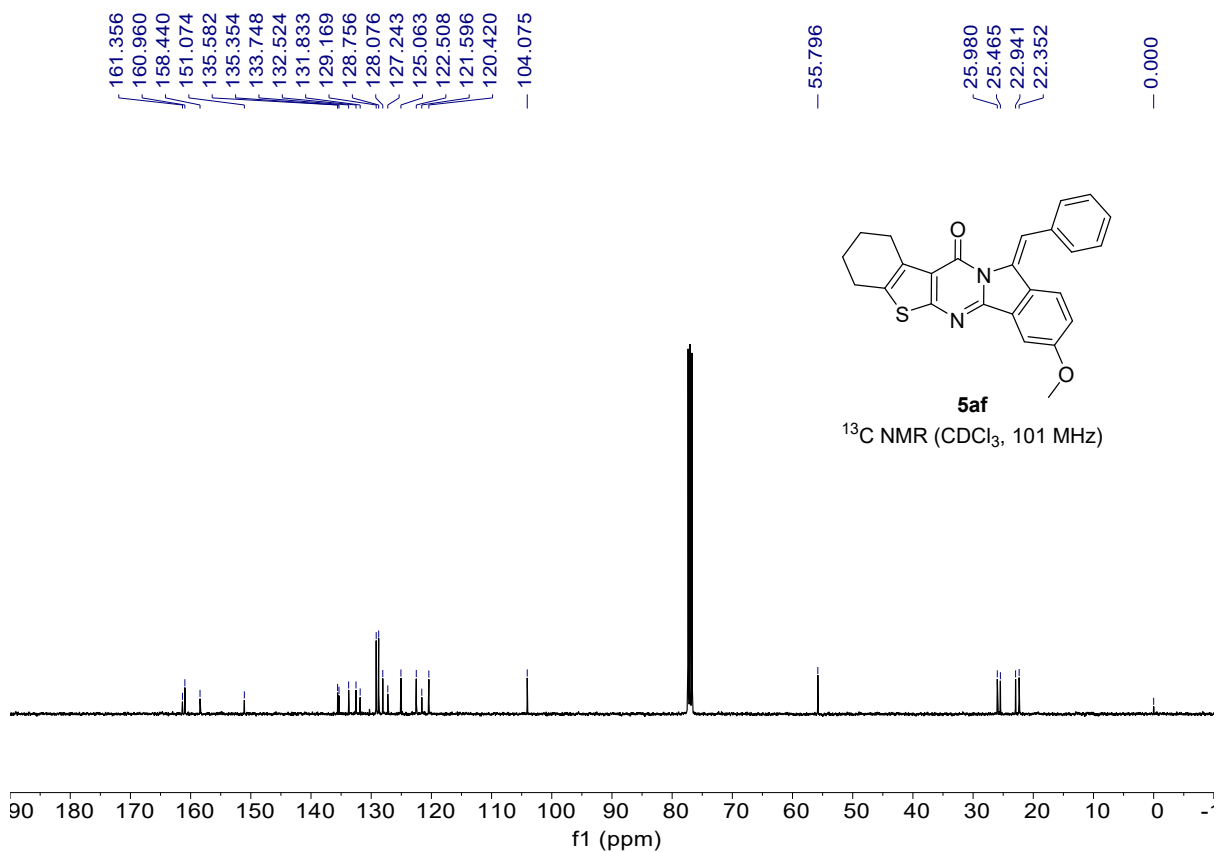
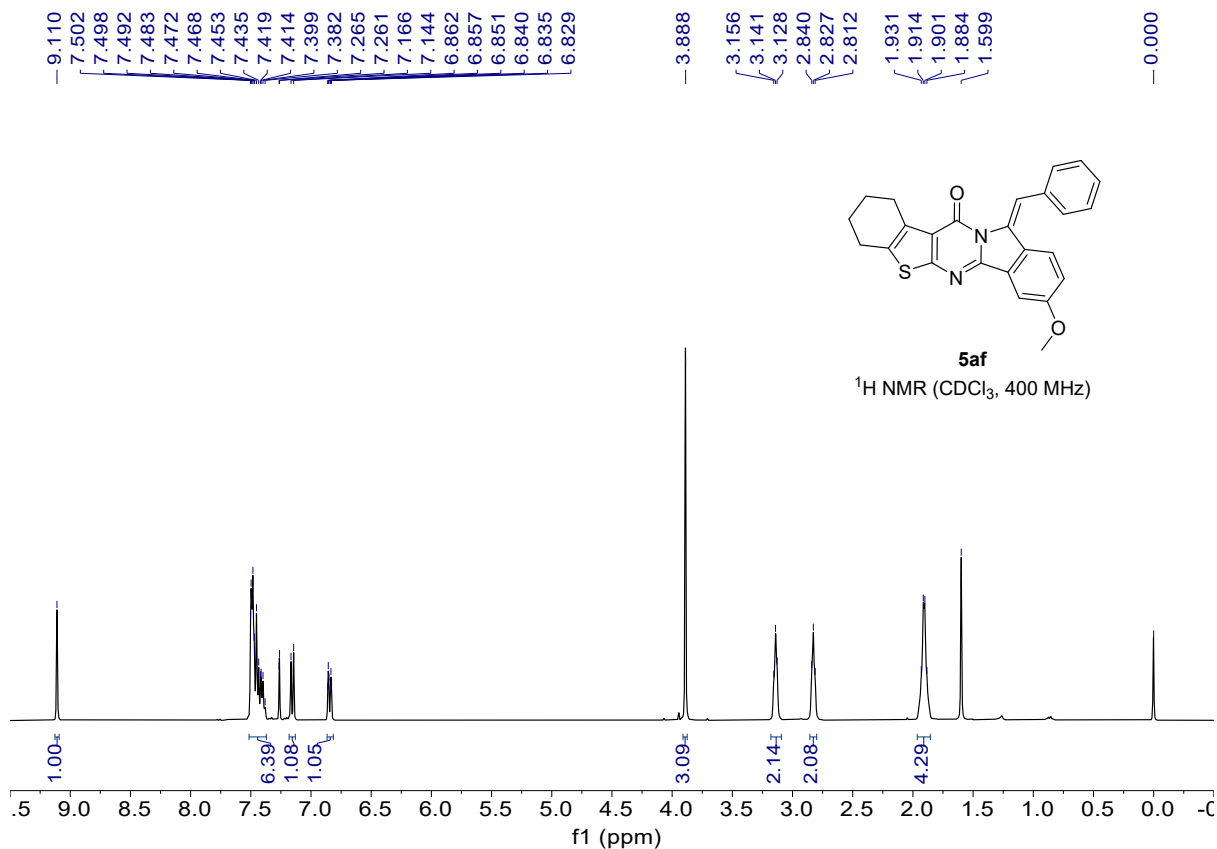
(E)-1-methyl-9-(3-methylbenzylidene)-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-*a*]isoindol-11-one (5ad)



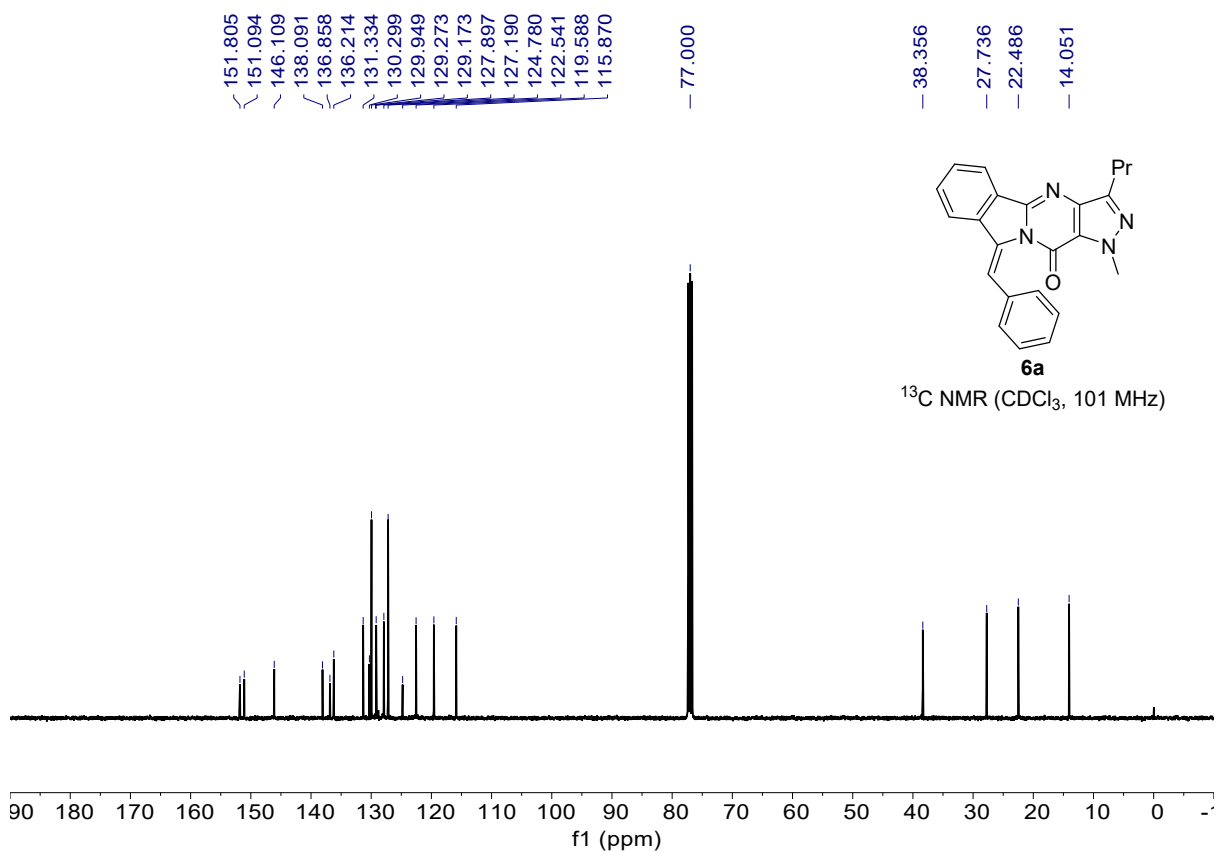
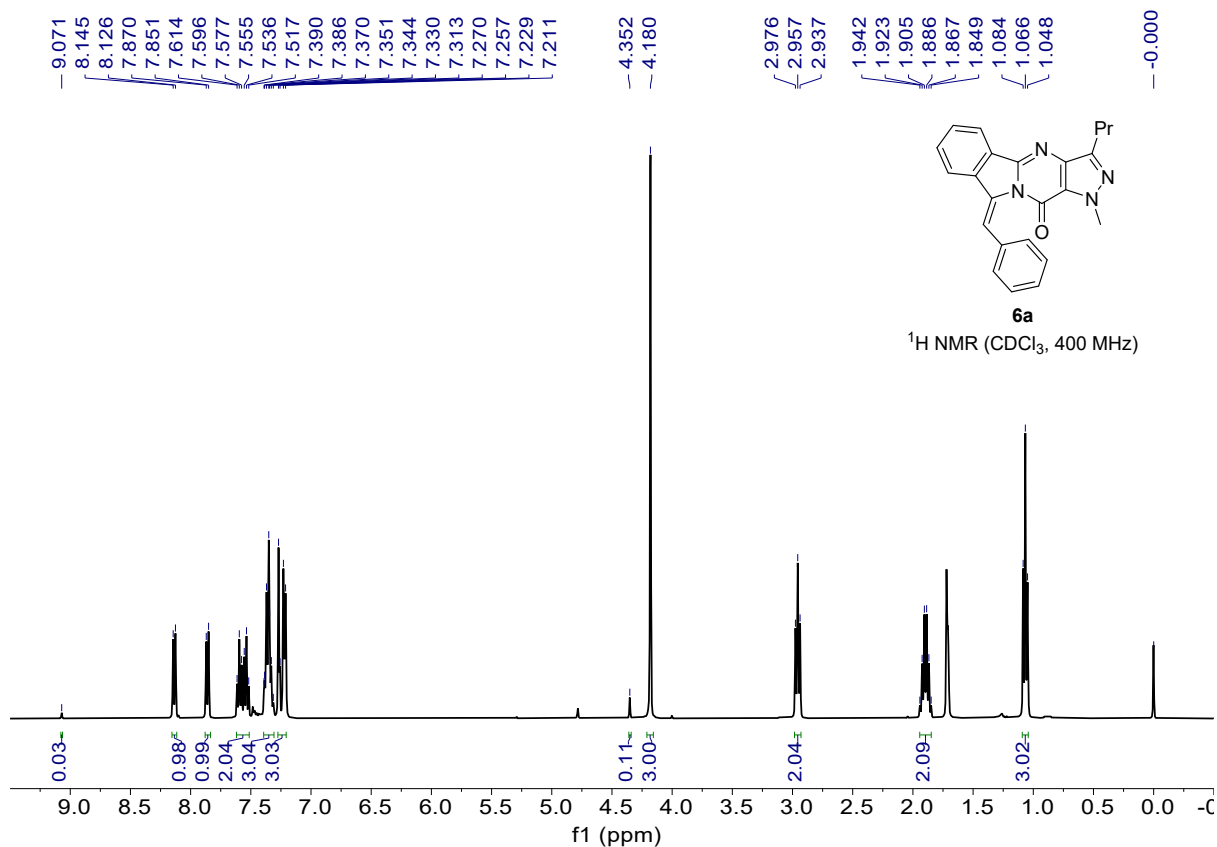
(E)-9-(3-methoxybenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (5ae)



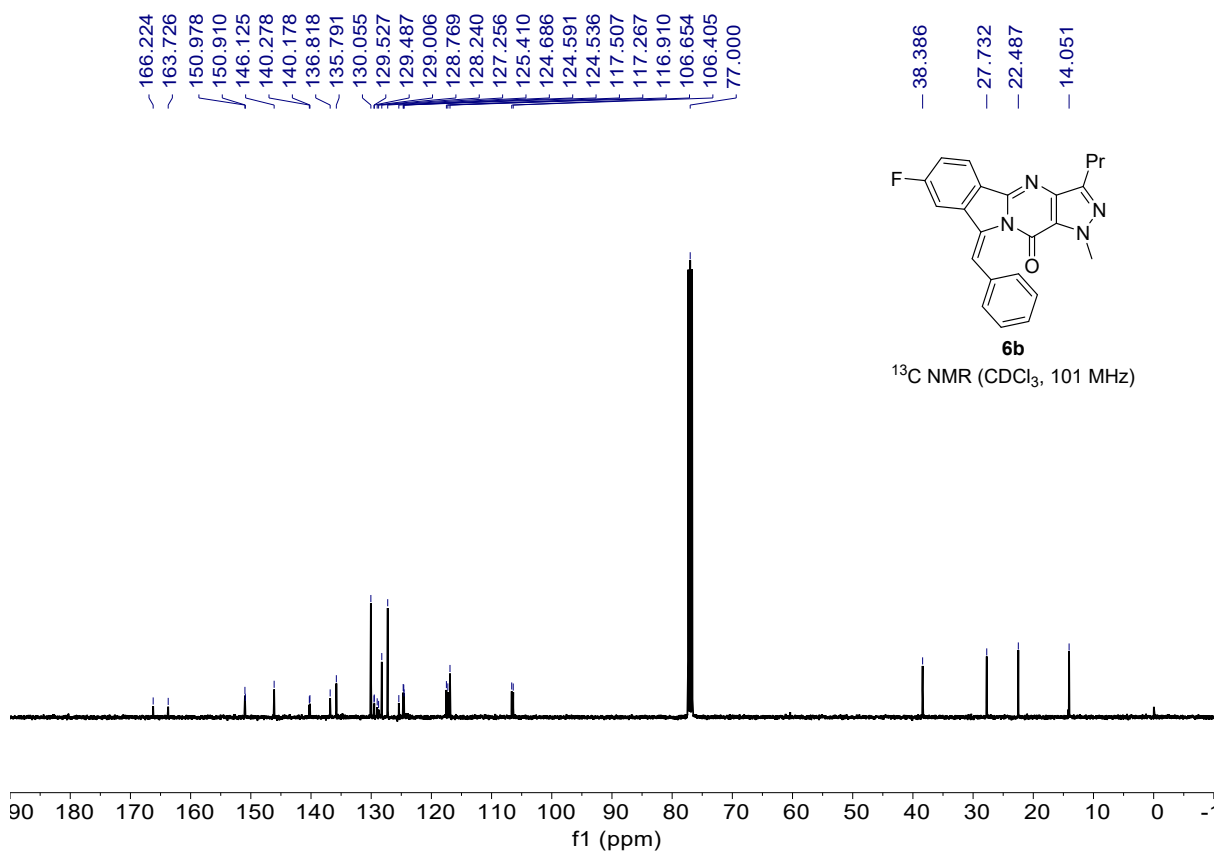
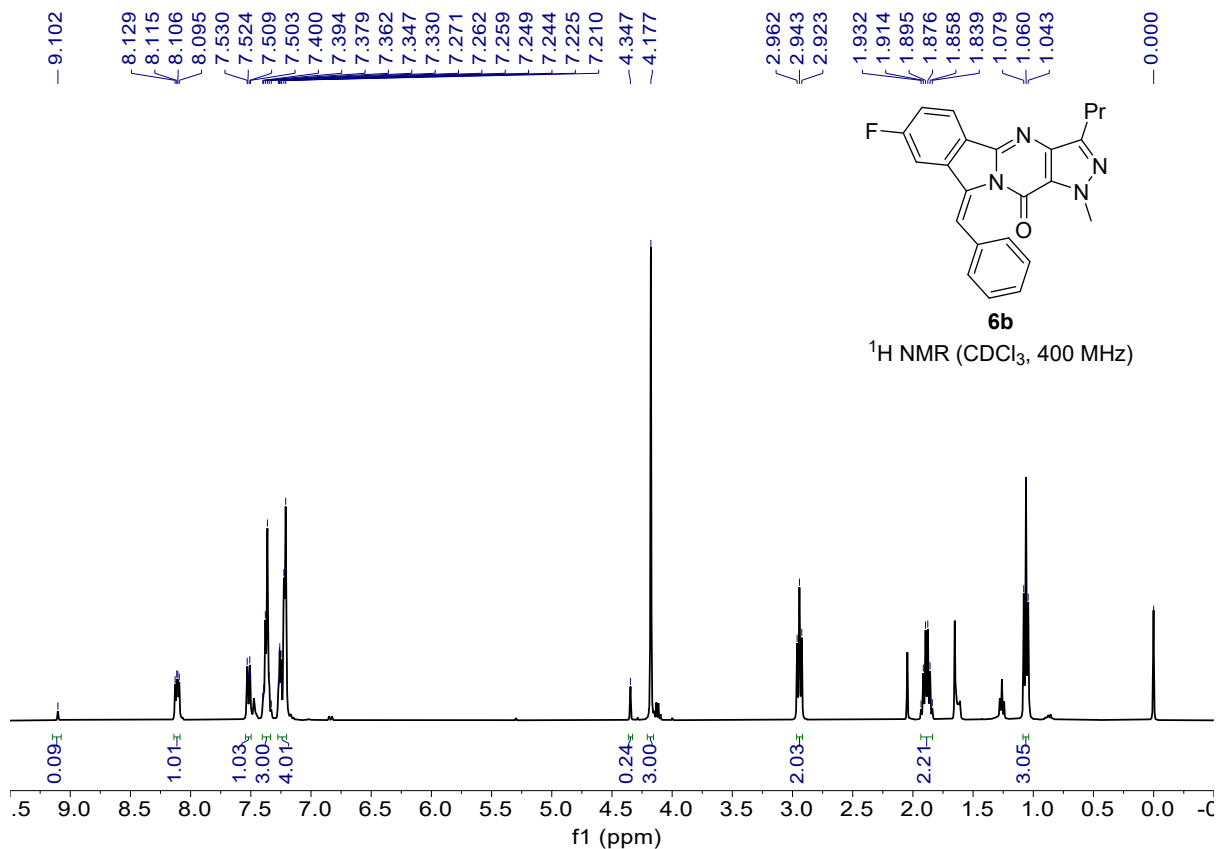
(E)-11-benzylidene-8-methoxy-2,3,4,11-tetrahydrobenzo[4',5']thieno[2',3':4,5]pyrimido[2,1-*a*]isoindol-13(1*H*)-one (5af)



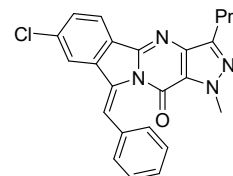
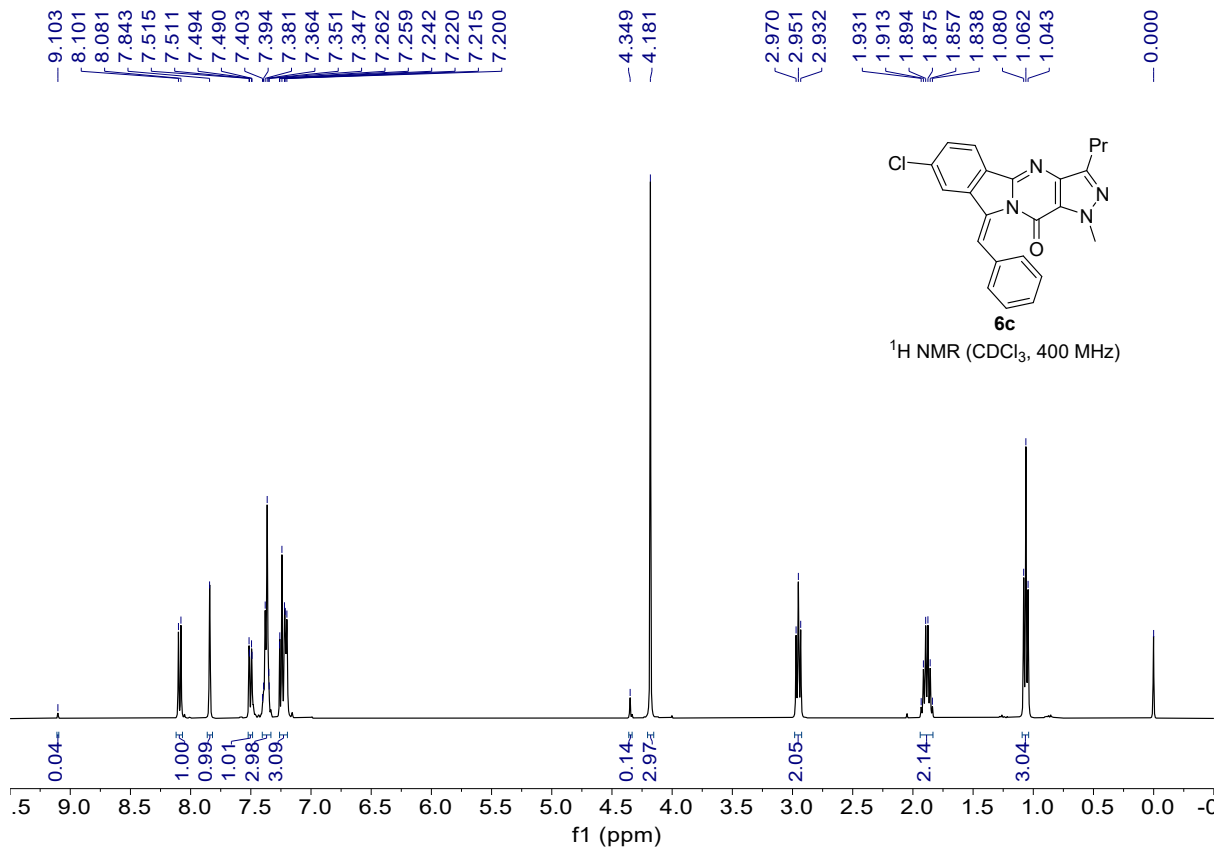
(Z)-9-benzylidene-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (6a)



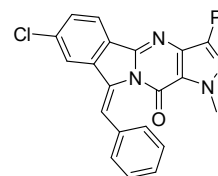
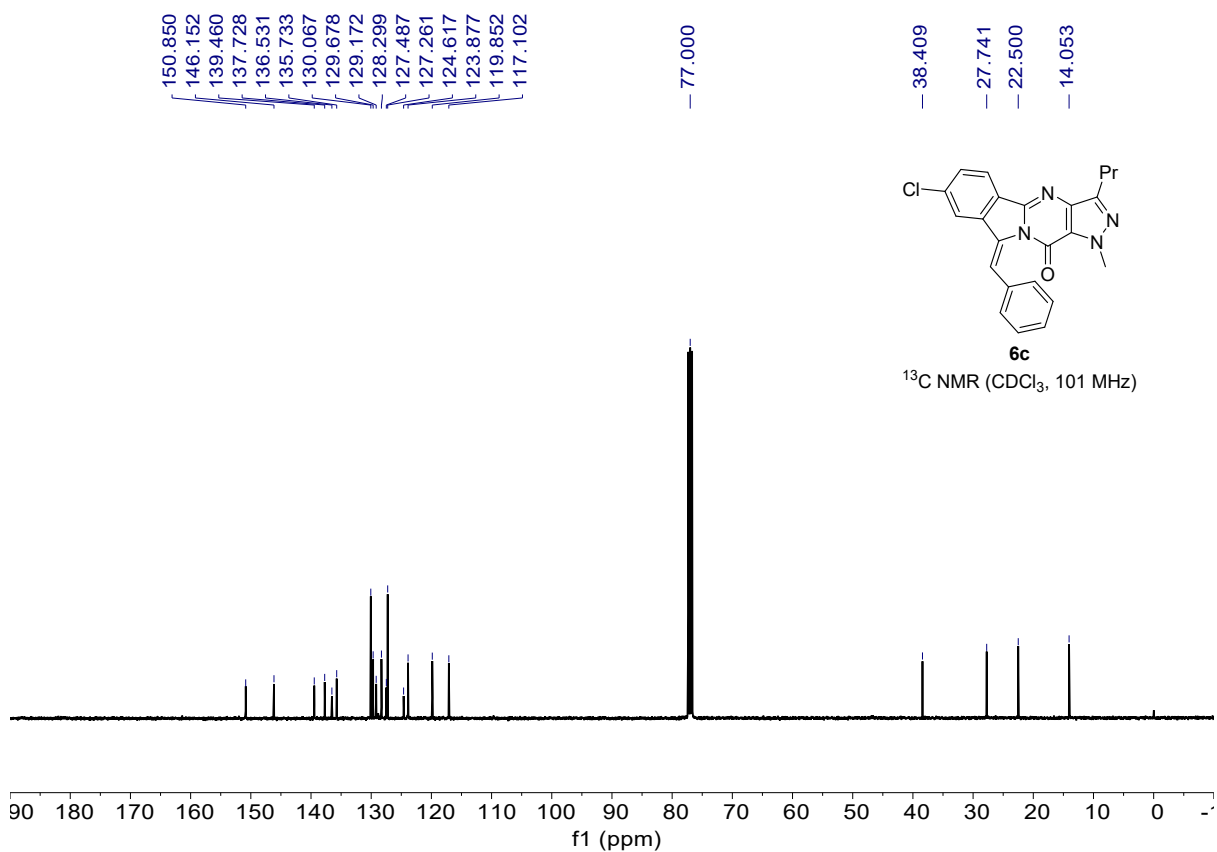
(Z)-9-benzylidene-7-fluoro-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (6b)



(Z)-9-benzylidene-7-chloro-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (6c)

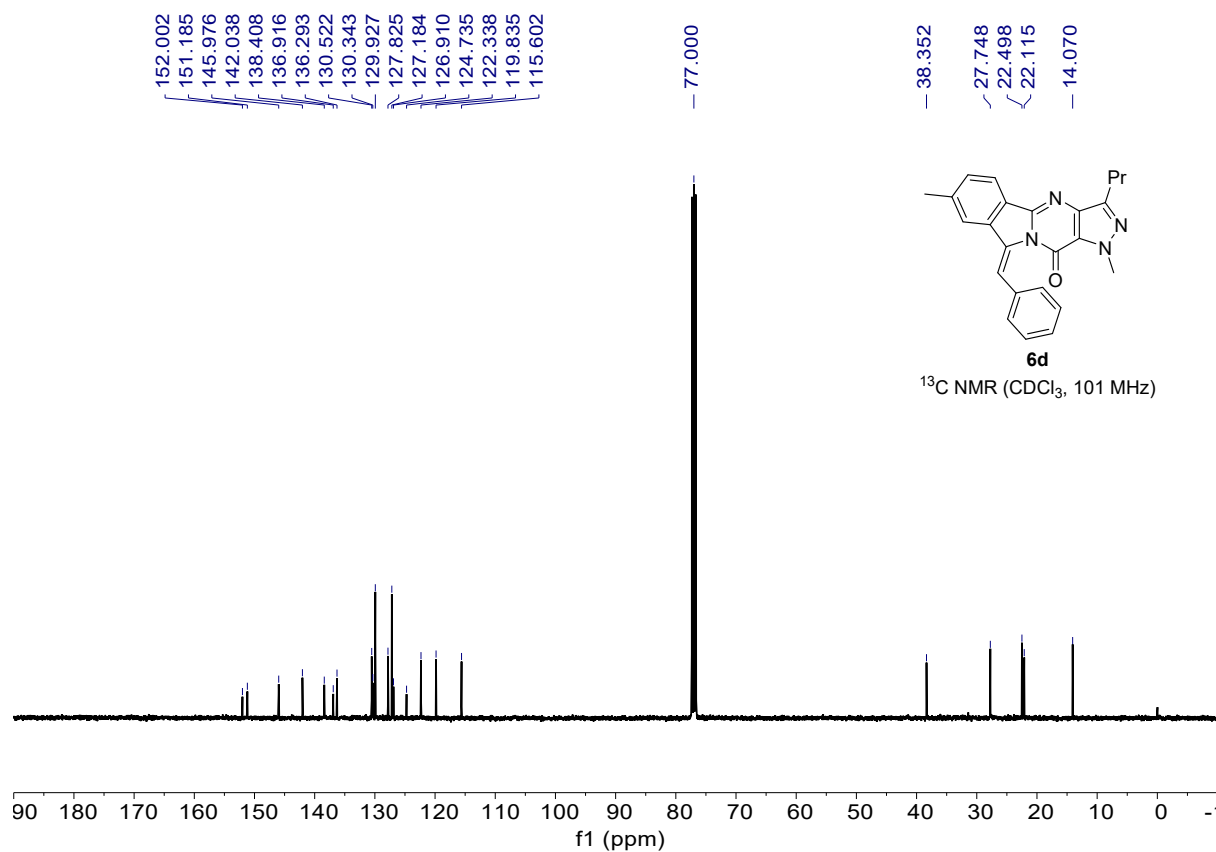
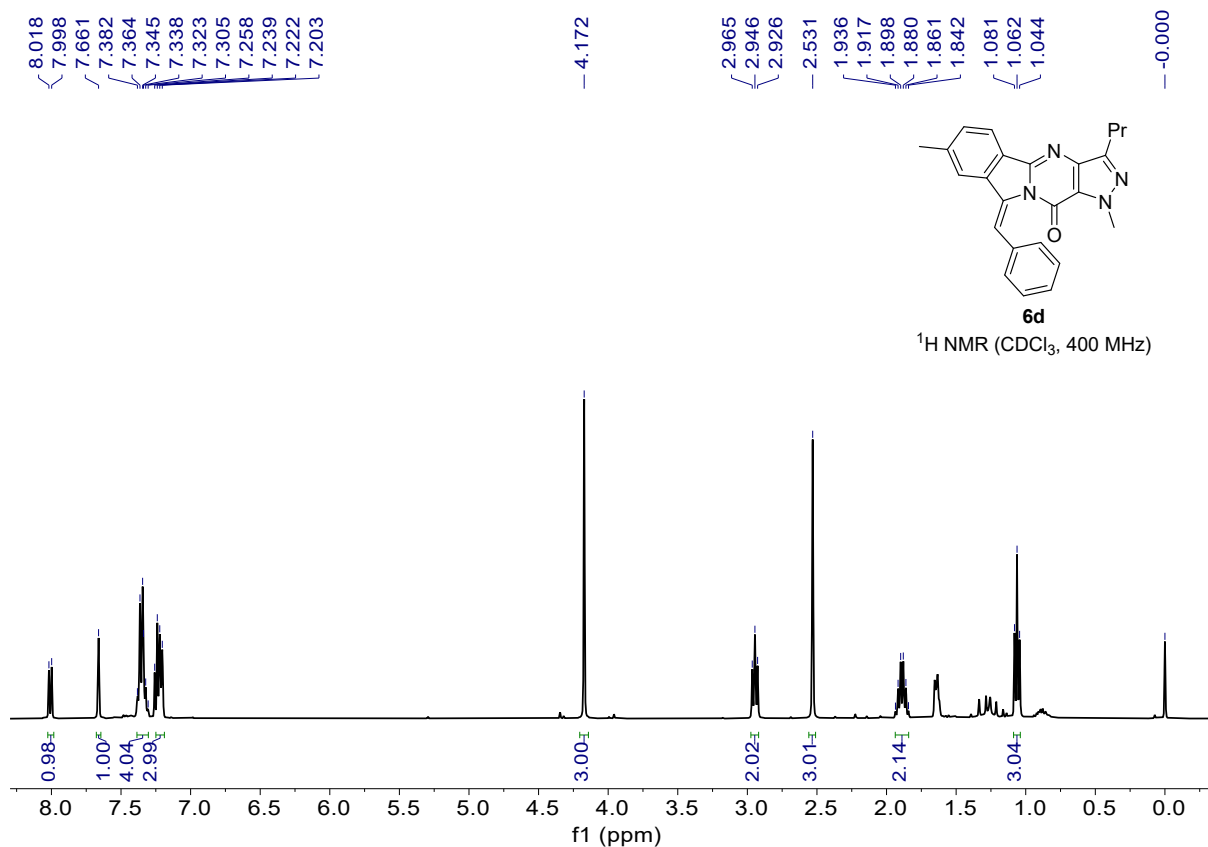


¹H NMR (CDCl₃, 400 MHz)

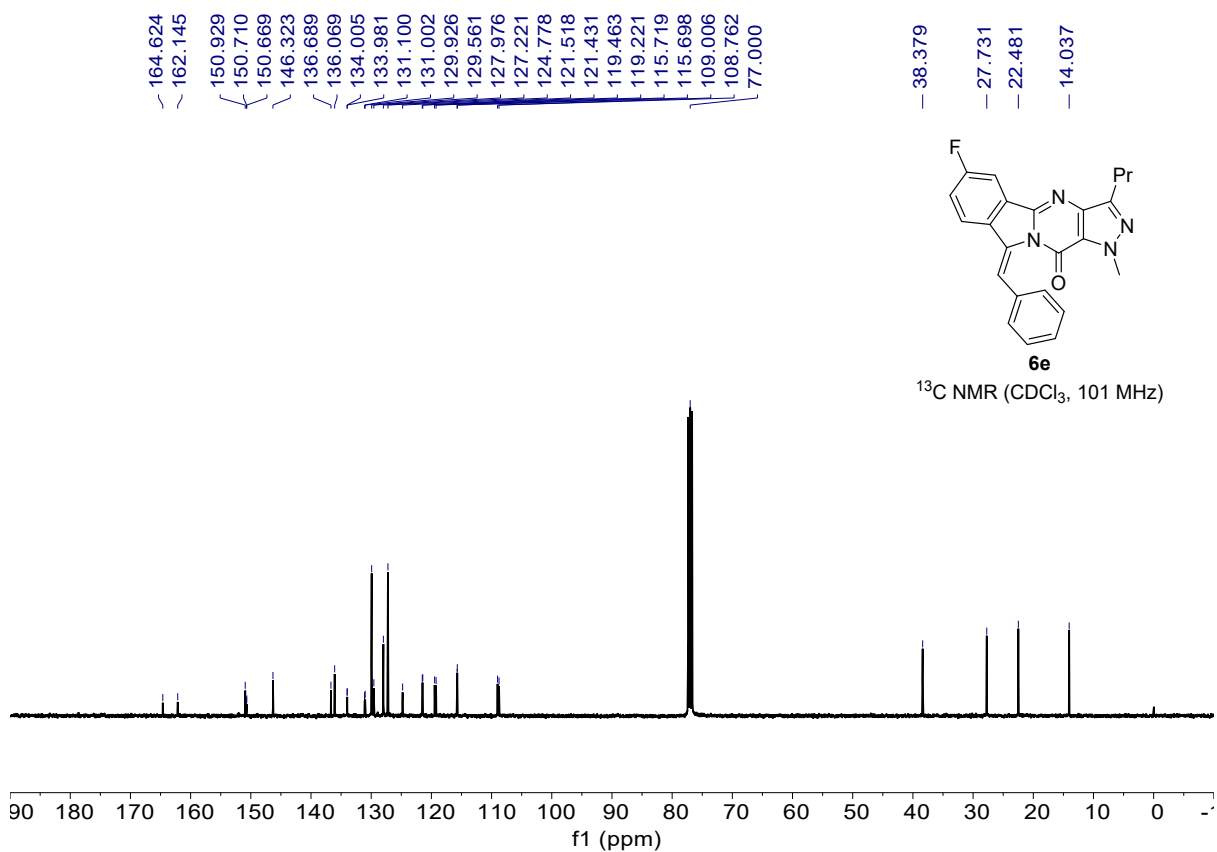
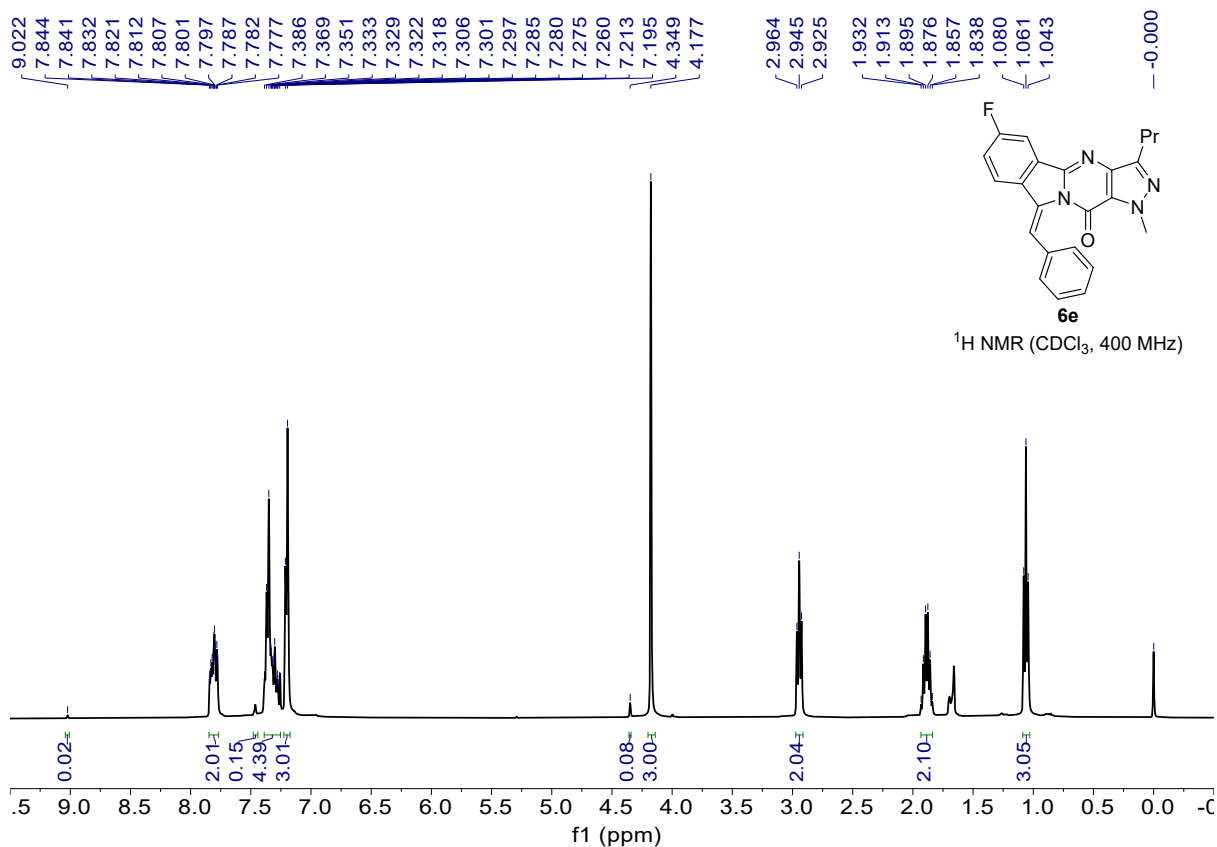


¹³C NMR (CDCl₃, 101 MHz)

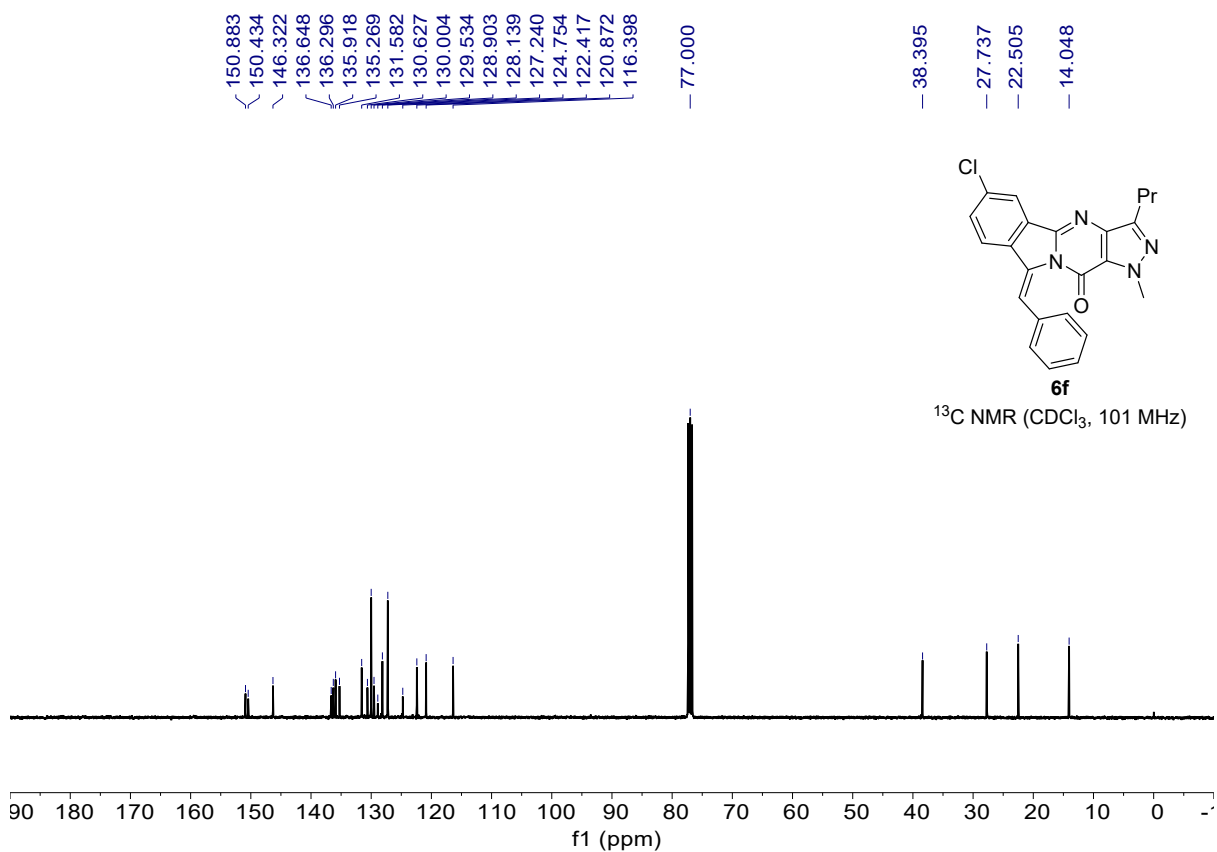
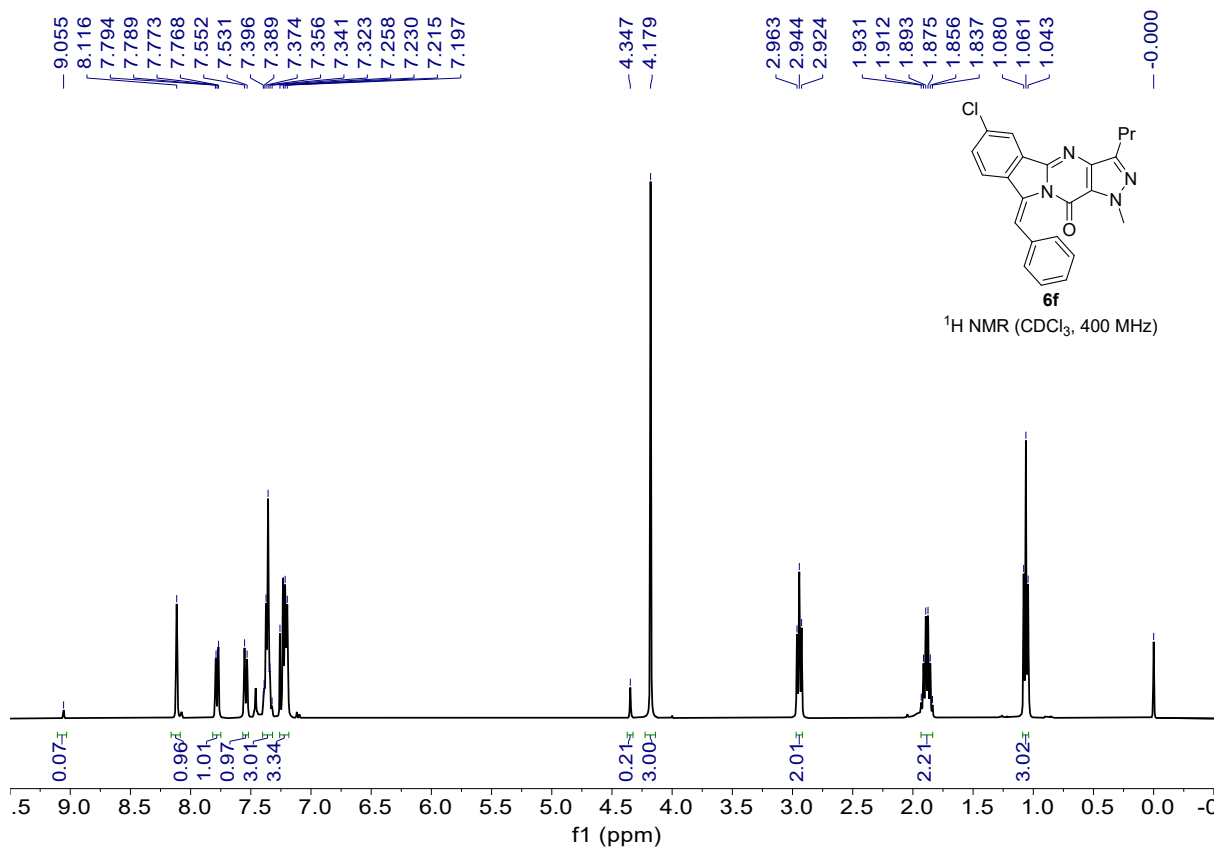
(Z)-9-benzylidene-1,7-dimethyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (6d)



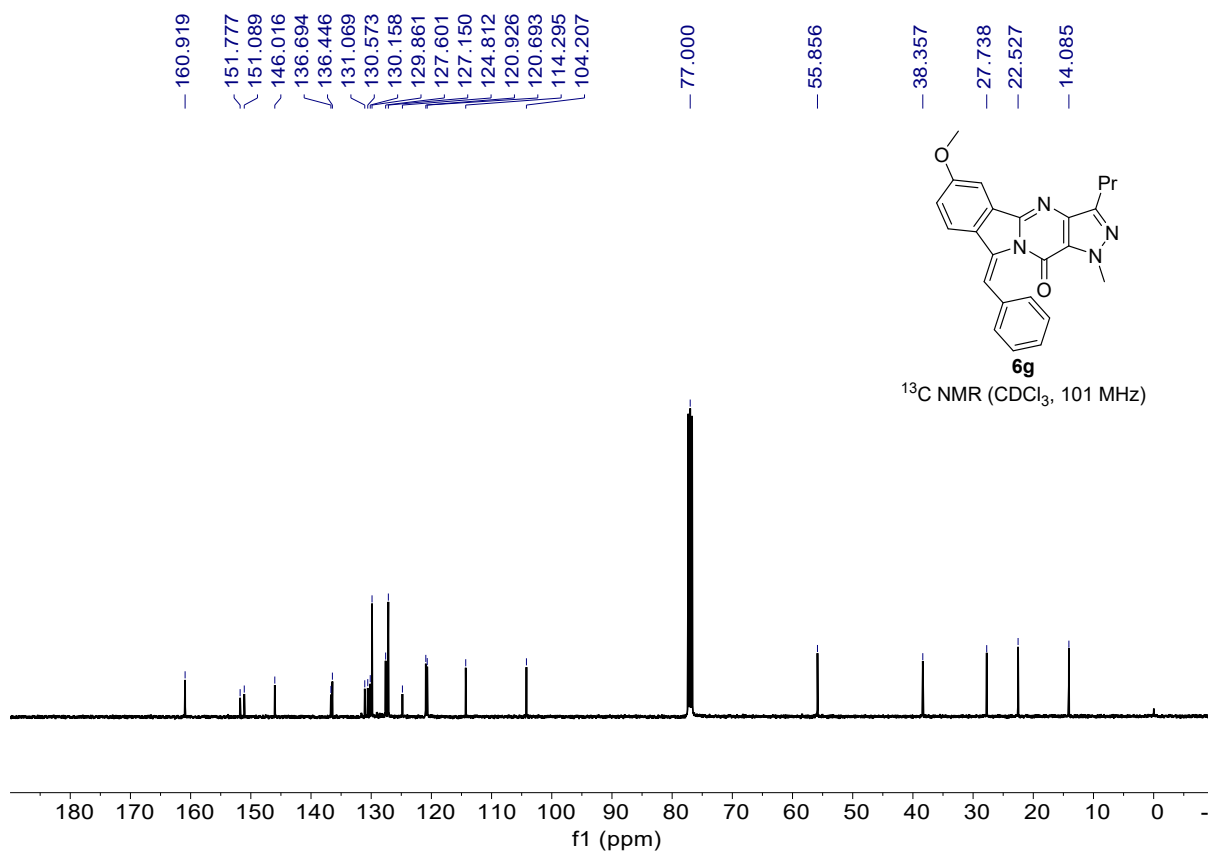
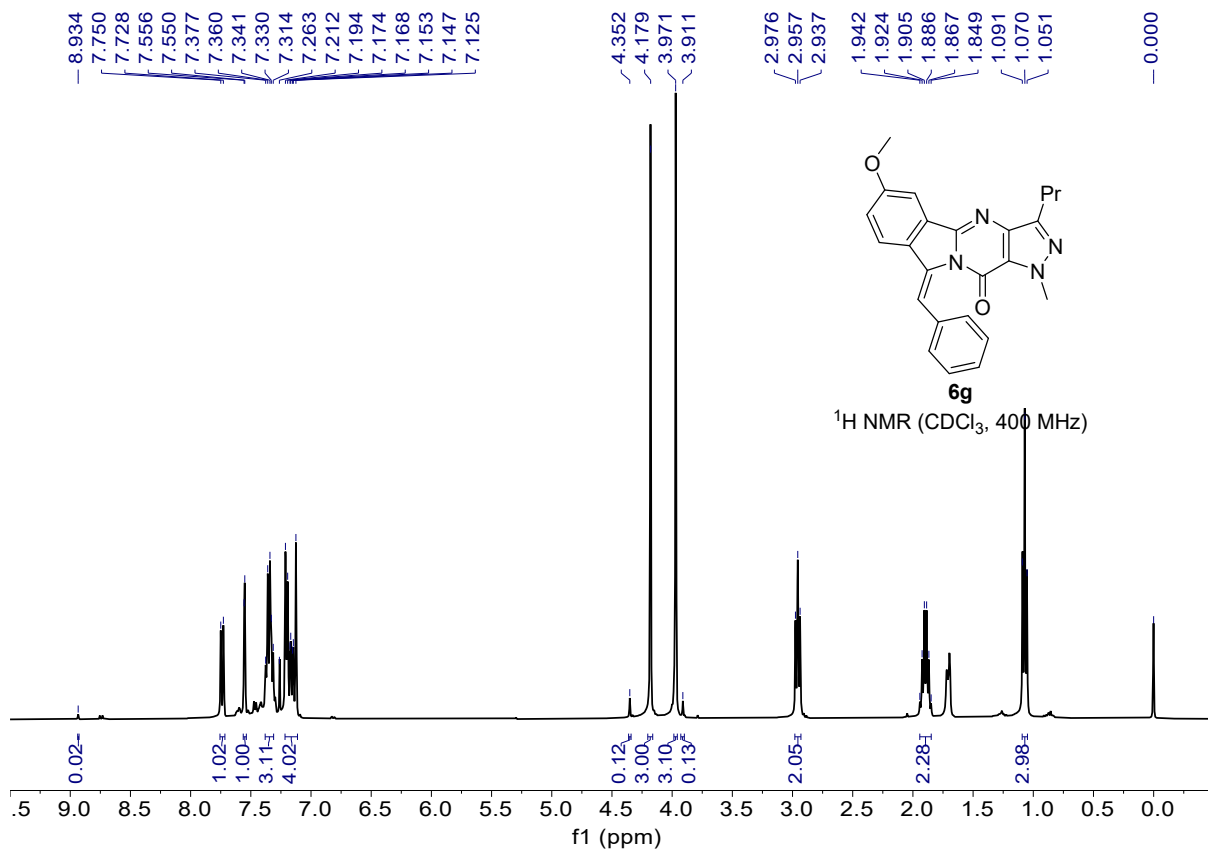
(Z)-9-benzylidene-6-fluoro-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (6e)



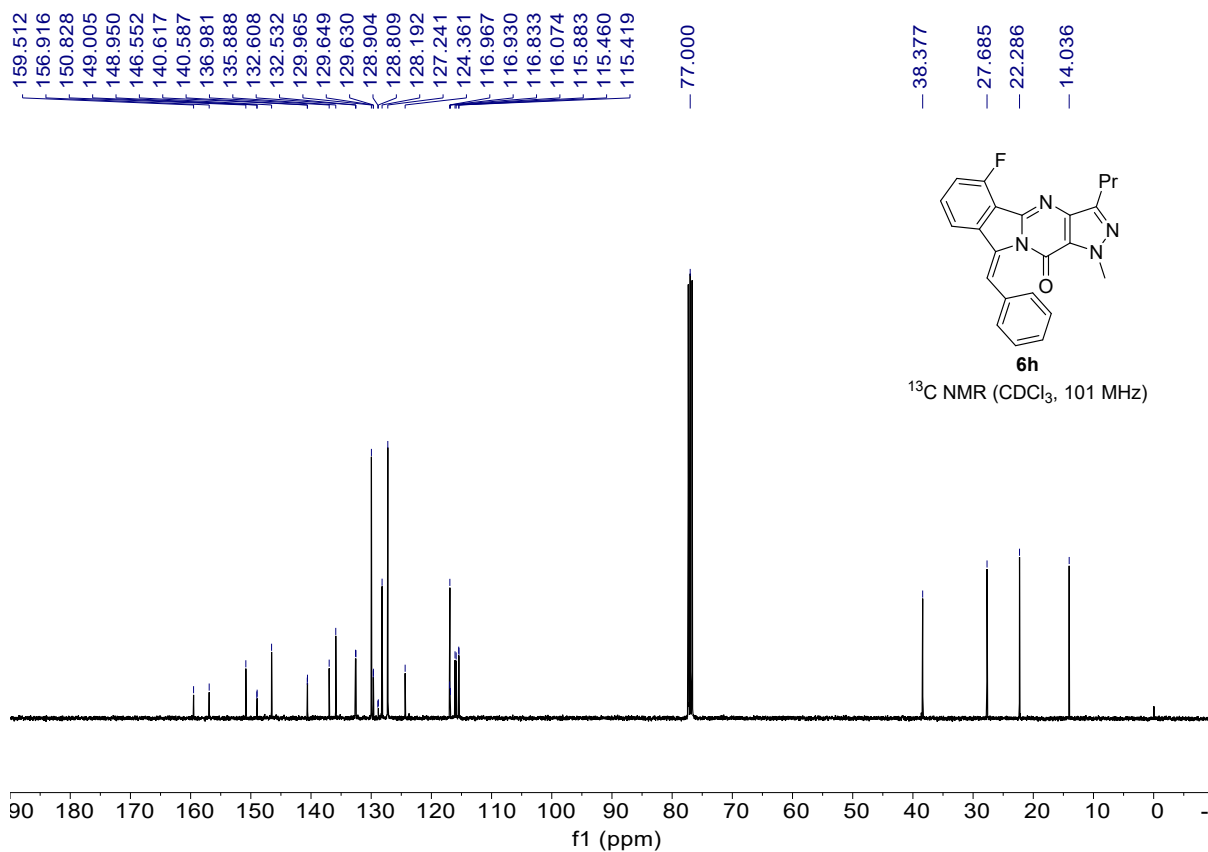
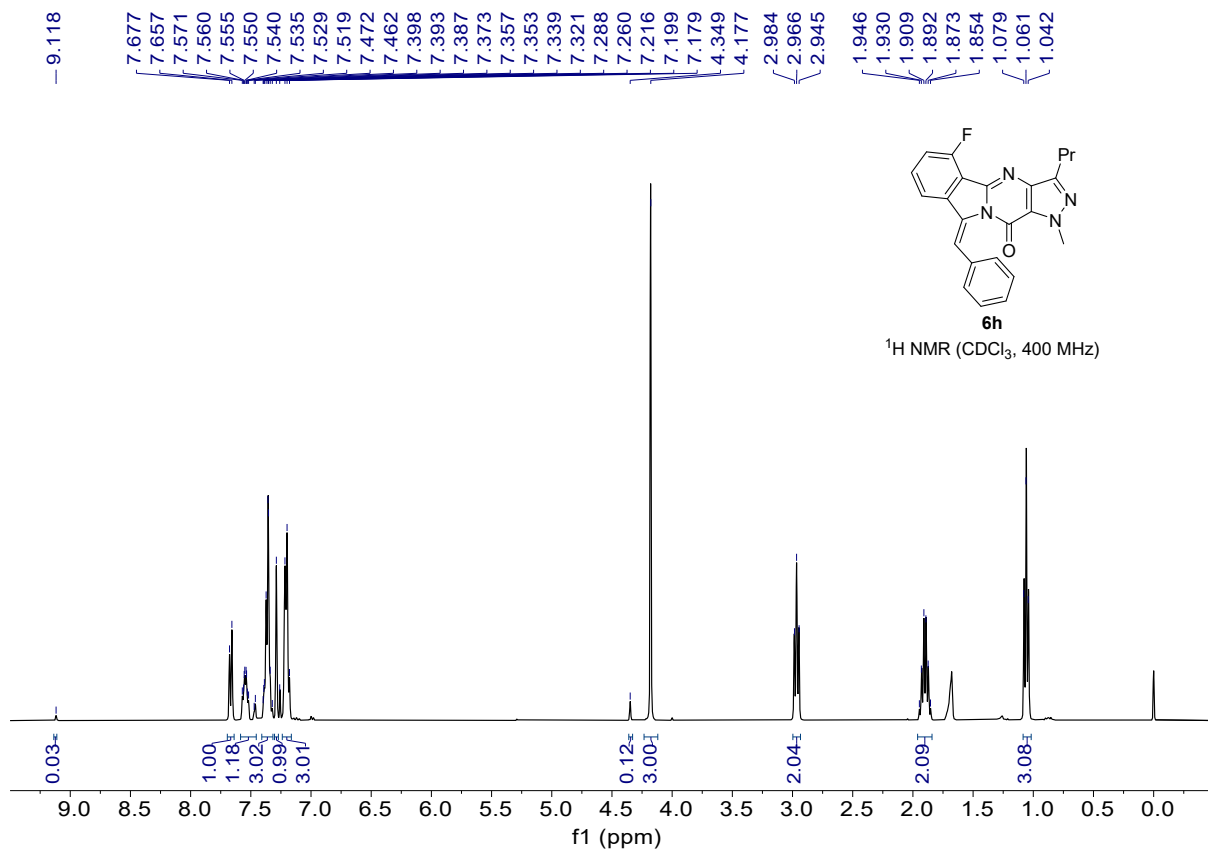
(Z)-9-benzylidene-6-chloro-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (6f)



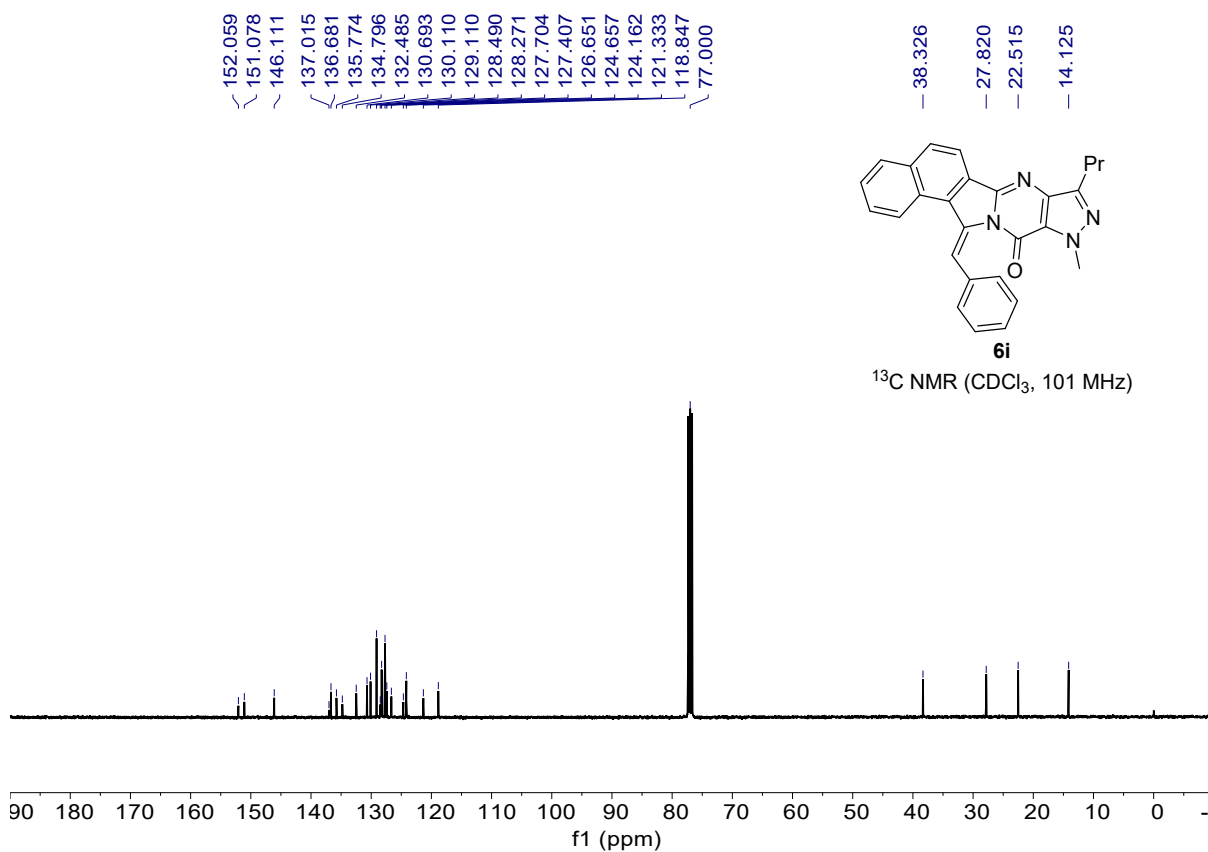
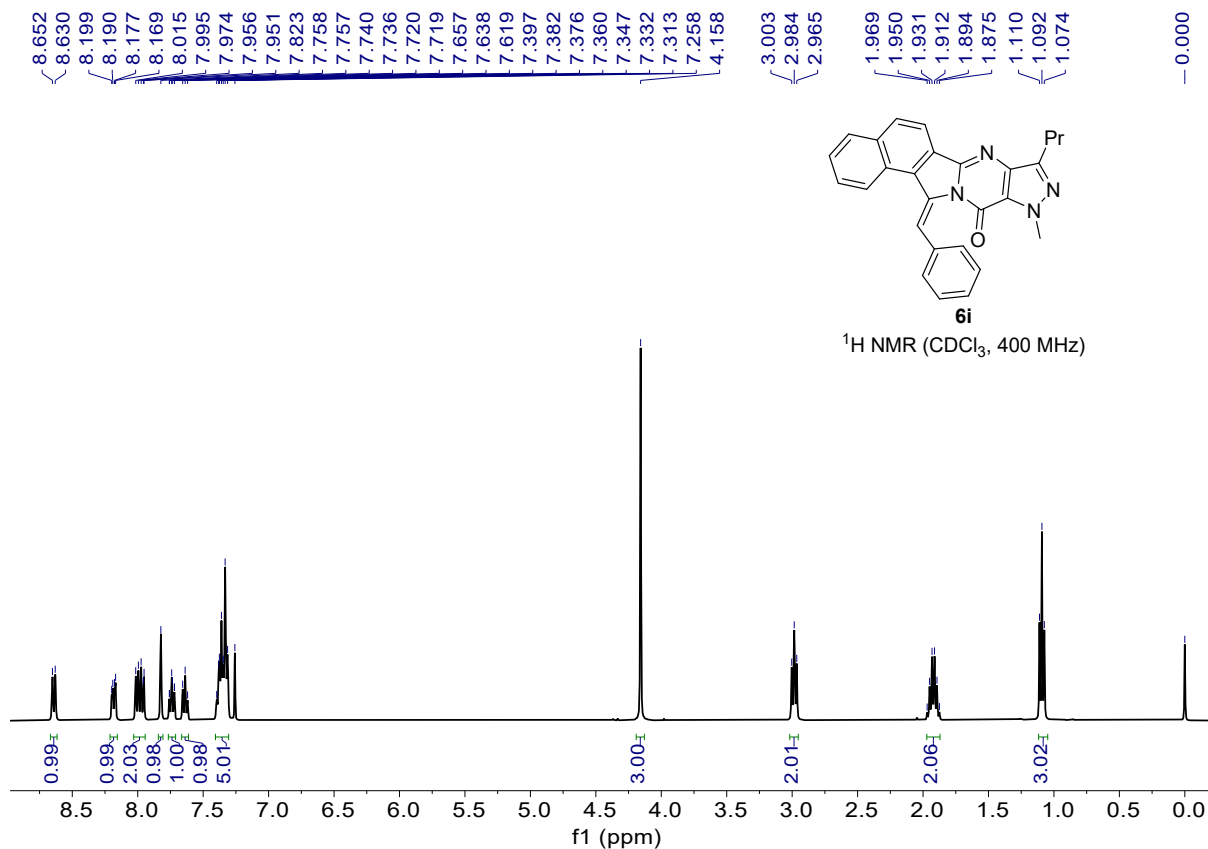
(Z)-9-benzylidene-6-methoxy-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (6g)



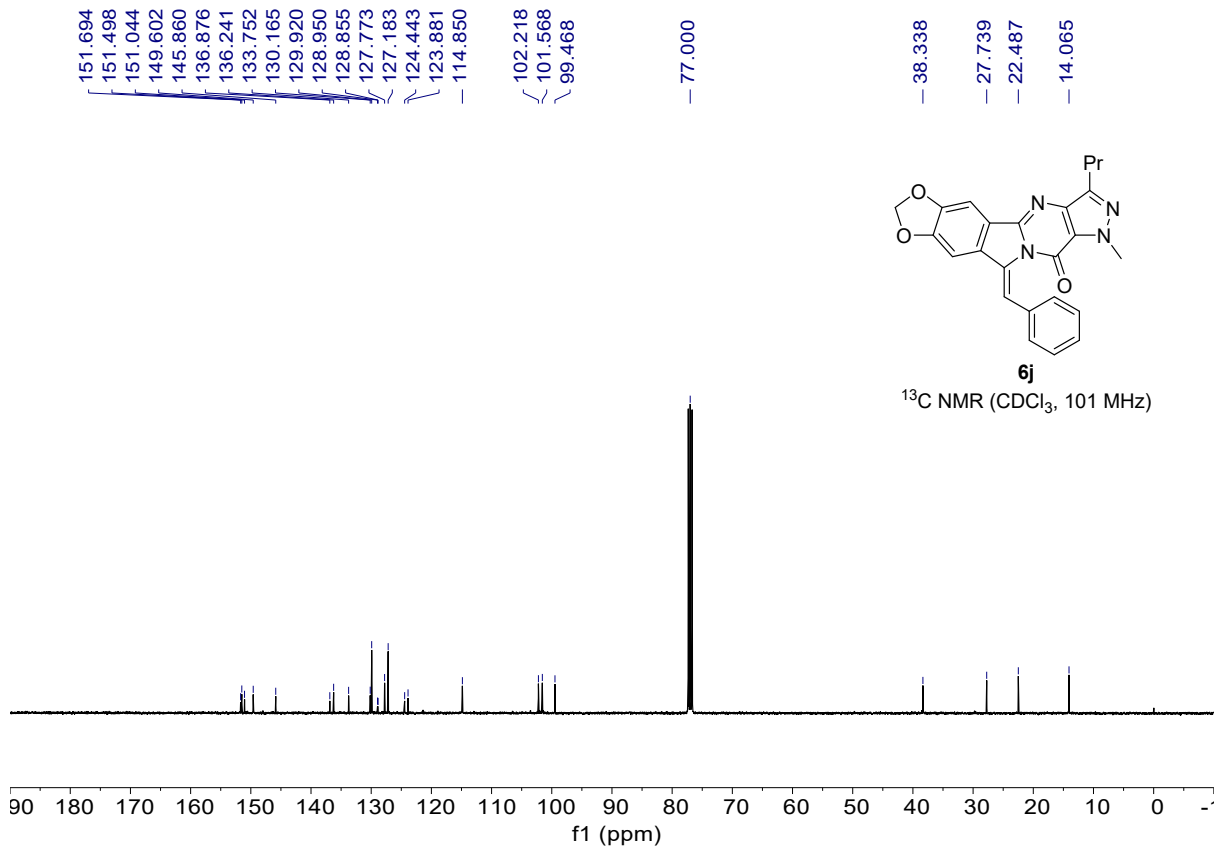
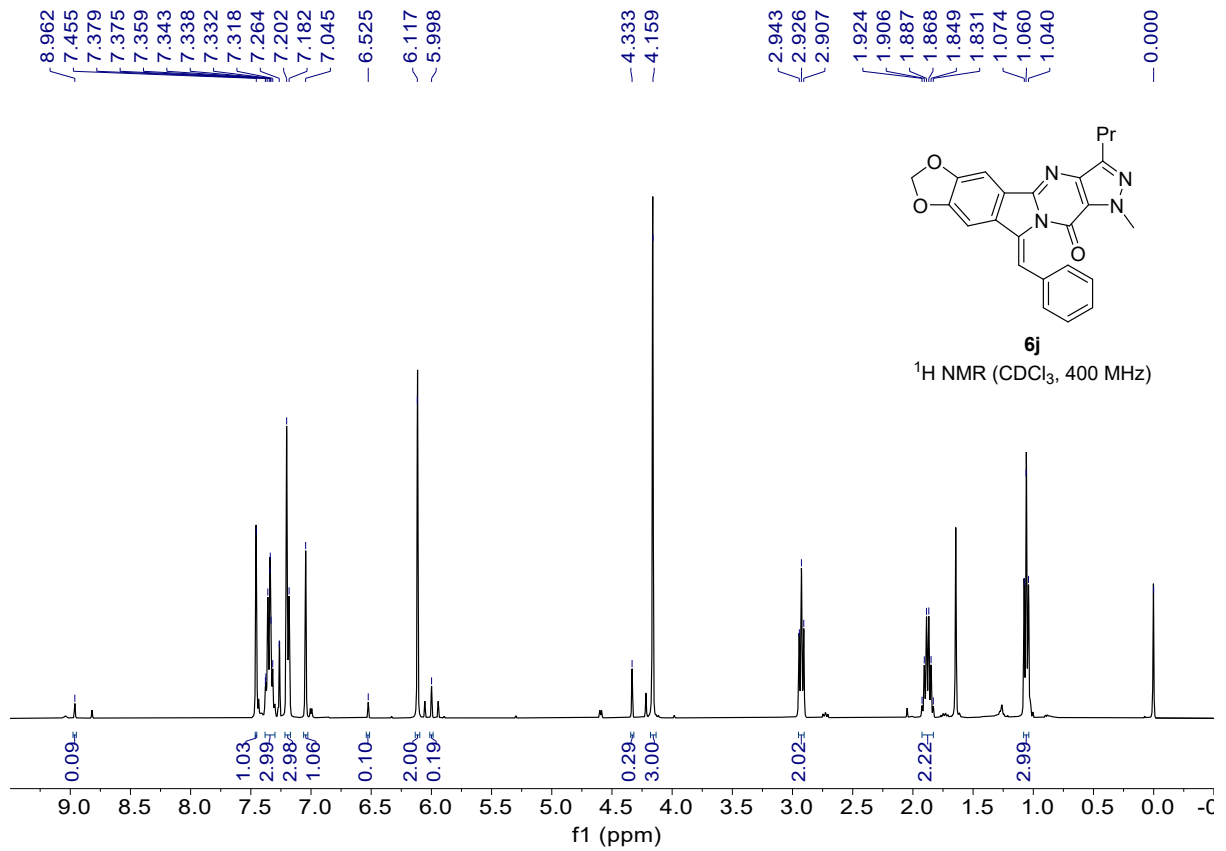
(Z)-9-benzylidene-5-fluoro-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (6h)



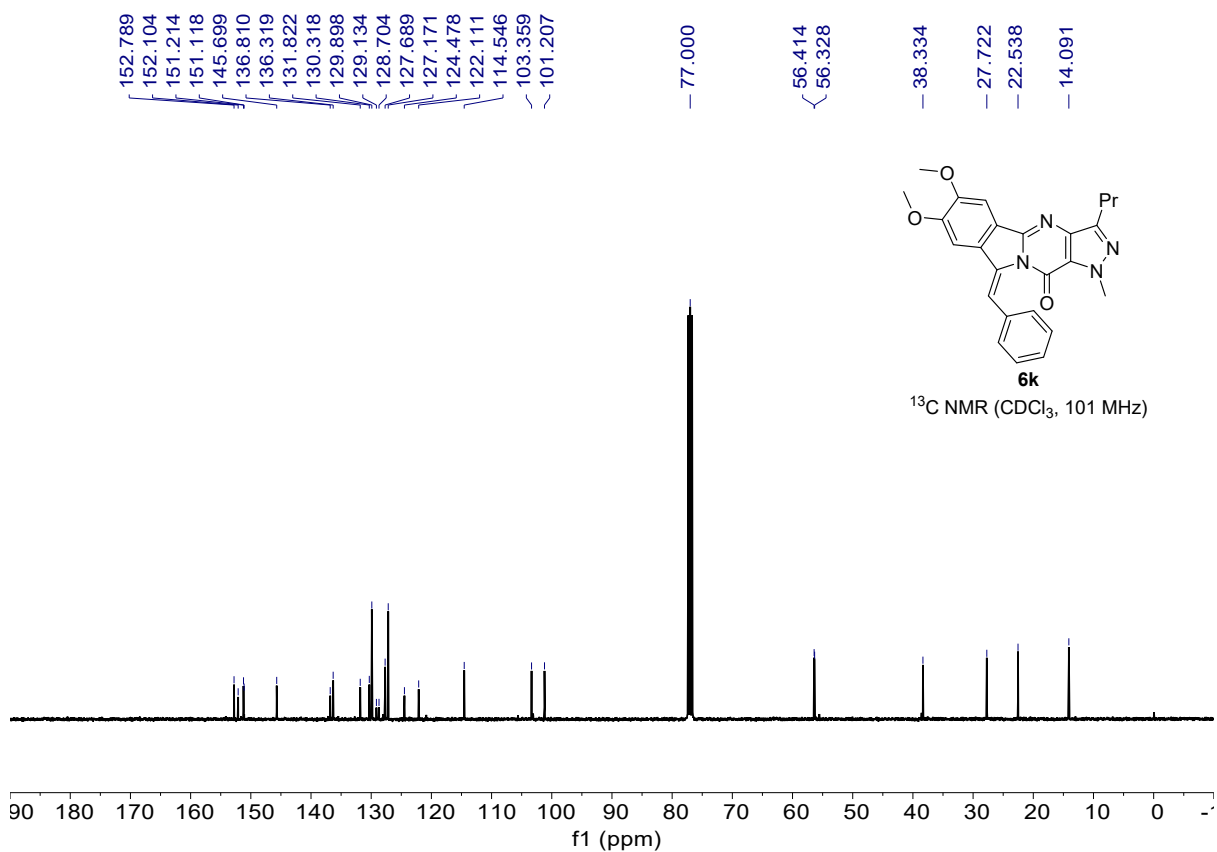
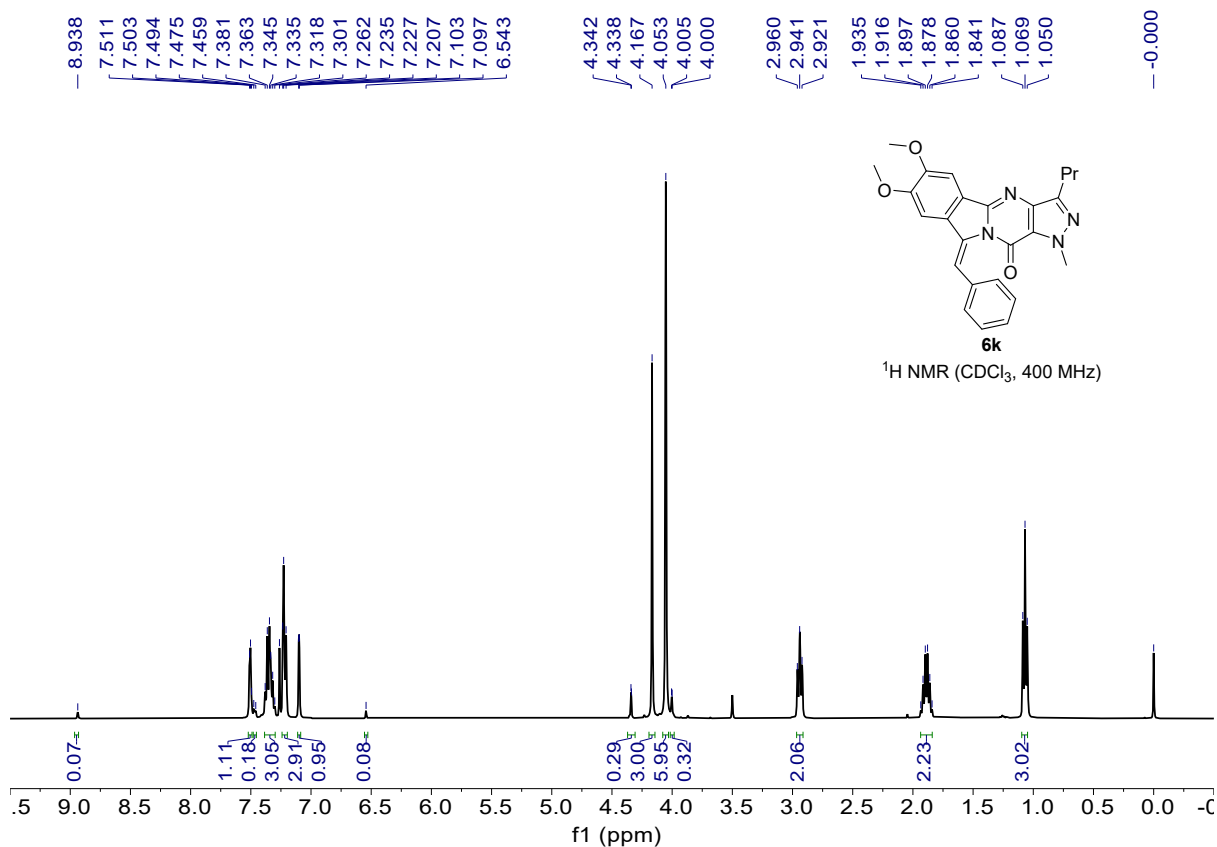
(Z)-11-benzylidene-1-methyl-3-propyl-1,11-dihydro-13H-benzo[f]pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-13-one (6i)



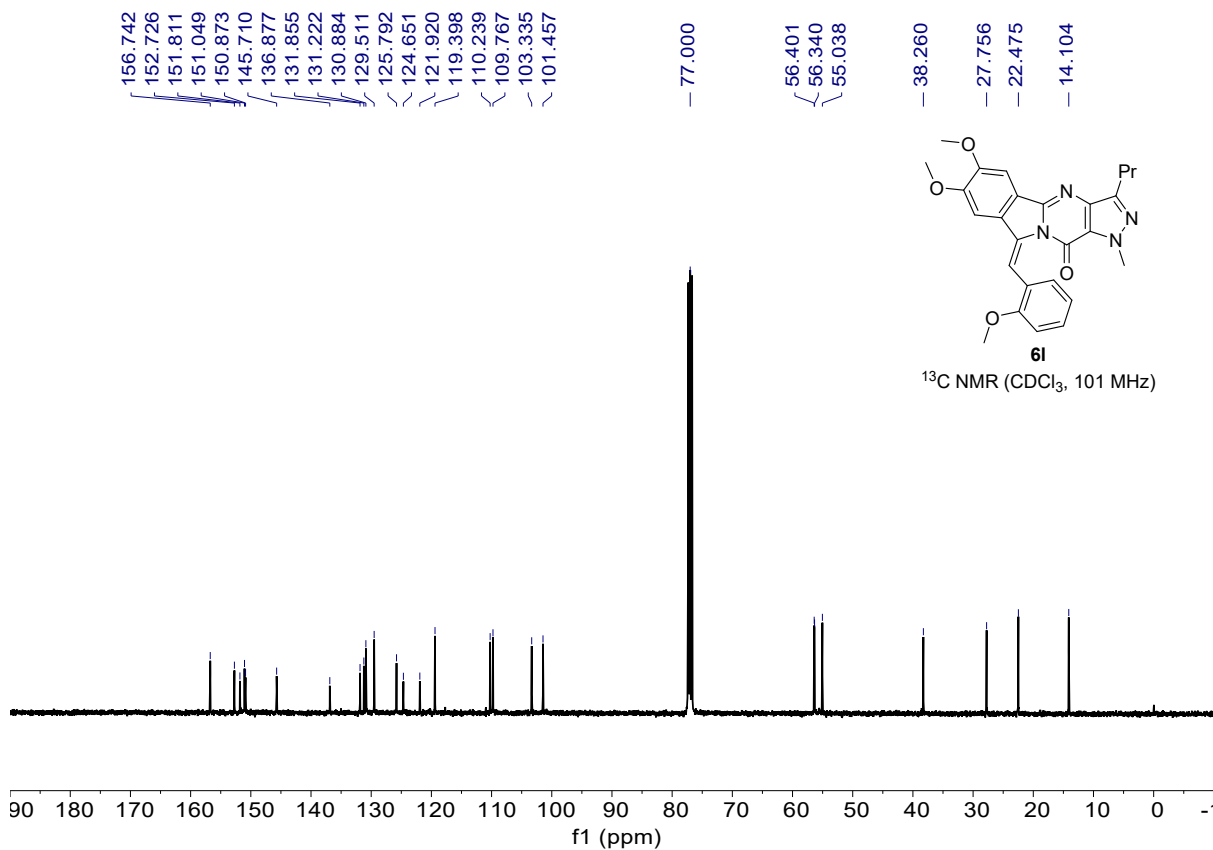
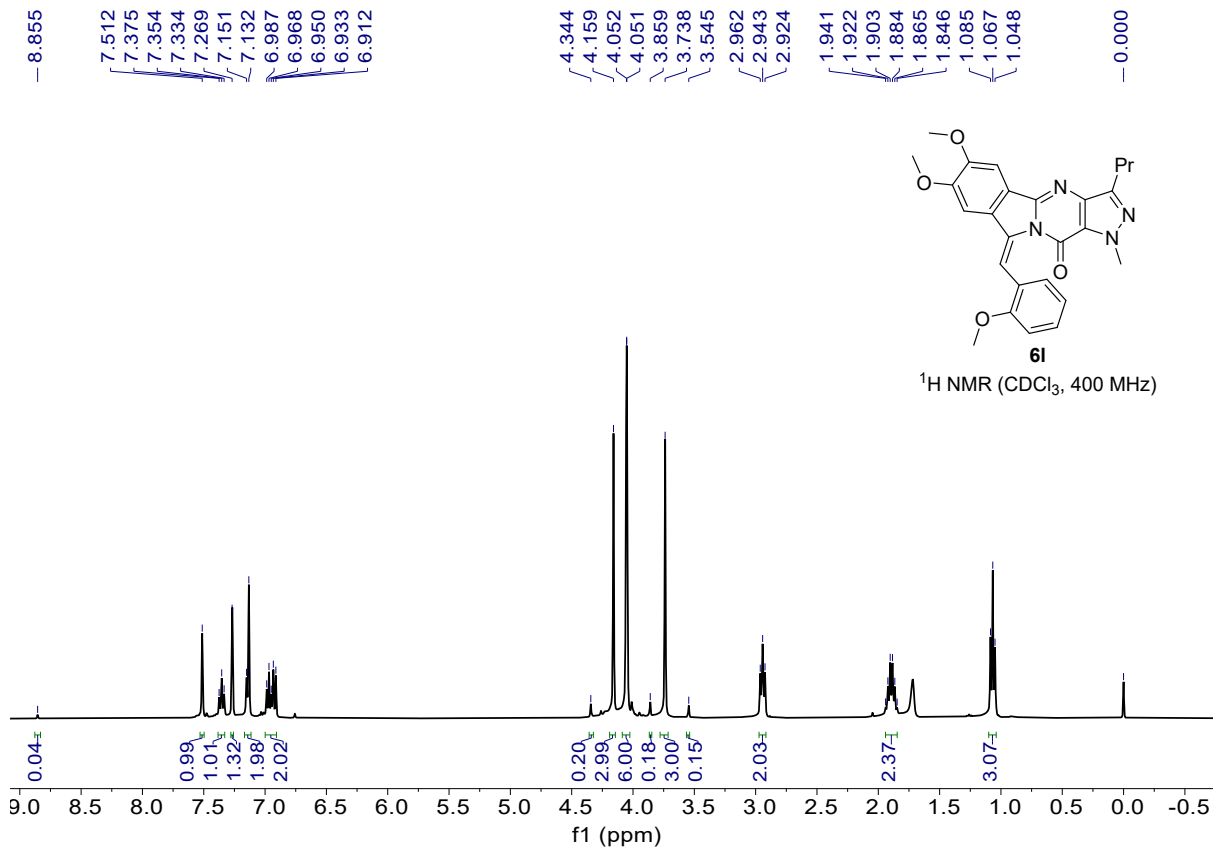
(Z)-10-benzylidene-1-methyl-3-propyl-1,10-dihydro-12H-[1,3]dioxolo[4,5-f]pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-12-one (6j)



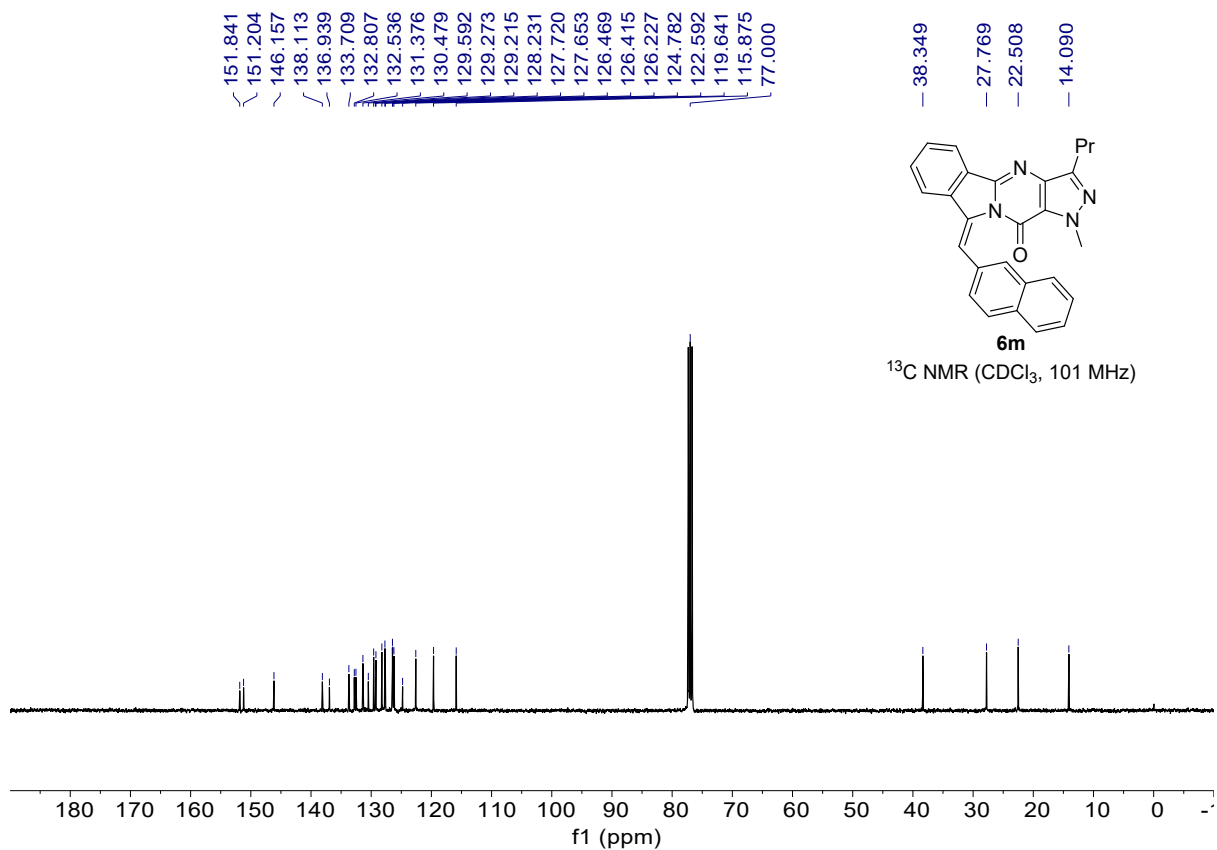
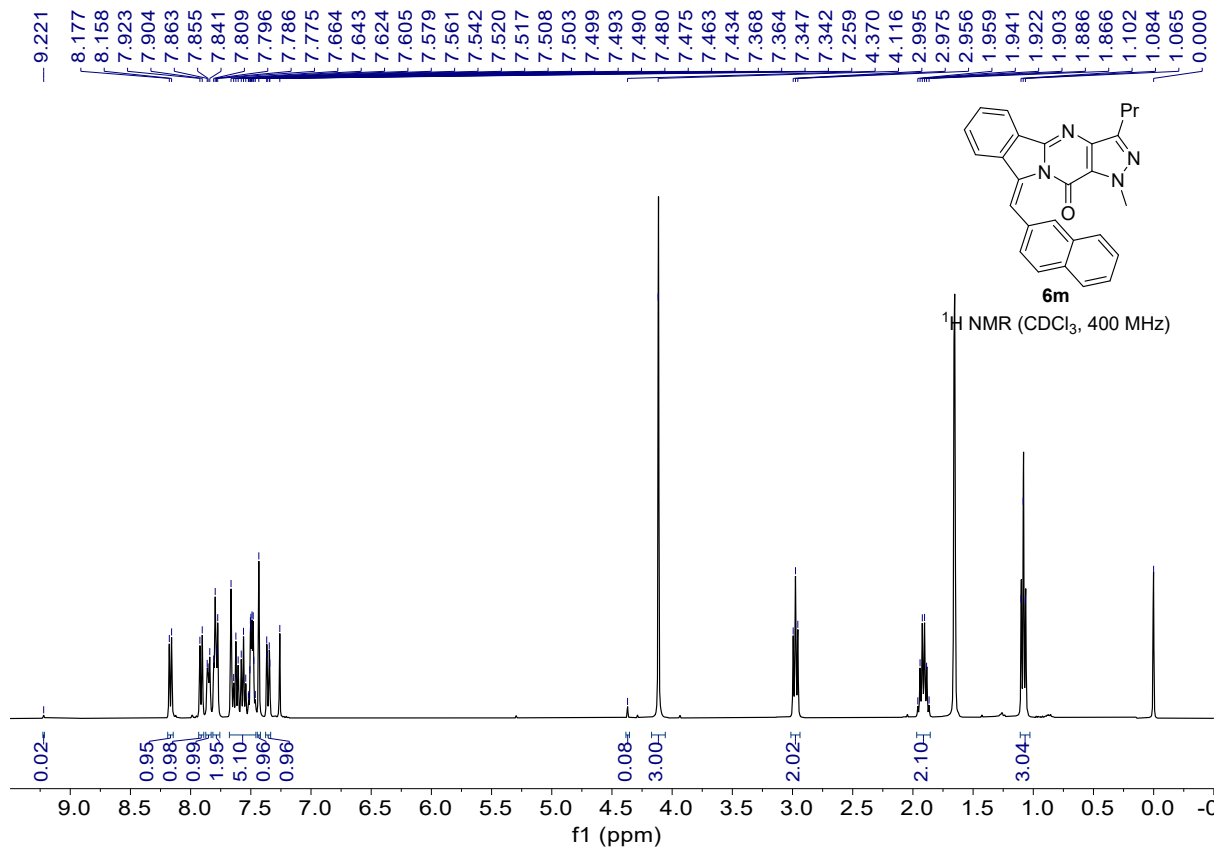
(Z)-9-benzylidene-6,7-dimethoxy-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (6k)



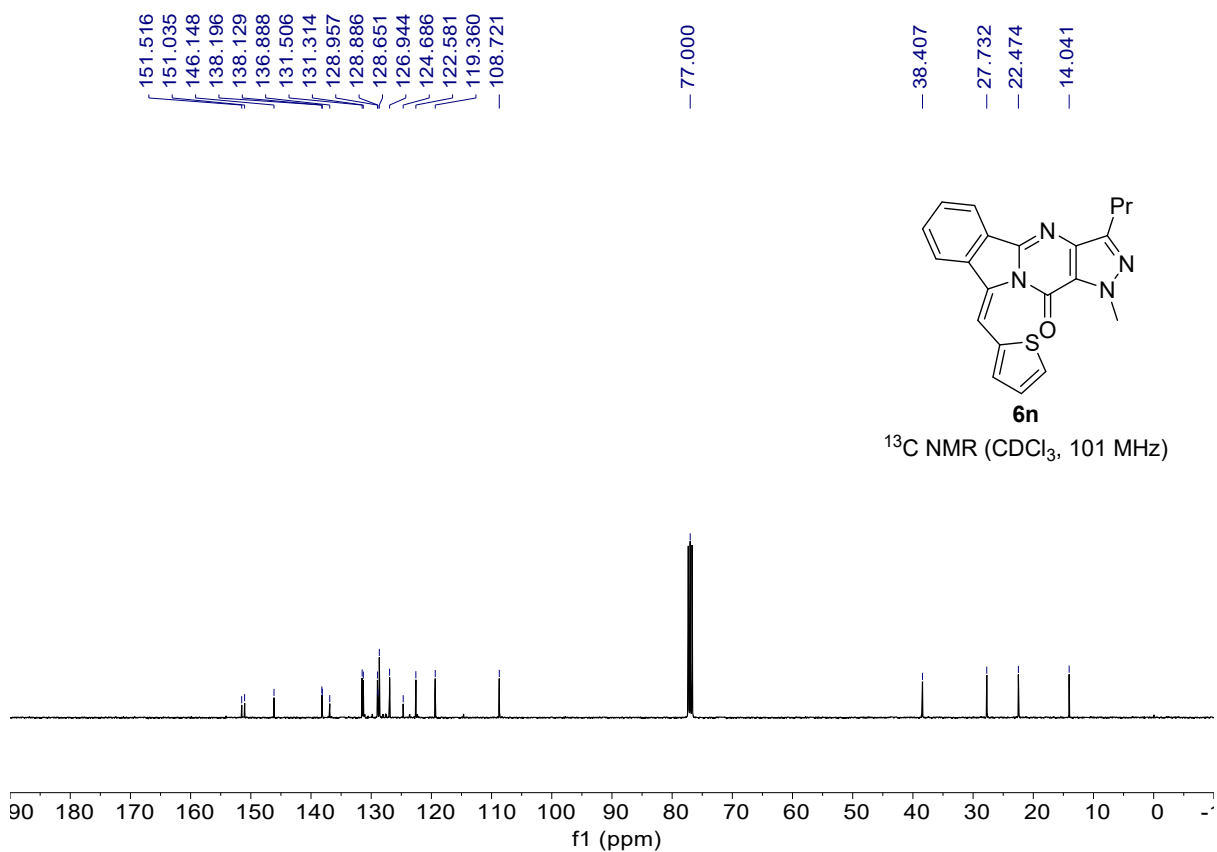
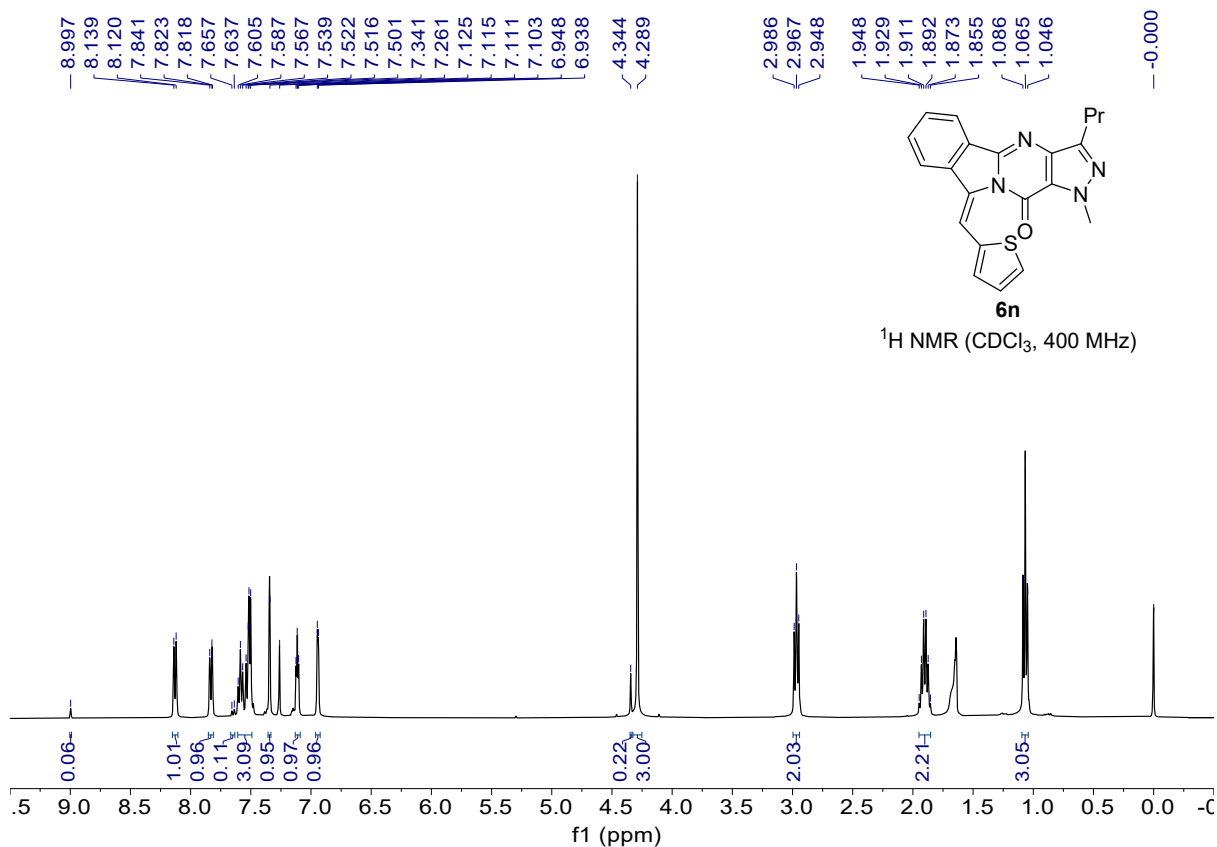
(Z)-6,7-dimethoxy-9-(2-methoxybenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (6I)



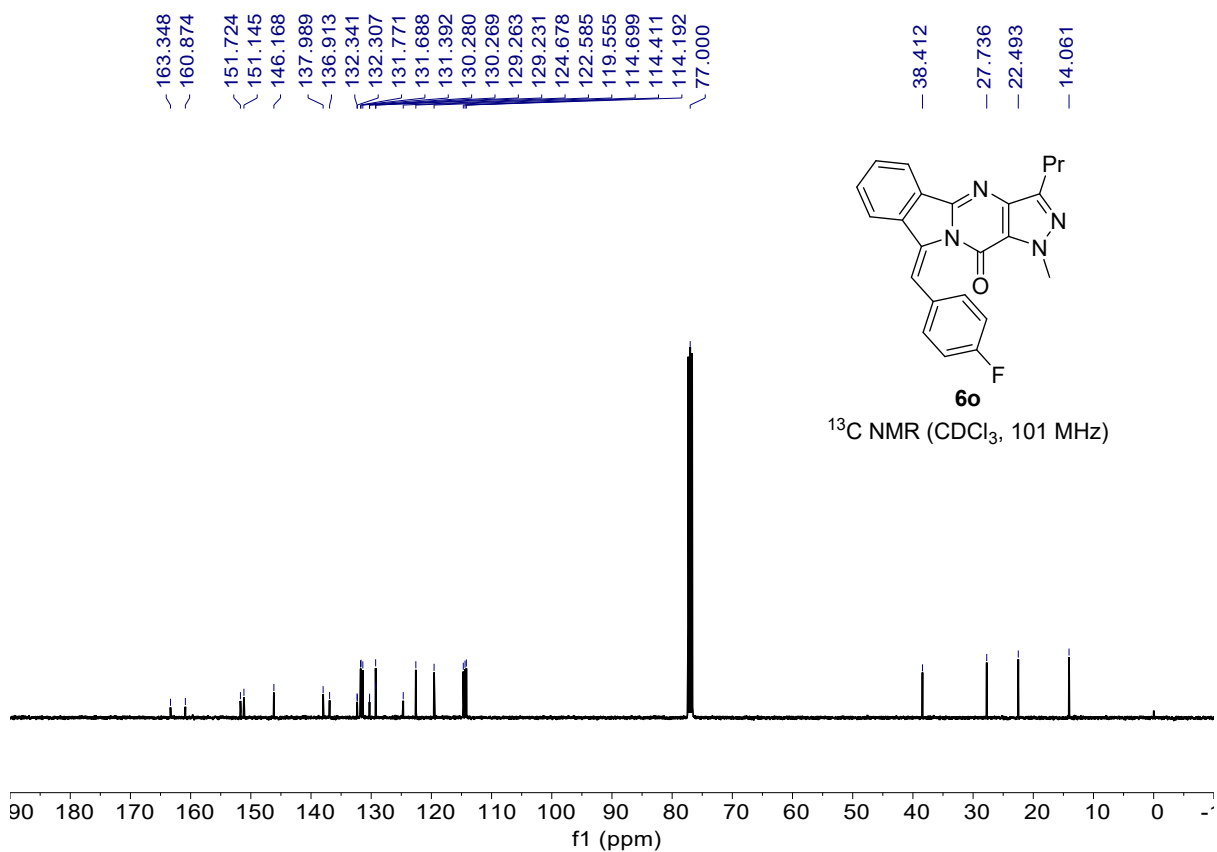
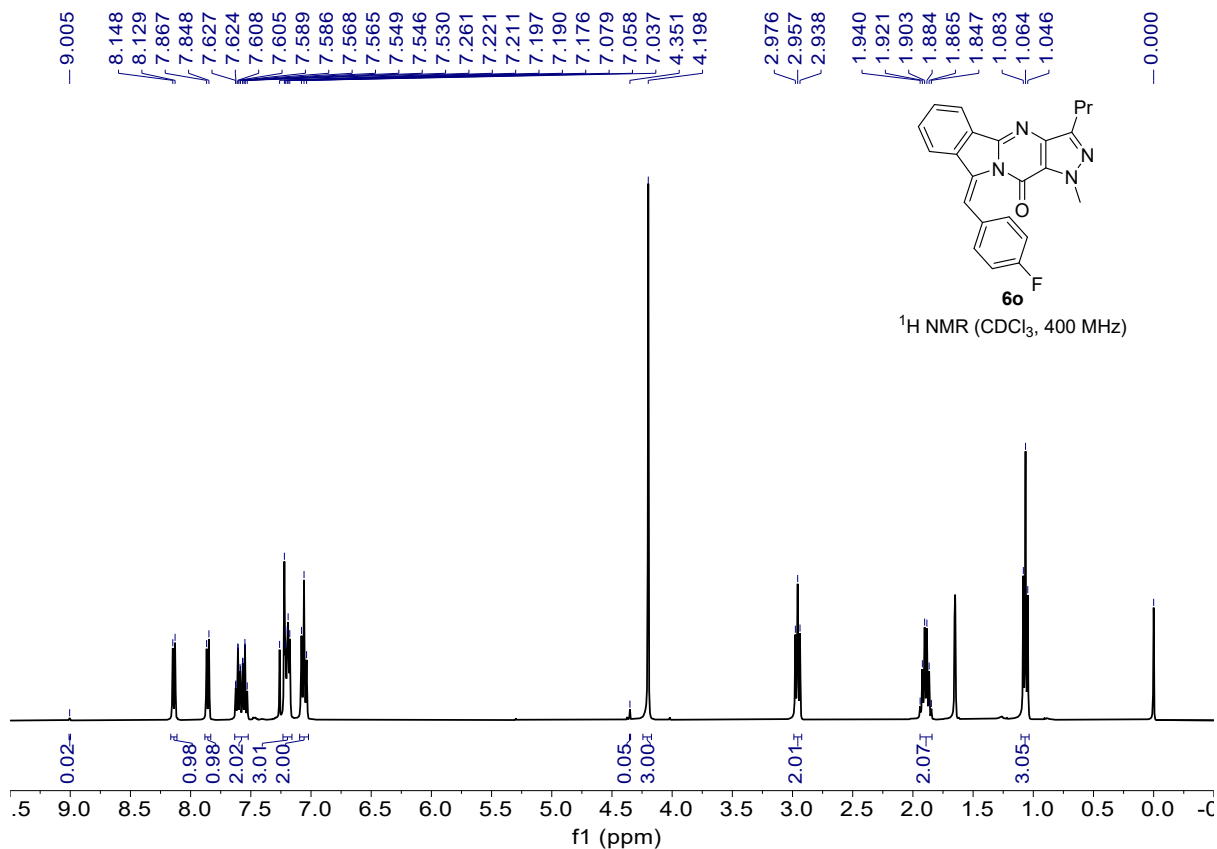
(Z)-1-methyl-9-(naphthalen-2-ylmethylene)-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (6m)



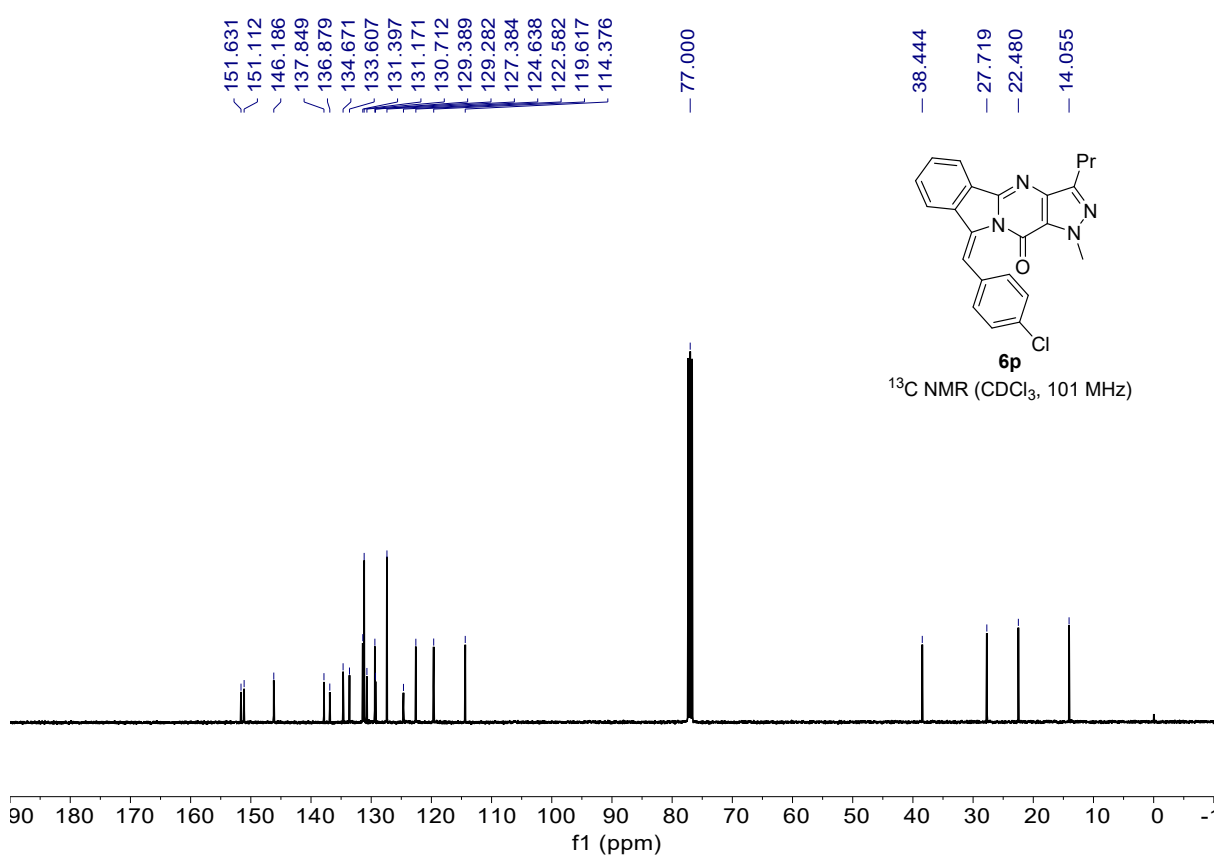
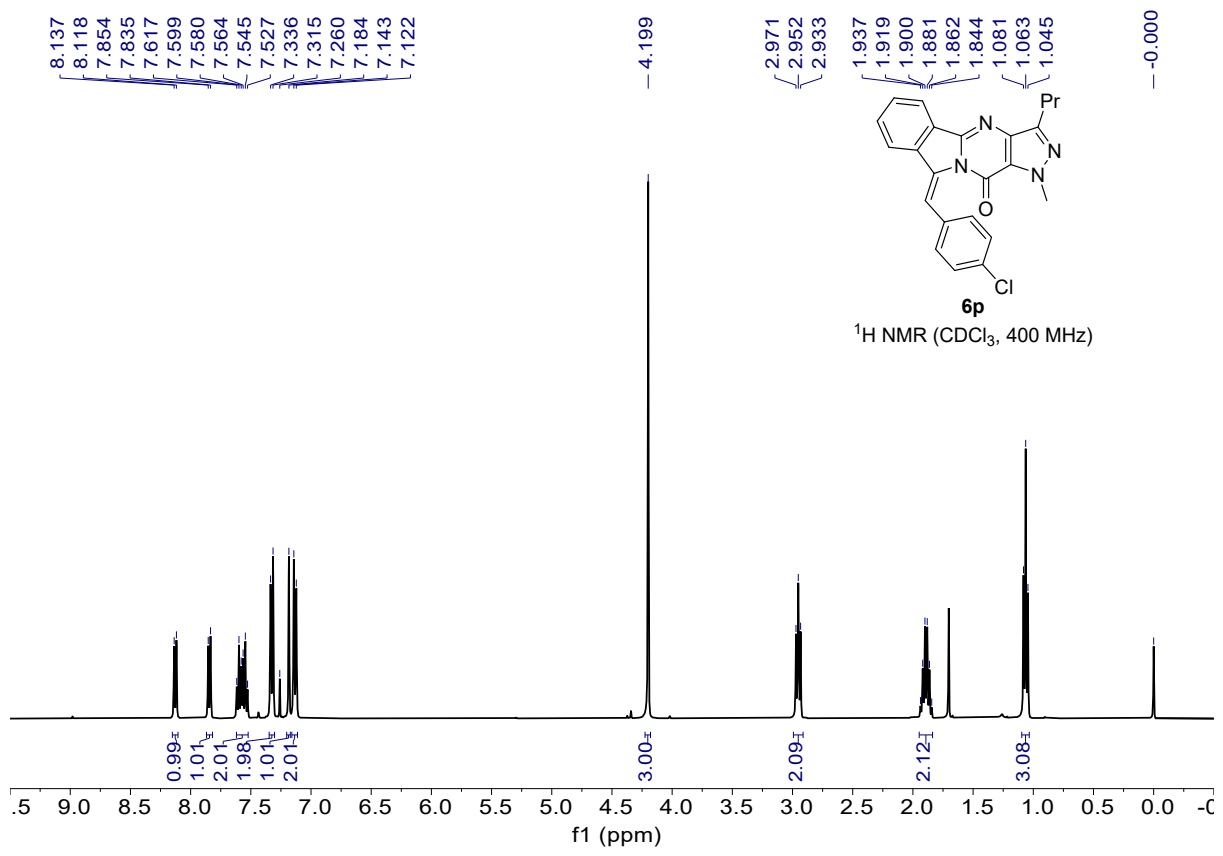
(Z)-1-methyl-3-propyl-9-(thiophen-2-ylmethylene)-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (6n)



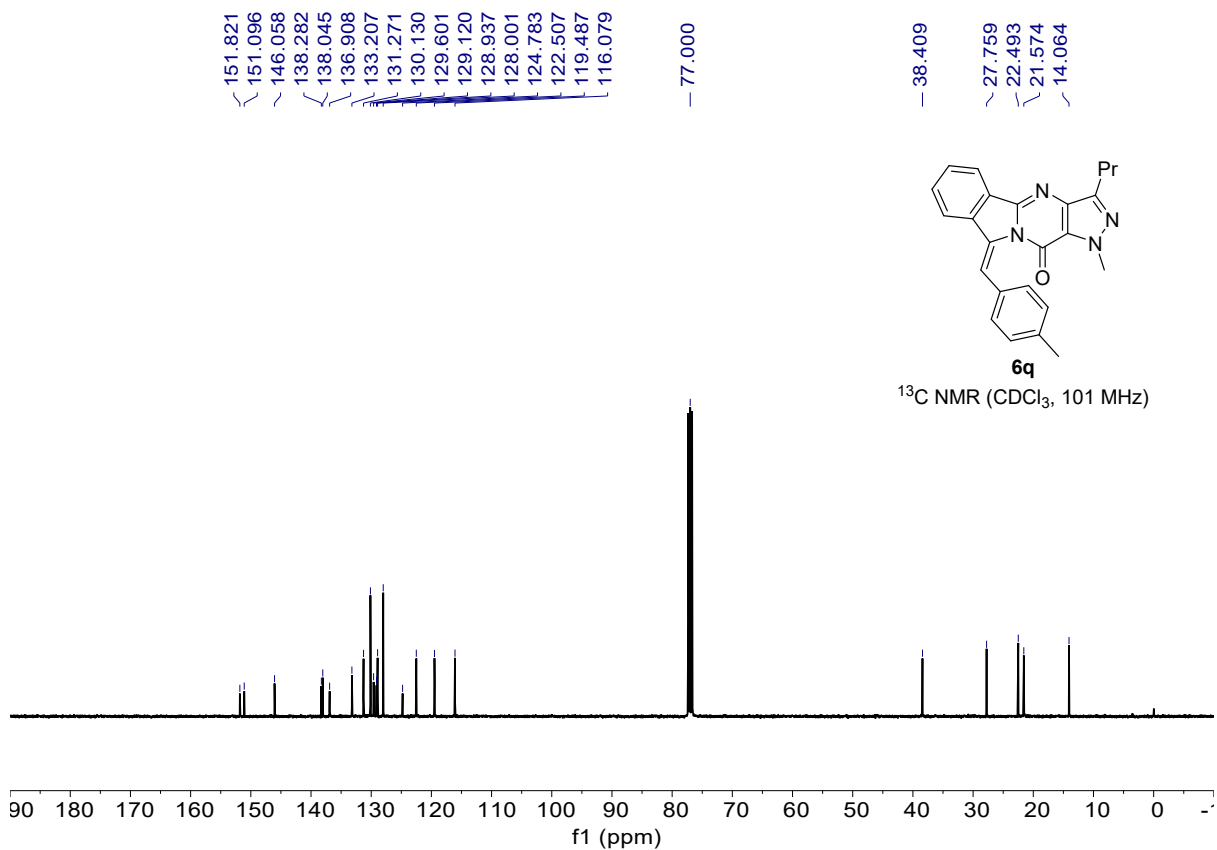
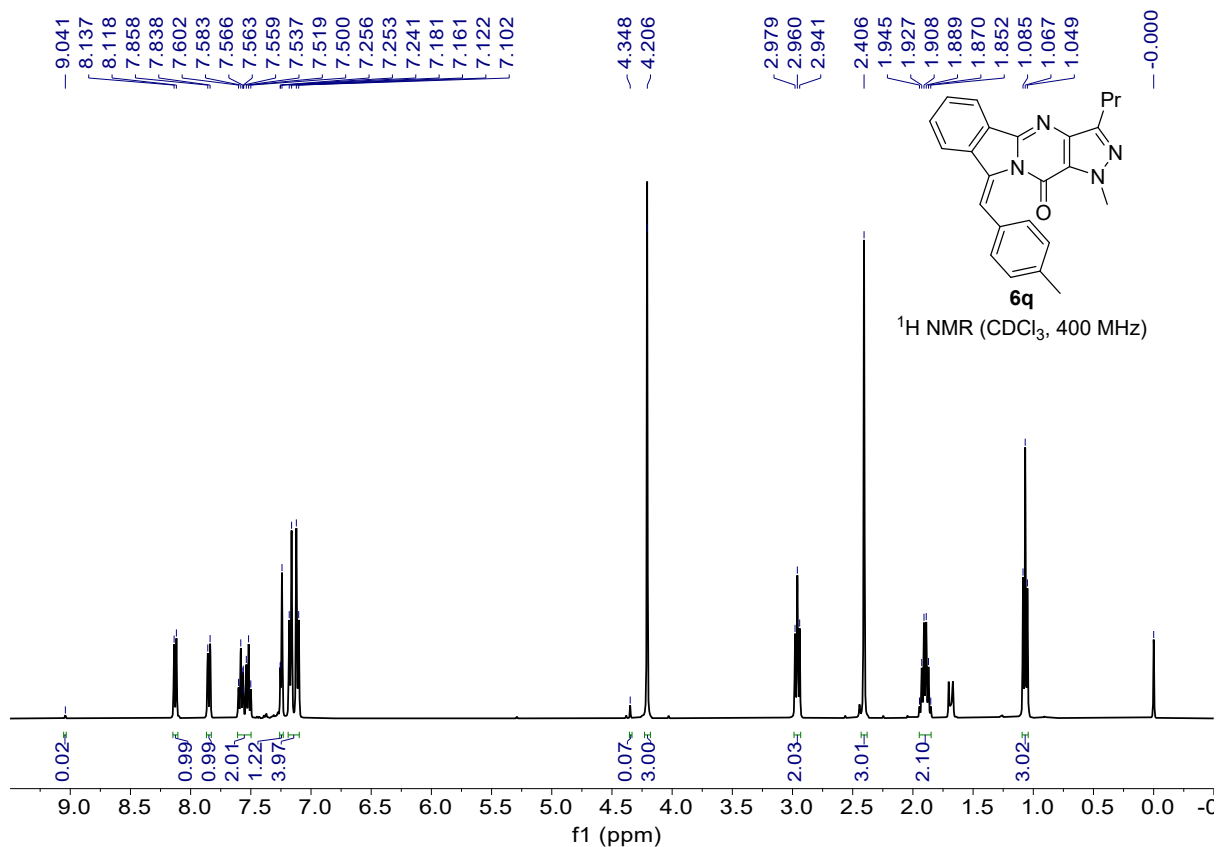
(Z)-9-(4-fluorobenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (6o)



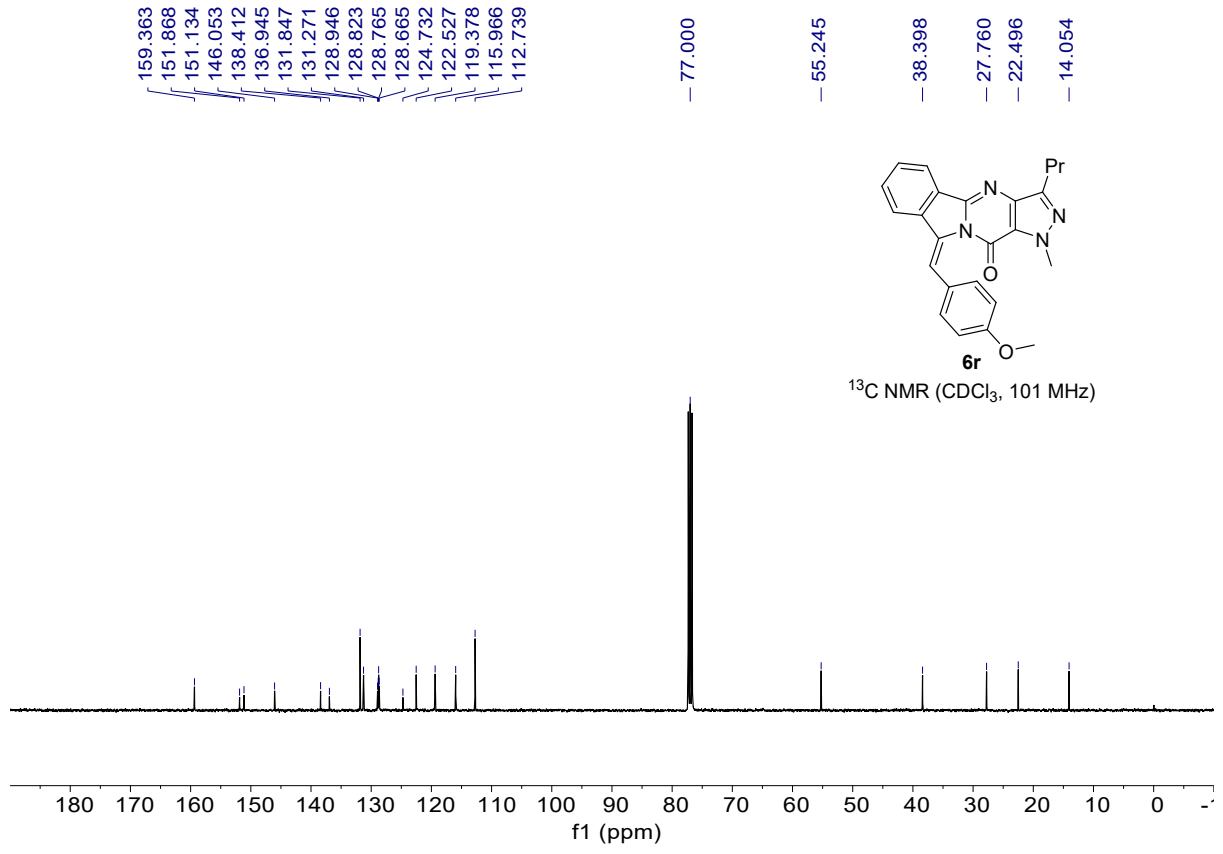
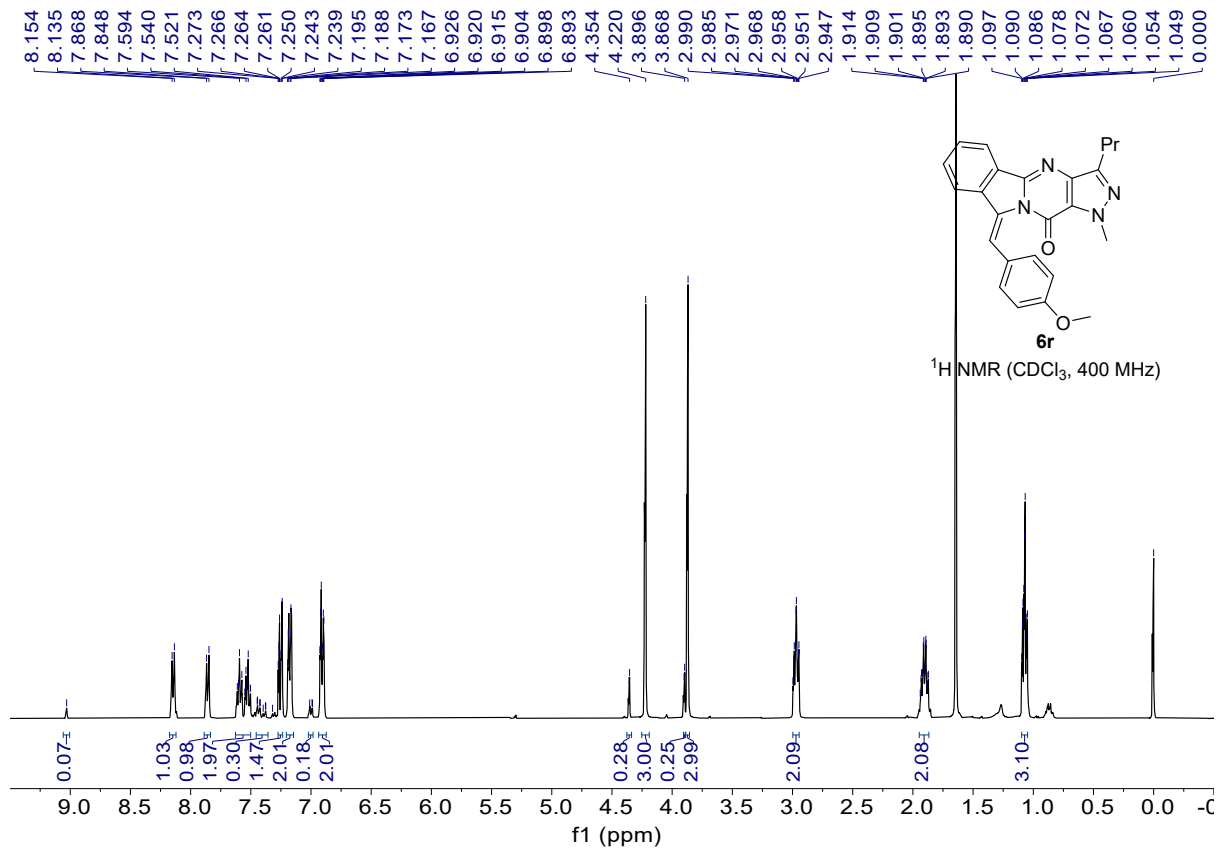
(Z)-9-(4-chlorobenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (6p)



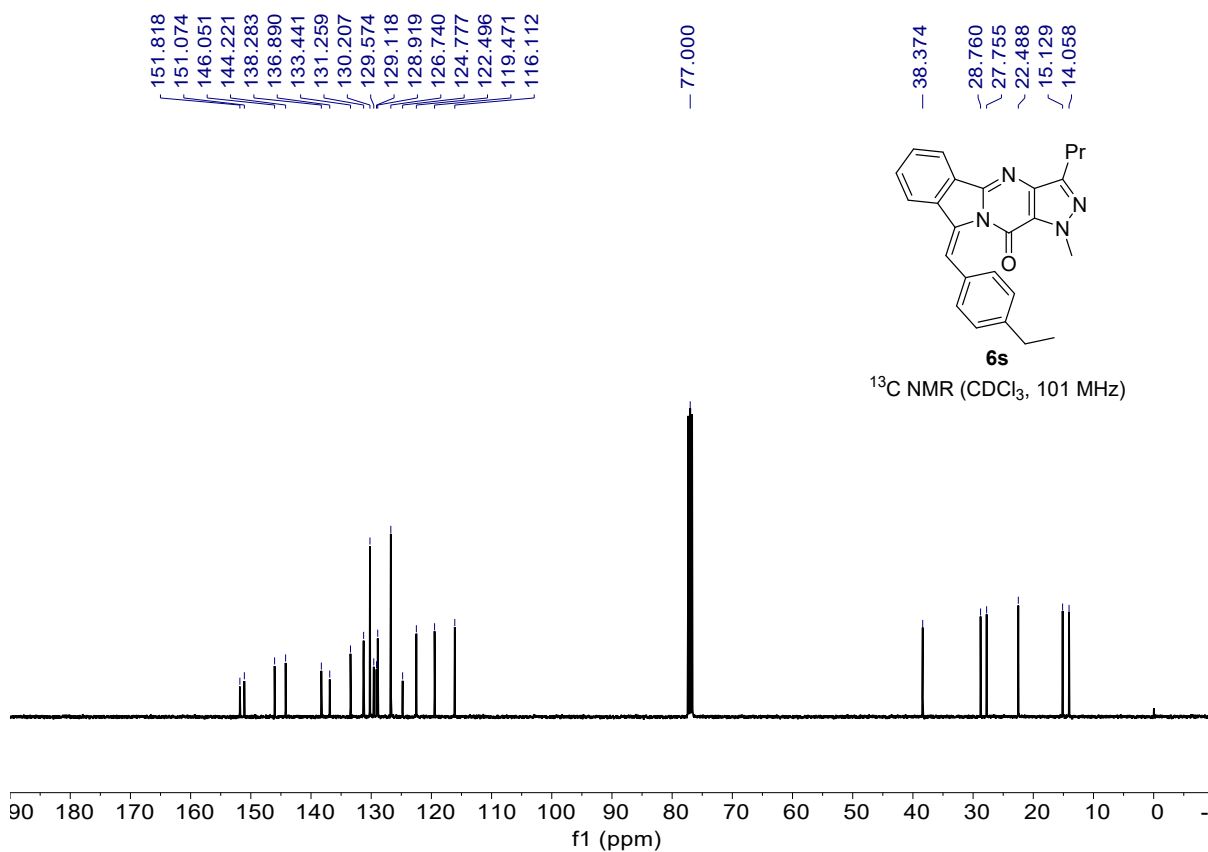
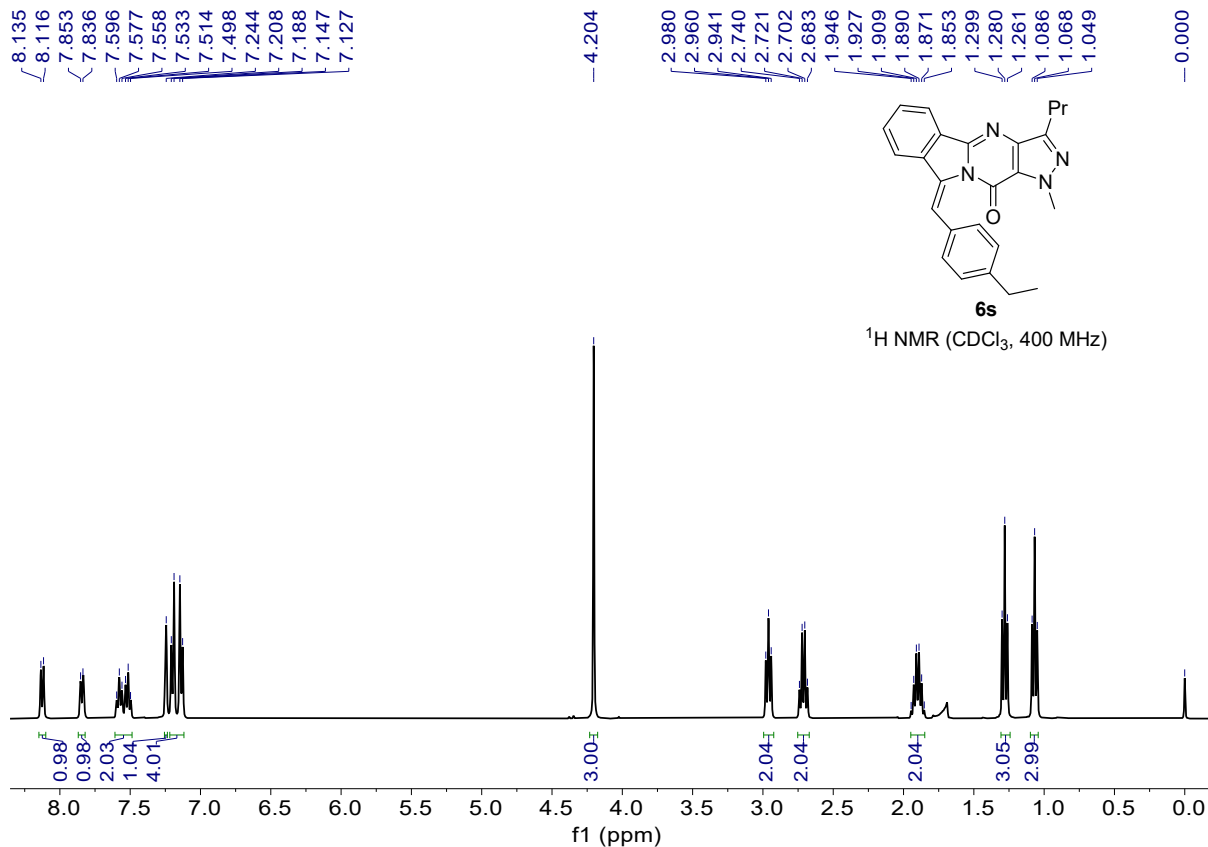
(Z)-1-methyl-9-(4-methylbenzylidene)-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-*a*]isoindol-11-one (6q)



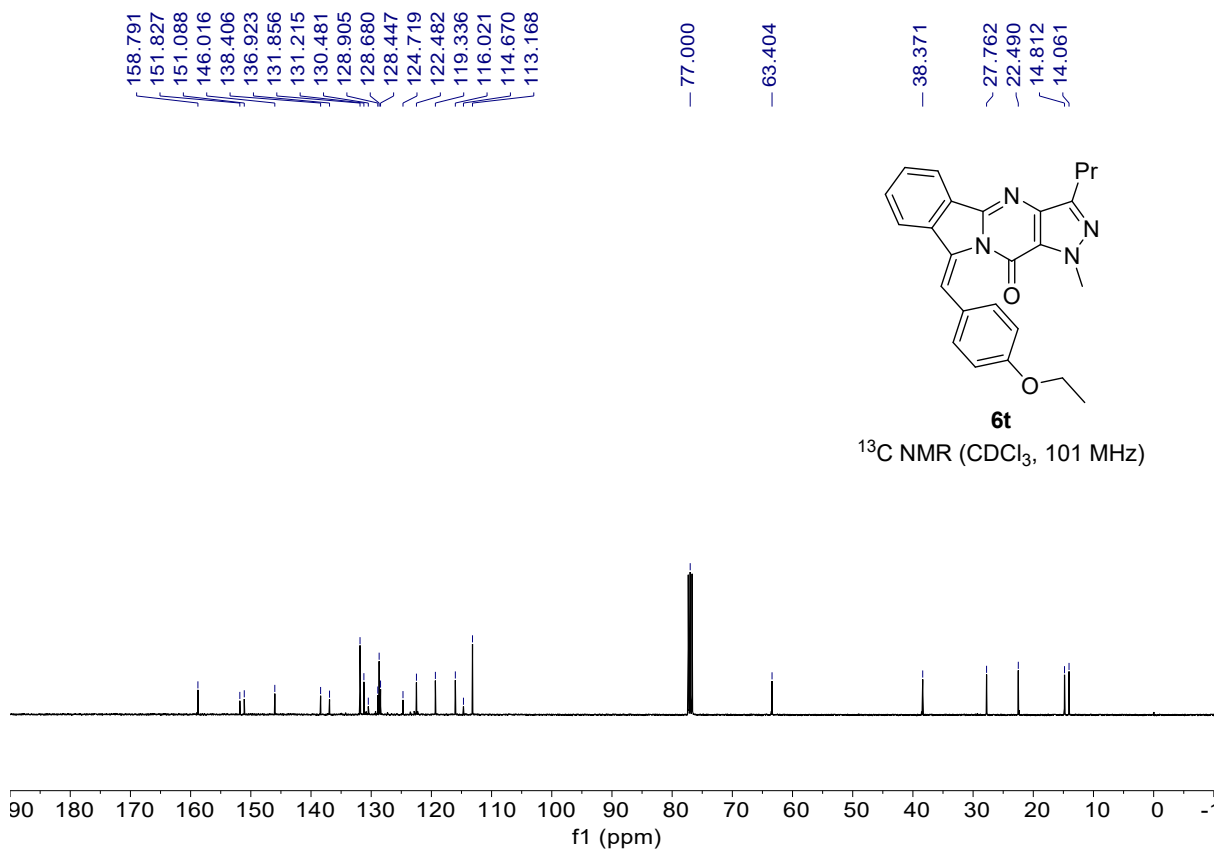
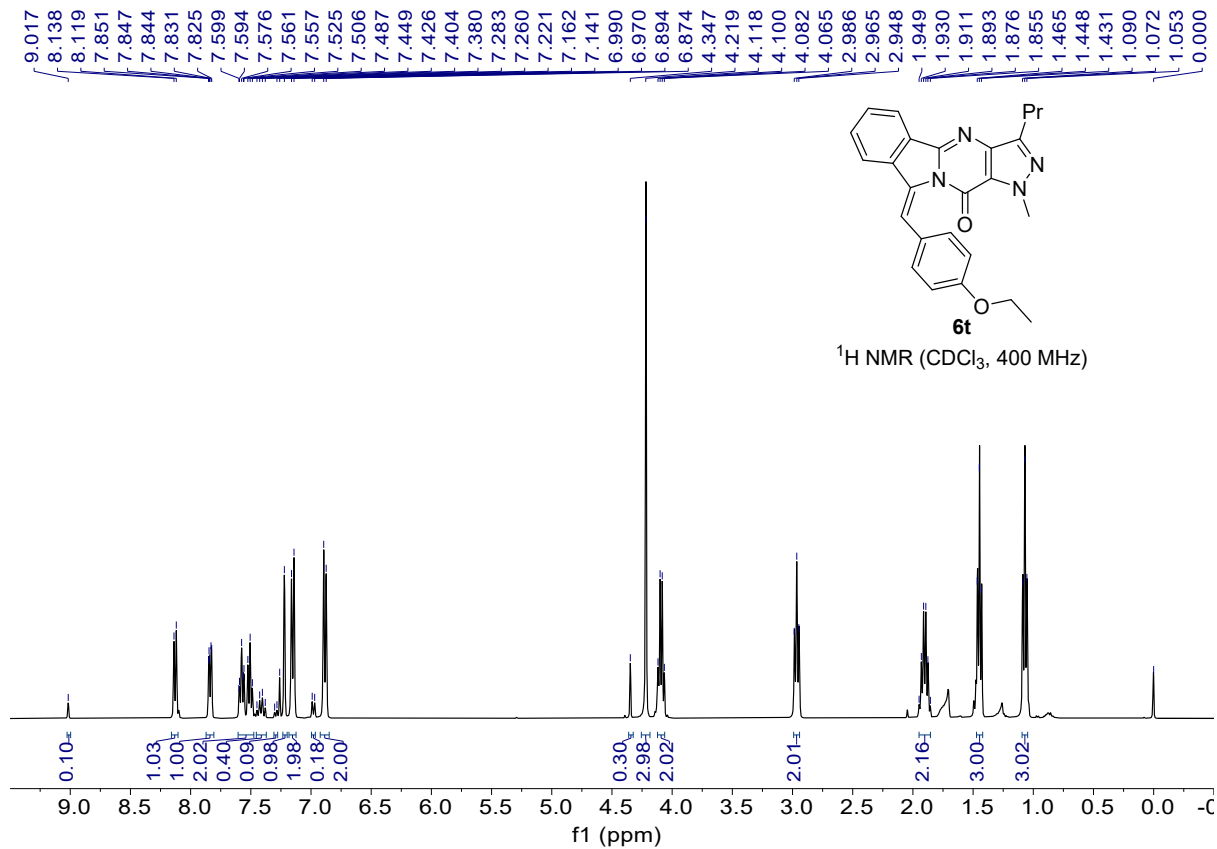
(Z)-9-(4-methoxybenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (6r)



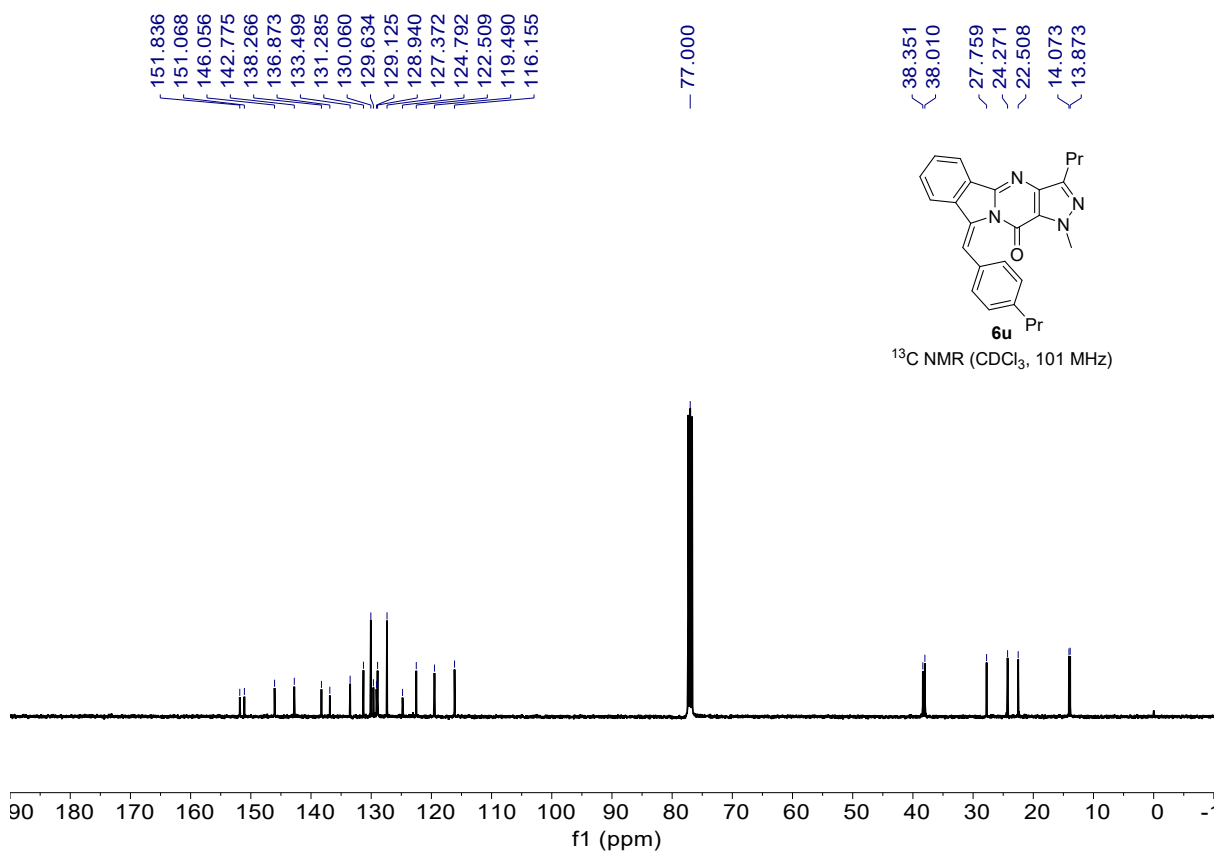
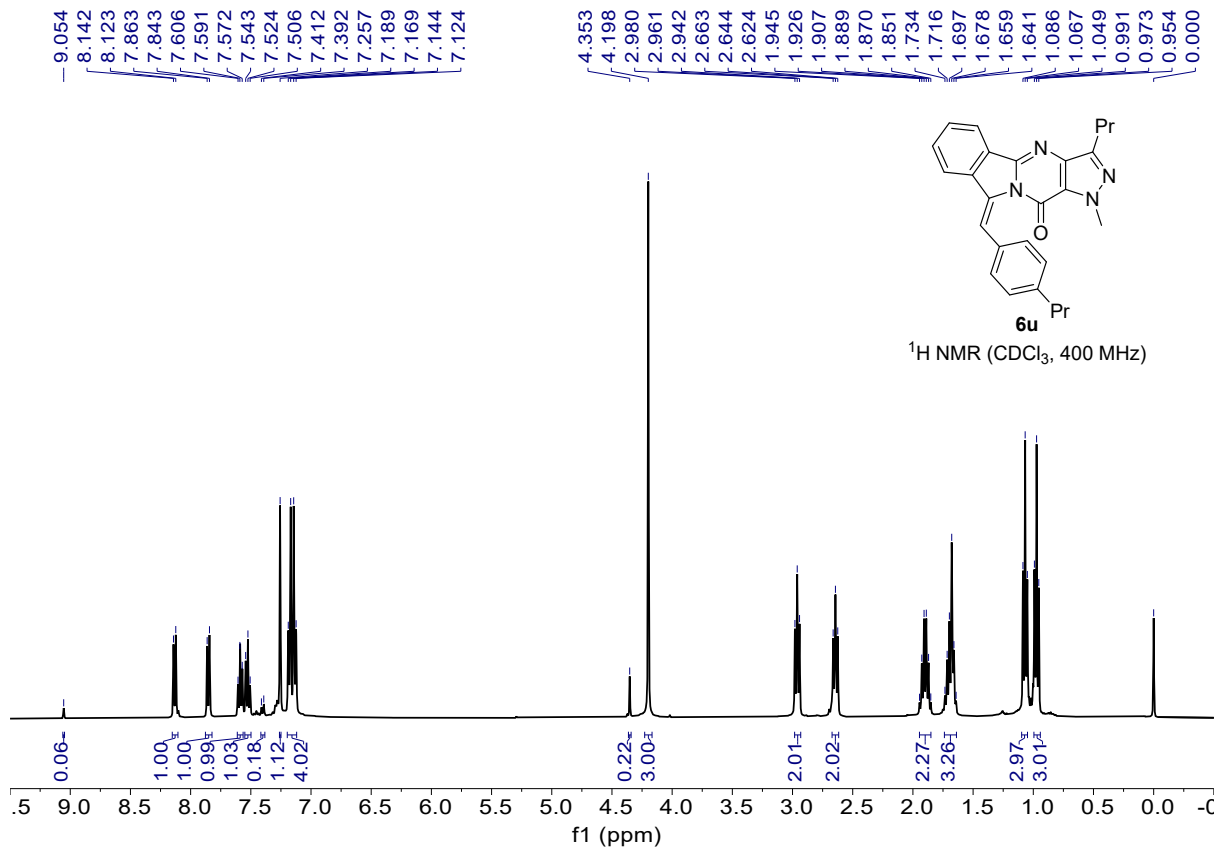
(Z)-9-(4-ethylbenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (6s)



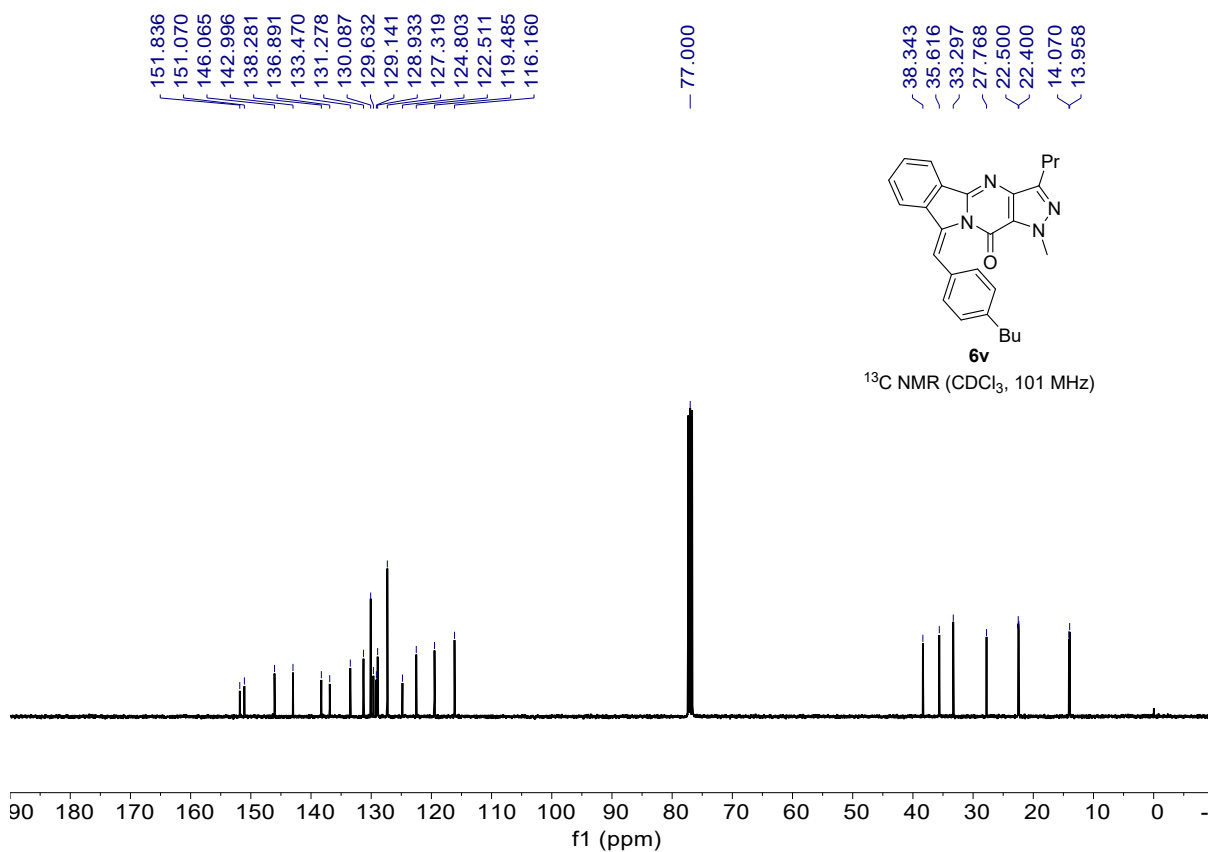
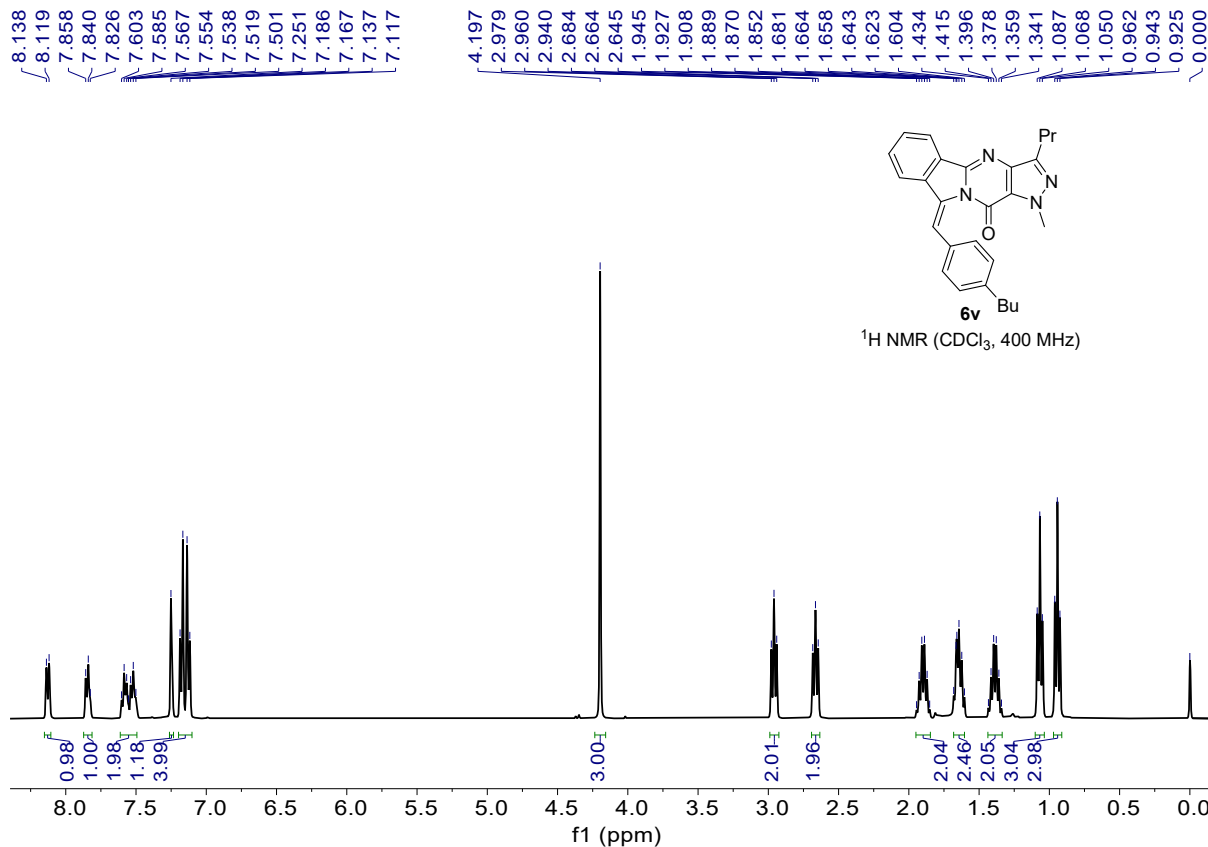
(Z)-9-(4-ethoxybenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (6t)



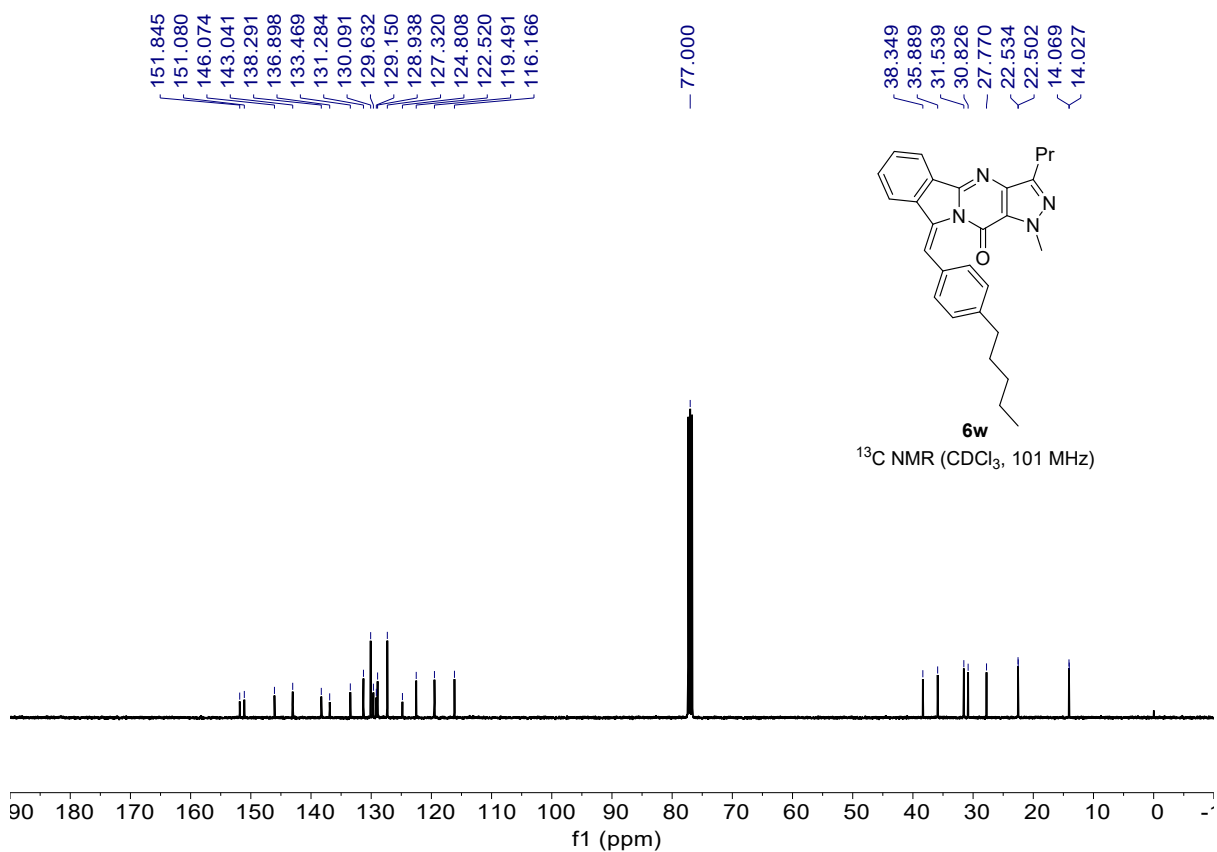
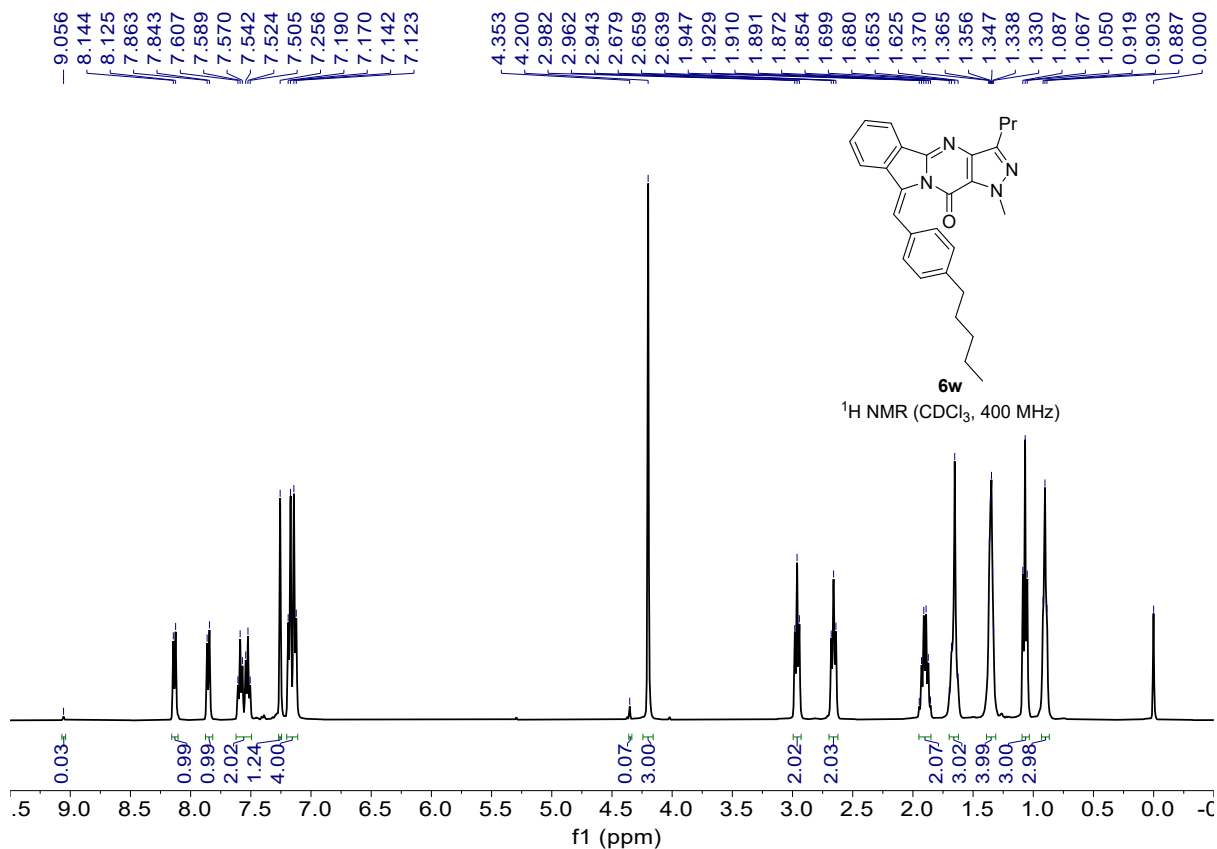
(Z)-1-methyl-3-propyl-9-(4-propylbenzylidene)-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (6u)



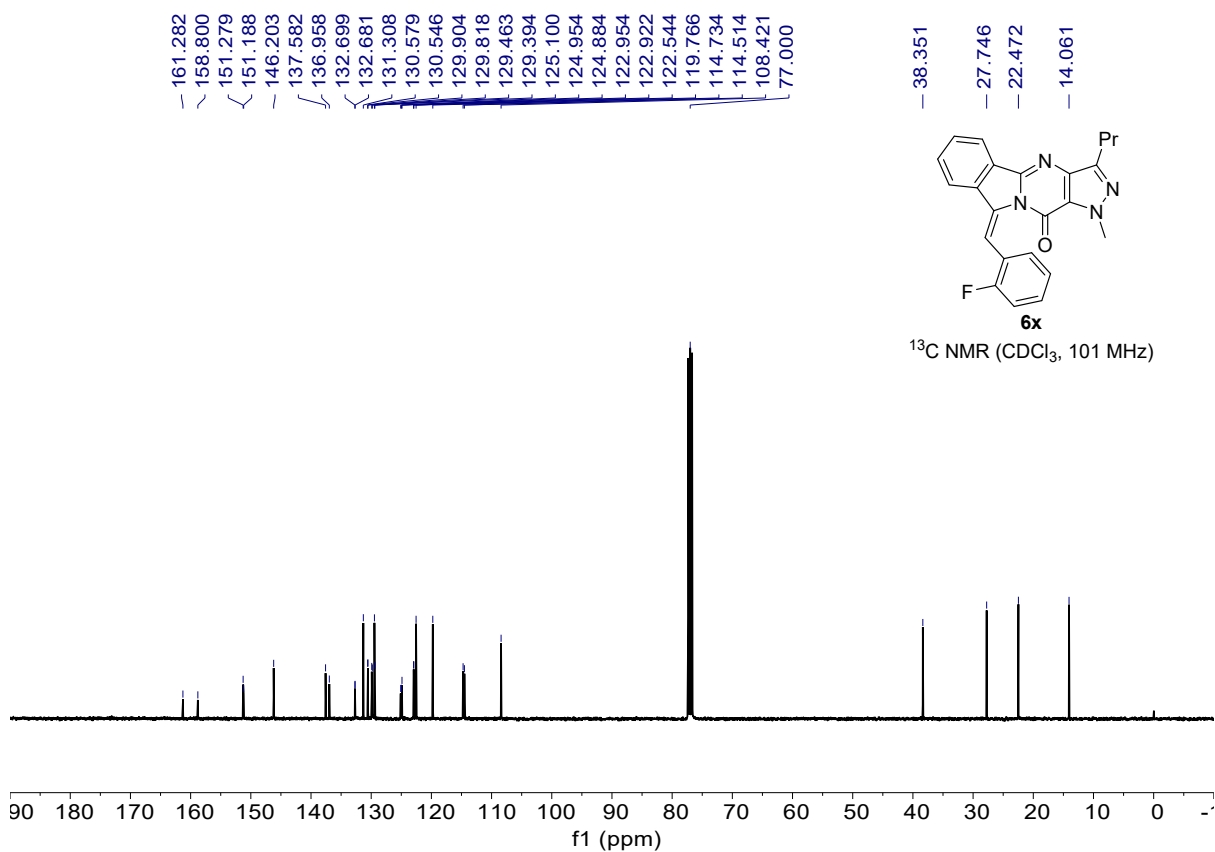
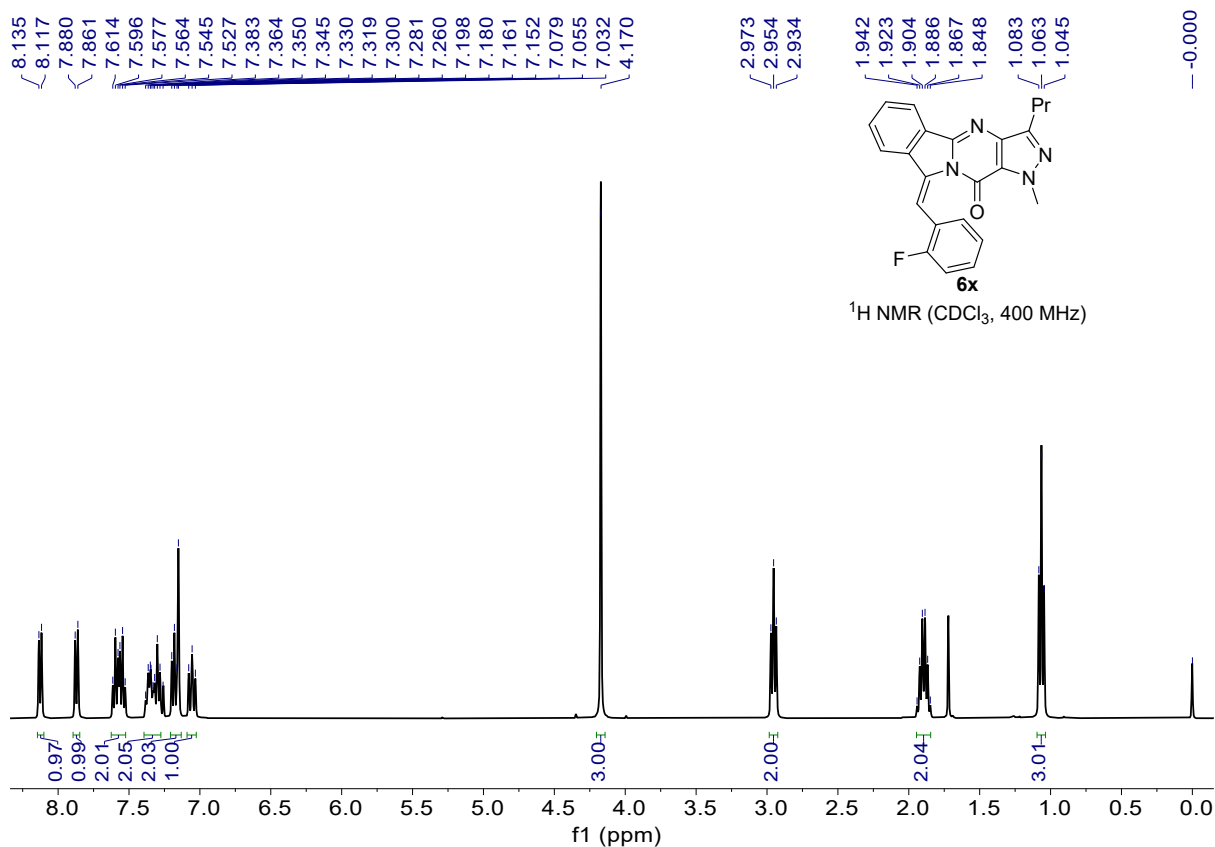
(Z)-9-(4-butylbenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (6v)



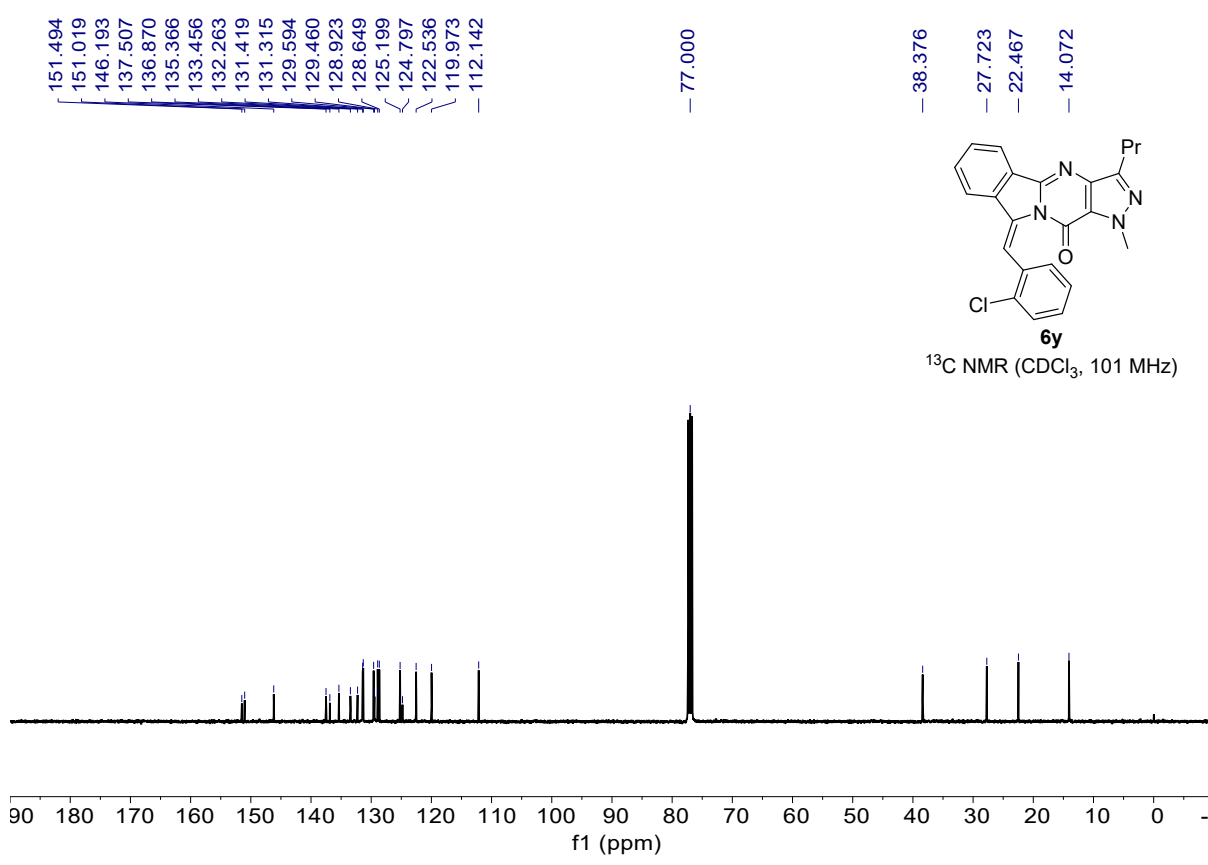
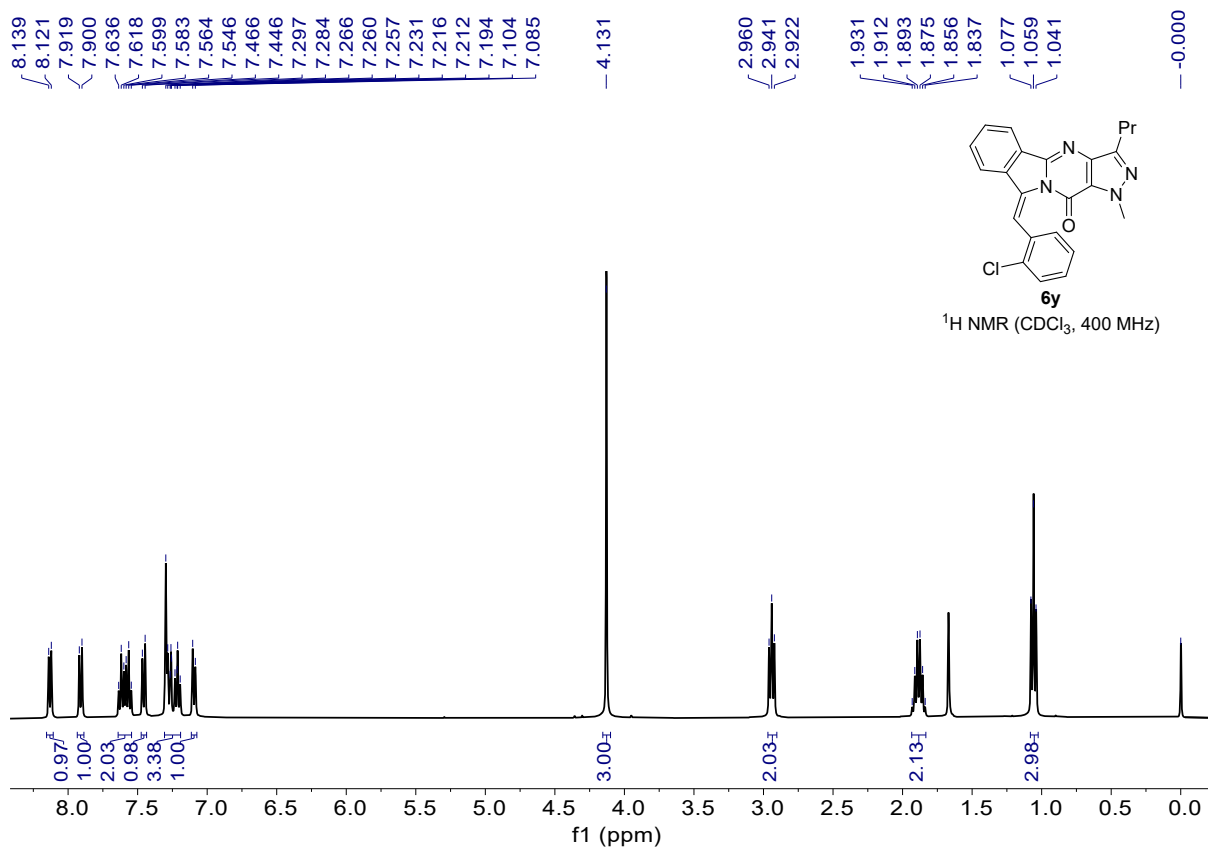
(Z)-1-methyl-9-(4-pentylbenzylidene)-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (6w)



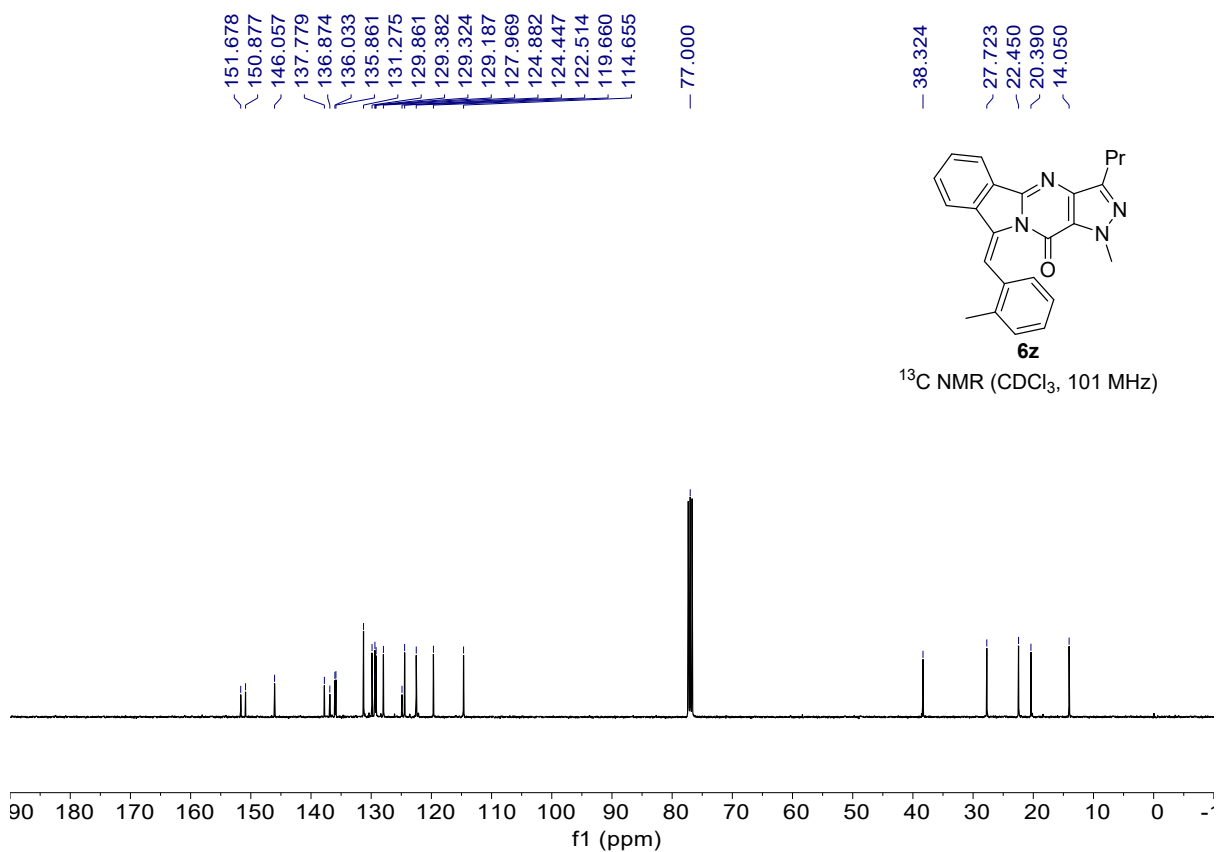
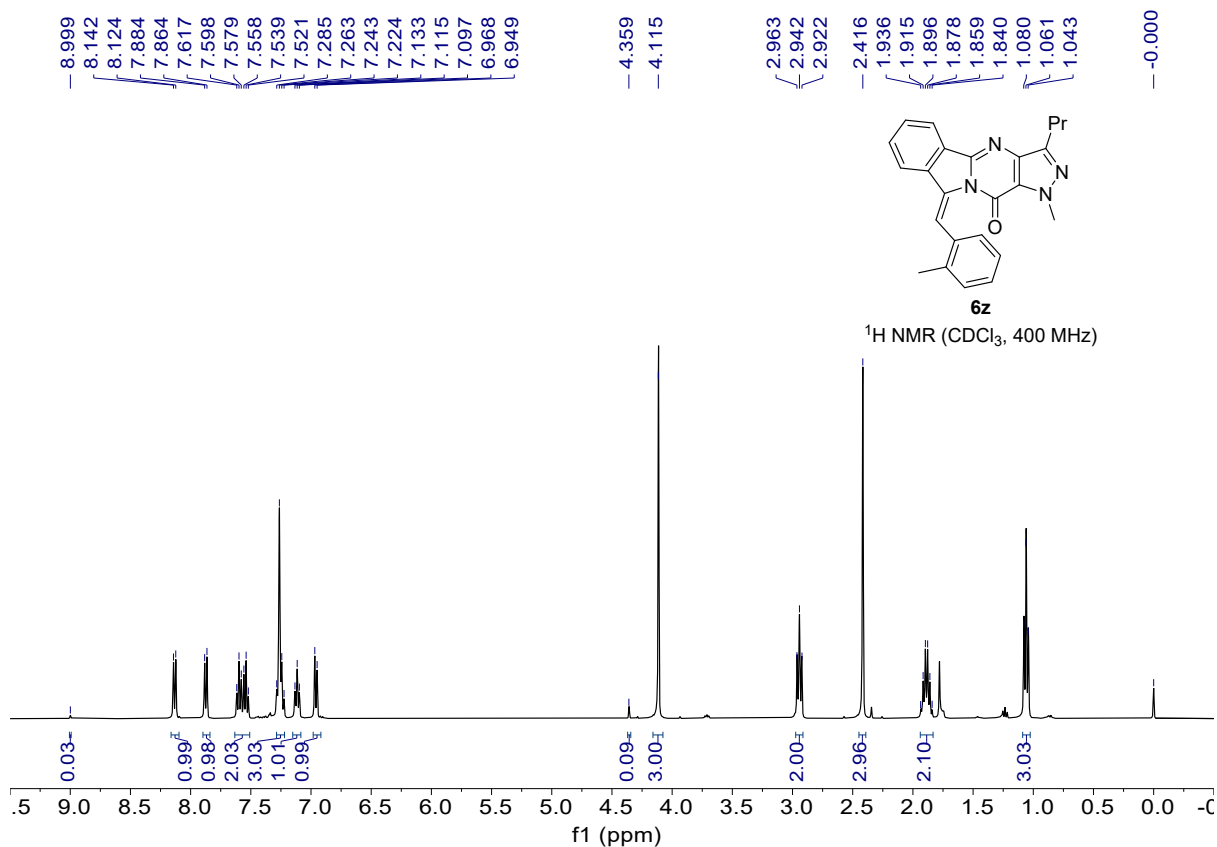
(Z)-9-(2-fluorobenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (6x)



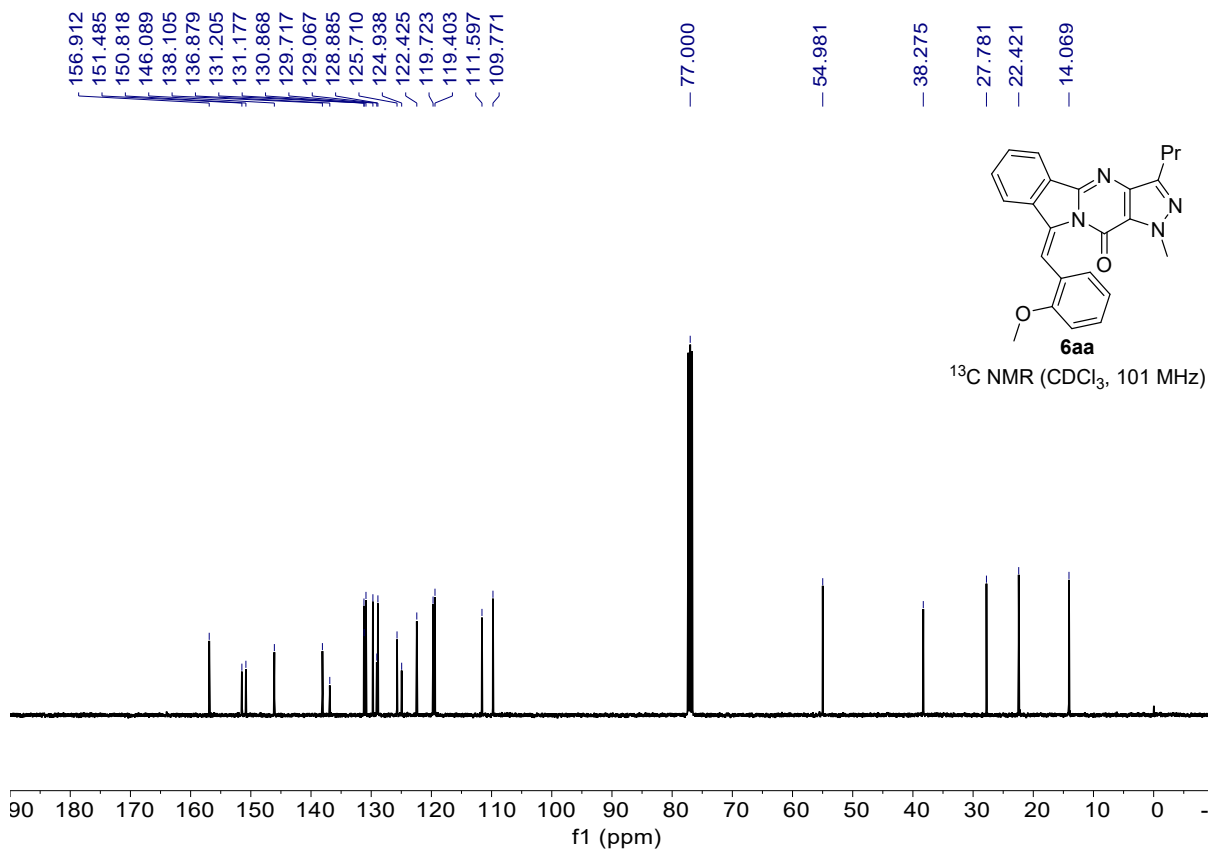
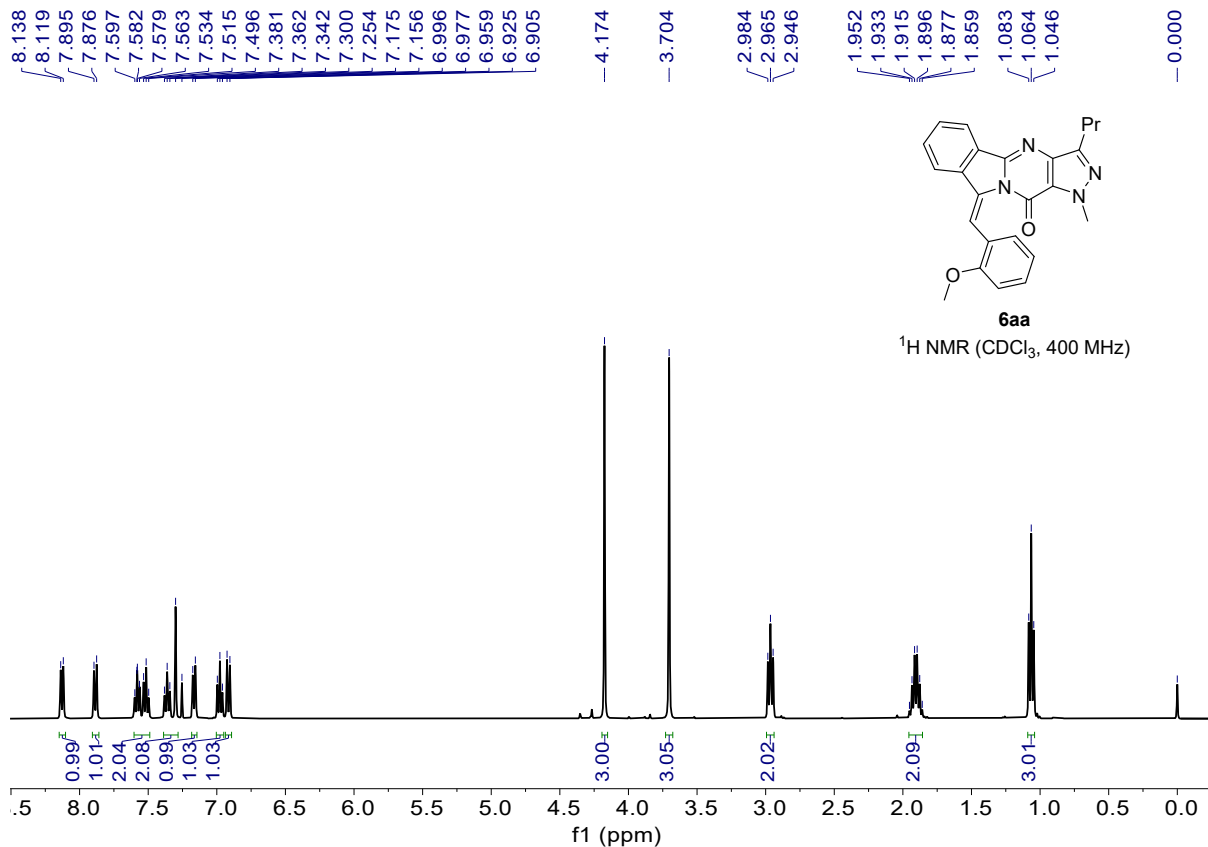
(Z)-9-(2-chlorobenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (6y)



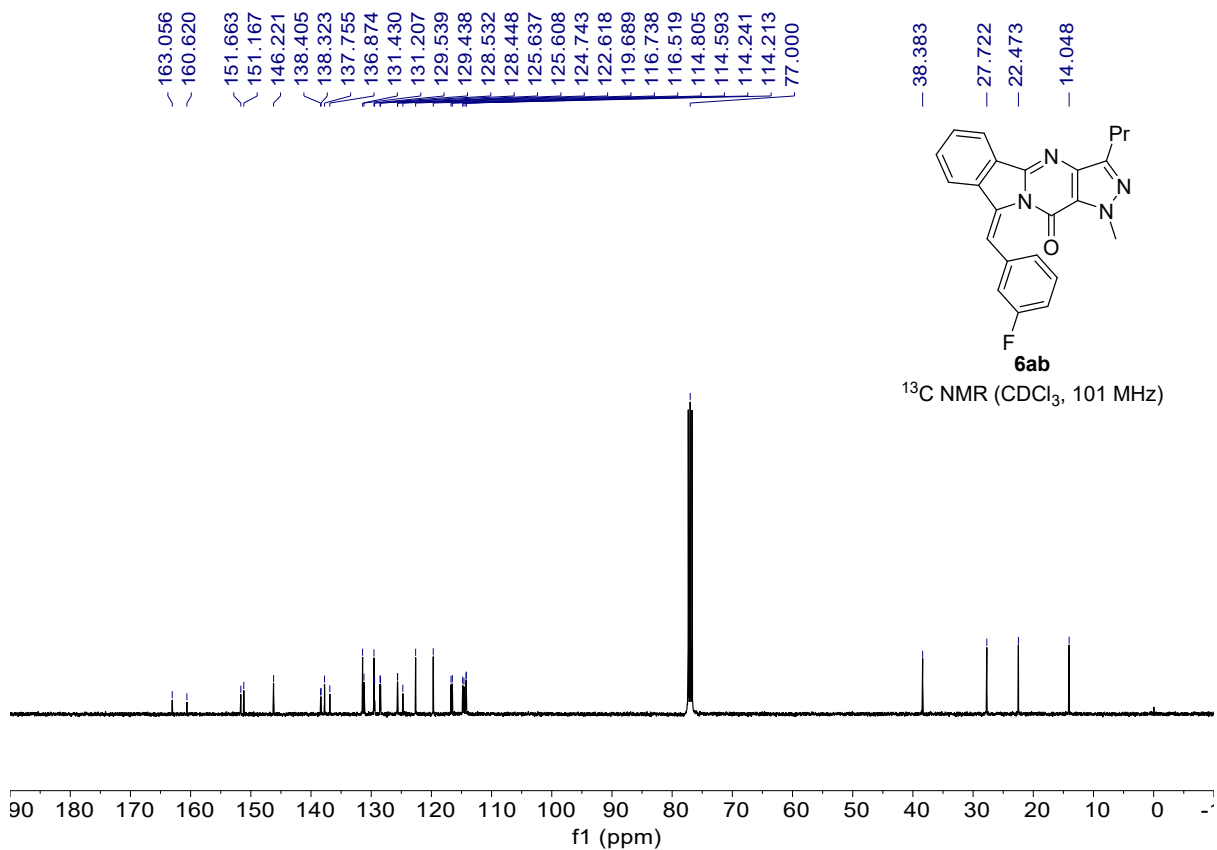
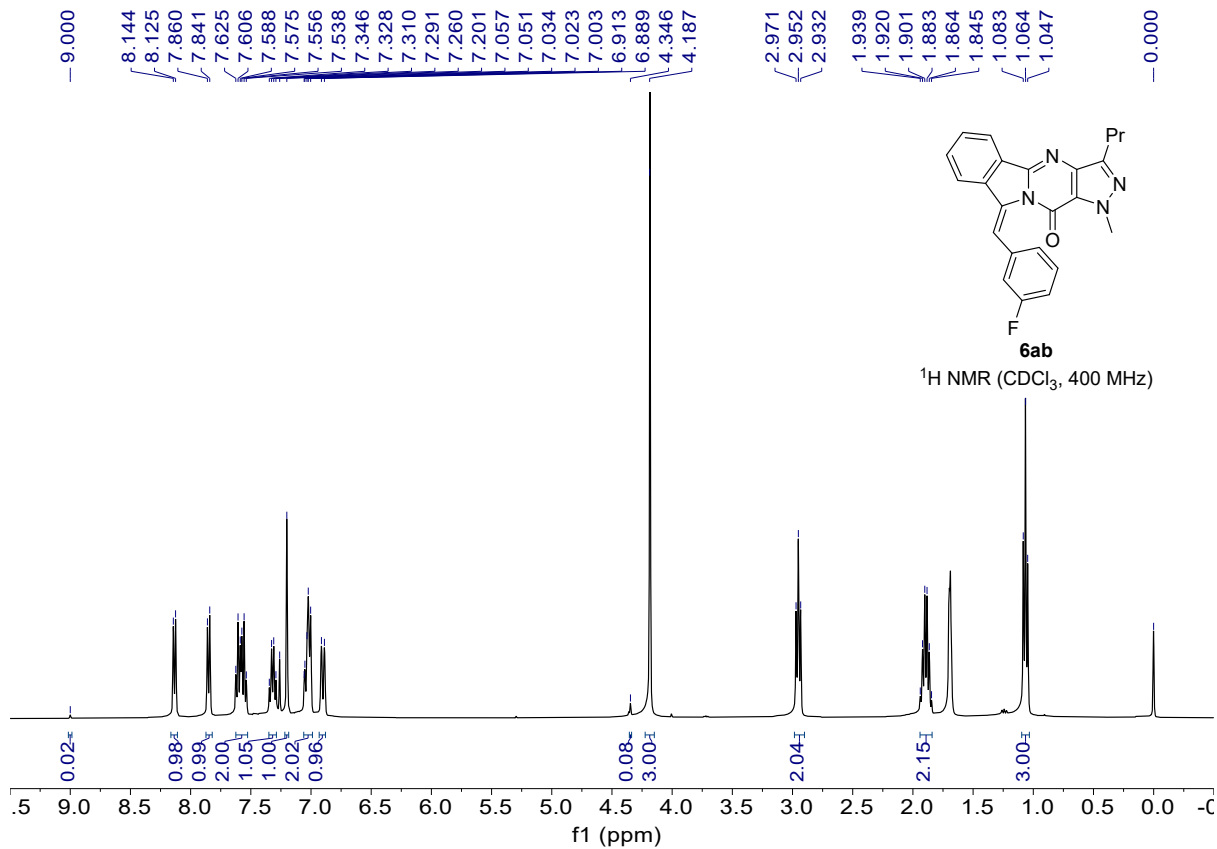
(Z)-1-methyl-9-(2-methylbenzylidene)-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (6z)



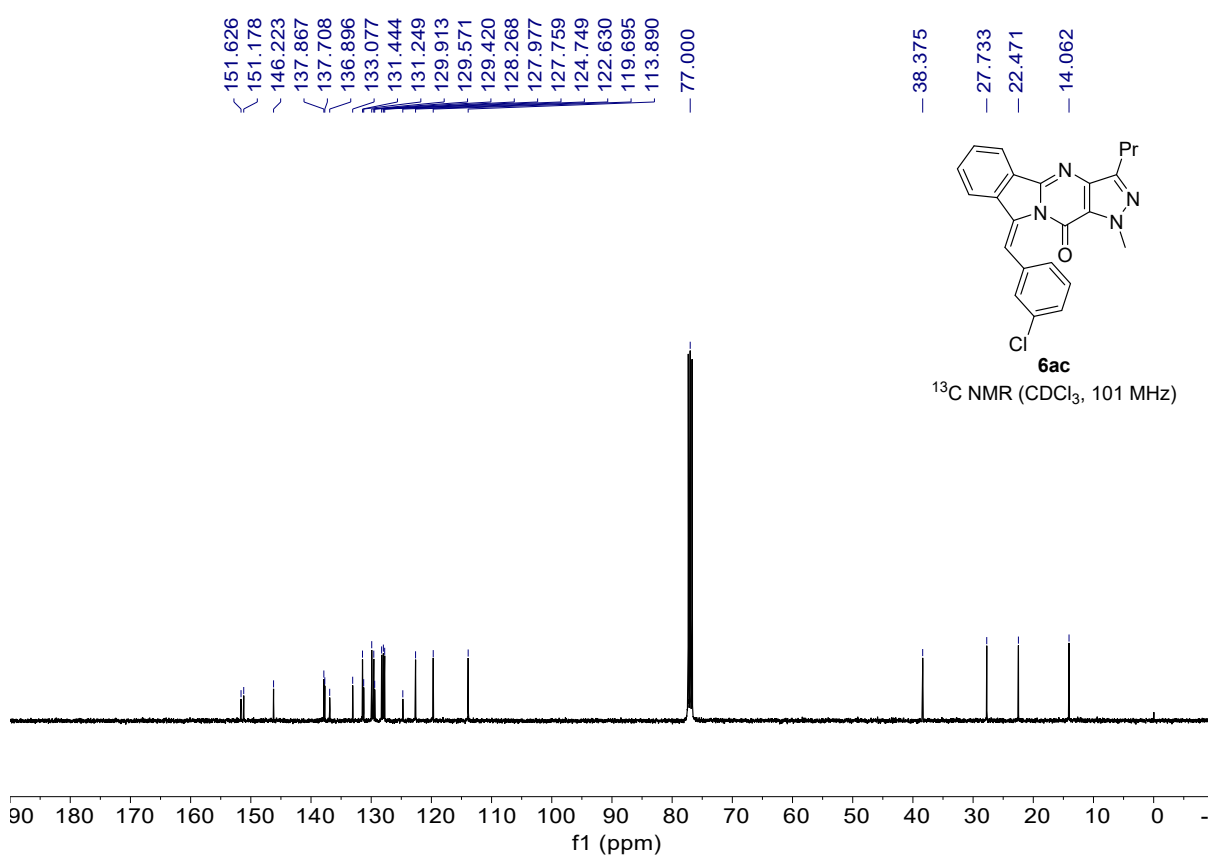
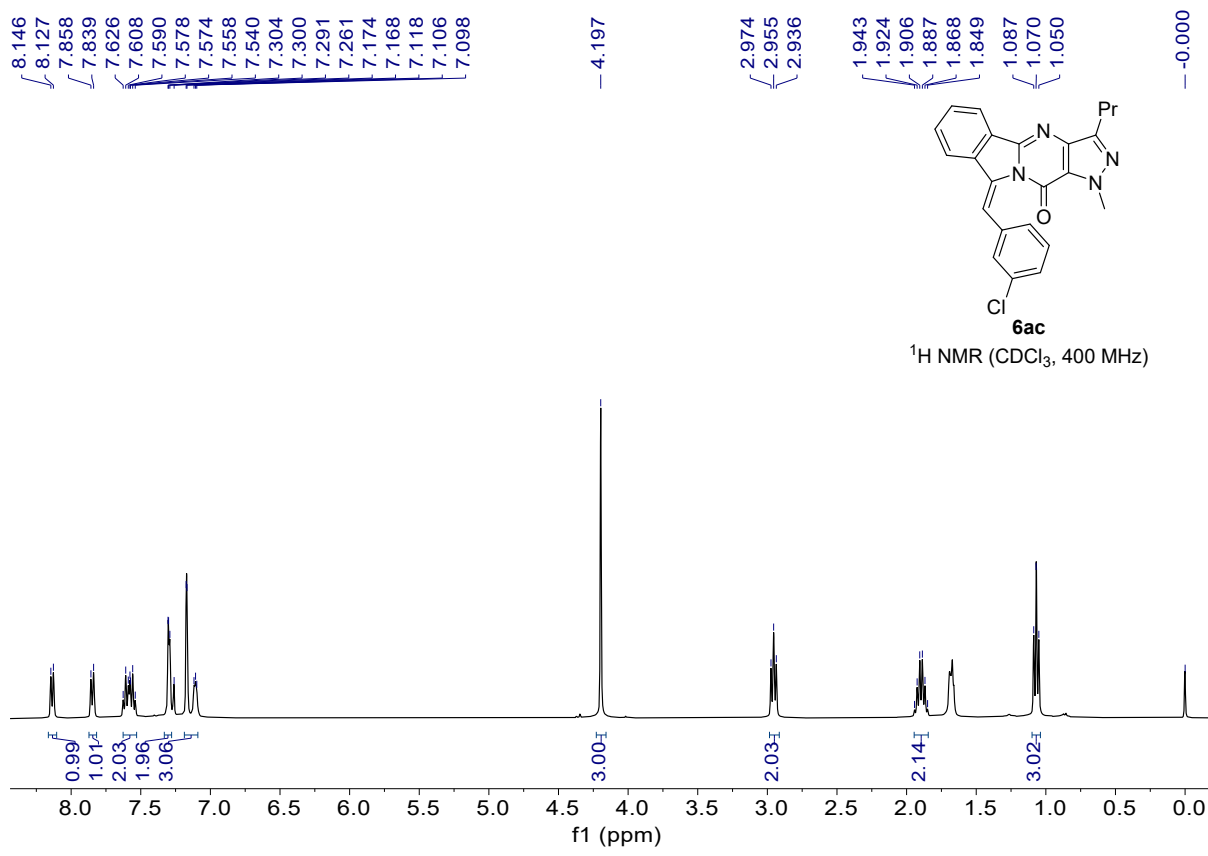
(Z)-9-(2-methoxybenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (6aa)



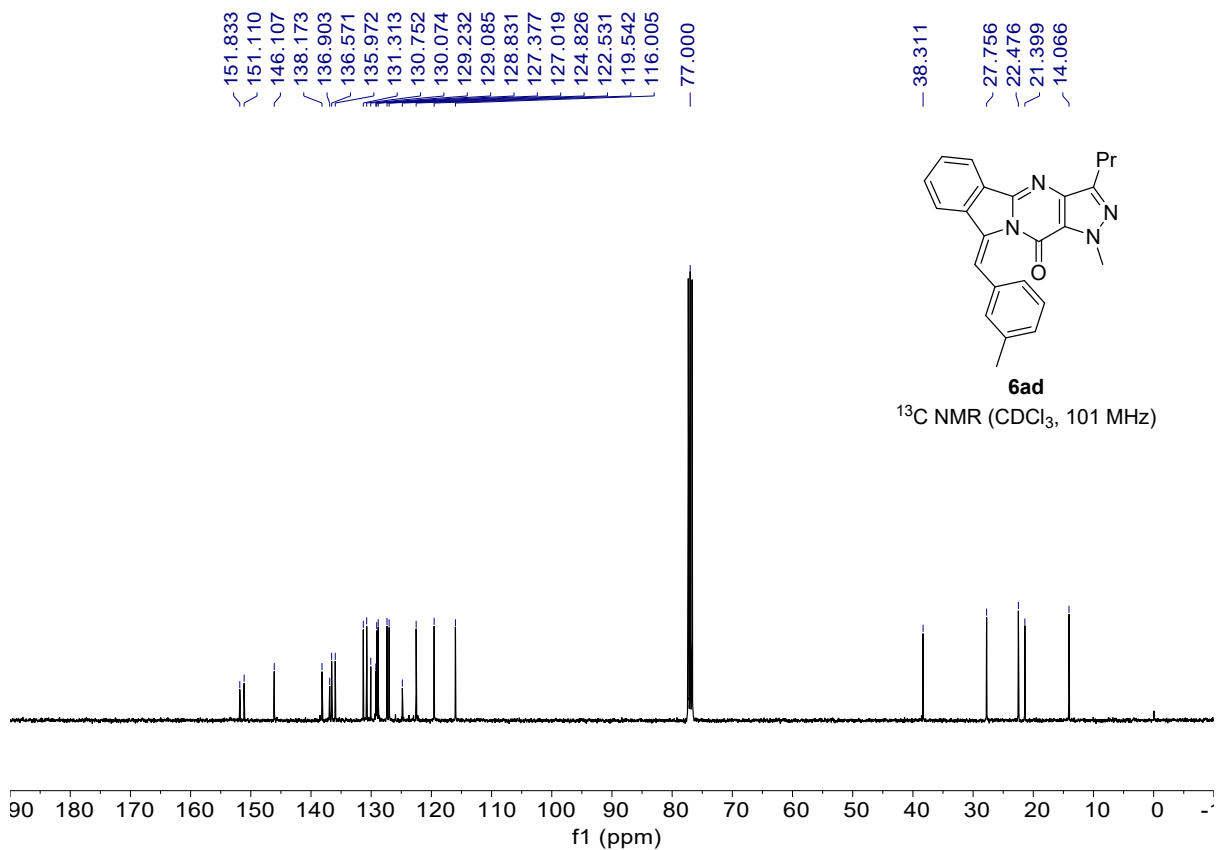
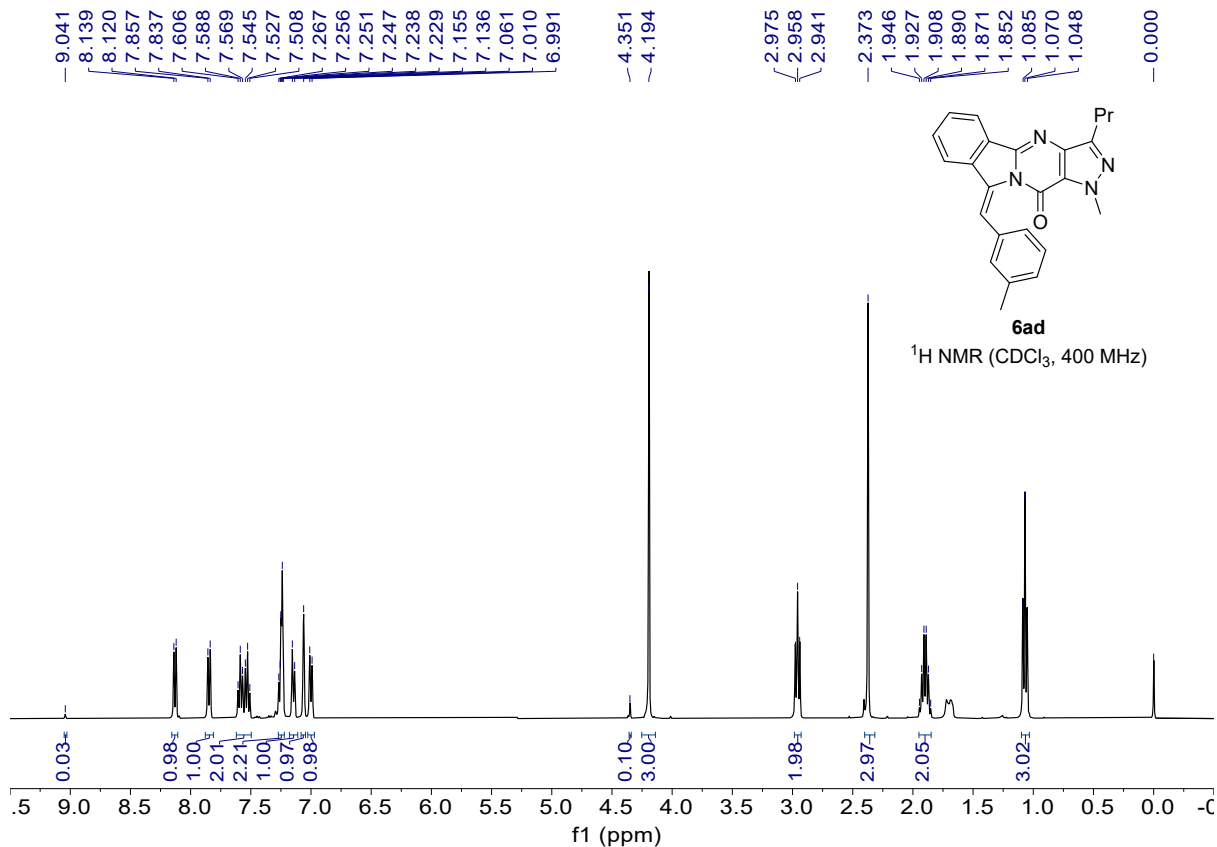
(Z)-9-(3-fluorobenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (6ab)



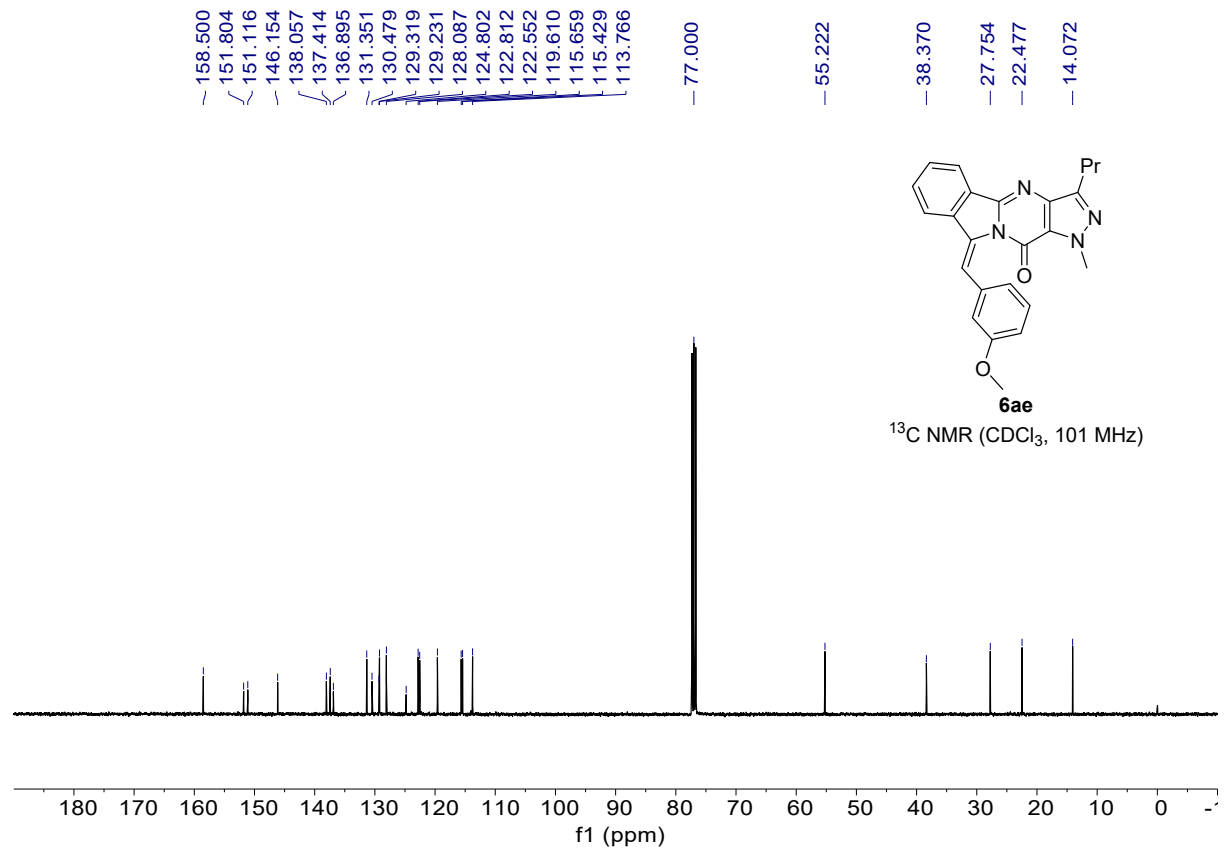
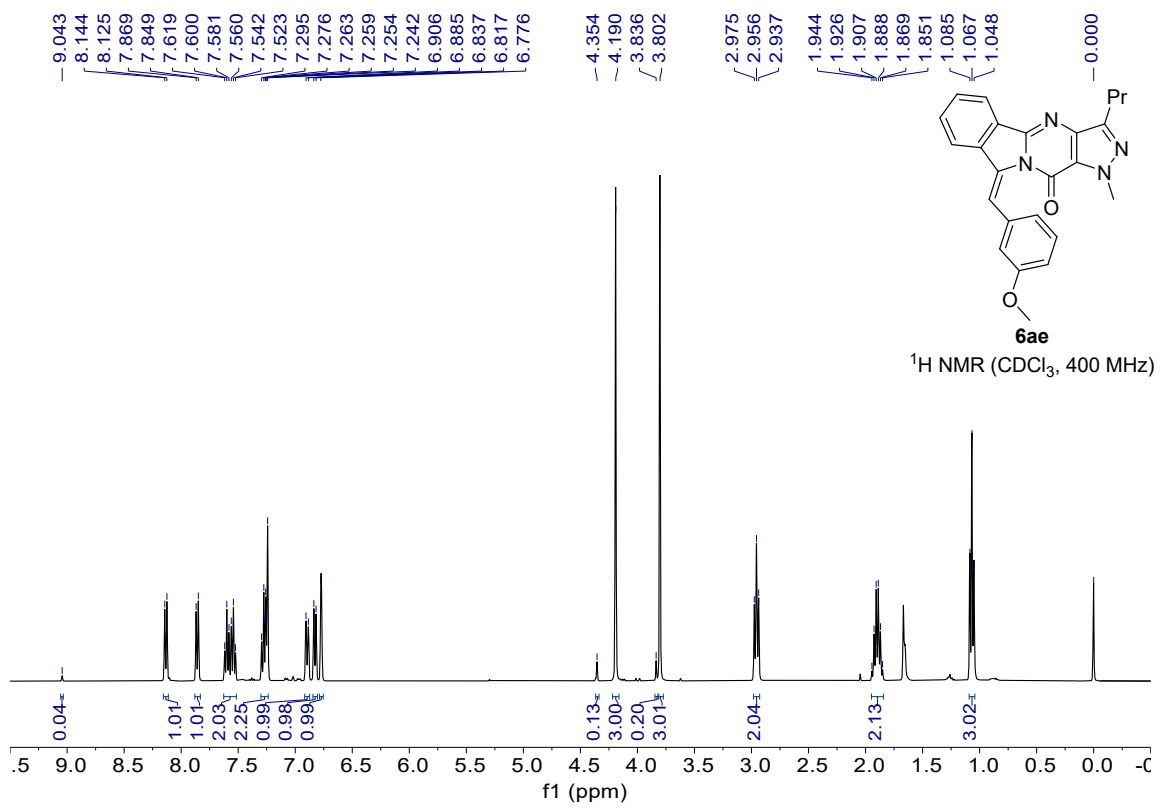
(Z)-9-(3-chlorobenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (6ac)



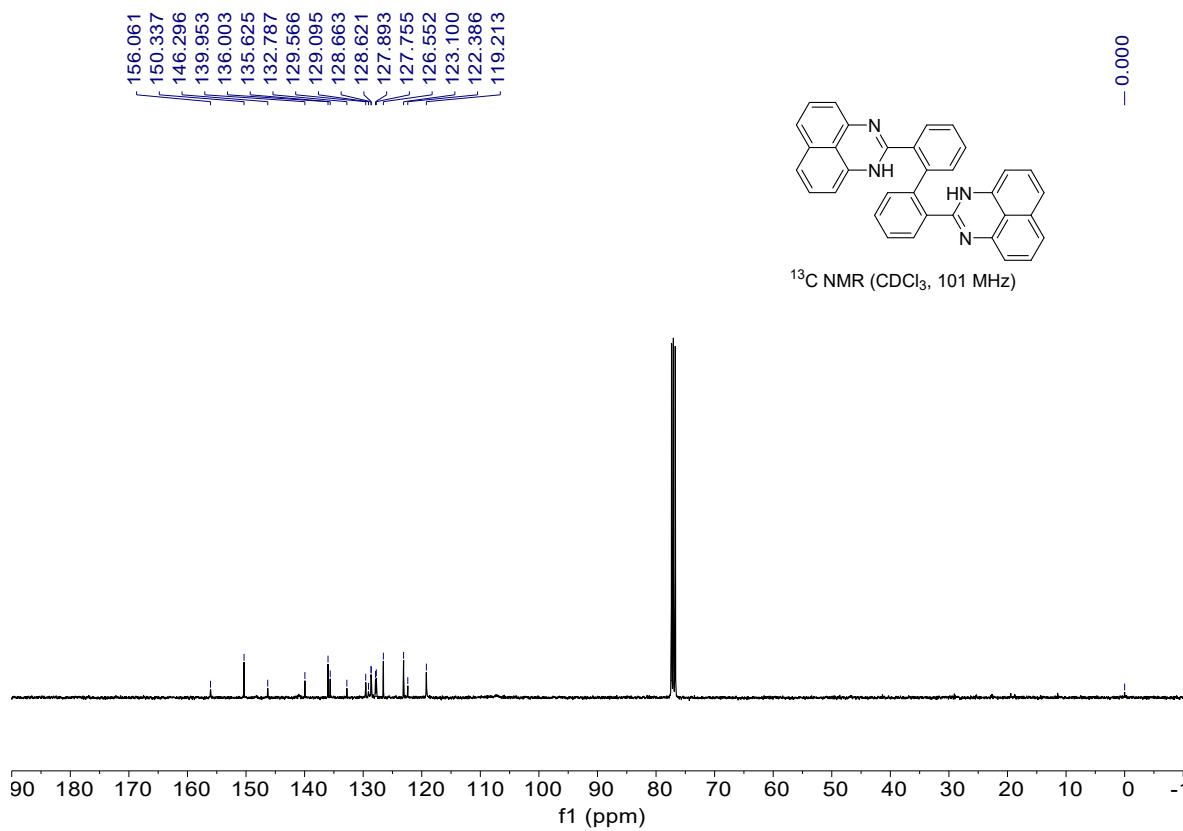
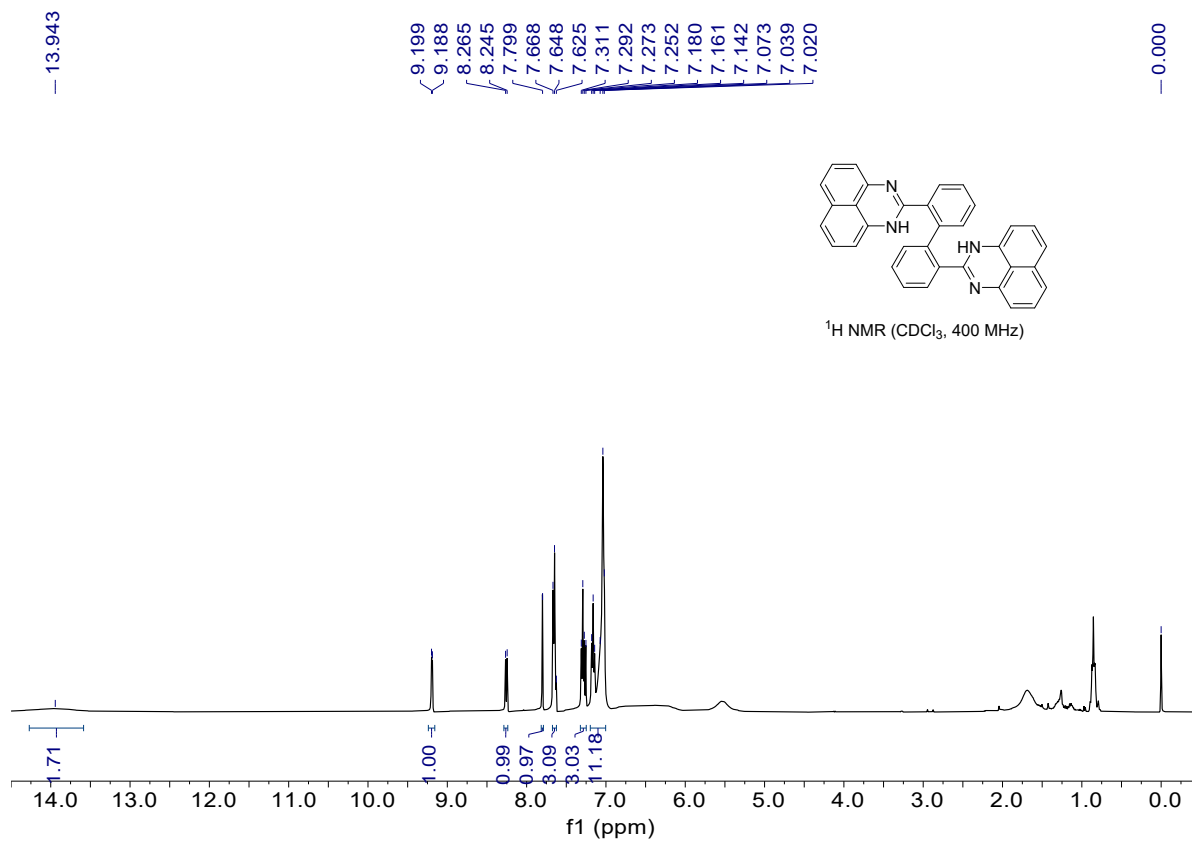
(Z)-1-methyl-9-(3-methylbenzylidene)-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (6ad)



(Z)-9-(3-methoxybenzylidene)-1-methyl-3-propyl-1,9-dihydro-11H-pyrazolo[4',3':4,5]pyrimido[2,1-a]isoindol-11-one (6ae)



2,2'-di(1*H*-perimidin-2-yl)-1,1'-biphenyl (3')



V. References

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