Development of a Solvent-Reagent Selection Guide for the Formation of Thioesters

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Experimental

Chemicals

All chemicals used were purchased from Sigma-Aldrich, TCI Europe, Across Organics or Fluorochem. All reagents were used without further purification. Solvents were dried over 3Å molecular sieves for 24 hours before use. Aluminium-backed Silicagel 60 F_{254} plates from E. Merck were used for thin layer chromatography. Puriflash 30 µm silica gel prepacked flash chromatography cartridges were used for all chromatographic separations.

NMR

The majority of NMR analysis was performed on a Bruker AC 400 MHz spectrometer operating at 400 MHz for ^{1}H-NMR and 101 MHz for ^{13}C-NMR. Samples were run in deuterated chloroform ($CDCl_3$) or deuterated dimethyl sulfoxide (DMSO) where appropriate. A 500 MHz Bruker spectrometer, operating at 500 MHz for ^{1}H-NMR and 126 MHz for ^{13}C-NMR was also used for analysis of some examples. All chemical shifts are reported in parts per million (ppm), are relative to the internal standard TMS and coupling constants (*J*) are measured in Hertz (Hz). Multiplicity is stated as follows: s-singlet, d-doublet, t-triplet, q-quartet, dd-doublet of doublets, dt-doublet of triplets, dq-doublet of quartets, tt-triplet of triplets, tq-triplet of quartets, ddd-doublet of doublet of doublets, m-multiplet, bs-broad singlet.

IR analysis

All IR analysis was carried out on a Bruker Alpha Platinum FT-IR spectrometer with ATR.

Melting point

Melting points were determined using a Stuart SMP20 melting point apparatus and the values are expressed in degrees Celsius (°C). The parameters for the melting point analysis were set at 5 °C per minute ramp and melting point was determined manually. Melting points are uncorrected.

ESI-MS

High resolution mass spectrometry (HRMS) with accurate mass measurement to four decimal places was obtained for all new compounds described. Mass spectra were recorded in both positive and negative electrospray ionisation mode on a Bruker ESI MicroTOF mass spectrometer.

HPLC Analysis

HPLC for reaction monitoring used an Agilent 1200 system, with a standard gradient elution method: Waters XBridge 2.1x30 mm column, stationary phase C_{18} 3.5 µm, 0.8 mL/min flow rate, detection at 254 nm; elution with 5-95% MeCN in 0.1% aqueous TFA over 4 minutes.

Chromatography

A Biotage SP4 was used for all chromatographic purifications using a petroleum ether: ethyl acetate gradient elution system with manual fraction collection. UV detector wavelength was set at 254 nm.

General Procedures

General Procedure A – Thioester formation using HATU, EDC.HCl or T3P for HPLC screening

To a stirred HPLC vial was added the appropriate carboxylic acid (0.2 mmol), solvent of choice (1 mL), thiol of choice (0.2 mmol) and DIPEA (0.4 mmol, 70µL). The reaction was stirred for ten minutes before the addition of the desired coupling reagent (0.24 mmol). Reaction progress was monitored by HPLC-UV at t=1, 2, 4, 8 and 24 h using calibration curves prepared for the alkyl and aryl thiols as appropriate.

General Procedure B – Thioester formation using CDI for HPLC screening

To a stirred HPLC vial was added the appropriate carboxylic acid (0.2 mmol), solvent of choice (1 mL) and CDI (0.2 mmol). The reaction was stirred at room temperature for one hour to pre-form the activated ester to avoid thiourea formation. After one hour the appropriate thiol was added (0.2 mmol) and the reaction was continued stirring at room temperature. Reaction progress was monitored by HPLC-UV at t=1, 2, 4, 8 and 24 h using calibration curves prepared for the alkyl and aryl thiols as appropriate.

General Procedure C – Thioester formation using T3P for building-block synthesis

To a stirred solution of carboxylic acid (1.0 mmol) in cyclopentanone (4 mL) was added DIPEA (348 µL, 2.0 mmol) and T3P (50 wt. % in ethyl acetate) (596 µL, 1.0 mmol). The solution was stirred at room temperature for 30 minutes before thiol of choice (1.0 mmol) was added in one portion. The solutions were stirred at room temperature for 12 hours before undergoing analysis by HPLC. Incomplete reactions were stirred for a further 12 hours. After completion, solvent was removed *in vacuo* and the resulting crude products were purified by silica gel chromatography using a 0-10% petrol - ethyl acetate gradient elution. Solvents were removed *in vacuo* and target compounds were dried under high vacuum for 24 hours.

General Procedure D – Thioester formation using CH_3CN-heptane extractions

To a stirred solution of carboxylic acid (10.0 mmol) in CH_3CN (25 mL) was added DIPEA (3.48 mL, 20.0 mmol) and HATU (4.00 g, 10.5 mmol). The solution was stirred at room temperature for 10 minutes before thiol of choice (10.0 mmol) was added in one portion. The solutions were stirred at room temperature for 12 hours before undergoing analysis by HPLC. After completion, the acetonitrile was extracted with heptane (3 x 90 mL) and the combined heptane layers were passed through a short plug of silica to remove polar impurities. The silica was washed with heptane (1 x 30 mL). The heptane was removed *in vacuo* to give the target product.

GSK Reagent Selection Guide – Amide Formation

Few Issues	Some Issues		Major Issues	
	Ghosez reagent	EEDQ		HCTU
	Mukaiyama reagent	BOP-Cl	DCC	CDI
			DPPA	
Enzyme	*i*-BuOCOCl	Thionyl chloride		HOAt
			Boric Acid	
	TFFH	CDMT		PyBOP®
			HOBt	
Activated silica	DMTMM	EDCI (WSCDI)		HBTU
			DIC	
	COMU®	T3P®		HATU
			Cyanuric chloride	
	SuOCOOSu	Oxalyl chloride		TBTU

This guide should only be used by the expert trained chemist. Before using any reagent listed on this guide, a complete risk assessment must be carried out.

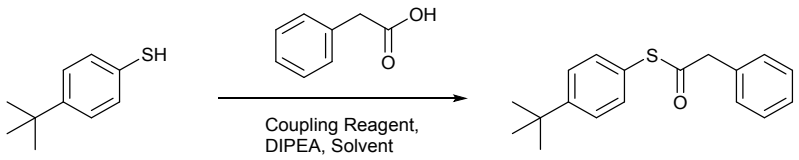
Revision Date: September, 2014

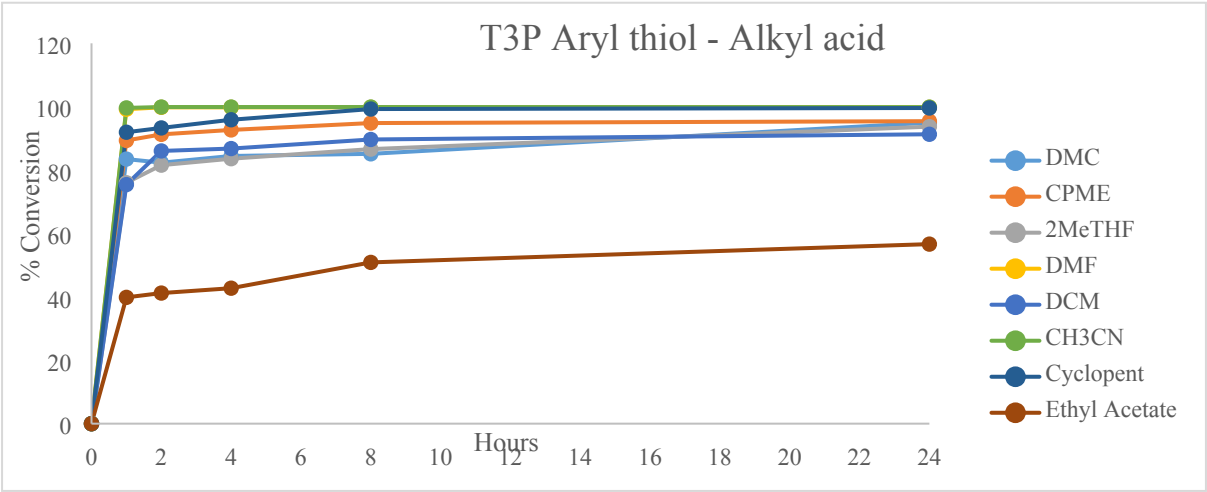
Material	Full Name	CAS number	EHS	Clean Chemistry	Greenness	Comments
Enzyme	Enzyme	N/A	10	8	8.8	
Activated silica	Thermally activated Kieselgel 60	7631-86-9	10	6	7.7	Activated at > 600 °C.
Ghosez reagent	1-Chloro-*N*,*N*,2-trimethyl-1-propenylamine	26189-59-3	7	7	6.6	Recommended storage at +4 °C.Amide by-product may be difficult to remove
Mukaiyama reagent	2-Chloro-1-methylpyridinium iodide	14338-32-0	10	4	6.5	Recommended storage at +4 °C.
i-BuOCOCl	Isobutyl chloroformate	543-27-1	7	6	6.3	Lachrymator, gaseous by-products. Recommended storage at +4 °C. Activated species forms quickly.
TFFH	Fluoro-*N*,*N*,*N*′,*N*′-tetramethylformamidinium hexafluorophosphate	164298-23-1	10	4	6.2	Fluoride by-product may limit vessel choice. Avoid acidic work-up.
DMTMM	4-Dimethoxy-1,3,5,triazin-2-yl)-4-methyl morpholinium	3945-69-5	7	5	6.1	Causes burns.
COMU®	(1-Cyano-2-ethoxy-2-oxoethylidenaminooxy)dimethylamino morpholino-carbenium hexafluorophosphate	1075198-30-9	10	4	6.0	Urea by-product may be difficult to remove. Fluoride content may limit vessel choice.
SuOCOOSu	*N*,*N*′-Disuccinimidyl carbonate	74124-79-1	9	4	5.8	Water sensitive. Recommended storage at +4 °C. Gaseous
EEDQ	2-Ethoxy-1-ethoxycarbonyl-1,2-dihydroquinoline	16357-59-8	9	4	5.6	Odour. Recommended storage at +4 °C
BOP-Cl	Bis(2- oxo- 3-oxazolidinyl) phosphinic chloride	68641-49-6	7	4	5.6	
Thionyl chloride	Thionyl chloride	7719-09-7	5	5	5.2	Lachrymator. Gaseous byproducts.
CDMT	2-Chloro-4,6-dimethoxy-1,3,5-triazine	3140-73-6	5	4	5.0	Sensitizer. Toxic to aquatic organisms.
EDCI (WSCDI)	[1-(3-Dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride]	25952-53-8	7	4	4.8	Water soluble by-products. Recommended storage at +4 °C. Known to test AMES positive, potential mutagen.
T3P®	2-Propanephosphonic acid anhydride	68957-94-8	5	4	4.7	Regulated chemical. Usage as 50% in EtOAc preferable to DMF
Oxalyl chloride	Oxalyl chloride	79-37-8	5	4	4.5	Lachrymator. Gaseous byproducts CO2 and HCl, toxic by-product CO. Scored without DMF, use with DMF not recommended as DMCC carcinogen may be produced.
DCC	*N*,*N*'-Dicyclohexylcarbodiimide	538-75-0	7	3	4.4	Urea byproduct is a sensitizer, also difficult to remove.
DPPA	Diphenylphosphoryl azide	26386-88-9	5	3	4.0	May form explosive hydrogen azide on contact with moisture.
Boric acid	Boric acid	10043-35-3	2	9	3.9	May damage fertility. May damage the unborn child.
HOBt	1-Hydroxybenzotriazole hydrate	123333-53-9	3	4	3.7	May cause explosion.
DIC	Diisopropyl carbodiimide	693-13-0	3	4	3.5	Flammable. Toxic by inhalation.
Cyanuric chloride	2,4,6-Trichloro-1,3,5-triazine	108-77-0	3	5	3.4	Reacts violently with water. Causes burns. Toxic by inhalation.
HCTU	1H-Benzotriazolium 1-[bis(dimethylamino)methylene] -5chloro-	330645-87-9	3	3	2.9	Toxic by-product.

CDI	1,1-Carbonyl diimidazole	530-62-1	2	6	2.9	Toxic imidazole by-product. Gaseous by-product needs abating.
HOAt	1-Hydroxy-7-azabenzotriazole	39968-33-7	2	4	2.8	May cause explosion. May cause harm to the unborn child..
PyBOP®	Benzotriazol-1-yl-oxytripyrrolidinophosphonium hexafluorophosphate	128625-52-5	3	2	2.4	Toxic by-product.
HBTU	*N*,*N*,*N*′,*N*′-Tetramethyl-*O*-(benzotriazol-1-yl)uronium hexafluorophosphate	94790-37-1	1	2	1.5	Risk of explosion. Cytotoxic urea by-product, can be difficult to remove.
HATU	1-[Bis(dimethylamino)methylene]-1*H*-1,2,3-triazolo[4,5-b]pyridinium 3-oxide hexafluorophosphate	148893-10-1	1	2	1.5	Toxic by-products.
TBTU	*O*-Benzotriazol-1-yl-*N*,*N*,*N*′,*N*′-tetramethyluronium tetrafluoroborate	125700-67-6	1	2	1.5	Risk of explosion. Cytotoxic urea by-product, can be difficult to remove.

Reaction 1: Performance by Coupling Reagent

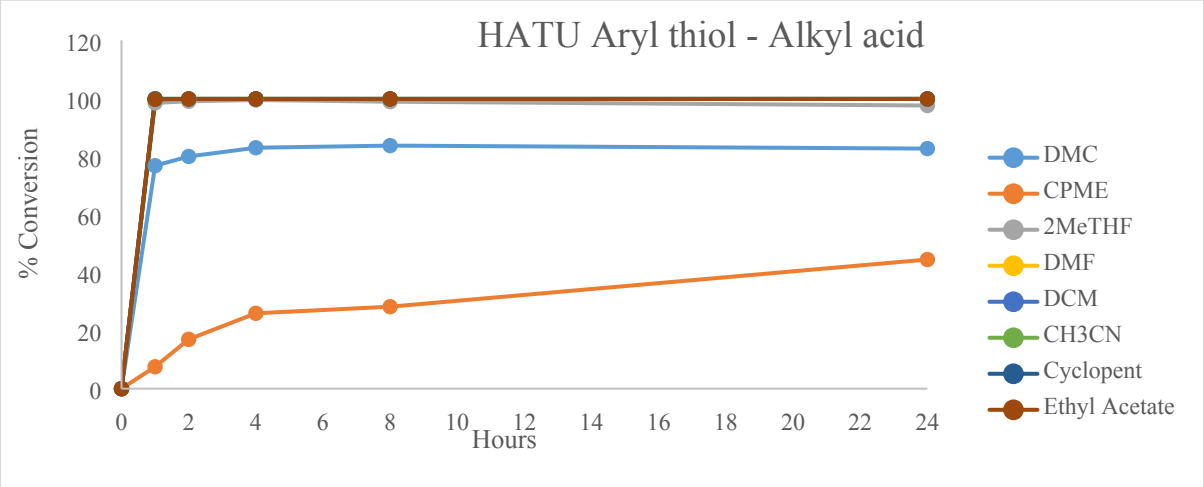
Reaction 1: T3P





Time	DMC	CPME	2-MeTHF	DMF	DCM	CH_3CN	Cyclopent	Ethyl Acetate
1	83	89	76	99	75	100	92	40
2	82	91	82	100	86	100	93	41
4	84	93	84	100	87	100	96	43
8	85	95	87	100	90	100	99	51
24	95	95	94	100	91	100	100	57

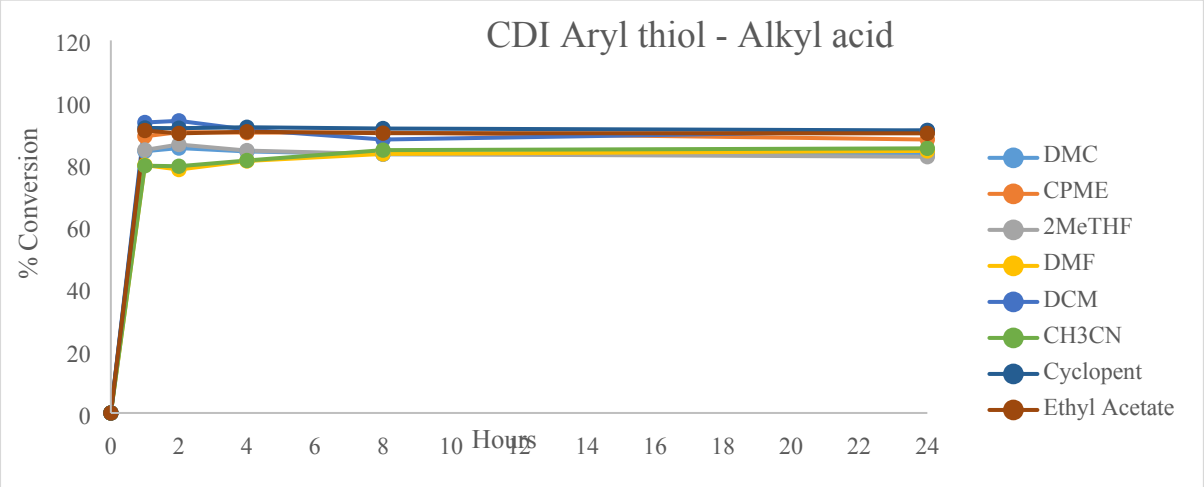
Reaction 1: HATU



Time h	DMC	CPME	2-MeTHF	DMF	DCM	CH_3CN	Cyclopent	Ethyl Acetate
1	77	8	98	100	100	100	100	100
2	80	17	99	100	100	100	100	100
4	83	26	99	100	100	100	100	100
8	84	28	99	100	100	100	100	100
24	83	44	98	100	100	*100	100	100

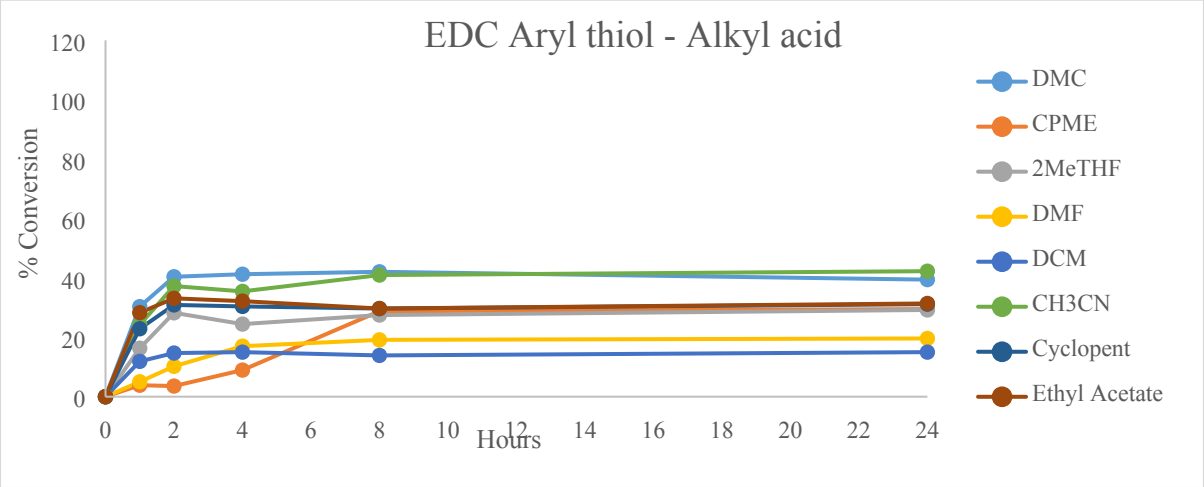
*Acetonitrile reaction isolated and purified by silica gel chromatography, 96% Yield (0.19 mmol, 54.6 mg).

Reaction 1: CDI



Time h	DMC	CPME	2-MeTHF	DMF	DCM	CH_3CN	Cyclopent	Ethyl Acetate
1	84	89	85	80	94	80	92	91
2	85	90	86	78	94	79	92	90
4	84	90	85	81	91	81	92	91
8	83	90	83	83	88	85	92	90
24	83	88	83	84	91	85	91	90

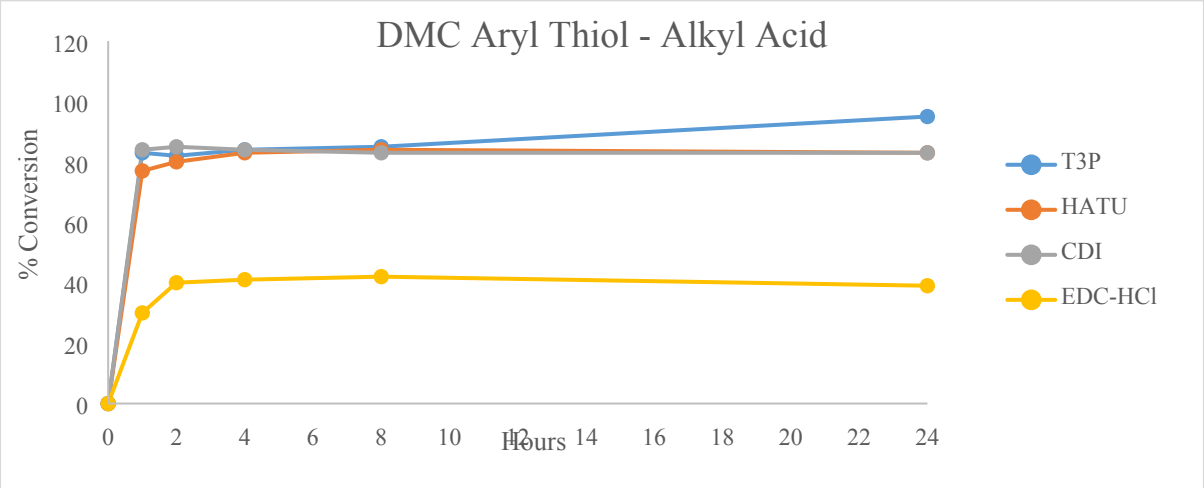
Reaction 1: EDC



Time h	DMC	CPME	2-MeTHF	DMF	DCM	CH_3CN	Cyclopent	Ethyl Acetate
1	30	4	16	5	12	24	23	28
2	40	4	28	10	15	37	31	33
4	41	9	24	17	15	35	30	32
8	42	29	27	19	14	41	30	30
24	39	29	29	20	15	42	31	31

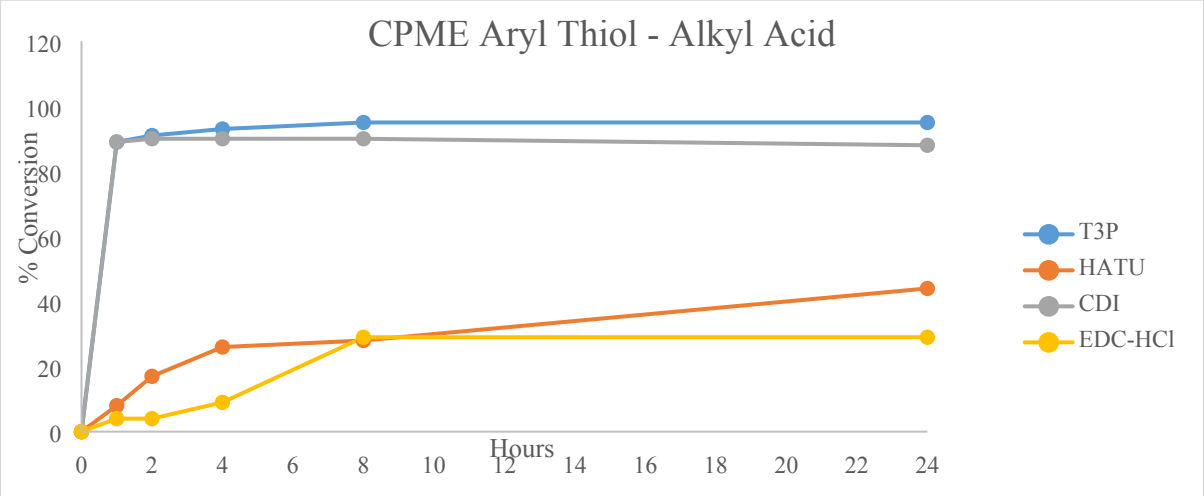
Reaction 1: Performance by Solvent

Reaction 1: DMC



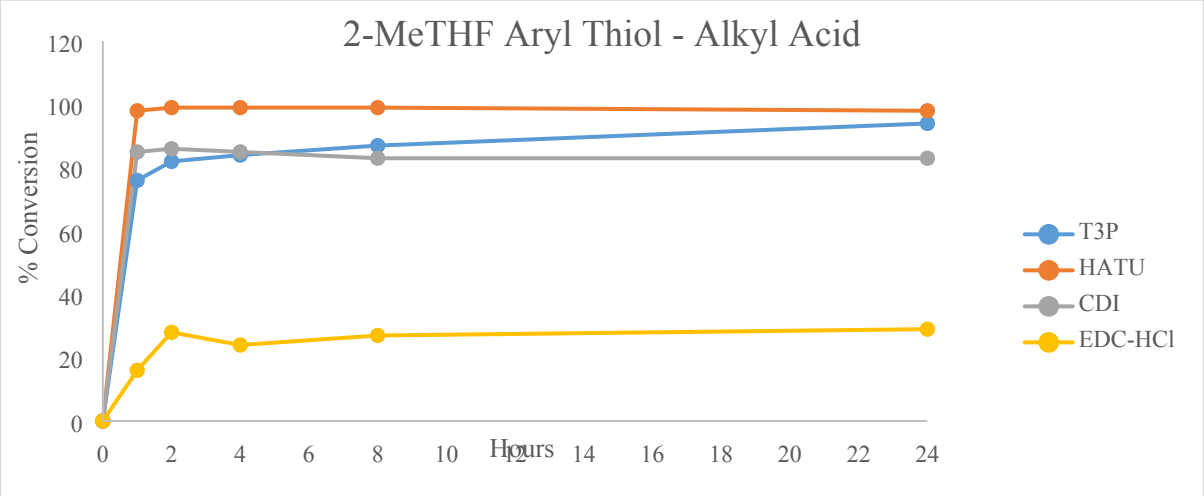
Time h	T3P	HATU	CDI	EDC-HCl
1	83	77	84	30
2	82	80	85	40
4	84	83	84	41
8	85	84	83	42
24	95	83	83	39

Reaction 1: CPME



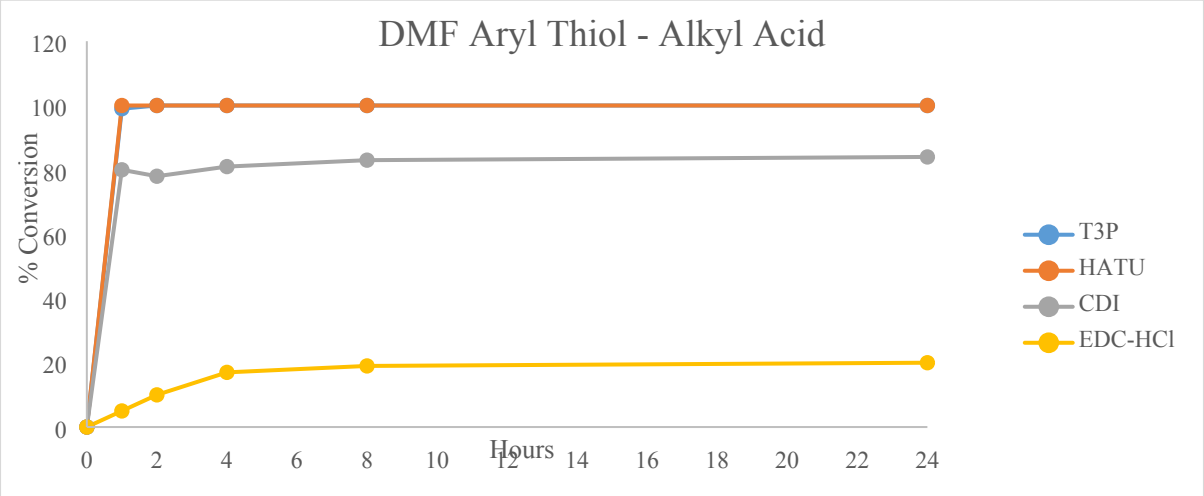
Time h	T3P	HATU	CDI	EDC-HCl
1	89	8	89	4
2	91	17	90	4
4	93	26	90	9
8	95	28	90	29
24	95	44	88	29

Reaction 1: 2-MeTHF



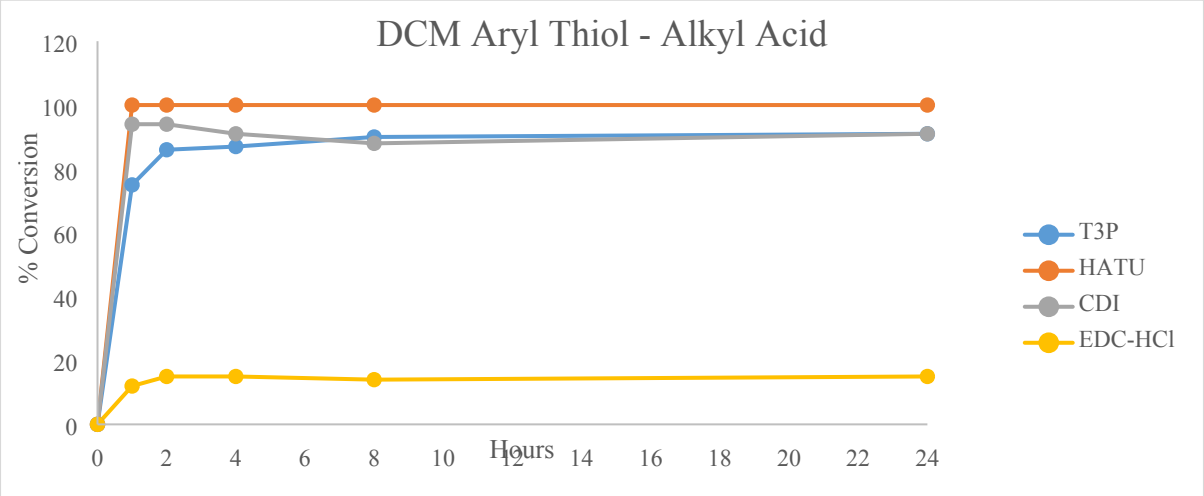
Time h	T3P	HATU	CDI	EDC-HCl
1	76	98	85	16
2	82	99	86	28
4	84	99	85	24
8	87	99	83	27
24	94	98	83	29

Reaction 1: DMF



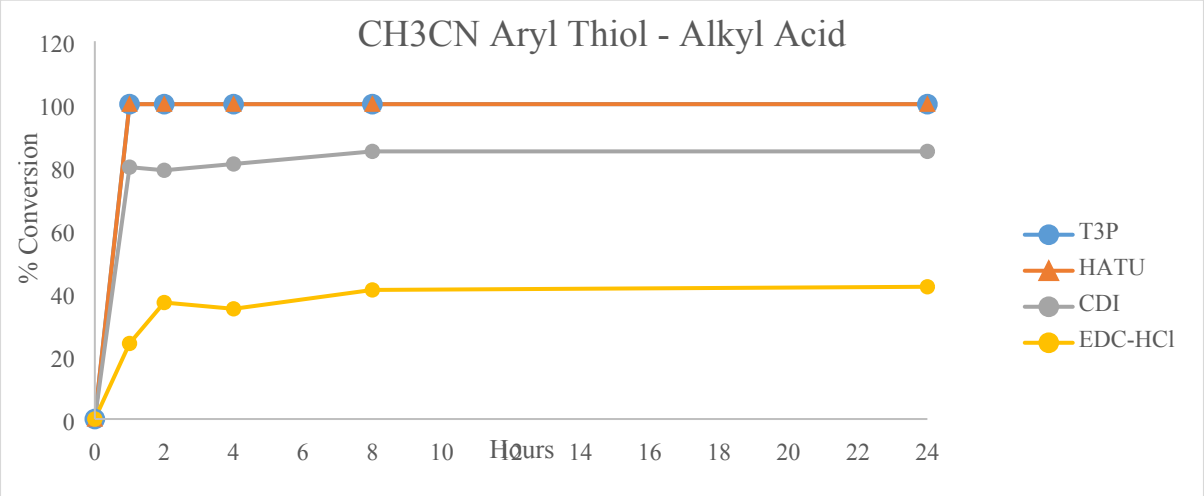
Time h	T3P	HATU	CDI	EDC-HCl
1	99	100	80	5
2	100	100	78	10
4	100	100	81	17
8	100	100	83	19
24	100	100	84	20

Reaction 1: DCM



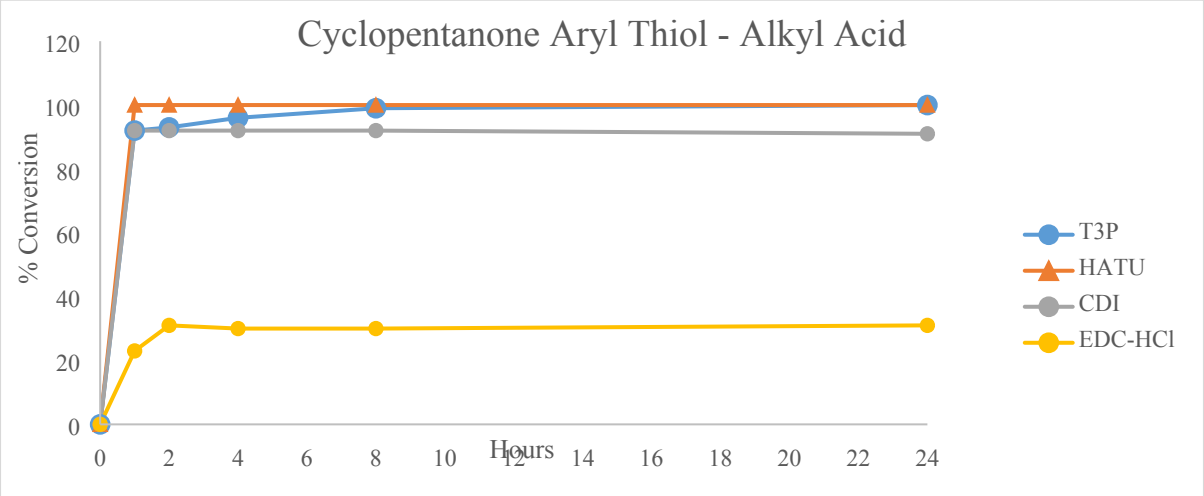
Time h	T3P	HATU	CDI	EDC-HCl
1	75	100	94	12
2	86	100	94	15
4	87	100	91	15
8	90	100	88	14
24	91	100	91	15

Reaction 1: CH_3CN



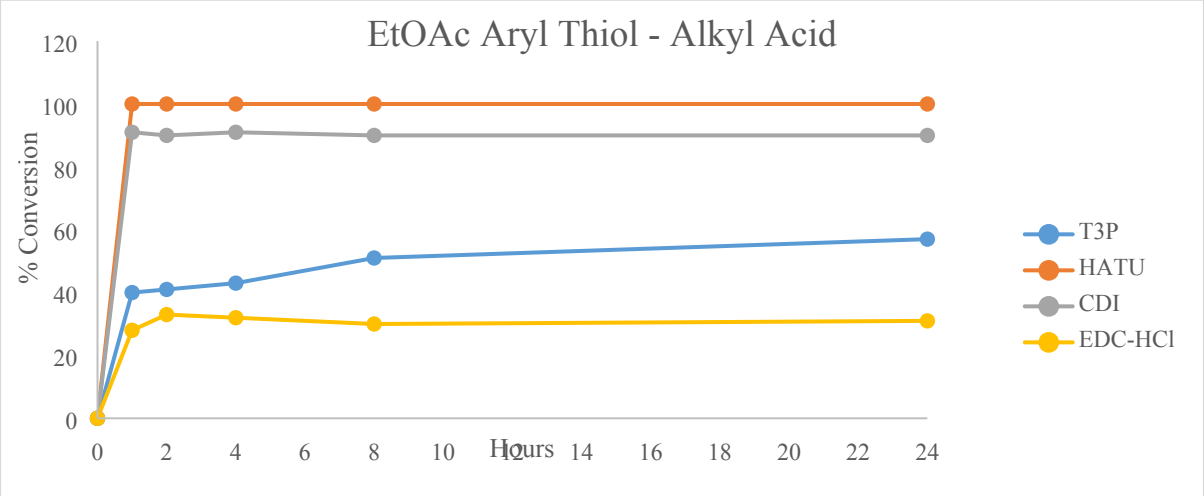
Time h	T3P	HATU	CDI	EDC-HCl
1	100	100	80	24
2	100	100	79	37
4	100	100	81	35
8	100	100	85	41
24	100	100	85	42

Reaction 1: Cyclopentanone



Time h	T3P	HATU	CDI	EDC-HCl
1	92	100	92	23
2	93	100	92	31
4	96	100	92	30
8	99	100	92	30
24	100	100	91	31

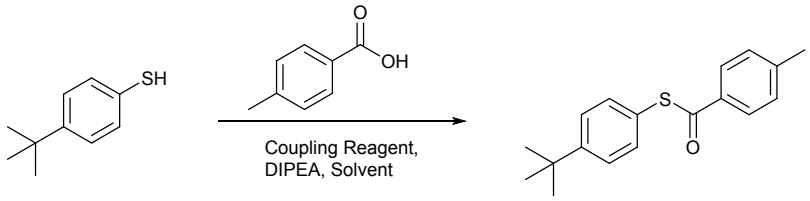
Reaction 1: Ethyl Acetate

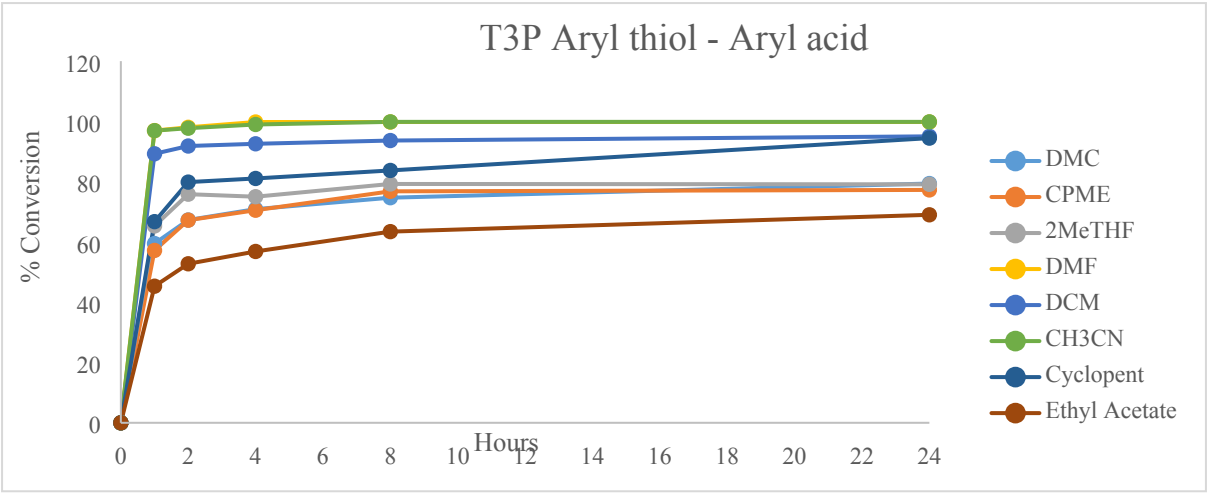


Time h	T3P	HATU	CDI	EDC-HCl
1	40	100	91	28
2	41	100	90	33
4	43	100	91	32
8	51	100	90	30
24	57	100	90	31

Reaction 2: Performance by Coupling Reagent

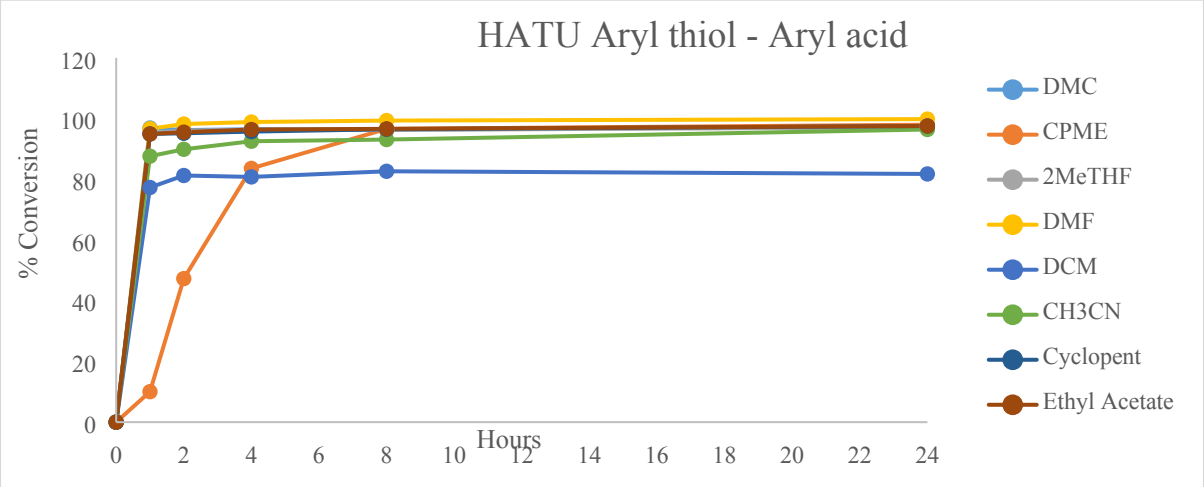
Reaction 2: T3P





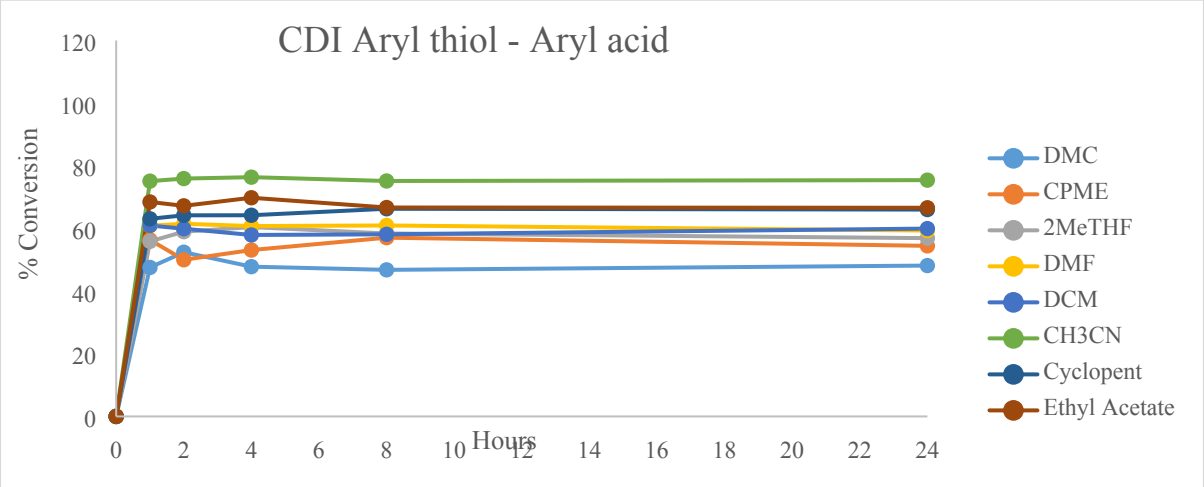
Time h	DMC	CPME	2-MeTHF	DMF	DCM	CH_3CN	Cyclopent	Ethyl Acetate
1	59	57	65	97	89	97	67	45
2	67	67	76	98	92	98	80	53
4	71	71	75	100	93	99	81	57
8	75	77	79	100	94	100	84	63
24	79	77	79	100	95	100	94	69

Reaction 2: HATU



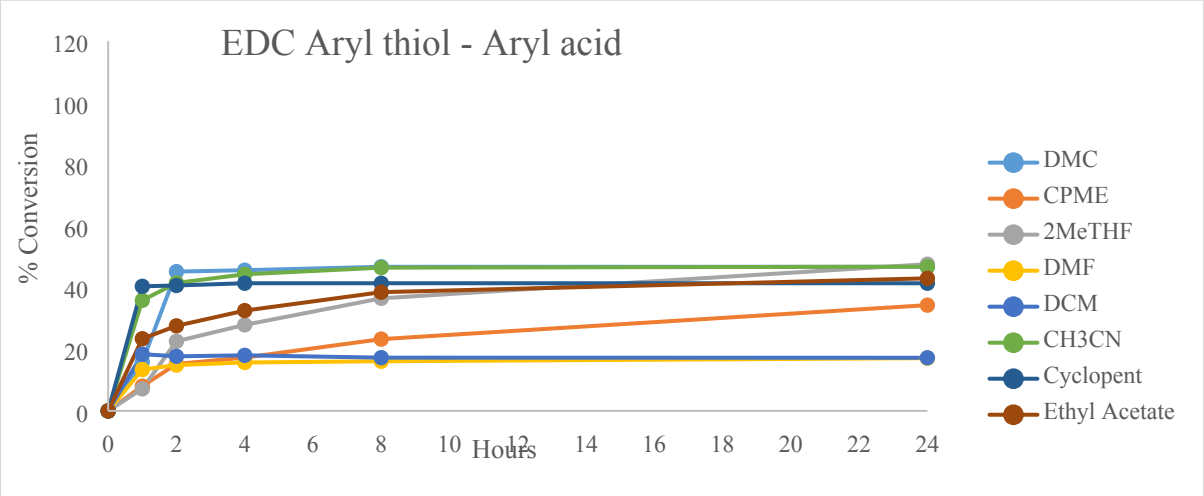
Time h	DMC	CPME	2-MeTHF	DMF	DCM	CH_3CN	Cyclopent	Ethyl Acetate
1	97	10	95	97	77	88	95	95
2	96	47	96	98	81	90	95	96
4	96	84	96	99	81	93	96	96
8	96	97	96	99	83	93	96	97
24	97	98	97	100	82	96	98	98

Reaction 2: CDI



Time h	DMC	CPME	2-MeTHF	DMF	DCM	CH_3CN	Cyclopent	Ethyl Acetate
1	48	56	56	61	61	75	63	68
2	52	50	59	61	60	76	64	67
4	48	53	60	61	58	76	64	70
8	47	57	58	61	58	75	66	67
24	48	54	57	59	60	75	66	67

Reaction 2: EDC

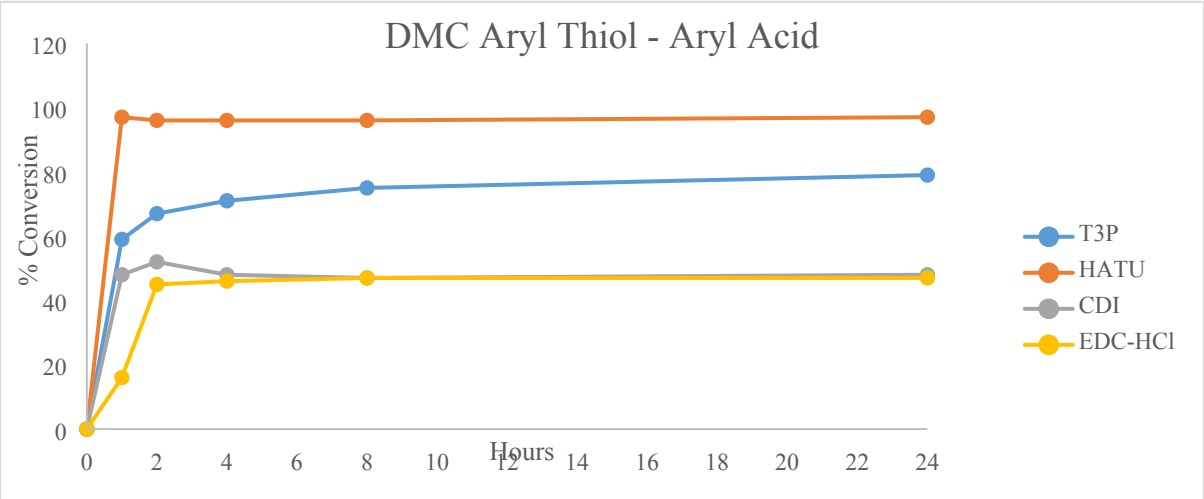


Time h	DMC	CPME	2-MeTHF	DMF	DCM	CH_3CN	Cyclopent	Ethyl Acetate
1	16	8	7	13	18	36	40	23
2	45	15	23	15	18	42	41	28
4	46	17	28	16	18	44	41	33
8	47	23	37	16	17	46	41	39
24	47	34	48	17	17	47	41	*43

*Isolated and purified by column chromatography, 45% yield (26.0 mg, 0.09 mmol)

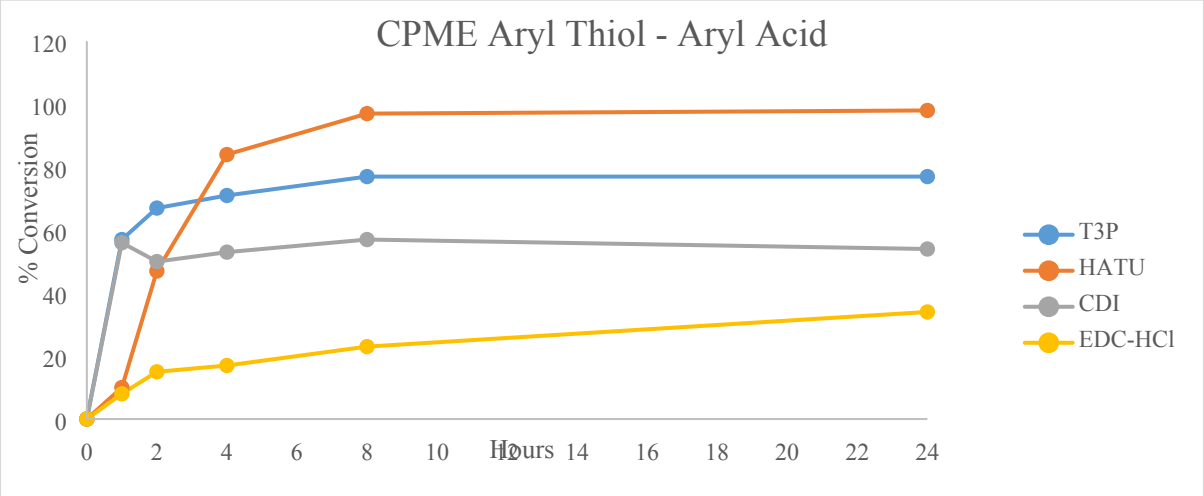
Reaction 2: Performance by Solvent

Reaction 2: DMC



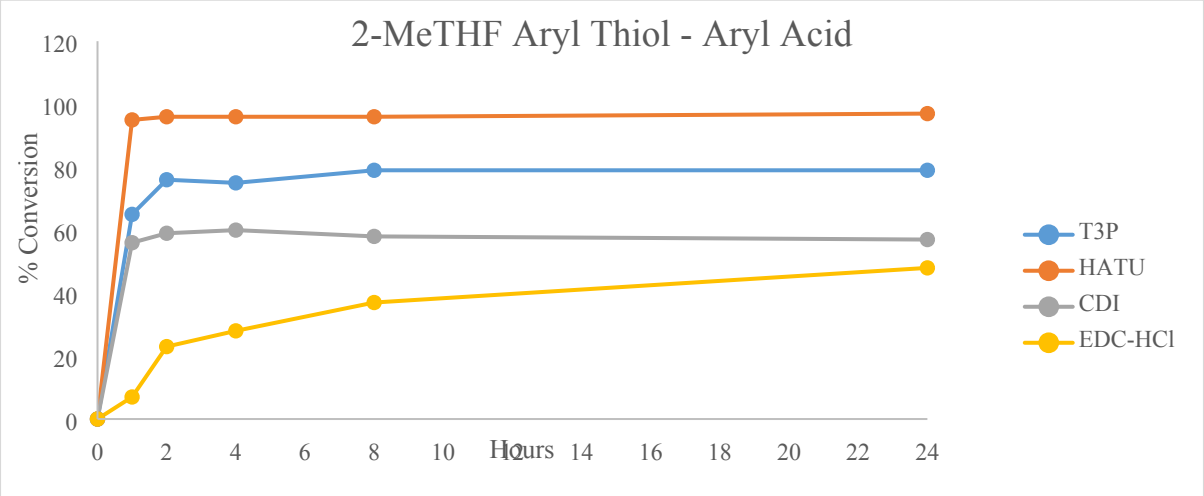
Time h	T3P	HATU	CDI	EDC-HCl
1	59	97	48	16
2	67	96	52	45
4	71	96	48	46
8	75	96	47	47
24	79	97	48	47

Reaction 2: CPME



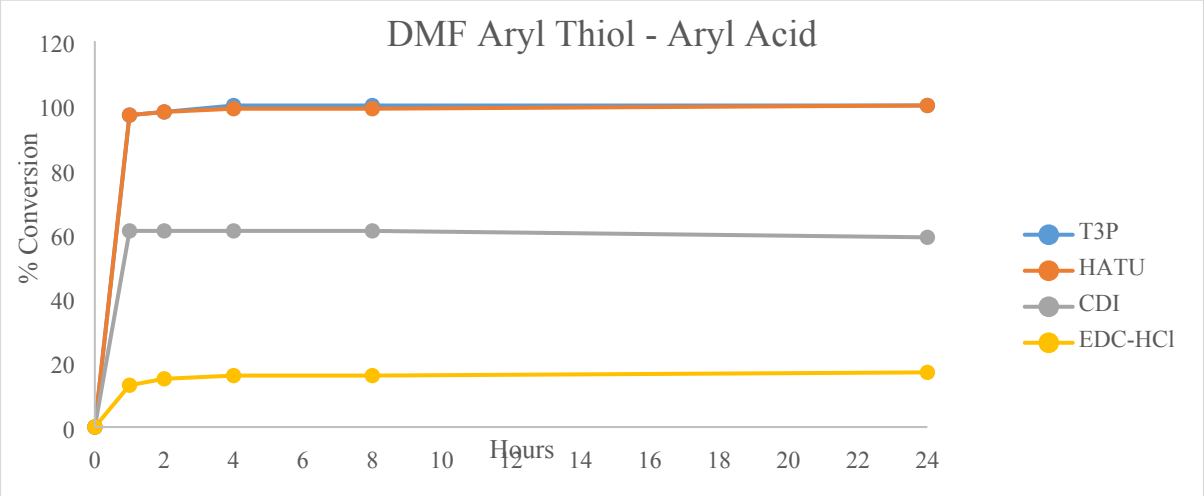
Time h	T3P	HATU	CDI	EDC-HCl
1	57	10	56	8
2	67	47	50	15
4	71	84	53	17
8	77	97	57	23
24	77	98	54	34

Reaction 2: 2-MeTHF



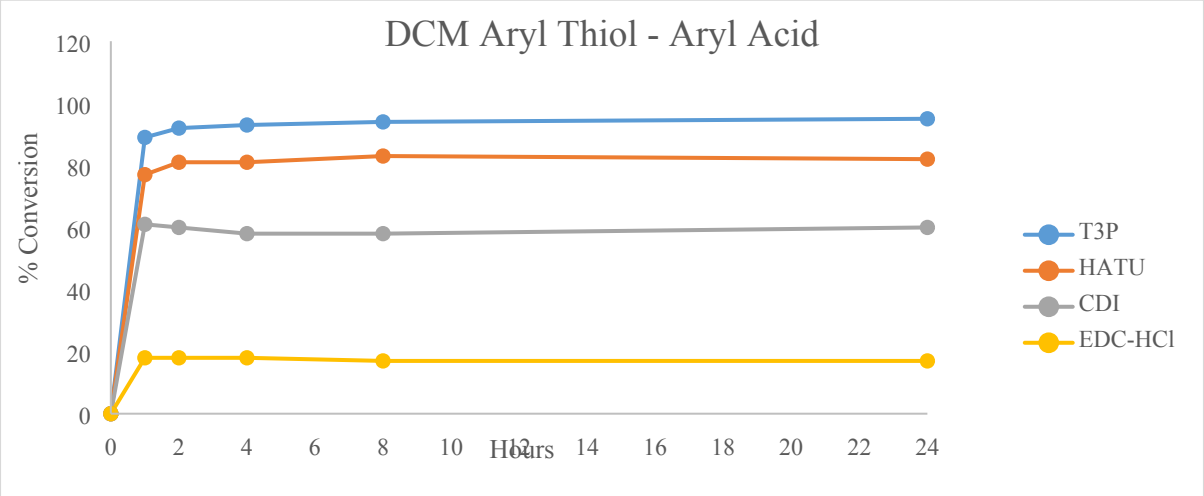
Time h	T3P	HATU	CDI	EDC-HCl
1	65	95	56	7
2	76	96	59	23
4	75	96	60	28
8	79	96	58	37
24	79	97	57	48

Reaction 2: DMF



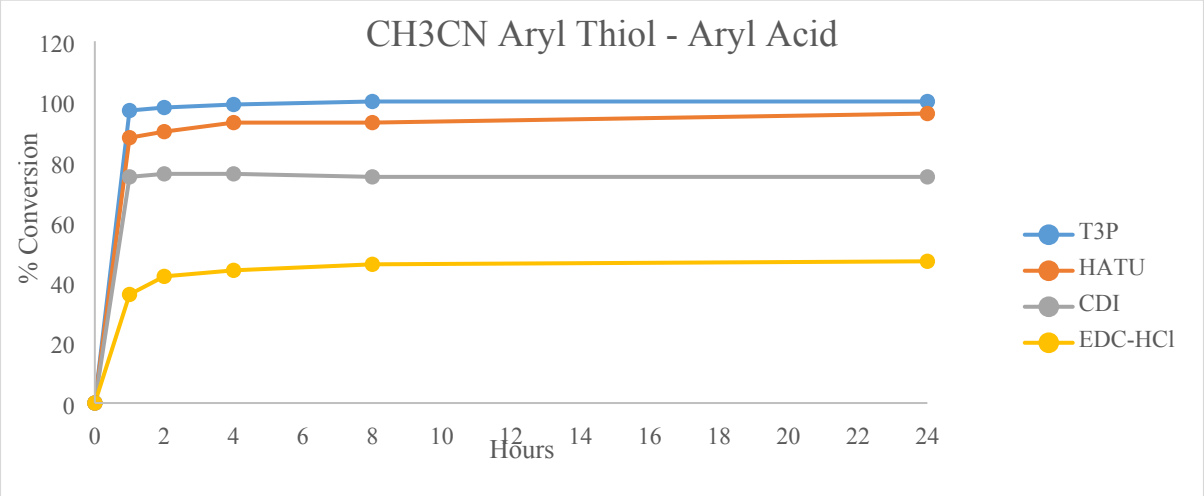
Time h	T3P	HATU	CDI	EDC-HCl
1	97	97	61	13
2	98	98	61	15
4	100	99	61	16
8	100	99	61	16
24	100	100	59	17

Reaction 2: DCM



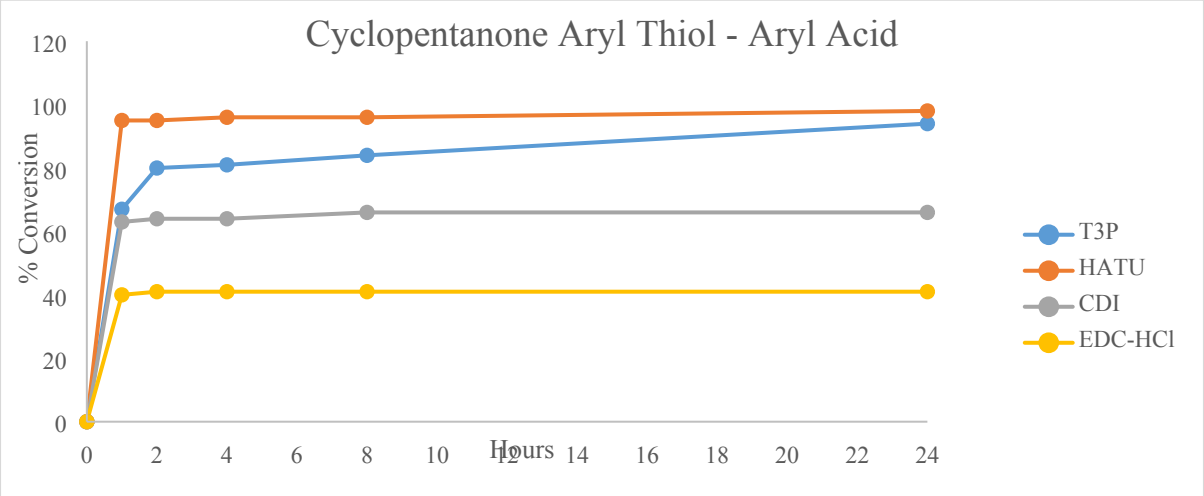
Time h	T3P	HATU	CDI	EDC-HCl
1	89	77	61	18
2	92	81	60	18
4	93	81	58	18
8	94	83	58	17
24	95	82	60	17

Reaction 2: CH_3CN



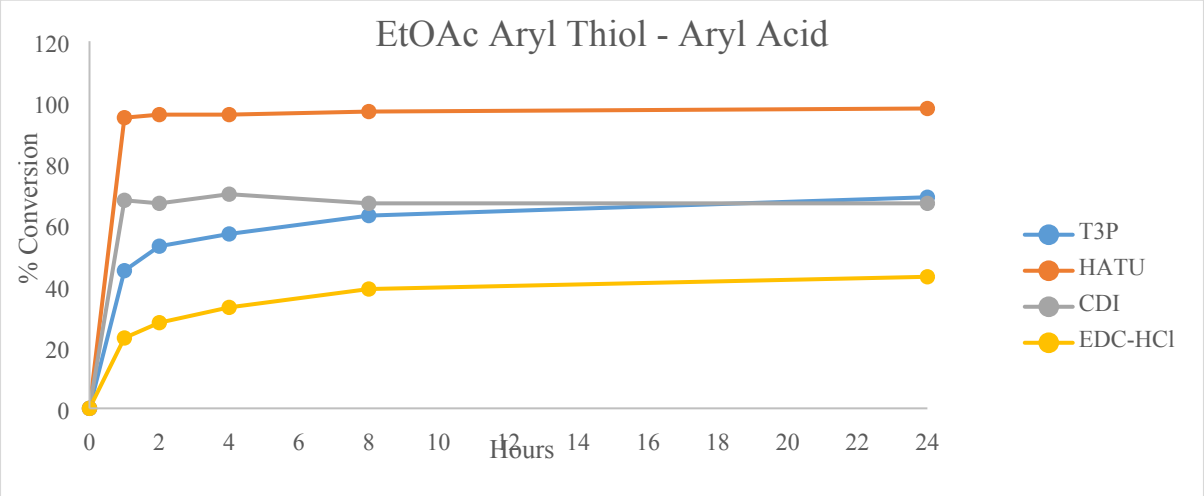
Time h	T3P	HATU	CDI	EDC-HCl
1	97	88	75	36
2	98	90	76	42
4	99	93	76	44
8	100	93	75	46
24	100	96	75	47

Reaction 2: Cyclopentanone



Time h	T3P	HATU	CDI	EDC-HCl
1	67	95	63	40
2	80	95	64	41
4	81	96	64	41
8	84	96	66	41
24	94	98	66	41

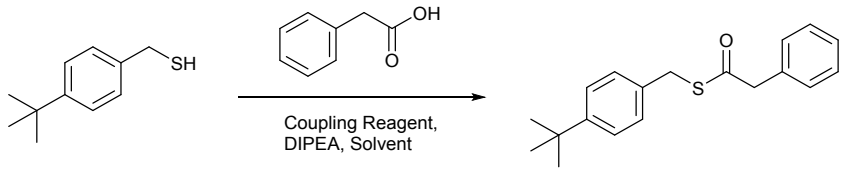
Reaction 2: Ethyl Acetate

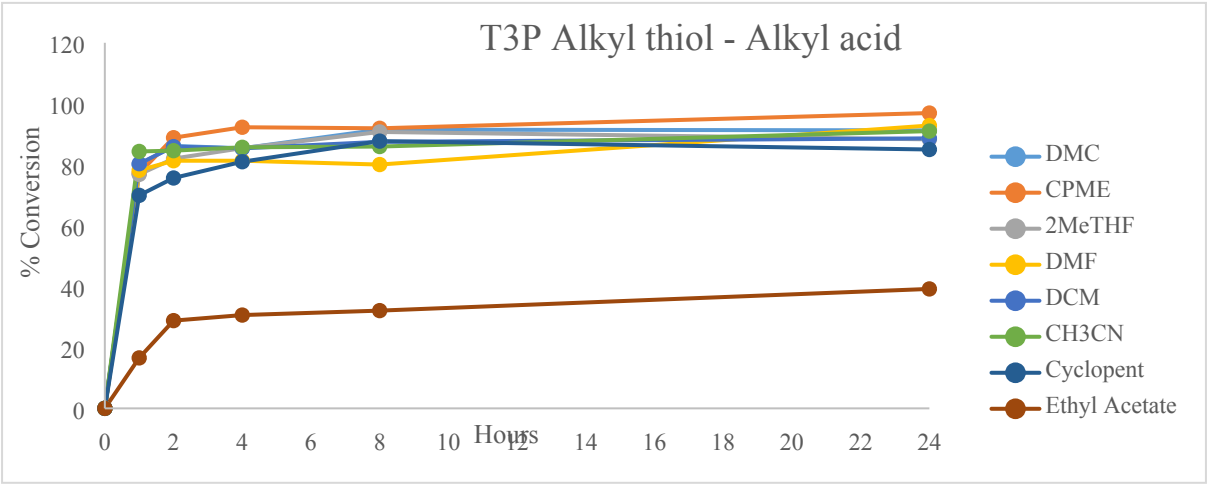


Time h	T3P	HATU	CDI	EDC-HCl
1	45	95	68	23
2	53	96	67	28
4	57	96	70	33
8	63	97	67	39
24	69	98	67	43

Reaction 3: Performance by Coupling Reagent

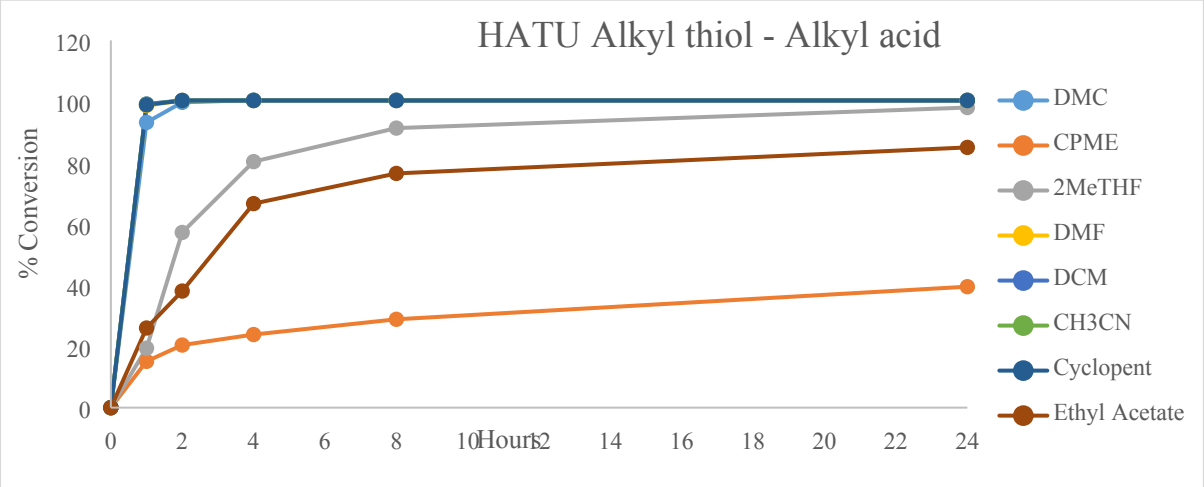
Reaction 3: T3P





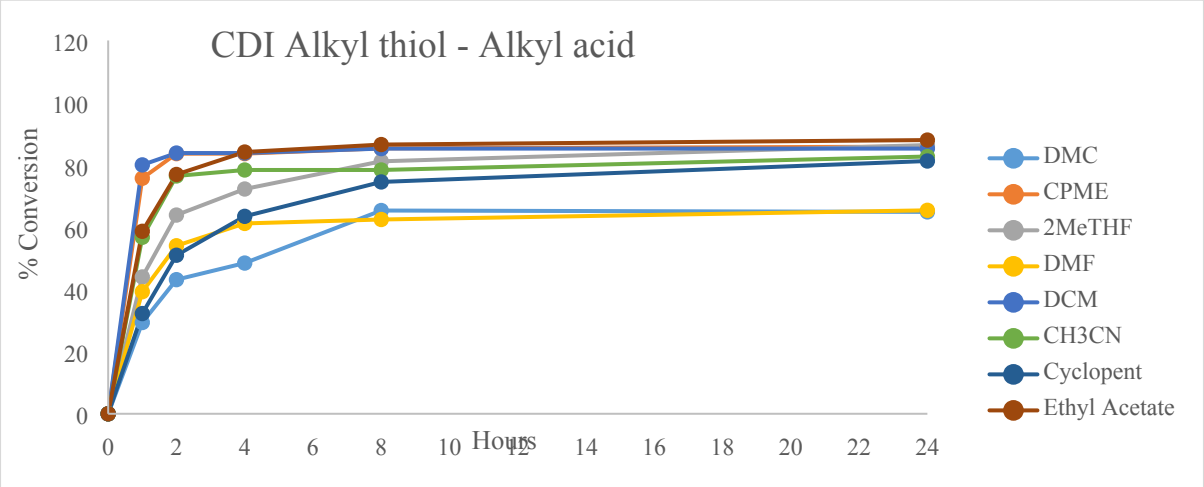
Time h	DMC	CPME	2MeTHF	DMF	DCM	CH3CN	Cyclopent	Ethyl Acetate
1	80	77	77	78	80	84	70	17
2	86	89	82	81	86	85	76	29
4	85	92	85	81	85	86	81	31
8	91	92	91	80	87	86	88	32
24	91	97	88	93	89	91	85	39

Reaction 3: HATU



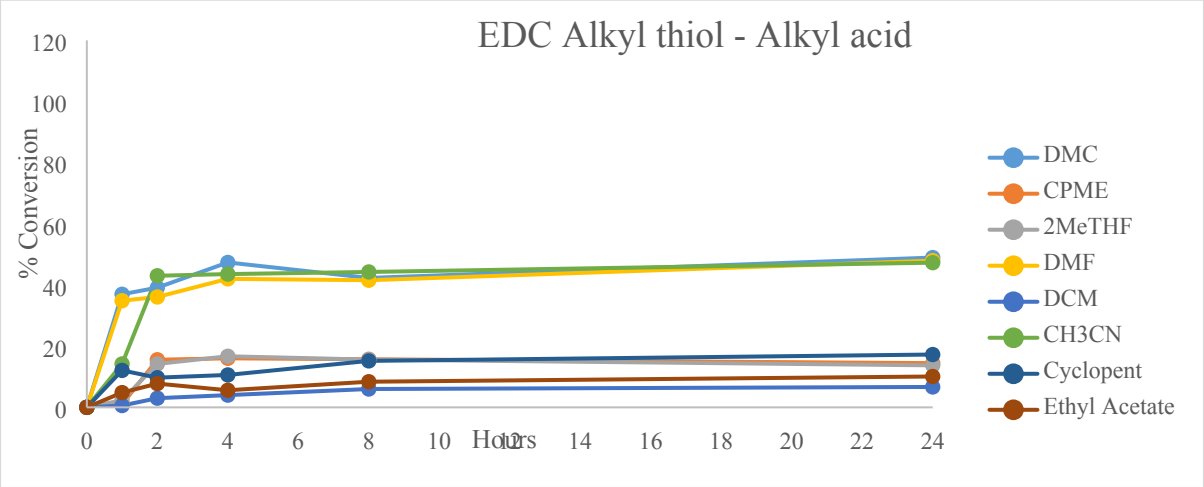
Time h	DMC	CPME	2MeTHF	DMF	DCM	CH3CN	Cyclopent	Ethyl Acetate
1	93	15	19	99	99	99	99	26
2	100	20	57	100	100	100	100	38
4	100	24	80	100	100	100	100	67
8	100	29	91	100	100	100	100	77
24	100	40	98	100	100	100	100	85

Reaction 3: CDI



Time h	DMC	CPME	2-MeTHF	DMF	DCM	CH_3CN	Cyclopent	Ethyl Acetate
1	29	76	44	39	80	57	32	59
2	43	84	64	54	84	76	51	77
4	48	84	72	61	84	78	63	84
8	65	85	81	62	85	78	75	87
24	65	86	86	65	85	83	81	88

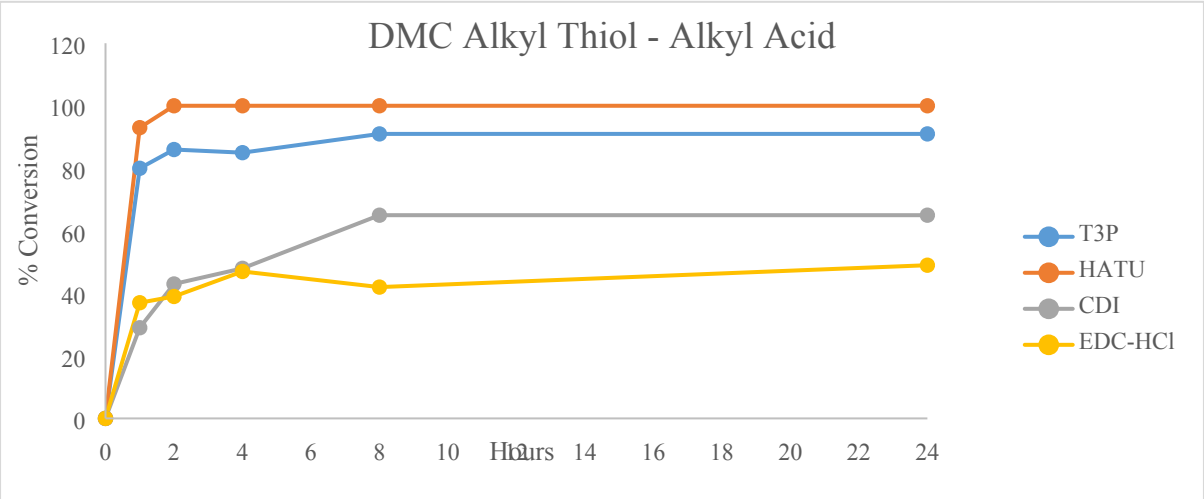
Reaction 3: EDC



Time h	DMC	CPME	2-MeTHF	DMF	DCM	CH_3CN	Cyclopent	Ethyl Acetate
1	37	1	2	35	1	14	12	5
2	39	16	14	36	3	43	10	8
4	47	16	17	42	4	44	11	6
8	42	16	16	42	6	44	15	8
24	49	14	14	48	7	47	17	10

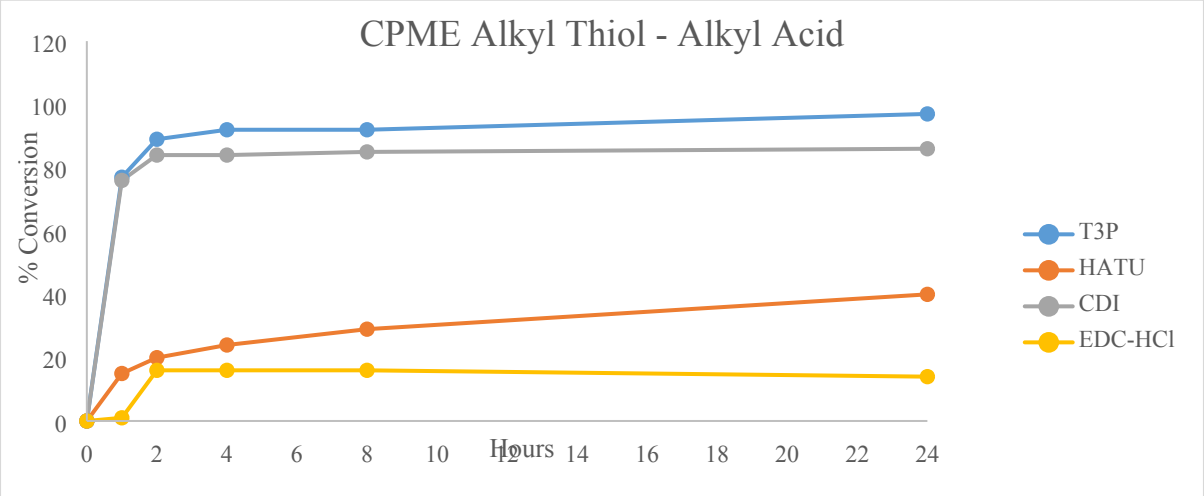
Reaction 3: Performance by Solvent

Reaction 3: DMC



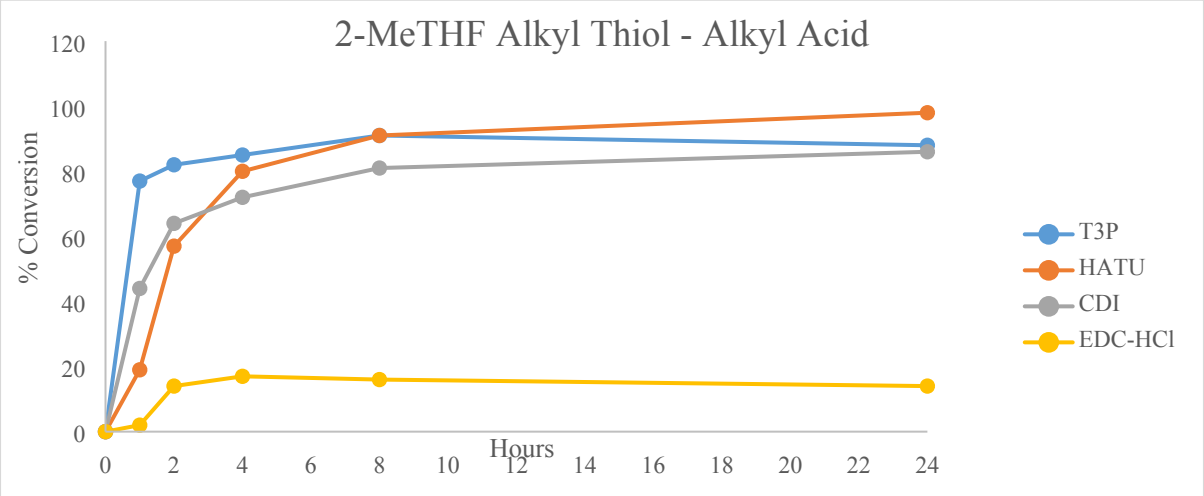
Time h	T3P	HATU	CDI	EDC-HCl
1	80	93	29	37
2	86	100	43	39
4	85	100	48	47
8	91	100	65	42
24	91	100	65	49

Reaction 3: CPME



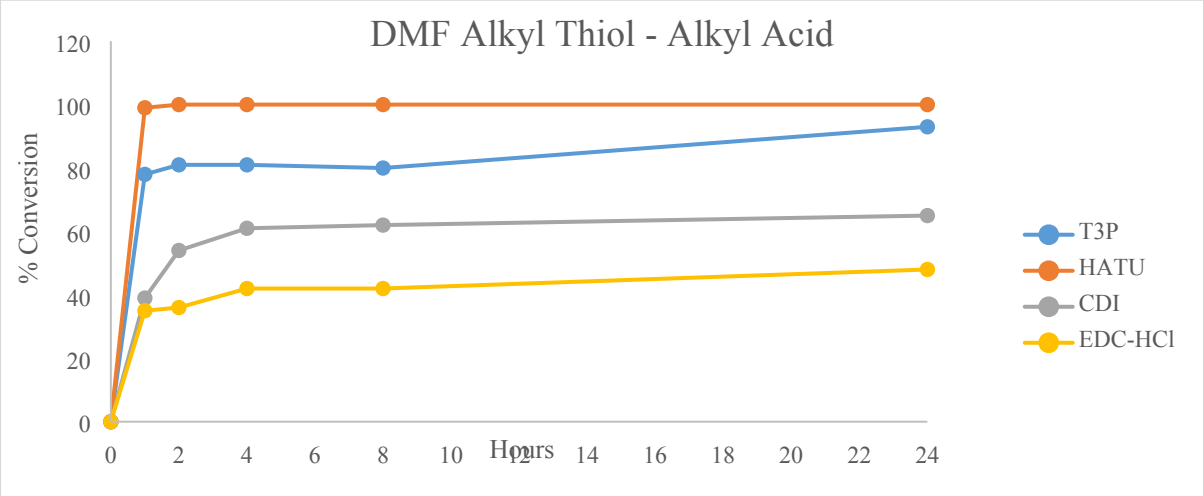
Time h	T3P	HATU	CDI	EDC-HCl
1	77	15	76	1
2	89	20	84	16
4	92	24	84	16
8	92	29	85	16
24	97	40	86	14

Reaction 3: 2-MeTHF



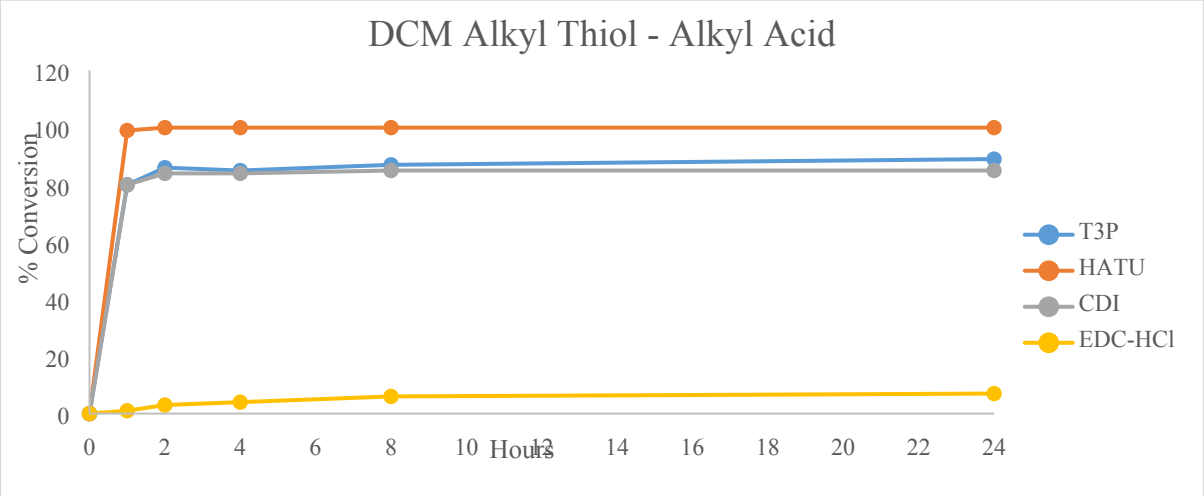
Time h	T3P	HATU	CDI	EDC-HCl
1	77	19	44	2
2	82	57	64	14
4	85	80	72	17
8	91	91	81	16
24	88	98	86	14

Reaction 3: DMF



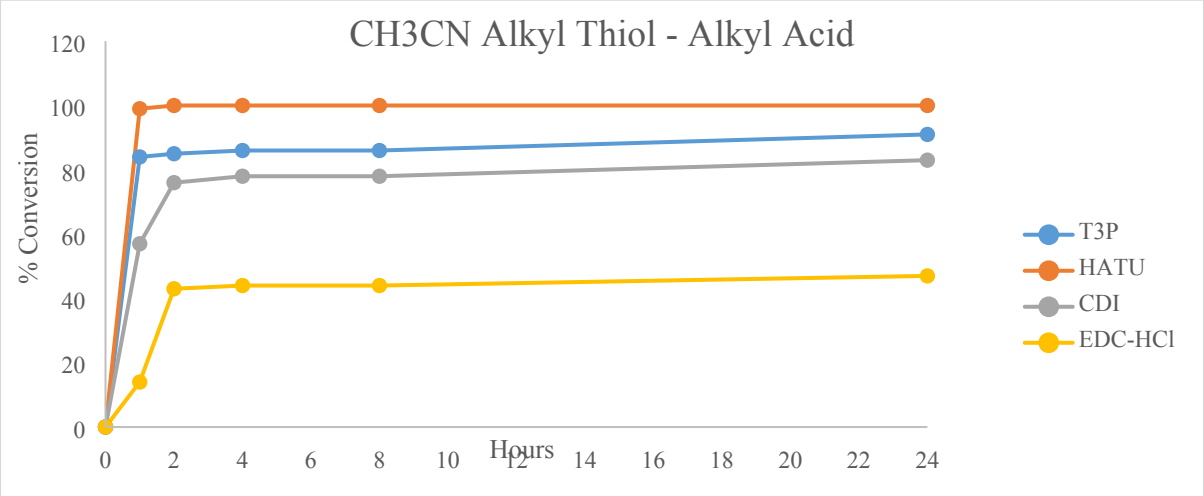
Time h	T3P	HATU	CDI	EDC-HCl
1	78	99	39	35
2	81	100	54	36
4	81	100	61	42
8	80	100	62	42
24	93	100	65	48

Reaction 3: DCM



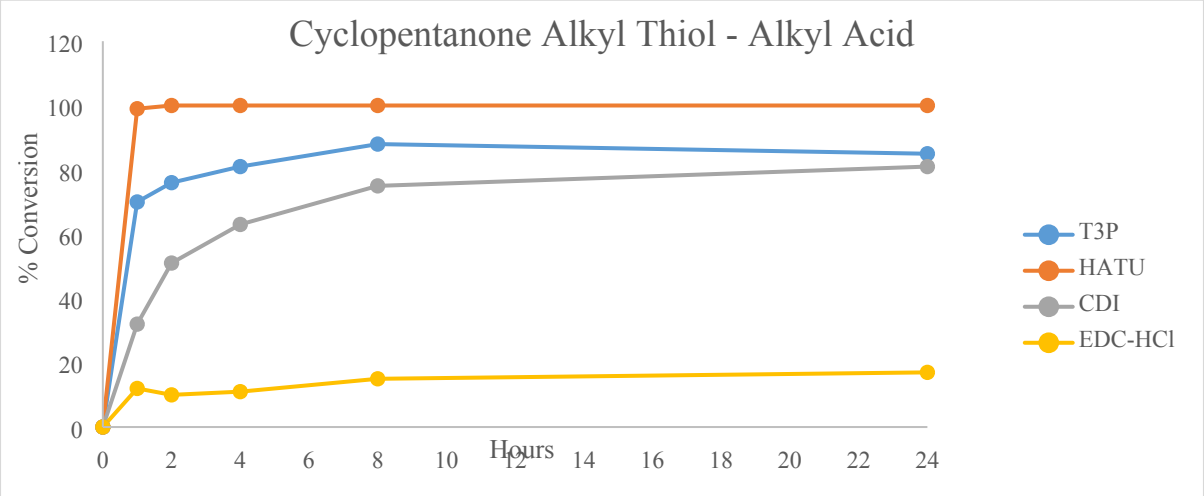
Time h	T3P	HATU	CDI	EDC-HCl
1	80	99	80	1
2	86	100	84	3
4	85	100	84	4
8	87	100	85	6
24	89	100	85	7

Reaction 3: CH_3CN



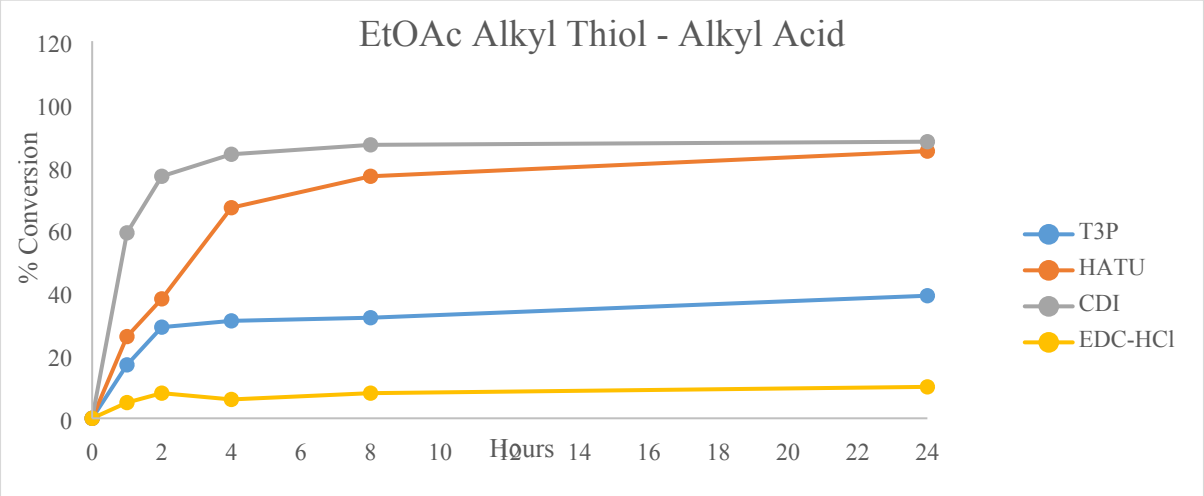
Time h	T3P	HATU	CDI	EDC-HCl
1	84	99	57	14
2	85	100	76	43
4	86	100	78	44
8	86	100	78	44
24	91	100	83	47

Reaction 3: Cyclopentanone



Time h	T3P	HATU	CDI	EDC-HCl
1	70	99	32	12
2	76	100	51	10
4	81	100	63	11
8	88	100	75	15
24	85	100	81	17

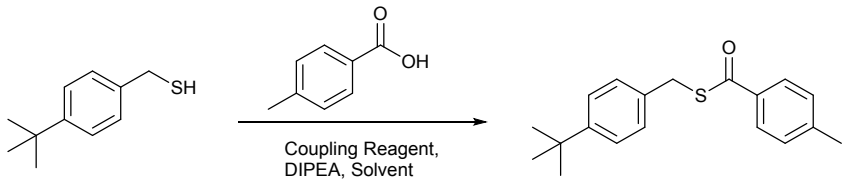
Reaction 3: Ethyl Acetate

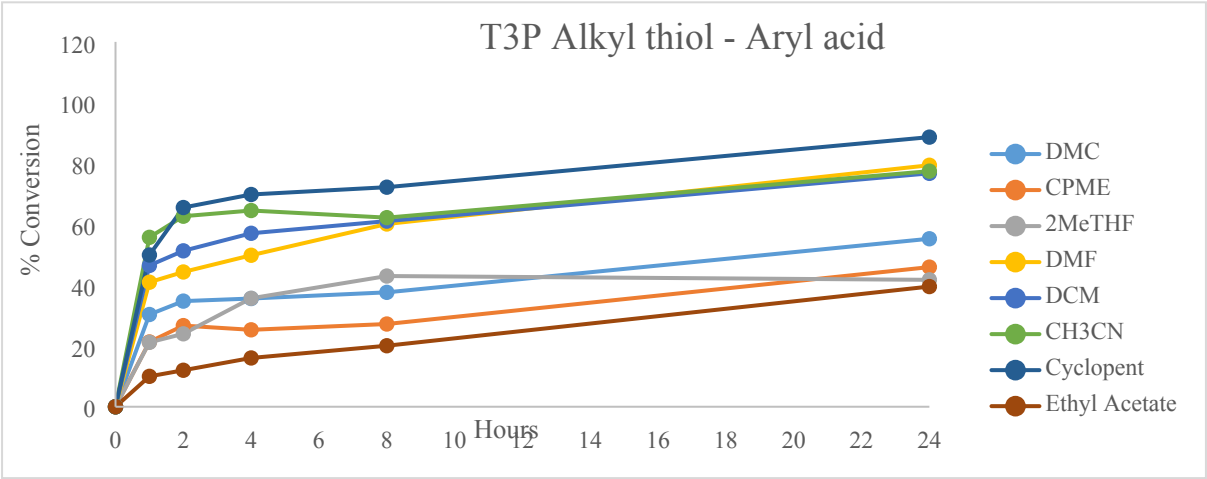


Time h	T3P	HATU	CDI	EDC-HCl
1	17	26	59	5
2	29	38	77	8
4	31	67	84	6
8	32	77	87	8
24	39	85	88	10

Reaction 4: Performance by Coupling Reagent

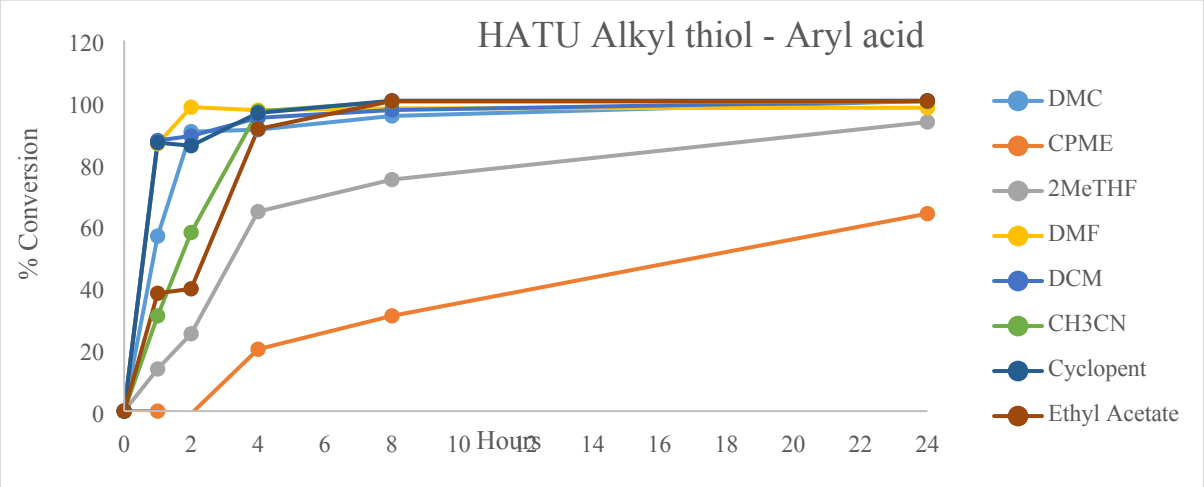
Reaction 4: T3P





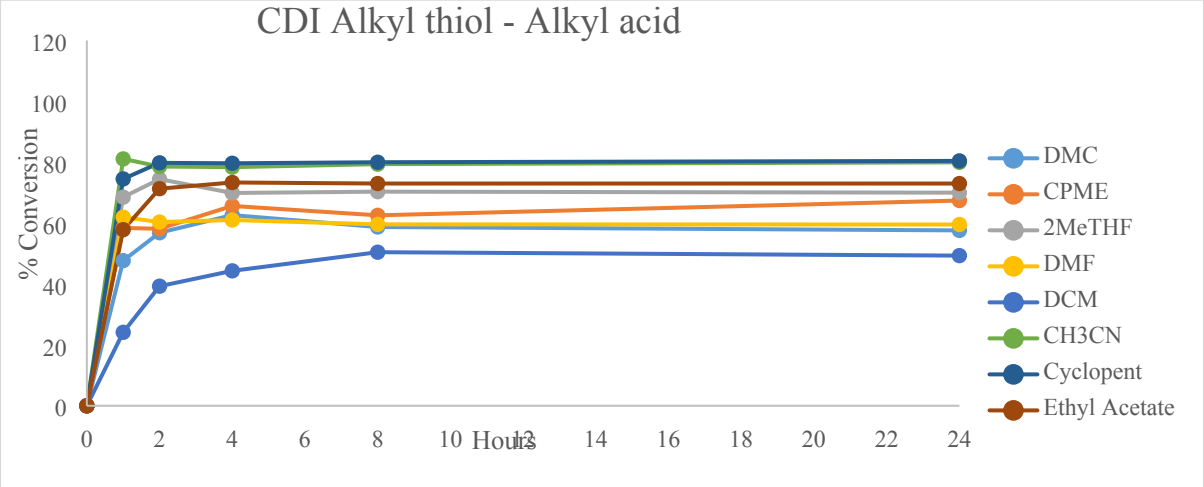
Time h	DMC	CPME	2-MeTHF	DMF	DCM	CH_3CN	Cyclopent	Ethyl Acetate
1	30	21	21	41	46	56	50	10
2	35	27	24	44	51	63	66	12
4	36	25	36	50	57	65	70	16
8	38	27	43	60	61	62	72	20
24	55	46	42	79	77	77	89	40

Reaction 4: HATU



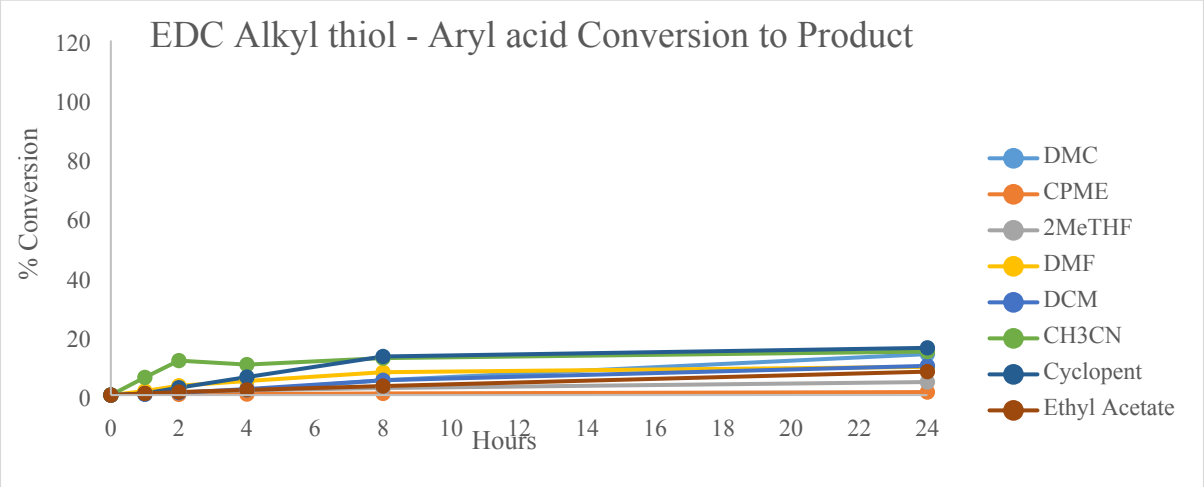
Time h	DMC	CPME	2-MeTHF	DMF	DCM	CH_3CN	Cyclopent	Ethyl Acetate
1	57	0	14	87	88	31	87	38
2	90	0	25	98	89	58	86	40
4	91	20	65	97	95	97	97	91
8	96	31	75	98	97	100	100	100
24	100	64	94	98	100	100	100	100

Reaction 4: CDI



Time h	DMC	CPME	2-MeTHF	DMF	DCM	CH_3CN	Cyclopent	Ethyl Acetate
1	48	58	69	62	24	81	75	58
2	57	58	74	60	39	79	80	71
4	63	66	70	61	44	78	80	73
8	59	63	70	60	50	79	80	73
24	58	67	70	60	49	80	80	73

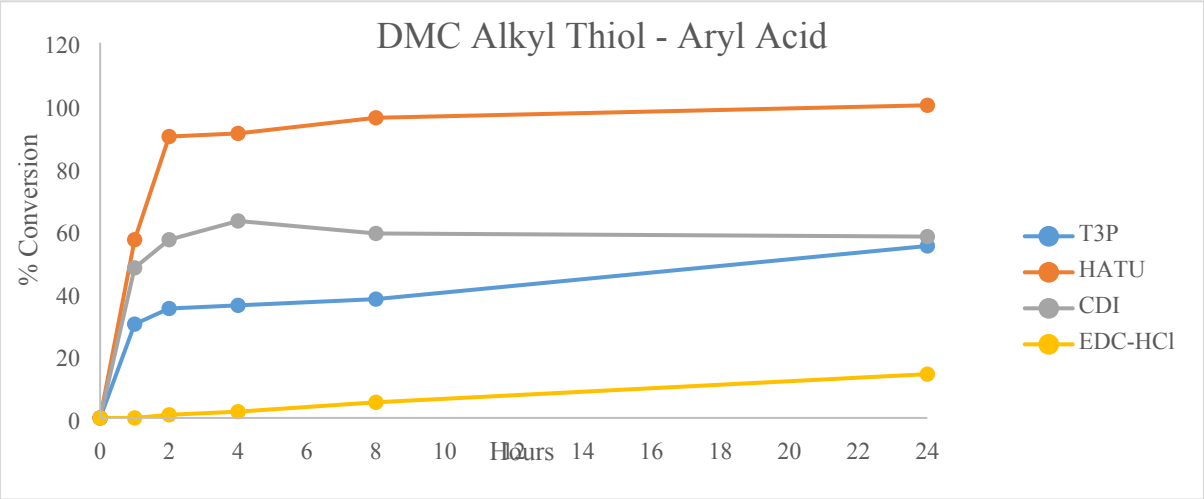
Reaction 4: EDC



Time h	DMC	CPME	2-MeTHF	DMF	DCM	CH_3CN	Cyclopent	Ethyl Acetate
1	0	0	0	1	0	6	1	1
2	1	0	1	3	1	12	2	1
4	2	0	2	5	2	10	6	2
8	5	1	2	8	5	13	13	3
24	14	1	4	10	10	15	16	8

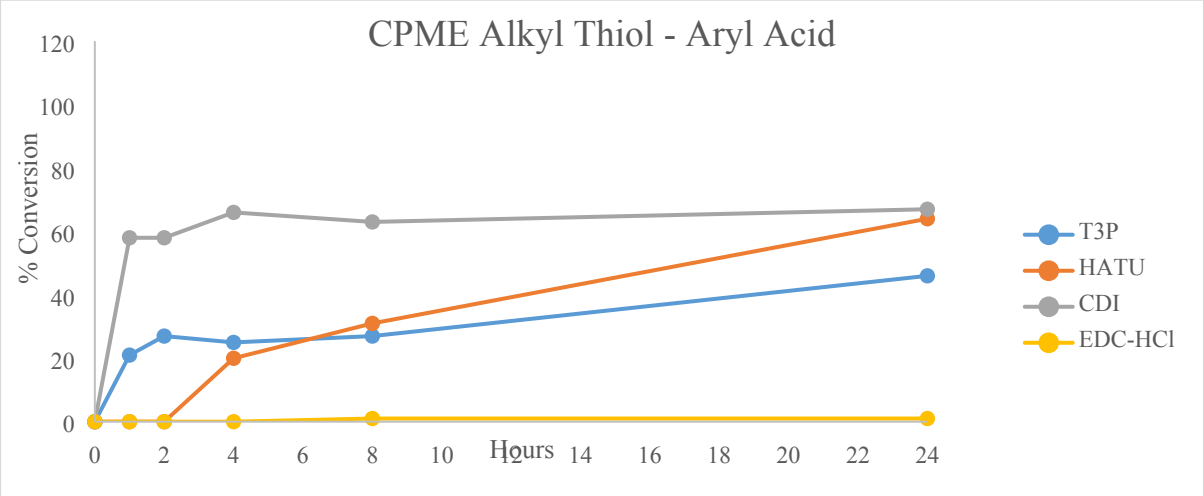
Reaction 4: Performance by Solvent

Reaction 4: DMC



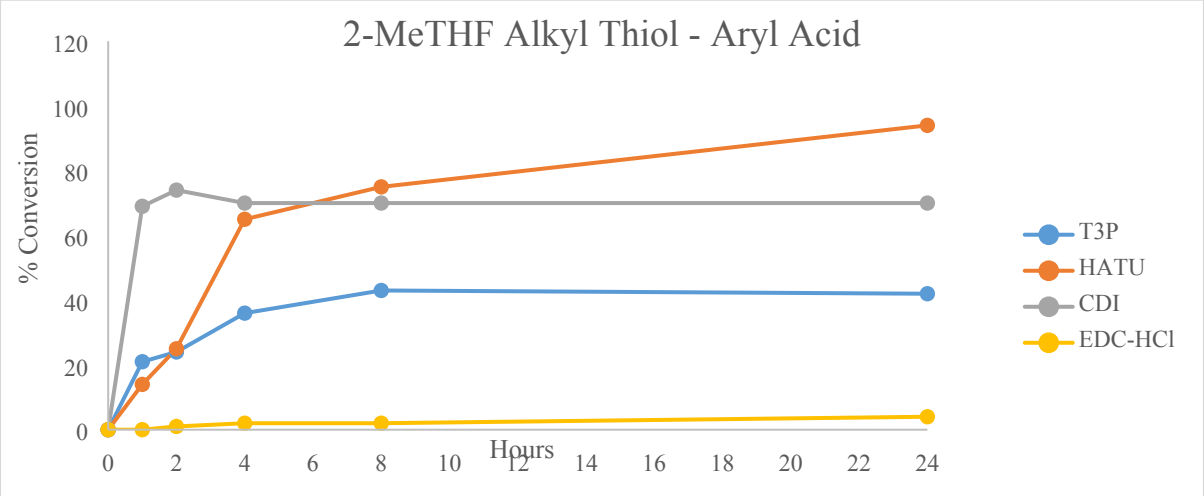
Time h	T3P	HATU	CDI	EDC-HCl
1	30	57	48	0
2	35	90	57	1
4	36	91	63	2
8	38	96	59	5
24	55	100	58	14

Reaction 4: CPME



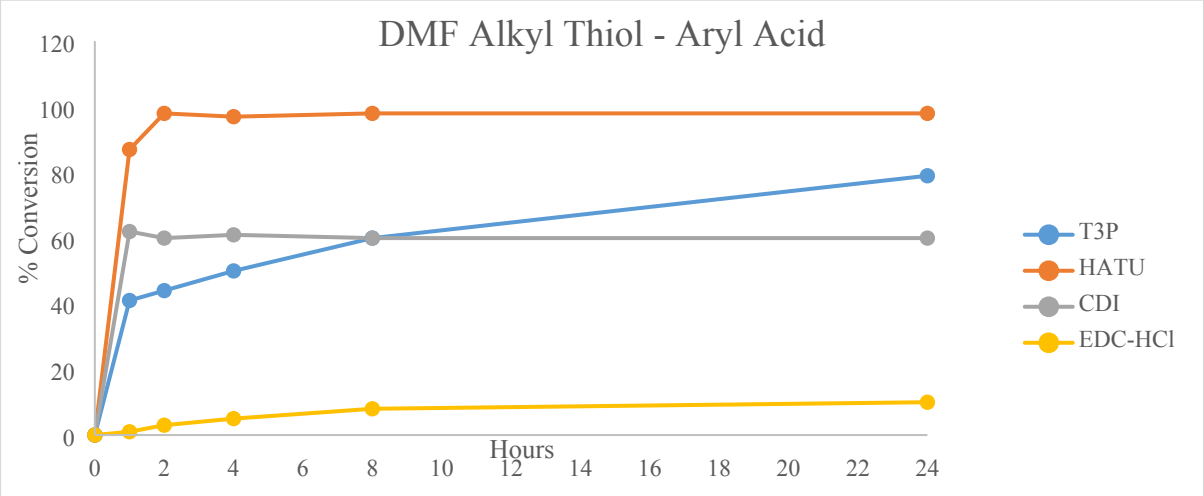
Time h	T3P	HATU	CDI	EDC-HCl
1	21	0	58	0
2	27	0	58	0
4	25	20	66	0
8	27	31	63	1
24	46	64	67	1

Reaction 4: 2-MeTHF



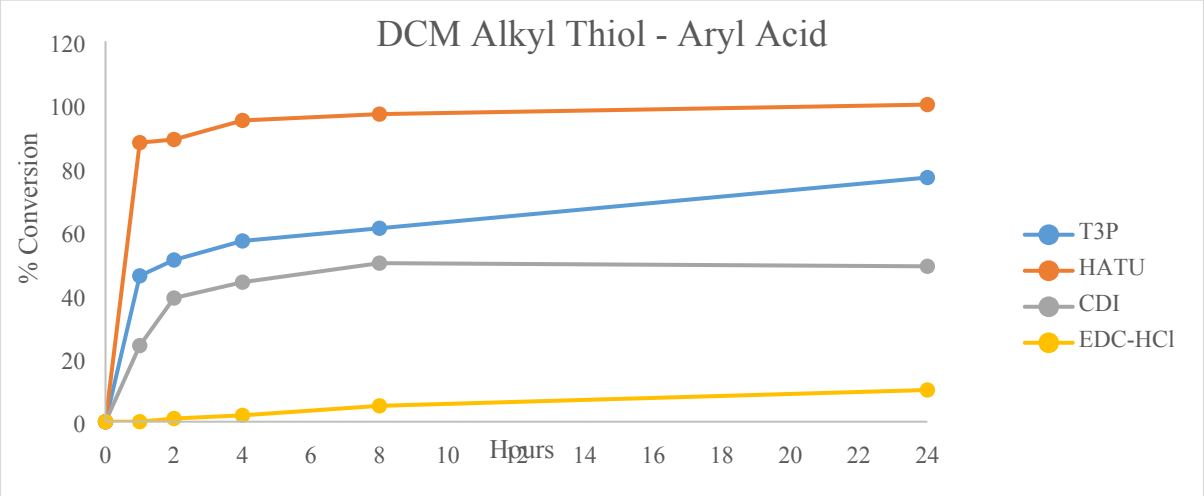
Time h	T3P	HATU	CDI	EDC-HCl
1	21	14	69	0
2	24	25	74	1
4	36	65	70	2
8	43	75	70	2
24	42	94	70	4

Reaction 4: DMF



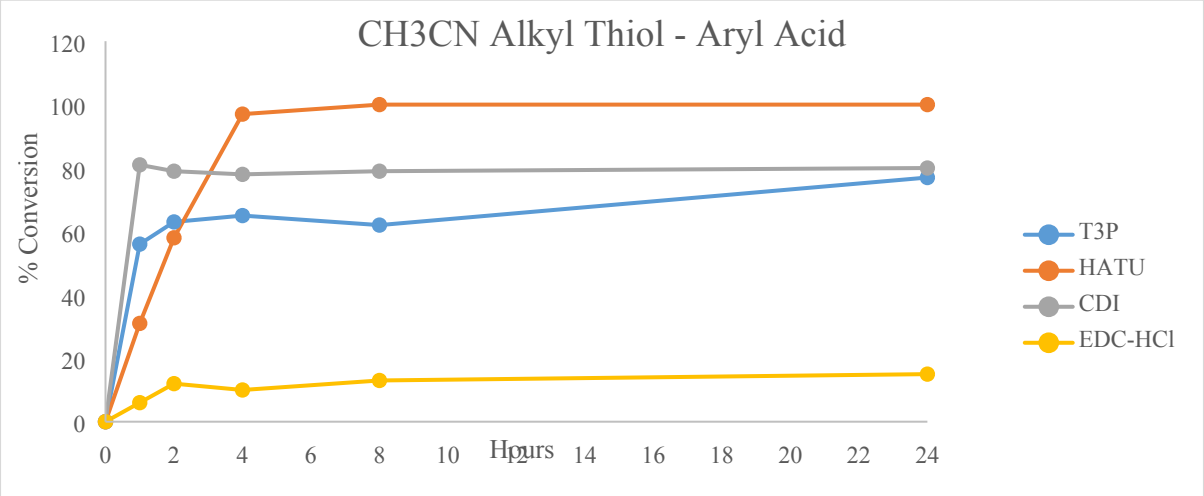
Time h	T3P	HATU	CDI	EDC-HCl
1	41	87	62	1
2	44	98	60	3
4	50	97	61	5
8	60	98	60	8
24	79	98	60	10

Reaction 4: DCM



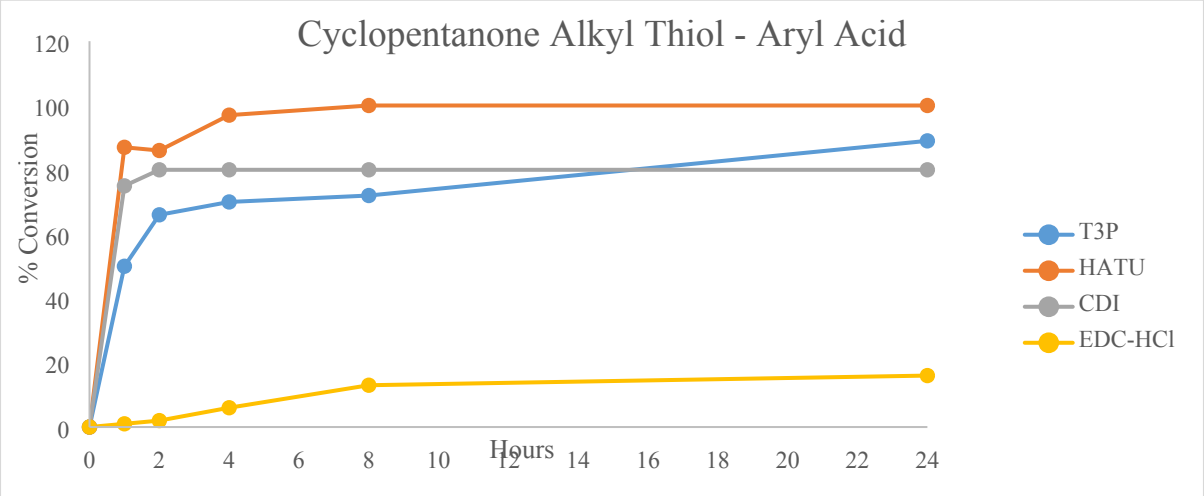
Time h	T3P	HATU	CDI	EDC-HCl
1	46	88	24	0
2	51	89	39	1
4	57	95	44	2
8	61	97	50	5
24	77	100	49	10

Reaction 4: CH_3CN



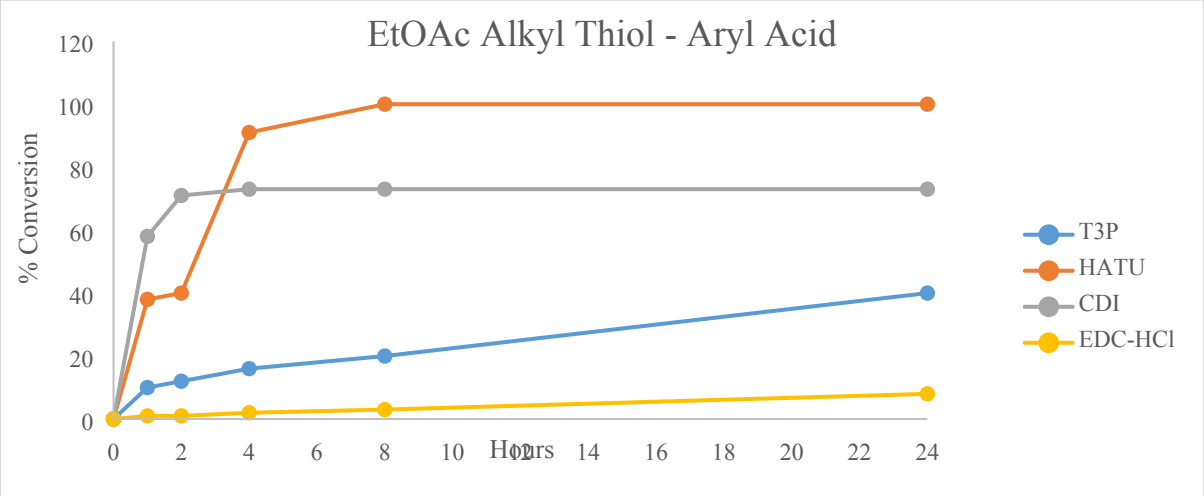
Time h	T3P	HATU	CDI	EDC-HCl
1	56	31	81	6
2	63	58	79	12
4	65	97	78	10
8	62	100	79	13
24	77	100	80	15

Reaction 4: Cyclopentanone



Time h	T3P	HATU	CDI	EDC-HCl
1	50	87	75	1
2	66	86	80	2
4	70	97	80	6
8	72	100	80	13
24	89	100	80	16

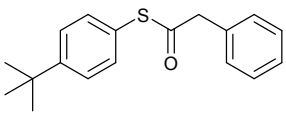
Reaction 4: Ethyl Acetate



Time h	T3P	HATU	CDI	EDC-HCl
1	50	87	75	1
2	66	86	80	2
4	70	97	80	6
8	72	100	80	13
24	89	100	80	16

Compound Characterisation

Compound **1**: S-(4-(*tert*-butyl)phenyl) 2-phenylethanethioate



Chemical Formula: $C_{18}H_{20}OS$
Exact Mass: 284.1235
Molecular Weight: 284.4170

Synthesised according to general procedure **D**.

Appearance: Colourless Oil.

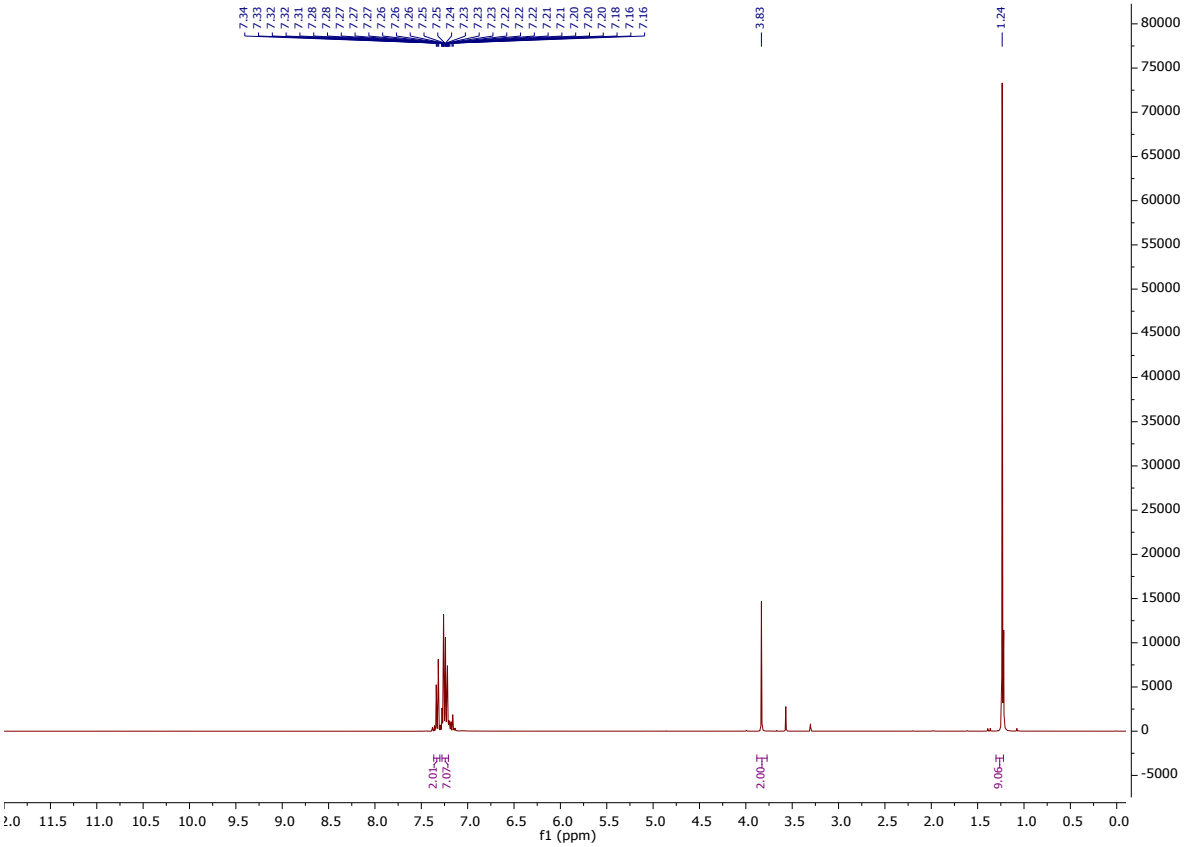
Yield: 96% (9.54 mmol, 2.71 g).

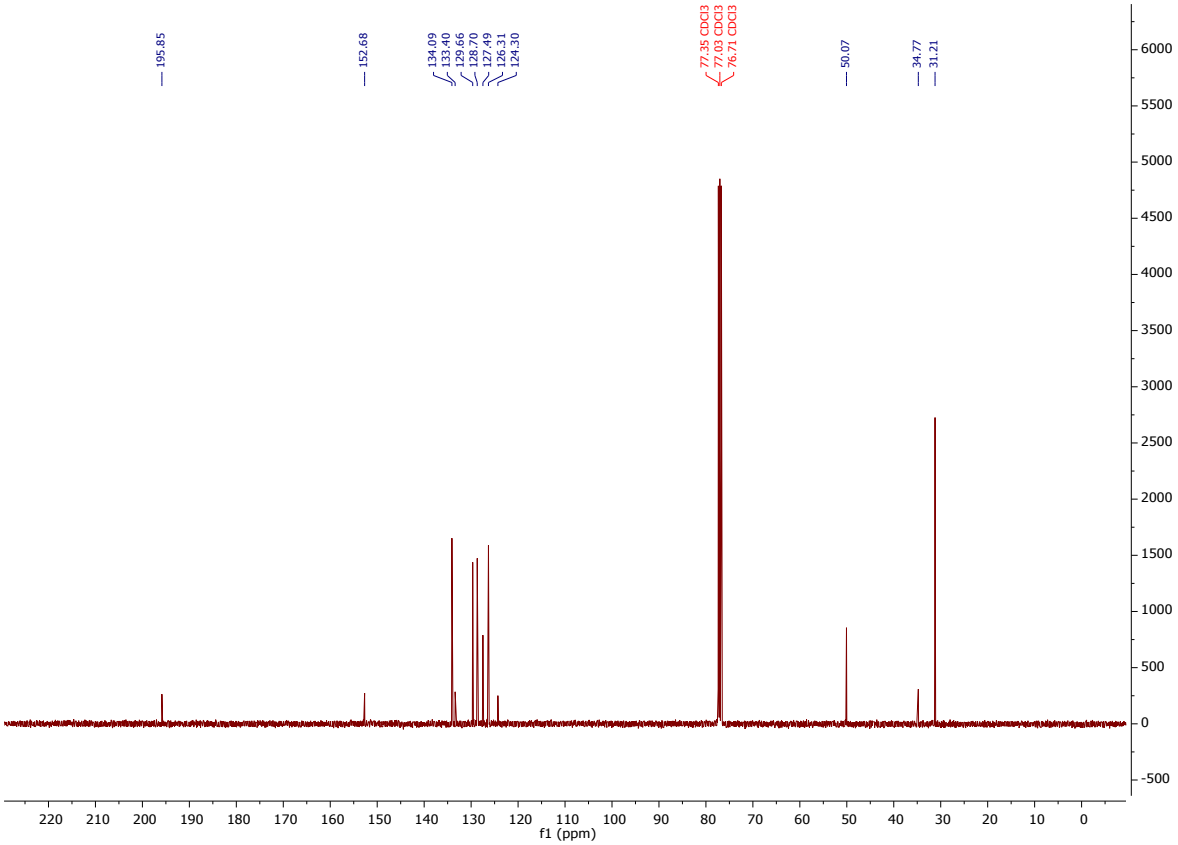
δ_H (400 MHz, Chloroform-*d*) 7.37 – 7.30 (2 H, m), 7.28 – 7.21 (7 H, m), 3.83 (2 H, s), 1.24 (9 H, s).

δ_C (101 MHz, Chloroform-*d*) 195.85, 152.68, 134.09, 133.40, 129.66, 128.70, 127.49, 126.31, 124.30, 50.07, 34.77, 31.21.

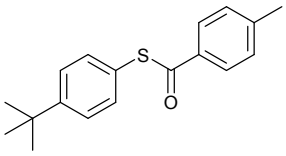
ν_{max}/cm^{-1}: 3241, 3030, 1701, 1499, 1398, 1009, 825, 700, 558.

ESI-MS (+ve) m/z: Found $[M+Na]^+$ 307.1127, $C_{18}H_{20}NaOS^+$ requires 307.1133.





Compound **2**: S-(4-(*tert*-butyl)phenyl) 4-methylbenzothioate



Chemical Formula: $C_{18}H_{20}OS$
Exact Mass: 284.1235
Molecular Weight: 284.4170

Appearance: White solid.

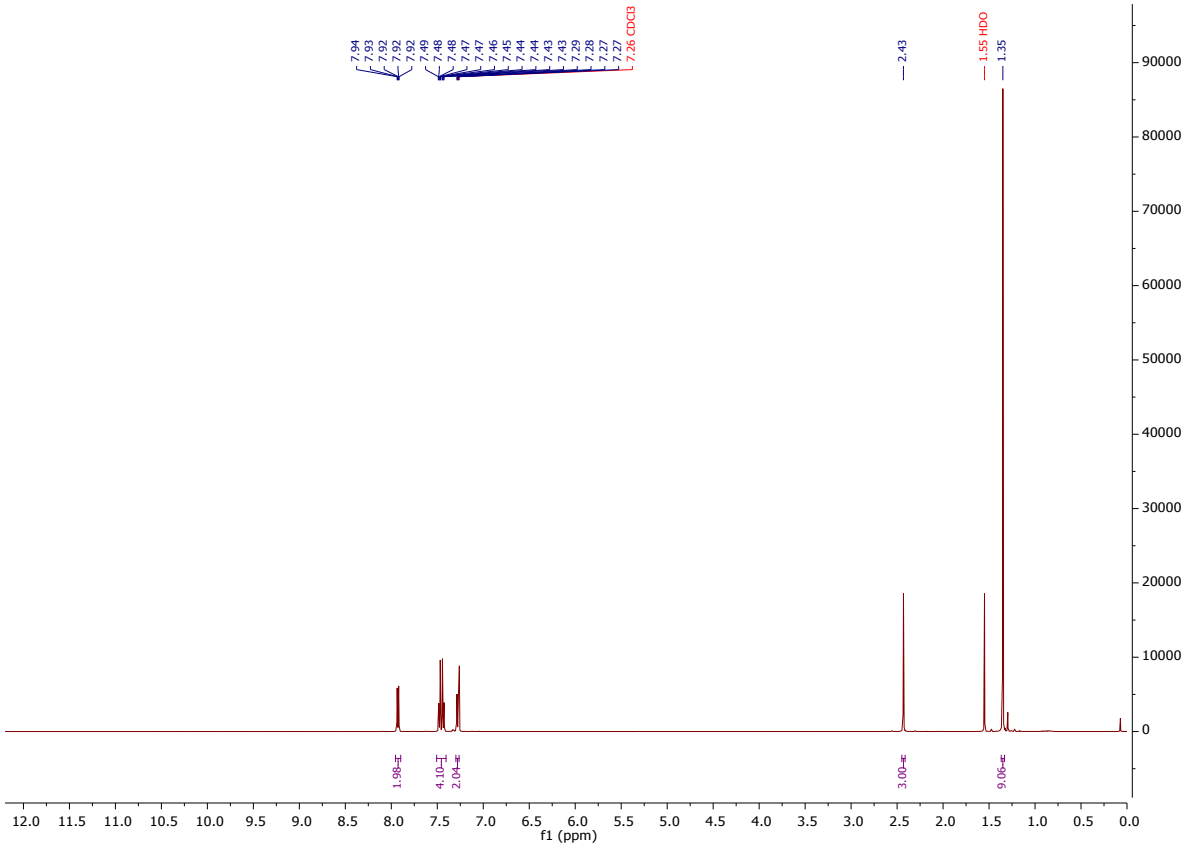
M.p.: 77-80 °C.

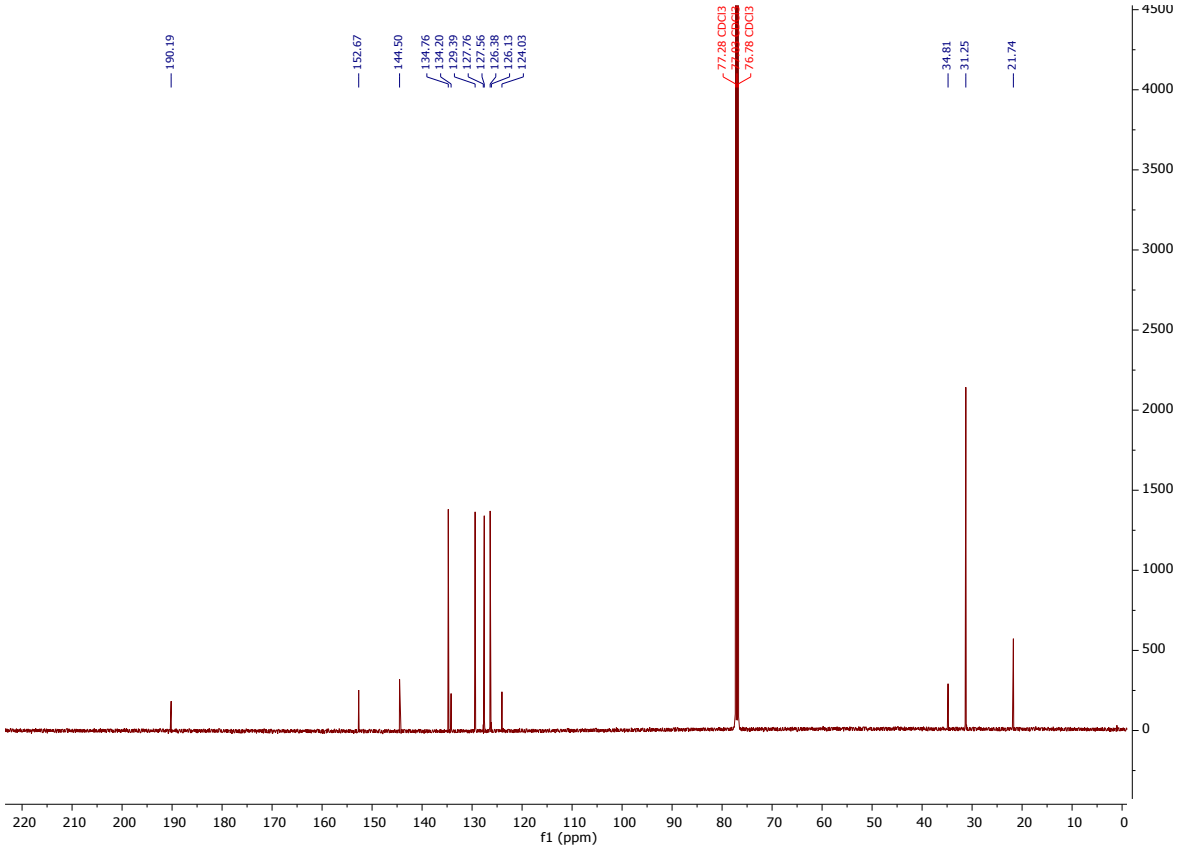
δ_H (500 MHz, Chloroform-*d*) 7.95 – 7.90 (2 H, m), 7.51 – 7.40 (4 H, m), 7.28 (2 H, d, *J* 8.1), 2.43 (3 H, s), 1.35 (9 H, s).

δ_C (126 MHz, Chloroform-*d*) 190.19, 152.67, 144.50, 134.76, 134.20, 129.39, 127.56, 126.38, 124.03, 34.81, 31.25, 21.74.

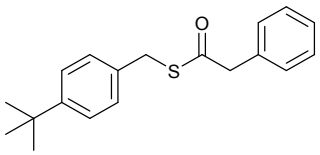
ν_{max}/cm^{-1}: 2963, 1669, 1606, 1488, 1361, 1202, 1172, 1113, 1042, 898, 821, 786, 718, 639, 622, 557.

ESI-MS (+ve) m/z: Found $[M+H]^+$ 285.1309, $C_{18}H_{21}OS^+$ requires 285.1308.


7.94
7.93
7.92
7.92
7.92
7.92
7.49
7.48
7.48
7.47
7.47
7.46
7.45
7.44
7.44
7.43
7.43
7.29
7.28
7.27
7.27
7.26 CDCl3
2.43
1.55 HDO
1.35
1.98
4.10
2.04
3.00
9.06
f1 (ppm)


190.19
152.67
144.50
134.76
134.20
129.39
127.76
127.56
126.38
126.13
124.03
77.28 CDCl3
77.03 CDCl3
76.78 CDCl3
34.81
31.25
21.74
f1 (ppm)

Compound **3**: S-(4-(*tert*-butyl)benzyl) 2-phenylethanethioate



Chemical Formula: $C_{19}H_{22}OS$
Exact Mass: 298.1391
Molecular Weight: 298.4440

Appearance: White Solid.

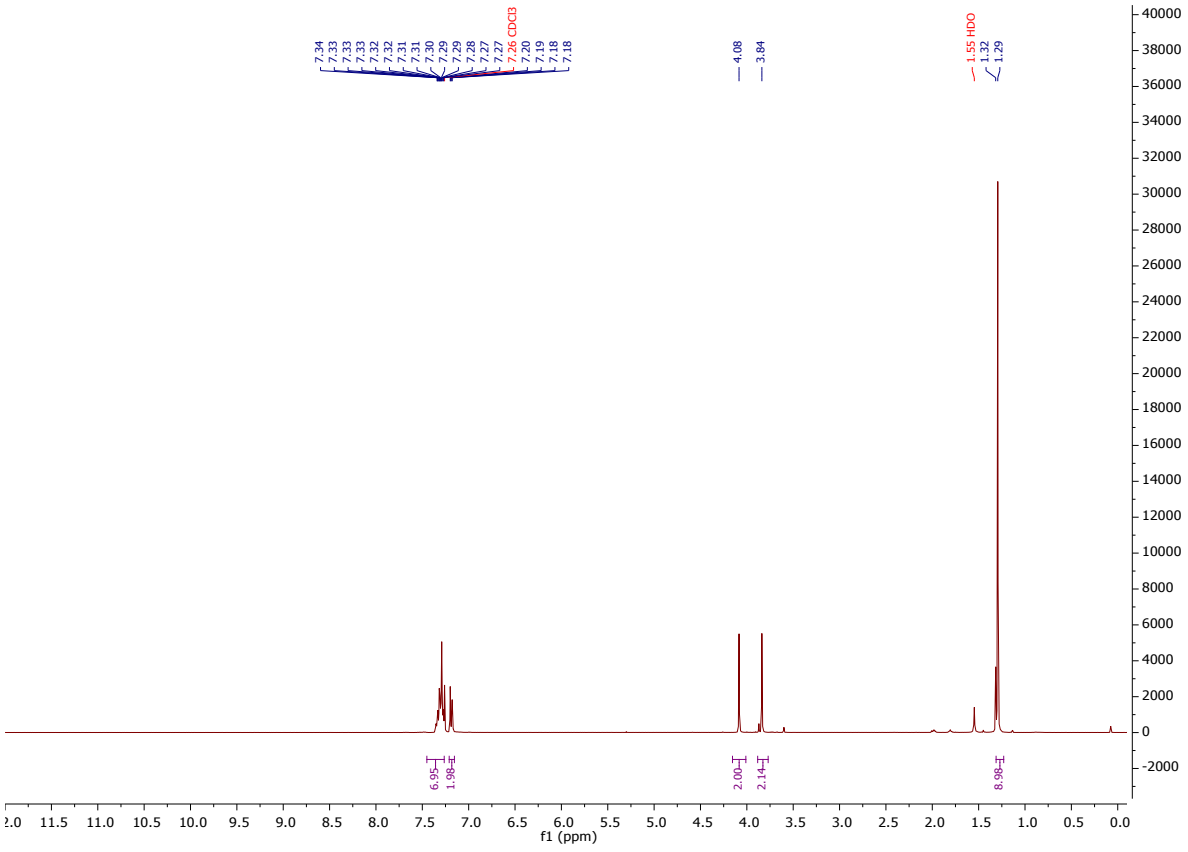
M.p.: 49-51 °C.

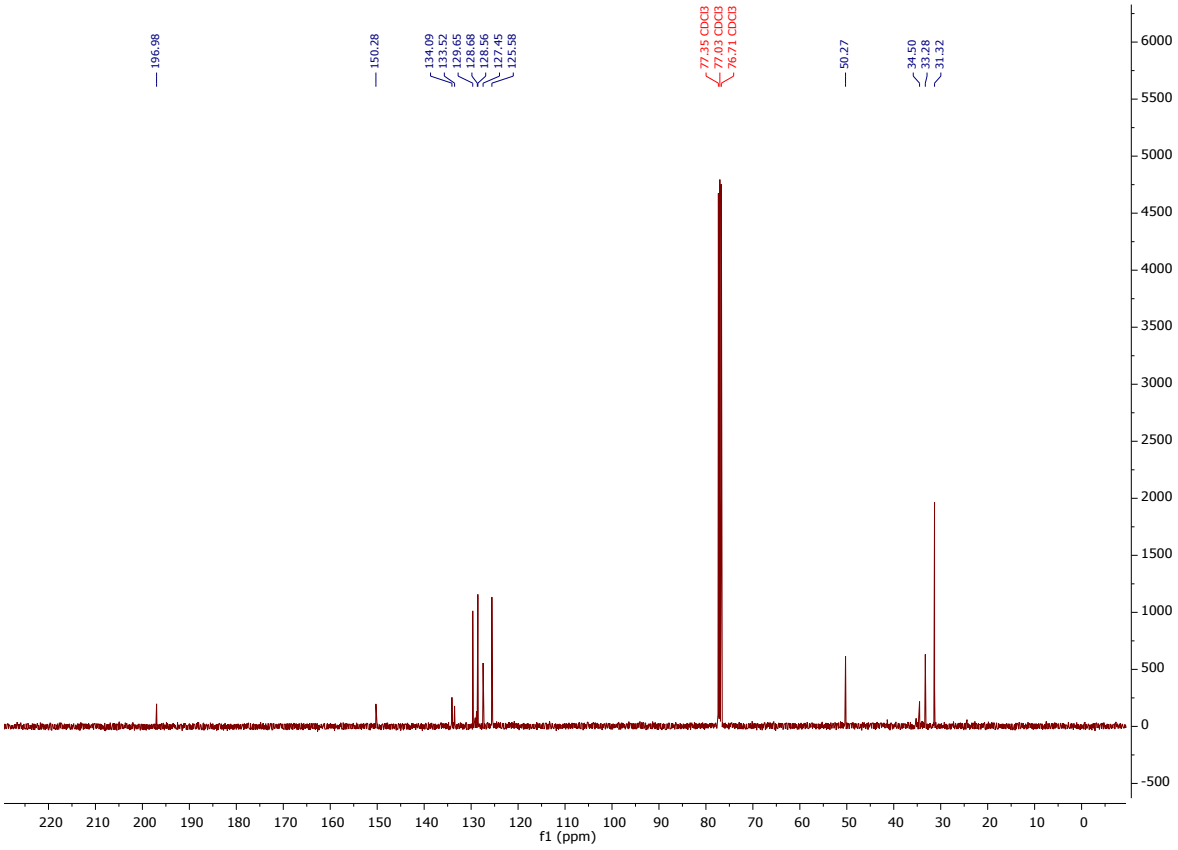
δ_H (400 MHz, Chloroform-*d*) 7.45 – 7.29 (7 H, m), 7.26 – 7.18 (2 H, m), 4.13 (2 H, s), 3.88 (2 H, s), 1.34 (9 H, s).

δ_C (101 MHz, Chloroform-*d*) 196.98, 150.28, 134.09, 133.52, 129.65, 128.68, 128.56, 127.45, 125.58, 50.27, 34.50, 33.28, 31.32.

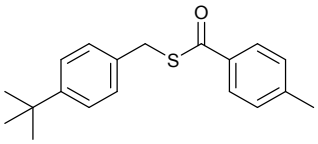
ν_{max}/cm^{-1}: 2955, 1677, 1491, 1411, 1361, 1268, 1176, 1012, 927, 850, 833, 787, 700, 654, 603, 558, 498.

ESI-MS (+ve) m/z: Found $[M+Na]^+$ 321.1284, $C_{19}H_{22}NaOS^+$ requires 321.1289.





Compound **4**: S-(4-(*tert*-butyl)benzyl) 4-methylbenzothioate



Chemical Formula: $C_{19}H_{22}OS$
Exact Mass: 298.1391
Molecular Weight: 298.4440

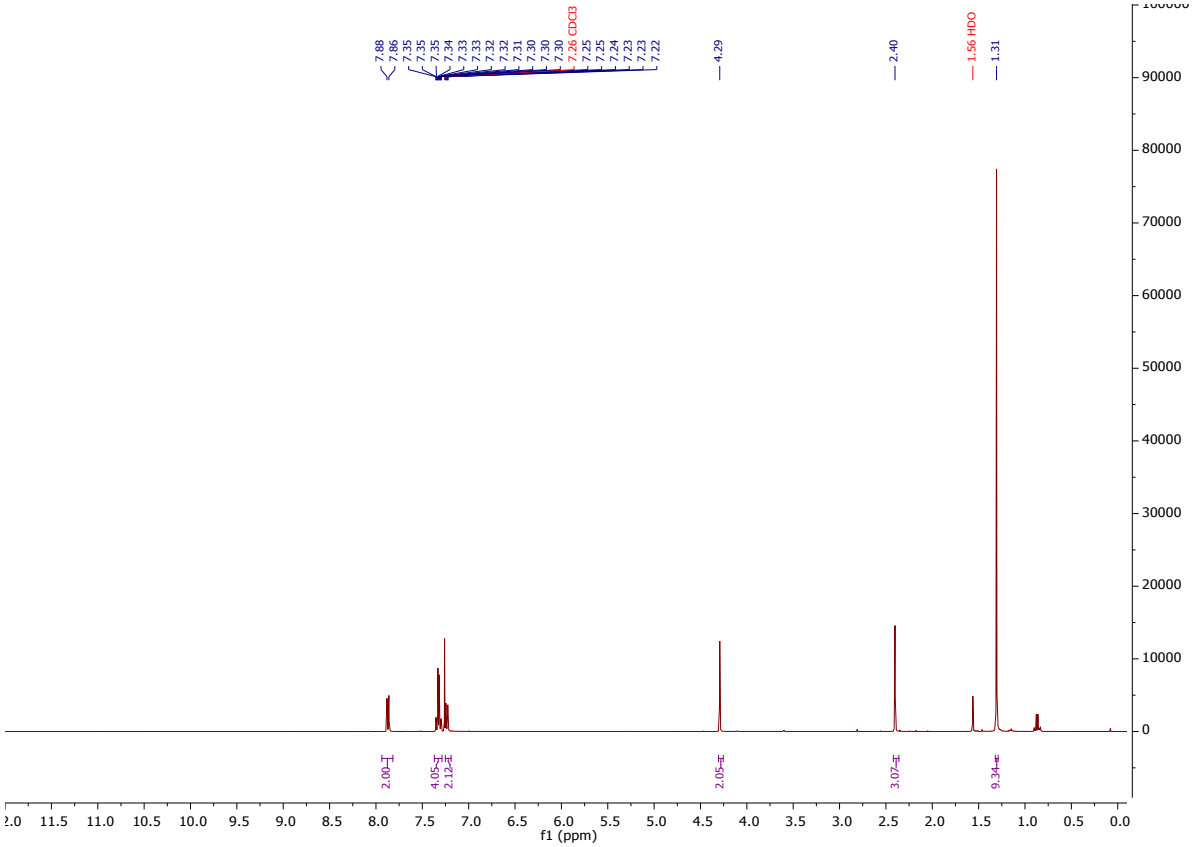
Appearance: Colourless oil.

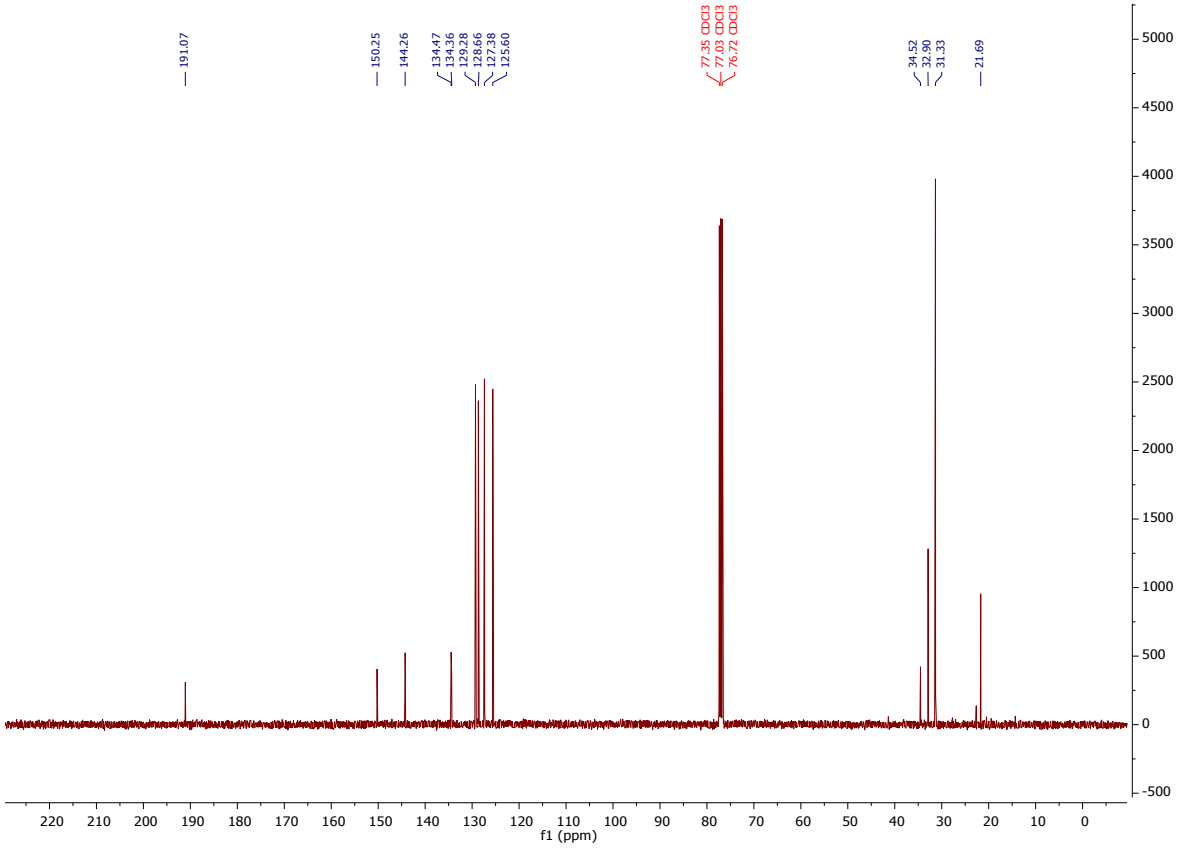
δ_H (400 MHz, Chloroform-*d*) 7.93 – 7.86 (2 H, m), 7.40 – 7.30 (4 H, m), 7.29 – 7.21 (2 H, m), 4.32 (2 H, s), 2.43 (3 H, s), 1.33 (9 H, s).

δ_C (101 MHz, Chloroform-*d*) 191.07, 150.25, 144.26, 134.47, 134.36, 129.28, 128.67, 127.38, 125.60, 34.52, 32.90, 31.33, 21.69.

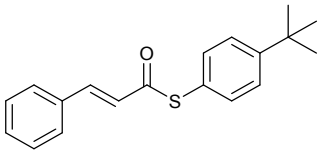
ν_{max}/cm^{-1}: 2959, 1657, 1605, 1204, 1173, 910, 820, 789, 642, 625, 559.

ESI-MS (+ve) m/z: Found $[M+Na]^+$ 321.1283, $C_{19}H_{22}NaOS^+$ requires 321.1289.


7.88
7.86
7.35
7.35
7.35
7.34
7.33
7.33
7.32
7.32
7.31
7.30
7.30
7.30
7.26 CDCl3
7.25
7.25
7.24
7.23
7.23
7.22
4.29
2.40
1.56 HDO
1.31
2.00
4.05
2.12
2.05
3.07
9.34
f1 (ppm)


191.07
150.25
144.26
134.47
134.36
129.28
128.66
127.38
125.60
77.35 CDCl3
77.03 CDCl3
76.72 CDCl3
34.52
32.90
31.33
21.69
f1 (ppm)

Compound **5**: *S*-(4-(tert-butyl)phenyl) (E)-3-phenylprop-2-enethioate



Chemical Formula: $C_{19}H_{20}OS$
Exact Mass: 296.1235
Molecular Weight: 296.4280

Synthesised according to general procedure **C** using 1.0 equivalents of 4-tert-butylbenzenethiol.

Appearance: White Solid.

M.p.: 118-121 °C.

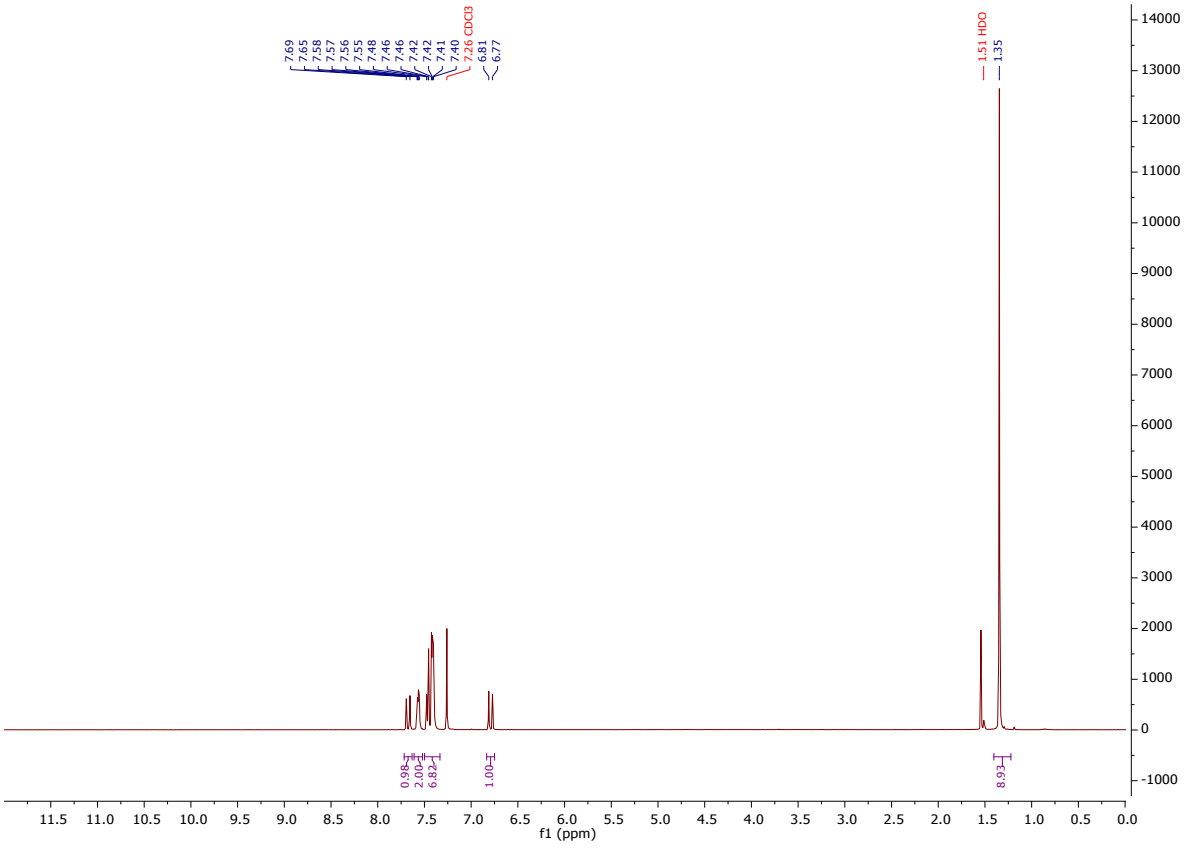
Yield: 72% (153 mg, 0.52 mmol).

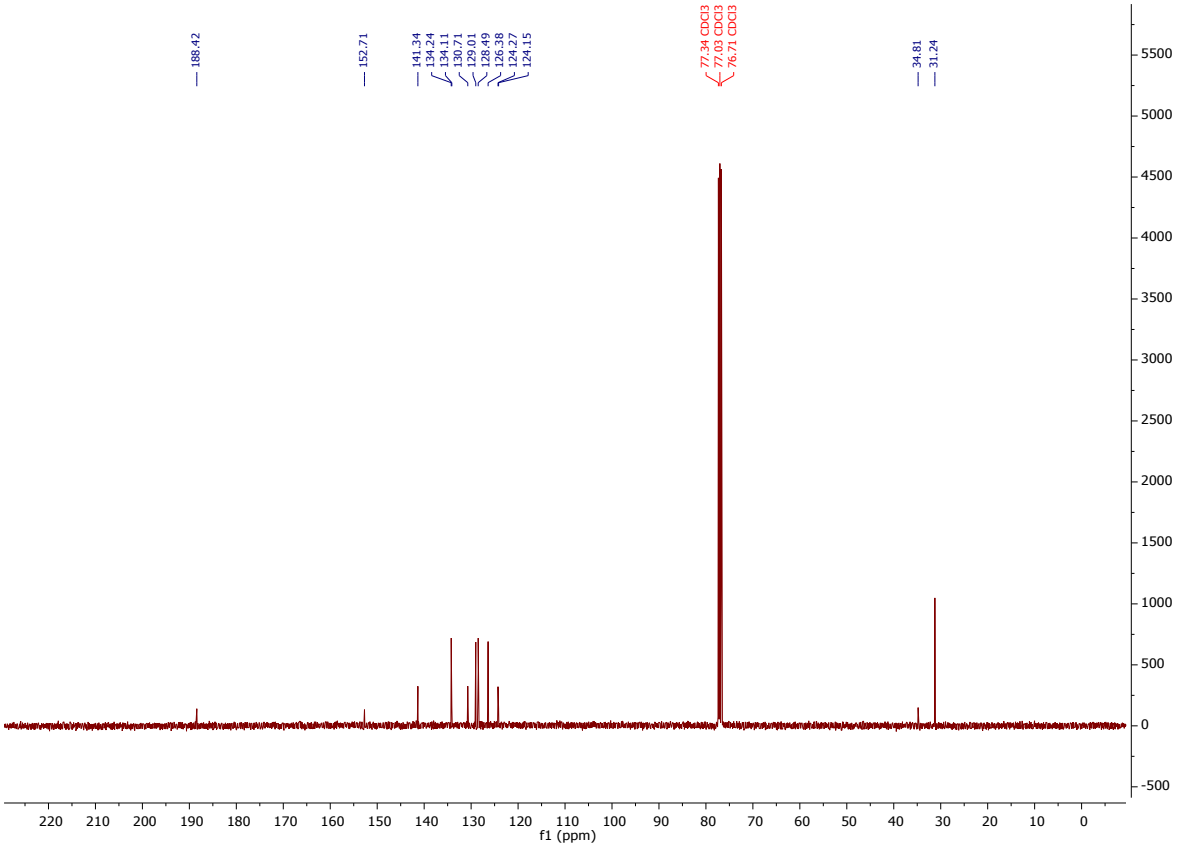
δ_H (400 MHz, Chloroform-*d*) 7.70 (1 H, d, *J* 15.8), 7.63 – 7.54 (2 H, m), 7.50-7.43 (7H, m), 6.79 (1 H, d, *J* 15.8), 1.39 (9 H, s).

δ_C (101 MHz, Chloroform-*d*) 188.42, 152.71, 141.34, 134.24, 134.11, 130.71, 129.01, 128.49, 126.38, 124.27, 124.15, 34.81, 31.24.

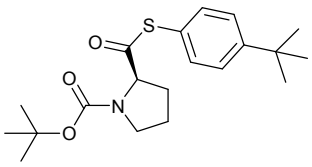
ν_{max}/cm^{-1}: 2951, 1694, 1615, 1491, 1394, 1331, 1026, 1010, 997, 820, 768, 749, 554.

ESI-MS (+ve) m/z: Found $[M+H]^+$ 297.1305, $C_{19}H_{20}OS^+$ requires 297.1308.





Compound **7**: S-(4-(tert-butyl)phenyl) (E)-3-phenylprop-2-enethioate



Chemical Formula: $C_{20}H_{29}NO_3S$
Exact Mass: 363.1868
Molecular Weight: 363.5160

Synthesised according to general procedure **C** using 0.85 equivalents of 4-tert-butylbenzenethiol.

Appearance: Colourless oil.

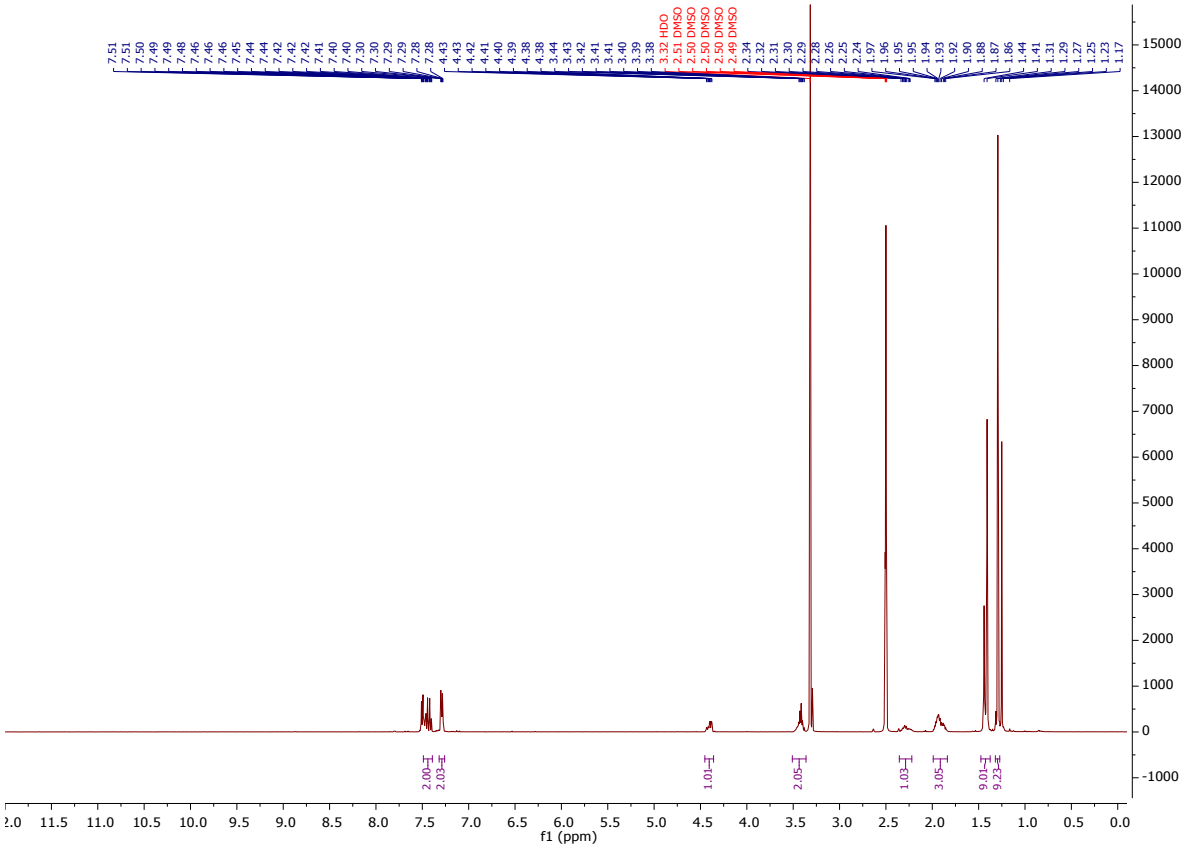
Yield: 80% (0.68 mmol, 246 mg).

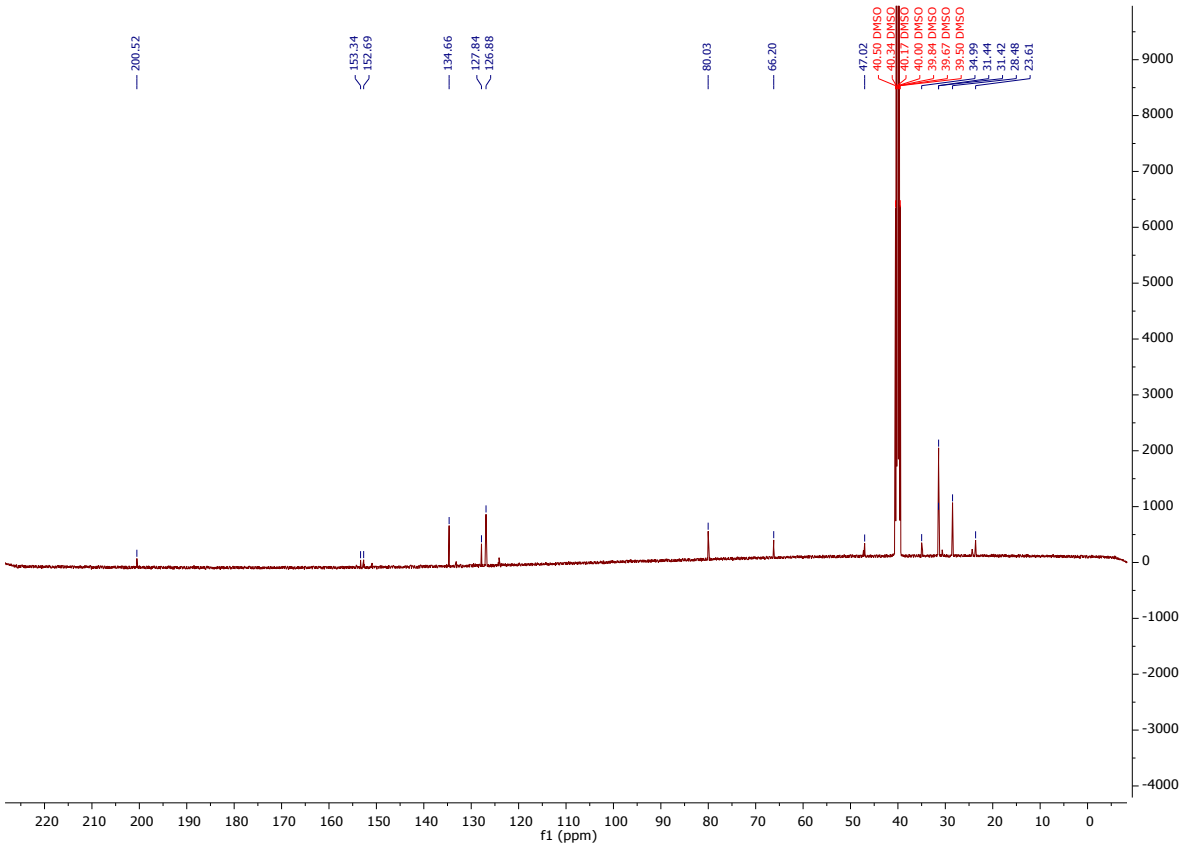
δ_H (500 MHz, DMSO-d6) 7.52 – 7.41 (2 H, m), 7.32 – 7.26 (2 H, m), 4.45 – 4.36 (1 H, m), 3.51 – 3.36 (2 H, m), 2.36 – 2.22 (1 H, m), 1.99 – 1.84 (3 H, m), 1.48 – 1.38 (9 H, m), 1.29 (9 H, s).

δ_C (126 MHz, DMSO-d_6) 200.52, 153.34, 152.69, 134.66, 127.84, 126.88, 80.03, 66.20, 47.02, 34.99, 31.44, 31.42, 28.48, 23.61.

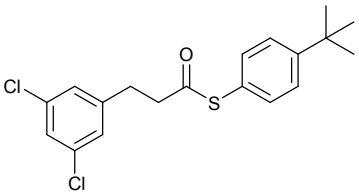
ν_{max}/cm^{-1}: 2958, 1660, 1569, 1448, 1362, 1210, 1087, 1019, 910, 831, 735, 697, 627, 557.

ESI-MS (+ve) m/z: Found $[M+H]^+$ 364.1933, $C_{20}H_{29}NO_3S^+$ requires 364.1941.


7.51
7.50
7.49
7.48
7.46
7.45
7.44
7.42
7.41
7.40
7.30
7.29
7.28
4.43
4.42
4.41
4.40
4.39
4.38
3.44
3.43
3.42
3.41
3.40
3.39
3.38
3.32 HDO
2.51 DMSO
2.50 DMSO
2.49 DMSO
2.34
2.32
2.31
2.30
2.29
2.28
2.26
2.25
2.24
1.97
1.96
1.95
1.94
1.93
1.92
1.90
1.88
1.87
1.86
1.44
1.41
1.31
1.29
1.27
1.25
1.23
1.17
2.00
2.03
1.01
2.05
1.03
3.05
9.01
9.23
f1 (ppm)


200.52
153.34
152.69
134.66
127.84
126.88
80.03
66.20
47.02
40.50 DMSO
40.34 DMSO
40.17 DMSO
40.00 DMSO
39.84 DMSO
39.67 DMSO
39.50 DMSO
34.99
31.44
31.42
28.48
23.61
f1 (ppm)

Compound **8**: *S*-(4-(tert-butyl)phenyl) 3-(3,5-dichlorophenyl)propanethioate



Chemical Formula: $C_{19}H_{20}Cl_2OS$
Exact Mass: 366.0612
Molecular Weight: 367.3280

Synthesised according to general procedure **C** using 1.0 equivalents of 4-tert-butylbenzenethiol.

Appearance: Pale yellow oil.

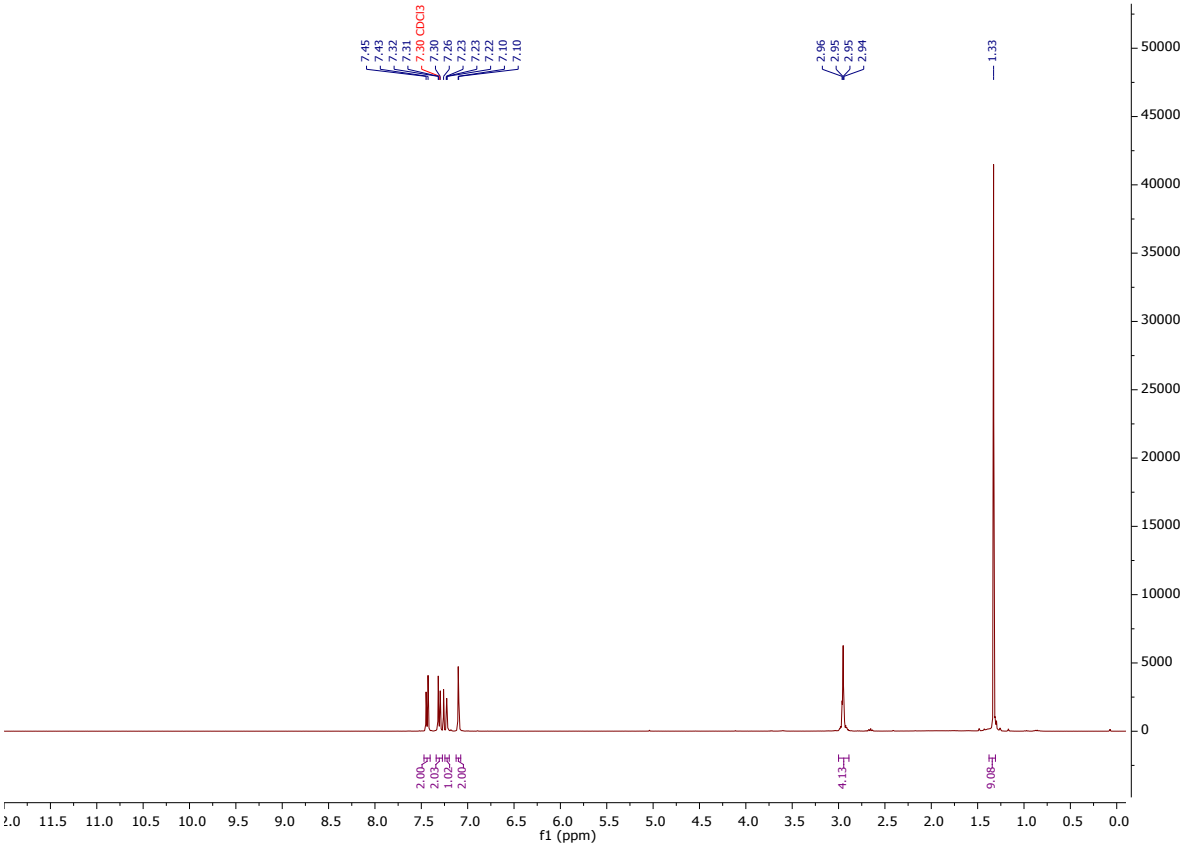
Yield: 95% (0.95 mmol, 349 mg).

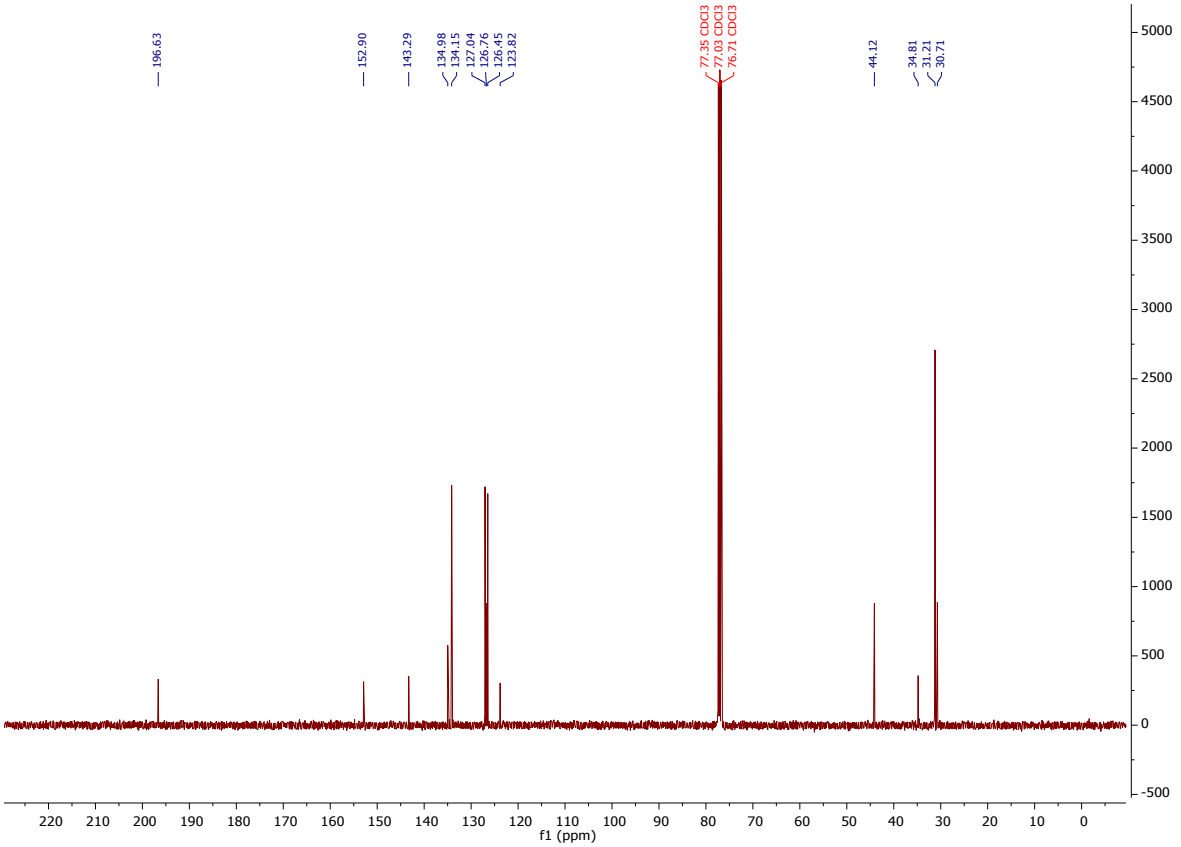
δ_H (400 MHz, Chloroform-*d*) 7.50 – 7.42 (2 H, m), 7.37 – 7.29 (2 H, m), 7.25 (1 H, t, *J* 1.9), 7.12 (2 H, d, *J* 1.9), 3.04 – 2.90 (4 H, m), 1.35 (9 H, s).

δ_C (101 MHz, Chloroform-*d*) 196.63, 152.90, 143.29, 134.98, 134.15, 127.04, 126.76, 126.45, 123.82, 44.12, 34.81, 31.21, 30.71.

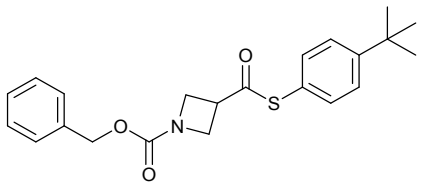
ν_{max}/cm^{-1}: 2948, 1693, 1566, 1431, 1117, 1102, 970, 798, 677, 554.

ESI-MS (+ve) m/z: Found $[M+Na]^+$ 389.0508, $C_{19}H_{20}Cl_2NaOS^+$ requires 389.0501.





Compound **9**: benzyl 3-(((4-(tert-butyl)phenyl)thio)carbonyl)azetidine-1-carboxylate



Chemical Formula: $C_{22}H_{25}NO_3S$
Exact Mass: 383.1555
Molecular Weight: 383.5060

Synthesised according to general procedure **C** using 0.9 equivalents of 4-tert-butylbenzenethiol.

Appearance: Colourless oil.

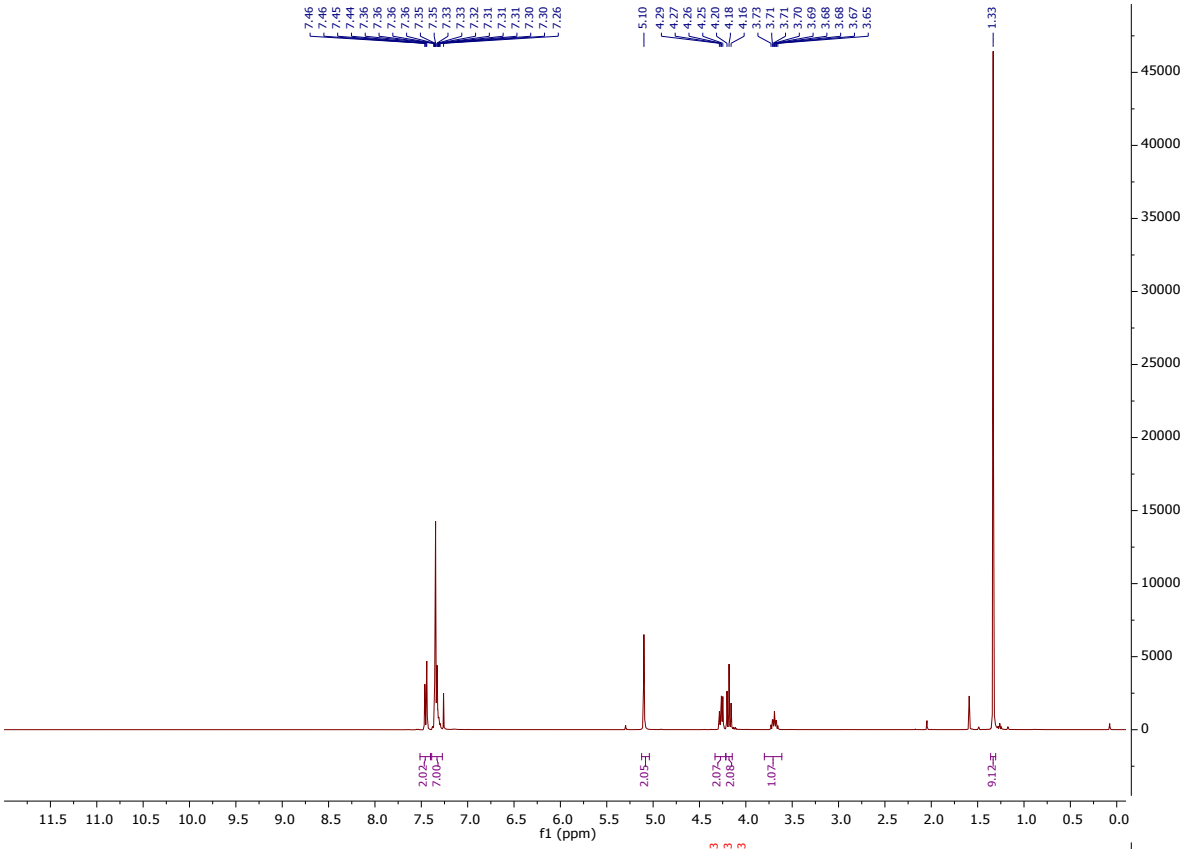
Yield: 92% (0.83 mmol, 317 mg).

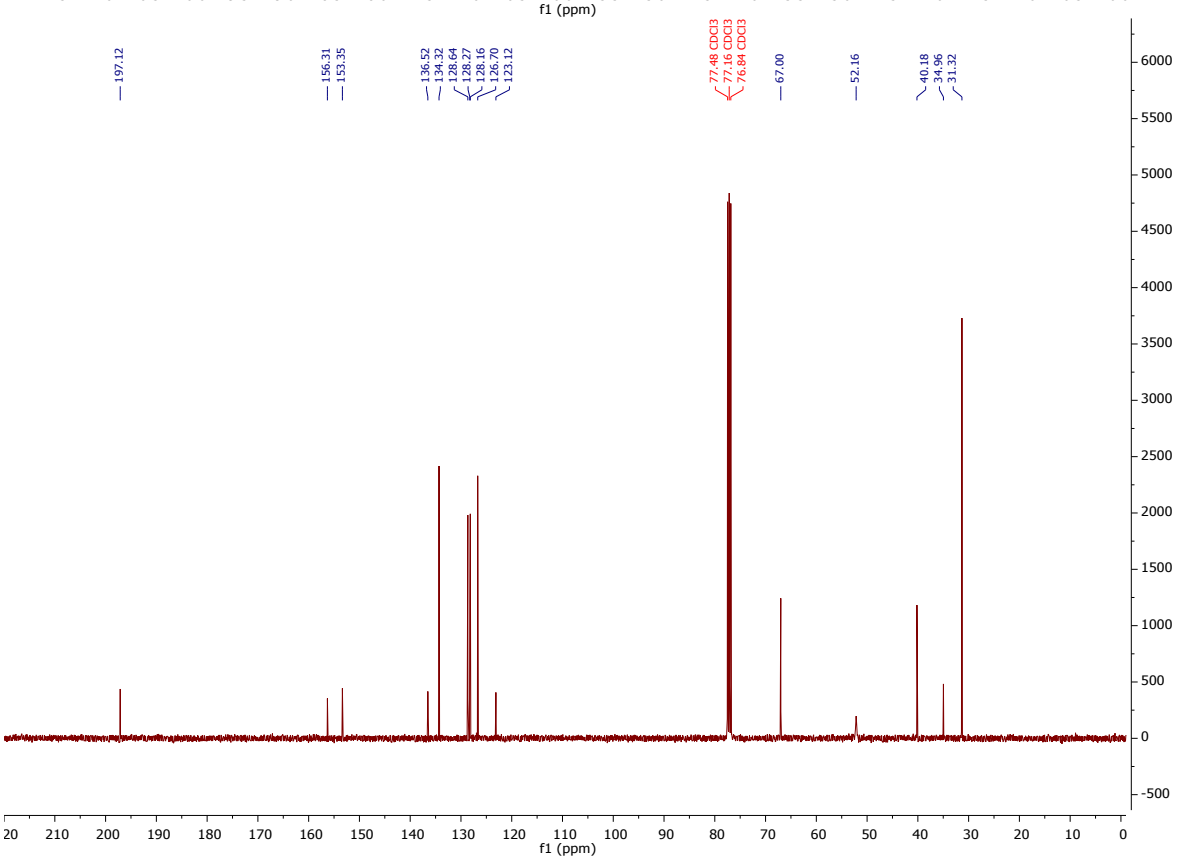
δ_H (400 MHz, Chloroform-*d*) 7.51 – 7.40 (2 H, m), 7.39 – 7.27 (7 H, m), 5.10 (2 H, s), 4.27 (2 H, dd, *J* 8.8, 6.0), 4.22 – 4.15 (2 H, m), 3.69 (1 H, tt, *J* 8.8, 6.0), 1.33 (9 H, s).

δ_C (101 MHz, Chloroform-*d*) 197.12, 156.31, 153.35, 136.52, 134.32, 128.64, 128.27, 128.16, 126.70, 123.12, 67.00, 52.16, 40.18, 34.96, 31.32.

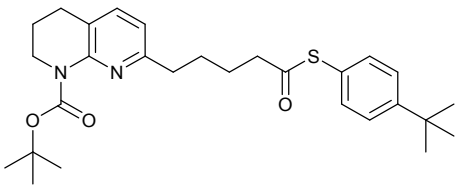
ν_{max}/cm^{-1}: 2958, 2889, 1703, 1410, 1354, 1326, 1120, 827, 766, 697, 556.

ESI-MS (+ve) m/z: Found $[M+H]^+$ 384.1621, $C_{22}H_{26}NO_3S^+$ requires 384.1628.


7.46
7.46
7.45
7.44
7.36
7.36
7.36
7.36
7.35
7.35
7.33
7.33
7.32
7.31
7.31
7.31
7.30
7.30
7.26
5.10
4.29
4.27
4.26
4.25
4.20
4.18
4.16
3.73
3.71
3.71
3.70
3.69
3.68
3.68
3.67
3.65
1.33
2.02
7.00
2.05
2.07
2.08
1.07
9.12
f1 (ppm)


197.12
156.31
153.35
136.52
134.32
128.64
128.27
128.16
126.70
123.12
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
67.00
52.16
40.18
34.96
31.32
f1 (ppm)

Compound **10**: Tert-butyl 7-(5-((4-(tert-butyl)phenyl)thio)-5-oxopentyl)-3,4-dihydro-1,8-naphthyridine-1(2H)-carboxylate



Chemical Formula: $C_{28}H_{38}N_2O_3S$
Exact Mass: 482.2603
Molecular Weight: 482.6830

Synthesised according to general procedure **C** using 0.9 equivalent of 4-tert-butylbenzenethiol.

Appearance: Yellow oil.

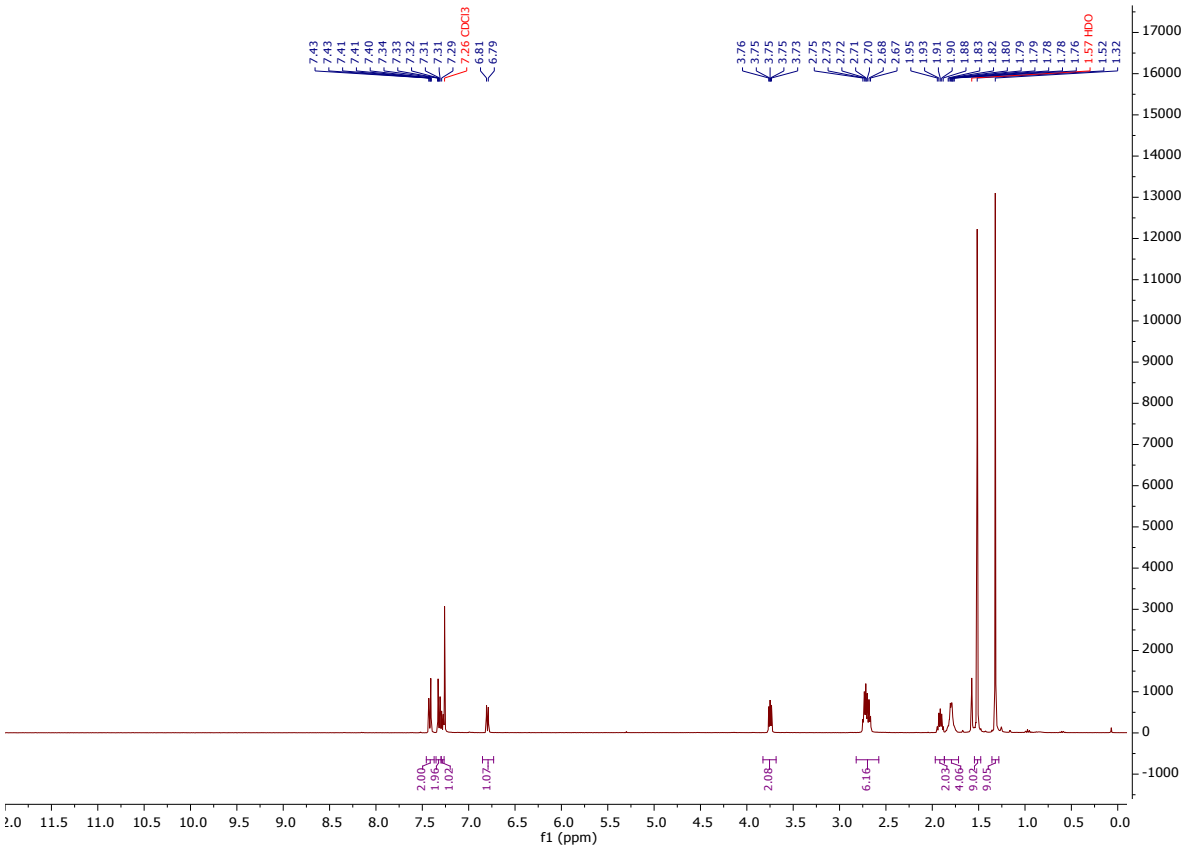
Yield: 61% (0.55 mmol, 265 mg).

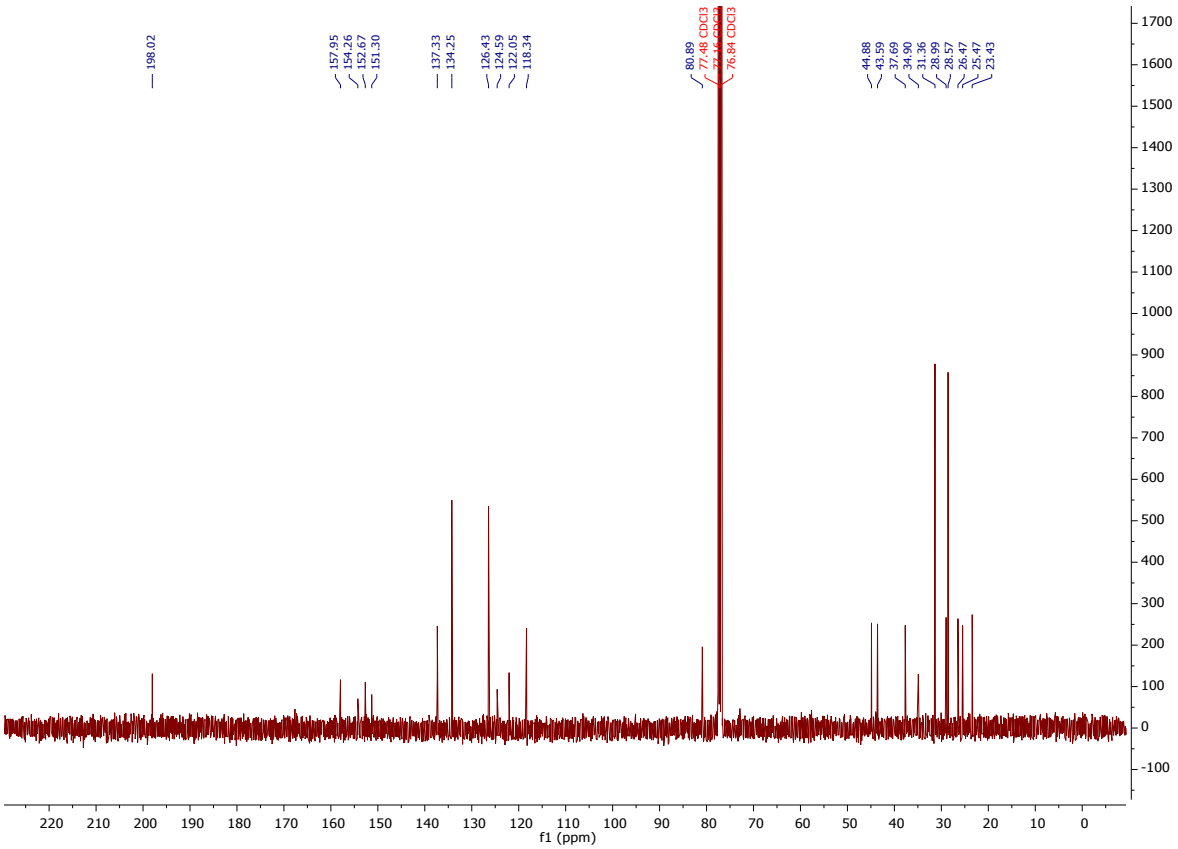
δ_H (400 MHz, Chloroform-d) 7.42 (2 H, d, J 8.5), 7.32 (2 H, d, J 8.4), 7.29 (1 H, s), 6.80 (1 H, d, J 7.6), 3.83 – 3.68 (2 H, m), 2.82 – 2.58 (6 H, m), 191 (2 H, p, J 6.5), 1.87 – 1.72 (4 H, m), 1.52 (9 H, s), 1.32 (9 H, s).

δ_C (101 MHz, Chloroform-*d*) 198.02, 157.95, 154.26, 152.67, 151.30, 137.33, 134.25, 126.43, 124.59, 122.05, 118.34, 80.89, 44.88, 43.59, 37.69, 34.90, 31.36, 28.99, 28.57, 26.47, 25.47, 23.43.

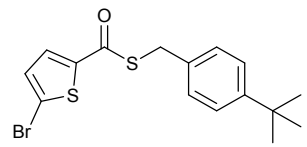
ν_{max}/cm^{-1}: 2960, 1689, 1494, 1462, 1409, 1364, 1320, 1196, 892, 656, 557.

ESI-MS (+ve) m/z: Found $[M+H]^+$ 483.2704, $C_{28}H_{39}N_2O_3S^+$ requires 483.2676.





Compound **12**: *S*-(4-(tert-butyl)benzyl) 5-bromothiophene-2-carbothioate



Chemical Formula: $C_{16}H_{17}BrOS_2$
Exact Mass: 367.9904
Molecular Weight: 369.3350

Synthesised according to general procedure **C** using 0.97 equivalents of 4-tert-butylbenzyl mercaptan.

Appearance: White solid.

Yield: 66% (224 mg, 0.64 mmol).

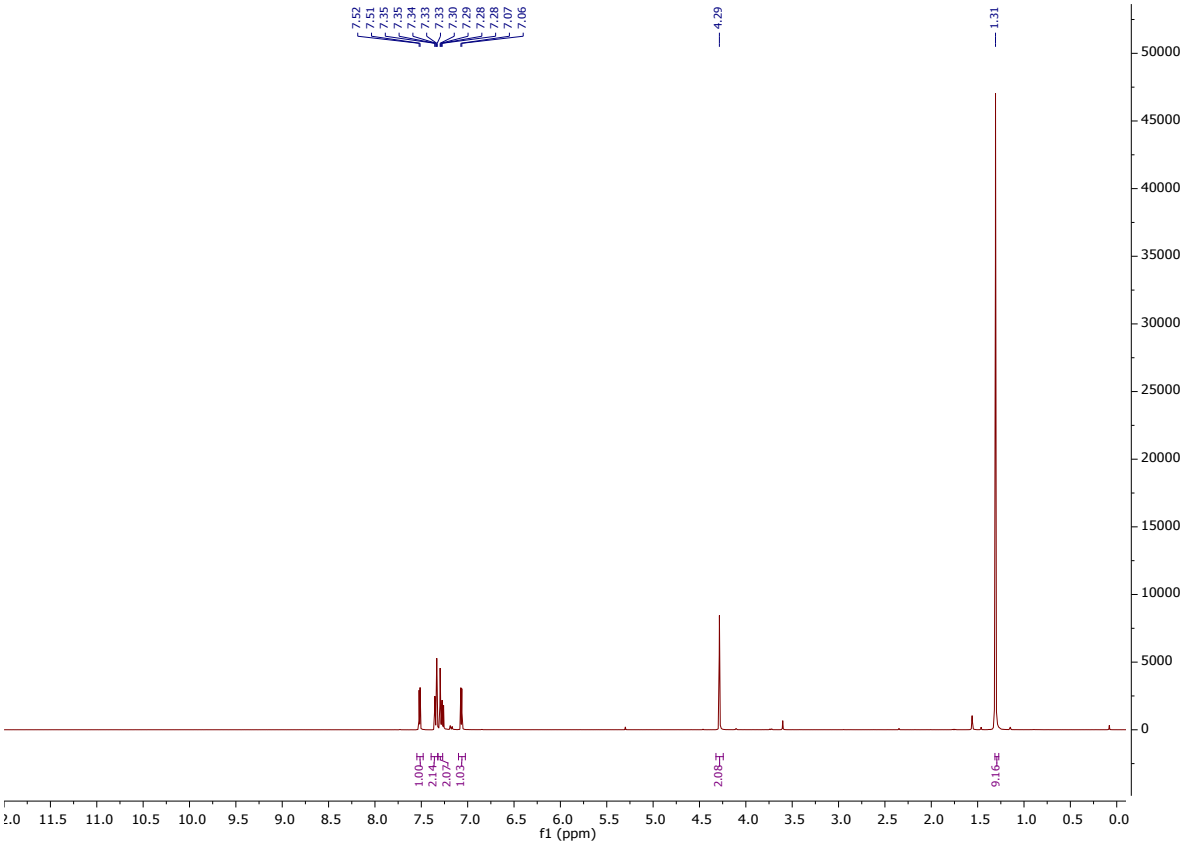
M.p.: 58-60 °C.

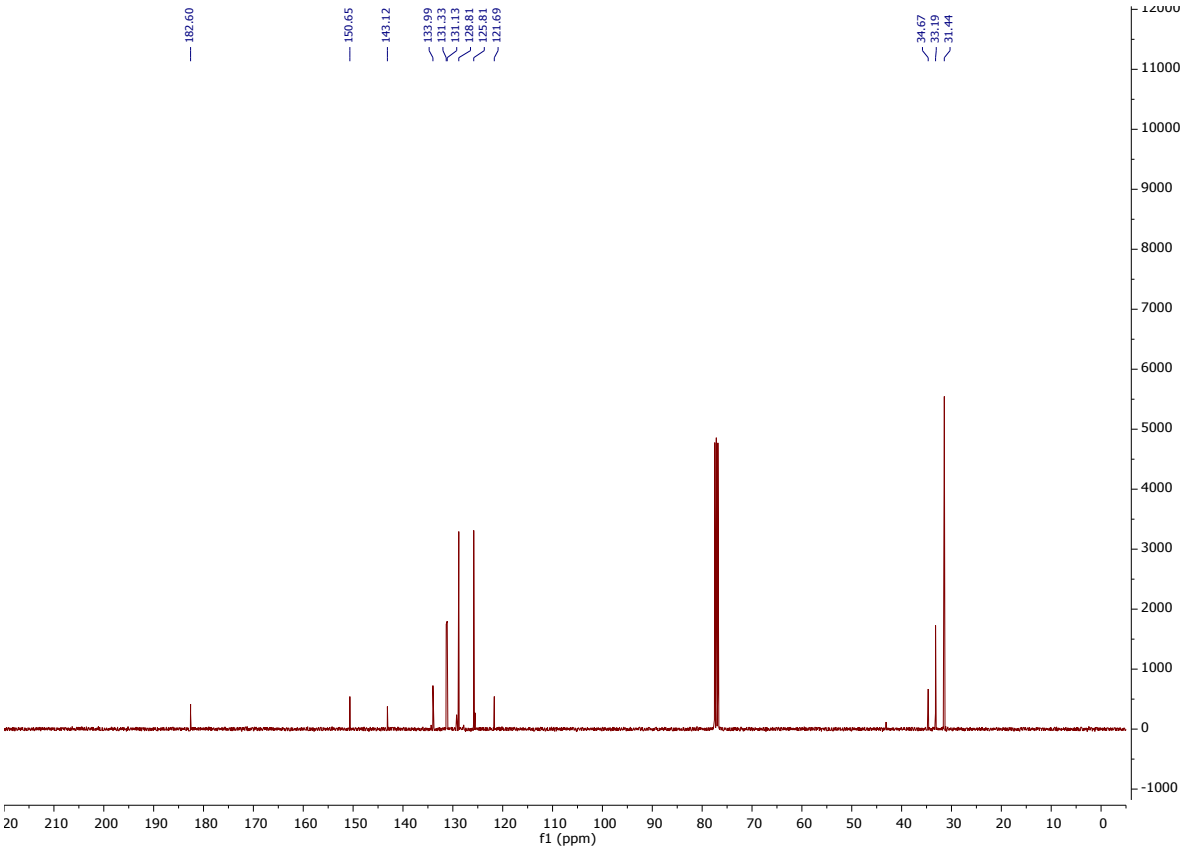
δ_H (400 MHz, Chloroform-d) 7.52 (1 H, d, J 4.1), 7.34 (2 H, d, J 8.4), 7.29 (2 H, d, J 8.4), 7.07 (1 H, d, J 4.1), 4.29 (2 H, s), 1.31 (9 H, s).

δ C (101 MHz, Chloroform-d) 182.60, 150.65, 143.12, 133.99, 131.33, 131.13, 128.81, 125.81, 121.69, 34.67, 33.19, 31.44.

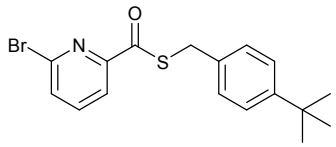
ν_{max}/cm^{-1}: 2960, 2865, 1565, 1622, 1406, 1197, 1020, 818, 798, 656, 557.

ESI-MS (+ve) m/z: Found $[M+Na]^+$ 392.9771, $C_{16}H_{17}BrNaOS_2^+$ requires 392.9781.


7.52
7.51
7.35
7.35
7.34
7.33
7.33
7.30
7.29
7.28
7.28
7.07
7.06
4.29
1.31
1.00
2.14
2.07
1.03
2.08
9.16
f1 (ppm)


182.60
150.65
143.12
133.99
131.33
131.13
128.81
125.81
121.69
34.67
33.19
31.44
f1 (ppm)

Compound **13**: *S*-(4-(tert-butyl)benzyl) 6-bromopyridine-2-carbothioate



Chemical Formula: $C_{17}H_{18}BrNOS$
Exact Mass: 363.0292
Molecular Weight: 364.3010

Synthesised according to general procedure **C** using 0.90 equivalents of 4-tert-butylbenzyl mercaptan.

Appearance: Off white solid.

Yield: 77% (0.69 mmol, 251 mg).

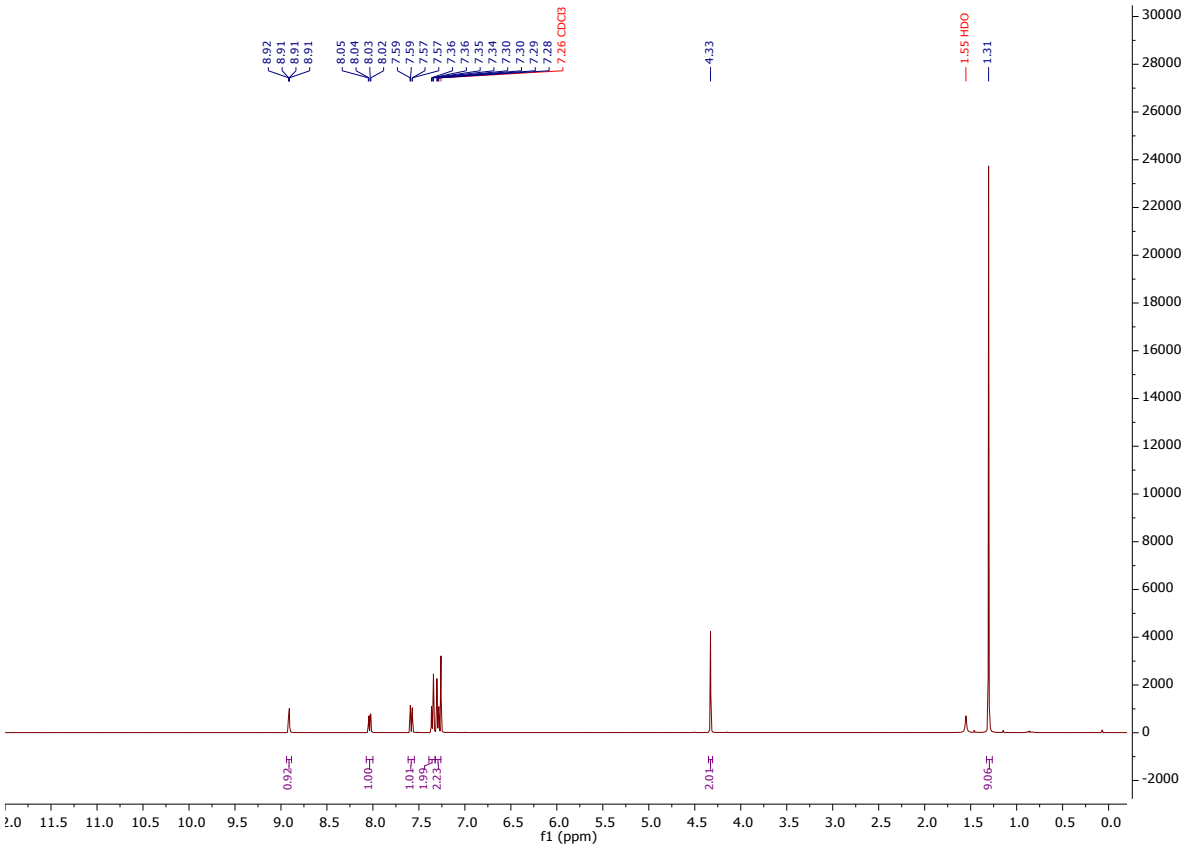
M.p.: 101-103 °C.

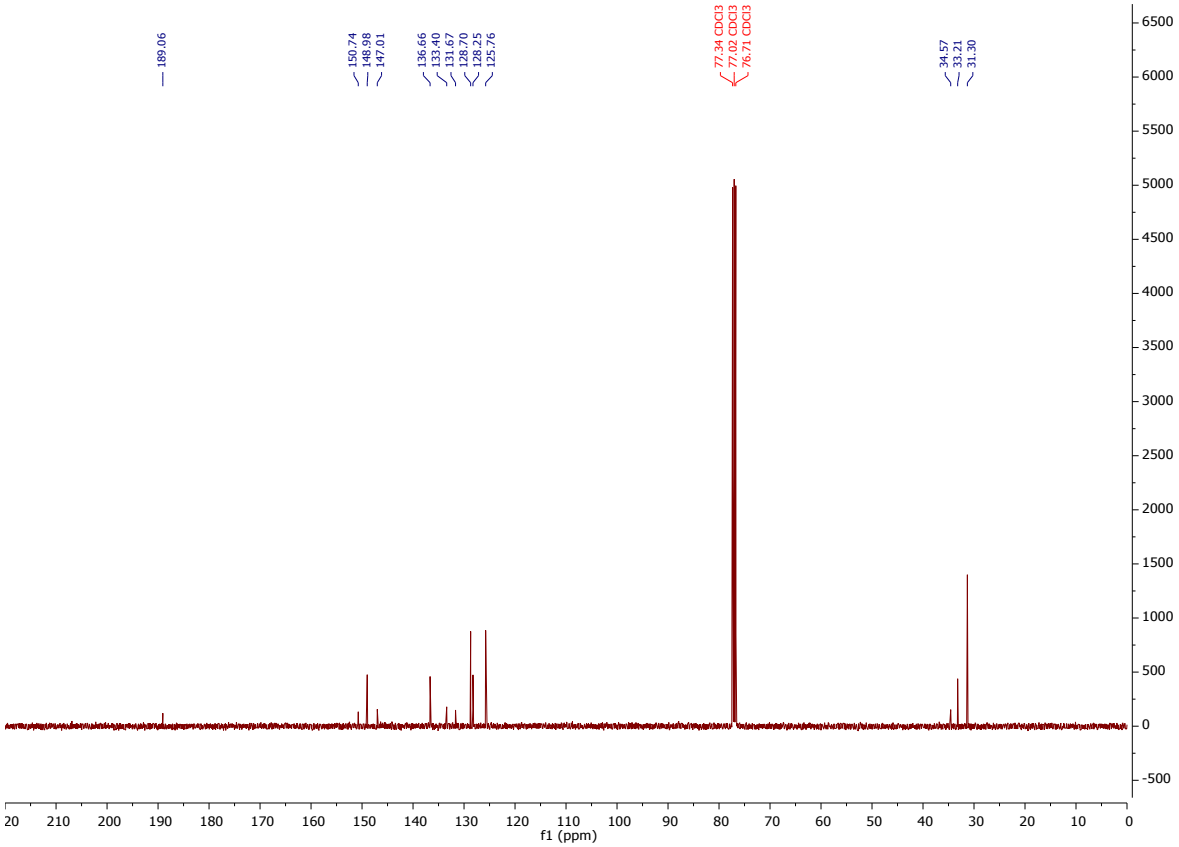
δ_H (400 MHz, Chloroform-*d*) 8.91 (1 H, dd, *J* 2.5, 0.8), 8.04 (1 H, dd, *J* 8.3, 2.5), 7.58 (1 H, dd, *J* 8.3, 0.8), 7.35 (2 H, d, *J* 8.6), 7.29 (2 H, d, *J* 8.4), 4.33 (2 H, s), 1.31 (9 H, s).

δ_C (101 MHz, Chloroform-*d*) 189.06, 150.74, 148.98, 147.01, 136.66, 133.40, 131.67, 128.70, 128.25, 125.76, 34.57, 33.21, 31.30.

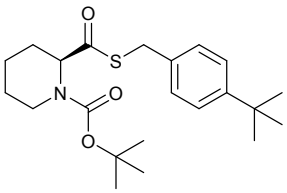
ν_{max}/cm^{-1}: 2963, 1665, 1650, 1569, 1450, 1363, 1105, 1018, 911, 831, 737, 696, 657, 558.

ESI-MS (+ve) m/z: Found $[M+H]^+$ 364.0360, $C_{17}H_{19}BrNOS^+$ requires 364.0365.





Compound **14**: tert-butyl (S)-2-(((4-(tert-butyl)benzyl)thio)carbonyl)piperidine-1-carboxylate



Chemical Formula: $C_{22}H_{33}NO_3S$
Exact Mass: 391.2181
Molecular Weight: 391.5700

Synthesised according to general procedure **C** using 0.73 equivalents of 4-tert-butylbenzyl mercaptan.

Appearance: Pale yellow oil.

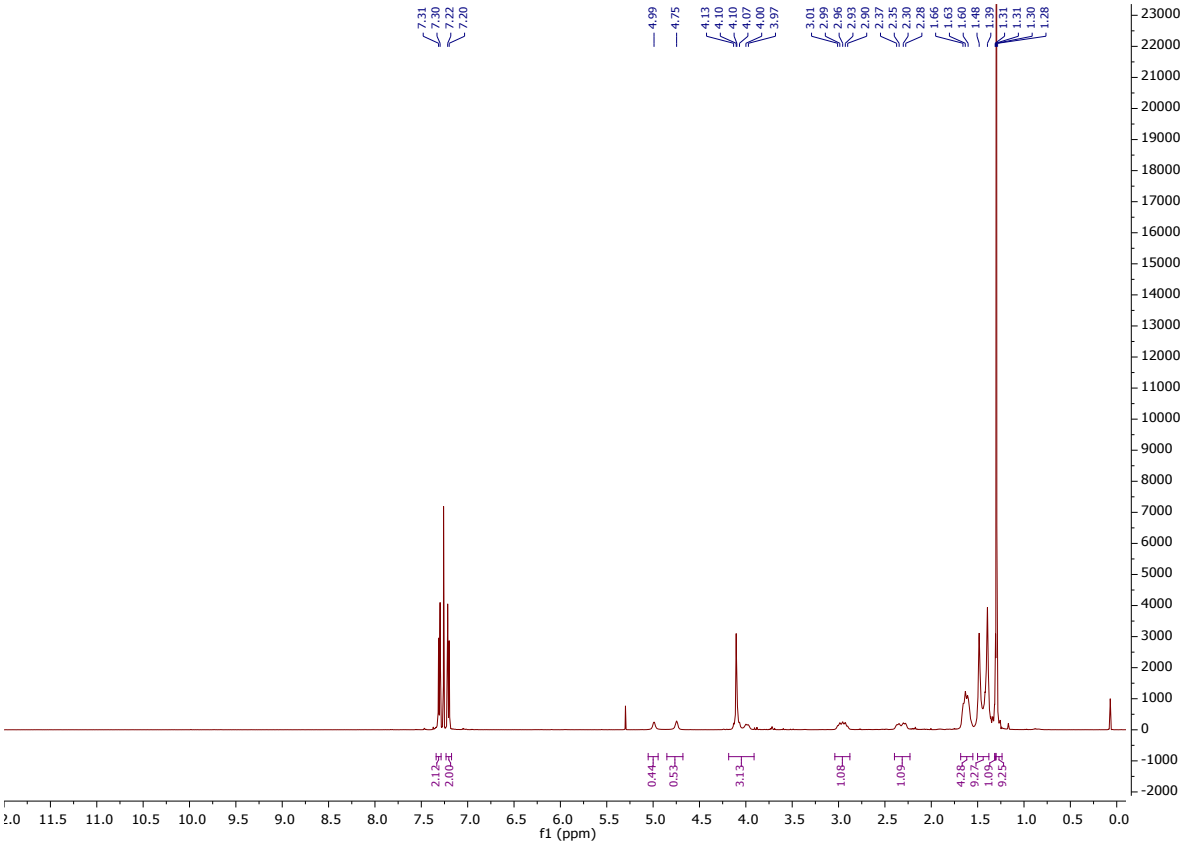
Yield: 43% (0.31 mmol, 123 mg).

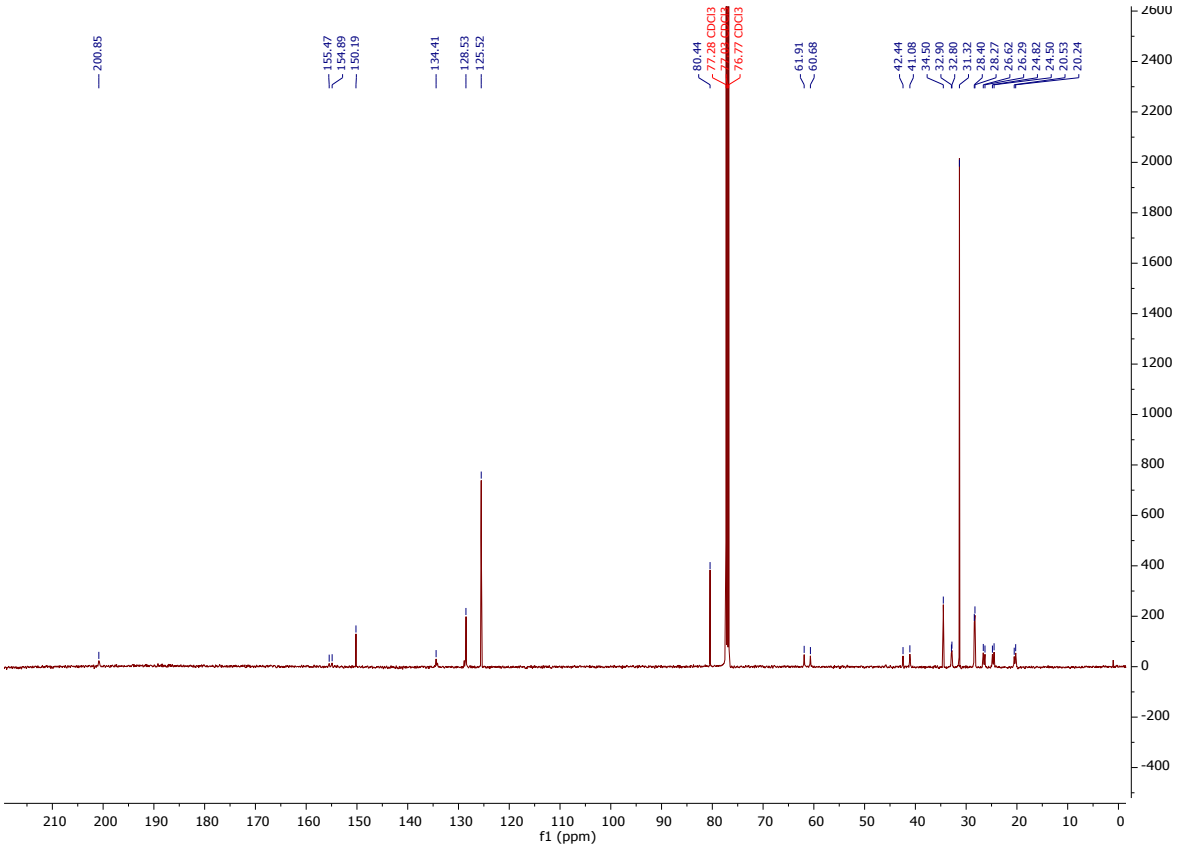
δ_H (500 MHz, Chloroform-*d*, rotamers) 7.31 (2 H, d, *J* 8.3), 7.21 (2 H, d, *J* 8.3), 4.99 (0.5 H, s), 4.75 (0.5 H, s), 4.18 – 3.96 (3 H, m) 3.01 – 2.90 (1 H, m), 2.37 – 2.28 (1 H, m), 1.68 – 1.55 (4 H, m), 1.50-1.38 (9 H, m), 1.31 – 1.30 (1 H, m), 1.28 (9 H, s).

δ_C (126 MHz, Chloroform-*d*, rotamers) 200.85, 155.47 &154.89, 150.19, 134.41, 128.53, 125.52, 80.44, 61.91 & 60.68, 42.44 & 41.08, 34.50, 32.92 & 32.80, 31.32, 28.40 & 28.27, 26.62 & 26.92, 24.82 & 24.50, 20.53 & 20.24.

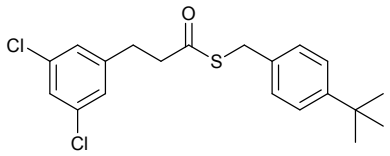
ν_{max}/cm^{-1}: 2962, 2865, 1682, 1518, 1407, 1366, 1266, 1114.

ESI-MS (+ve) m/z: Found $[M+H]^+$ 392.2245, $C_{22}H_{34}NO_3S^+$ requires 392.2254.


7.31
7.30
7.22
7.20
4.99
4.75
4.13
4.10
4.10
4.07
4.00
3.97
3.01
2.99
2.96
2.93
2.90
2.37
2.35
2.30
2.28
1.66
1.63
1.60
1.48
1.39
1.31
1.31
1.30
1.28
2.12
2.00
0.44
0.53
3.13
1.08
1.09
4.28
9.27
1.09
9.25
f1 (ppm)


200.85
155.47
154.89
150.19
134.41
128.53
125.52
80.44
77.28 CDCl3
76.77 CDCl3
61.91
60.68
42.44
41.08
34.50
32.90
32.80
31.32
28.40
28.27
26.62
26.29
24.82
24.50
20.53
20.24
f1 (ppm)

Compound **15**: *S*-(4-(tert-butyl)benzyl) 3-(3,5-dichlorophenyl)propanethioate



Chemical Formula: $C_{20}H_{22}Cl_2OS$
Exact Mass: 380.0768
Molecular Weight: 381.3550

Synthesised according to general procedure **C** using 0.9 equivalents of 4-tert-butylbenzyl mercaptan.

Appearance: Colourless Oil.

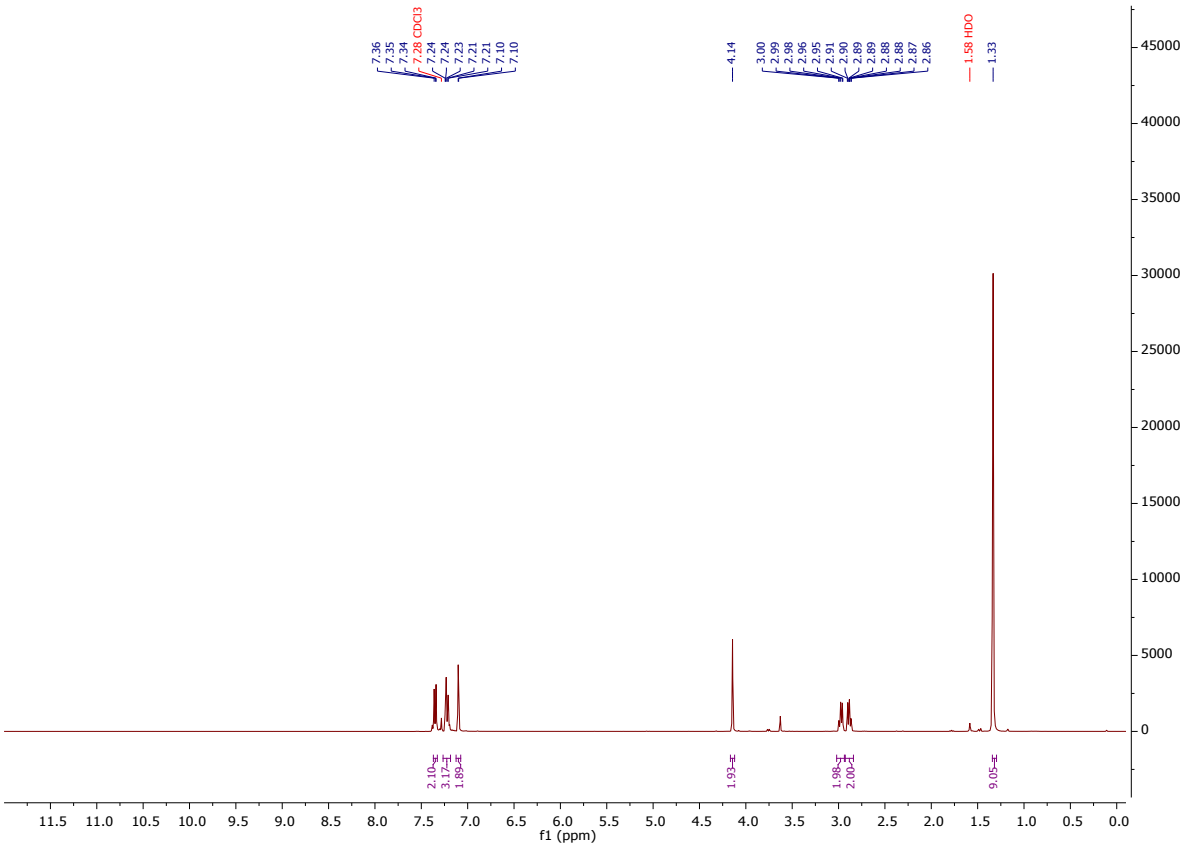
Yield: 71% (0.64 mmol, 243 mg).

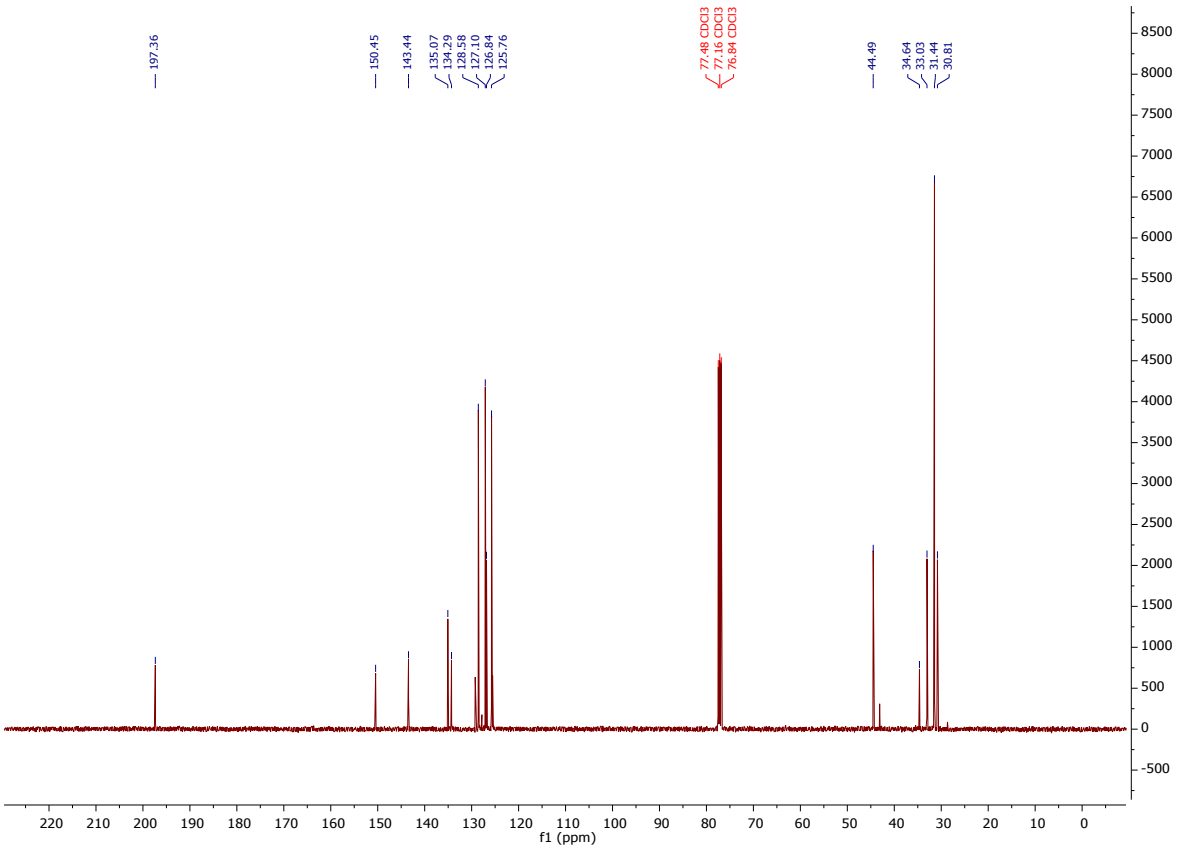
δ_H (400 MHz, Chloroform-*d*) 7.37 – 7.33 (2 H, m), 7.27 – 7.18 (3 H, m), 7.12 – 7.08 (2 H, m), 4.14 (2 H, s), 3.03 – 2.94 (2 H, m), 2.93 – 2.84 (2 H, m), 1.33 (9 H, s).

δ_C (101 MHz, Chloroform-*d*) 197.36, 150.45, 143.44, 135.07, 134.29, 128.58, 127.10, 126.84, 125.76, 44.49, 34.64, 33.03, 31.44, 30.81.

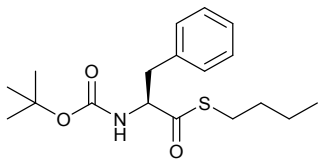
ν_{max}/cm^{-1}: 2960, 1685, 1566, 1462, 1050, 974, 852, 834, 679, 558.

ESI-MS (+ve) m/z: Found $[M+Na]^+$ 403.0663, $C_{20}H_{22}Cl_2NaOS^+$ requires 403.0666.





Compound **16**: *S*-butyl (S)-2-((tert-butoxycarbonyl)amino)-3-phenylpropanethioate



Chemical Formula: $C_{18}H_{27}NO_3S$
Exact Mass: 337.1712
Molecular Weight: 337.4780

Synthesised according to general procedure **C** using 0.97 equivalents of 1-butanethiol

Appearance: White solid.

Yield: 55% (0.53 mmol, 180 mg).

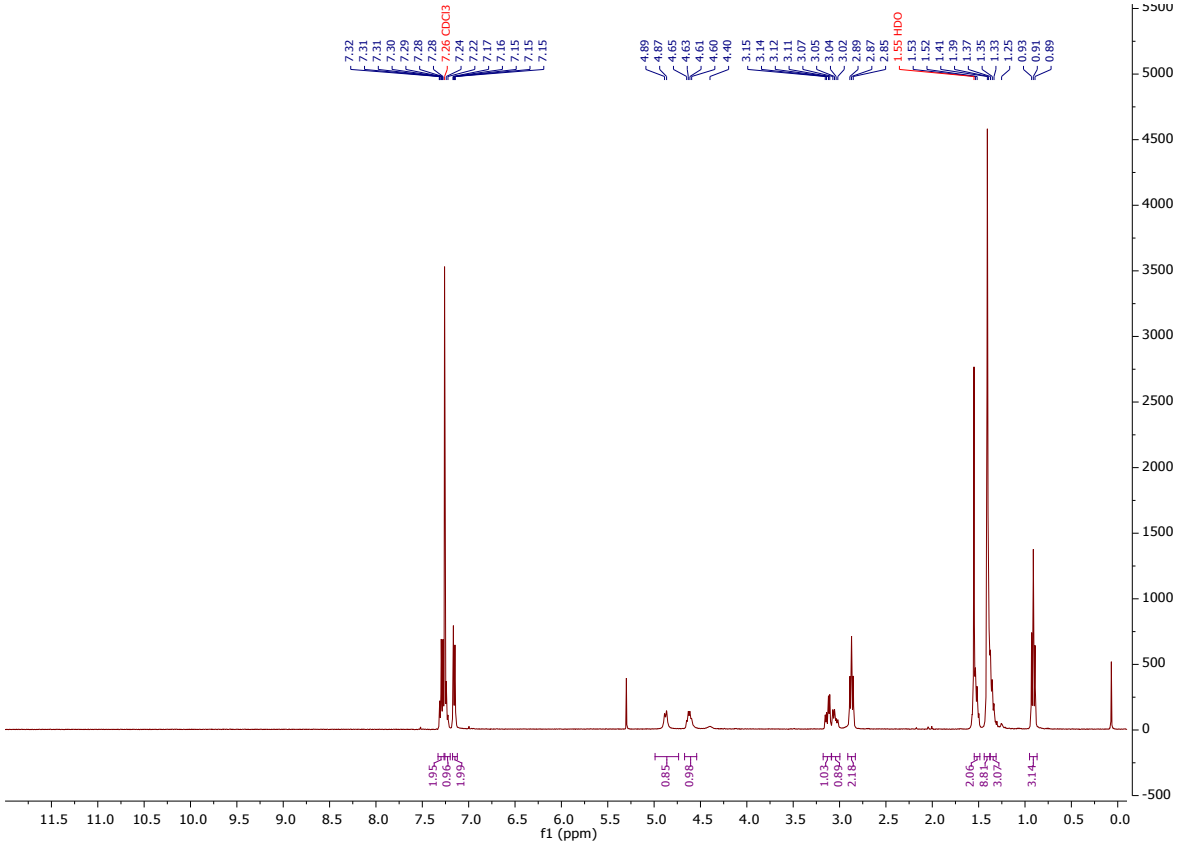
M.p.: 83-86 °C.

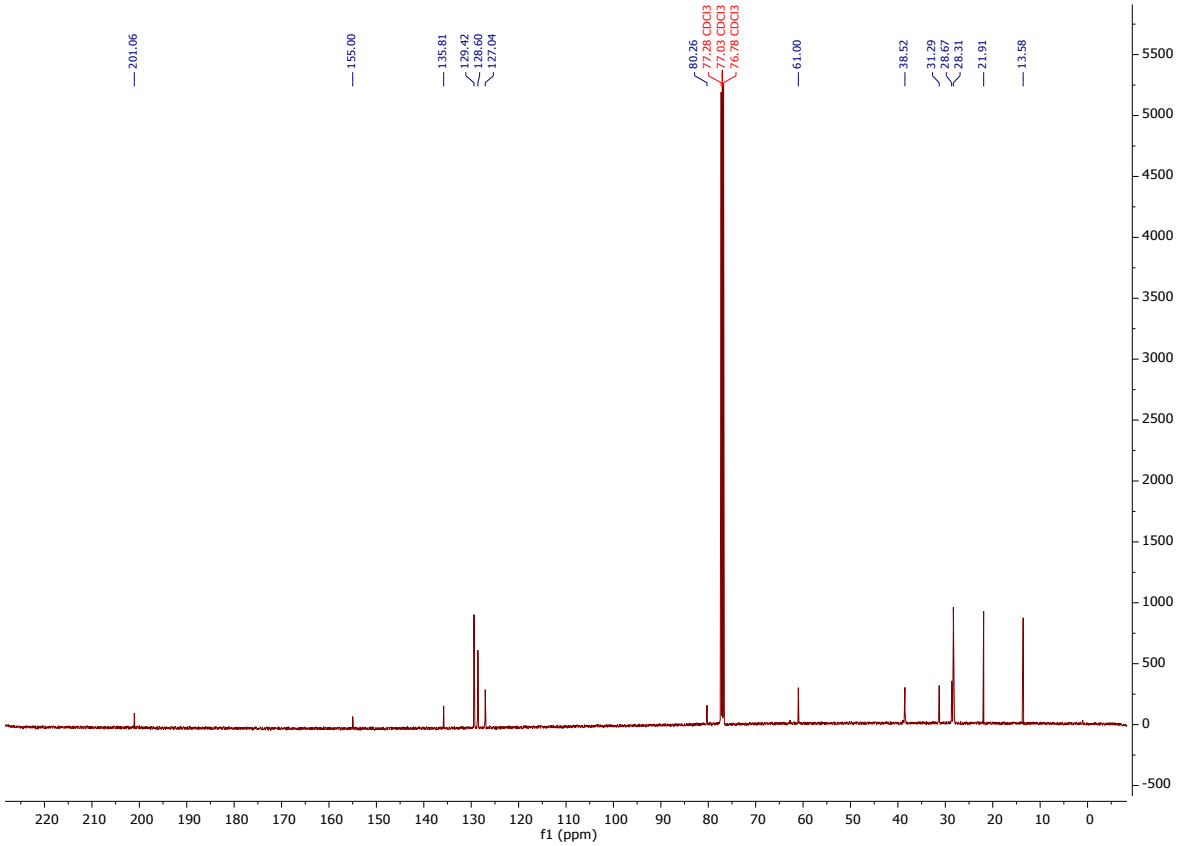
δ_H (400 MHz, Chloroform-*d*) 7.33 – 7.27 (2 H, m), 7.25 – 7.20 (1 H, m), 7.17 – 7.12 (2 H, m), 4.89 – 4.87 (1 H, m), 4.67 – 4.54 (1 H, m), 3.13 (1 H, dd, *J* 14.0, 5.5), 3.05 (1 H, dd, *J* 14.0, 7.1), 2.87 (2 H, t, *J* 7.3), 1.55 – 1.49 (2 H, m), 1.41 (9 H, s), 1.38 – 1.31 (2 H, m), 0.91 (3 H, t, *J* 7.3).

δ_C (126 MHz, Chloroform-*d*) 201.06, 155.00, 135.81, 129.42, 128.60, 127.04, 80.26, 61.00, 38.52, 31.29, 28.67, 28.31, 21.91, 13.58.

ν_{max}/cm^{-1}: 3340, 2963, 2930, 1681, 1520, 1323, 1248, 1163, 992, 720, 621, 530.

ESI-MS (+ve) m/z: Found $[M+H]^+$ 338.1779, $C_{18}H_{27}NO_3S^+$ requires 338.1784.


7.32
7.31
7.31
7.30
7.29
7.28
7.28
7.26 CDCl3
7.24
7.22
7.17
7.16
7.15
7.15
7.15
4.89
4.87
4.65
4.63
4.61
4.60
4.40
3.15
3.14
3.12
3.11
3.07
3.05
3.04
3.02
2.89
2.87
2.85
1.55 HDO
1.53
1.52
1.41
1.39
1.37
1.35
1.33
1.25
0.93
0.91
0.89
1.95
0.96
1.99
0.85
0.98
1.03
0.89
2.18
2.06
8.81
3.07
3.14
f1 (ppm)


201.06
155.00
135.81
129.42
128.60
127.04
80.26
77.28 CDCl3
77.03 CDCl3
76.78 CDCl3
61.00
38.52
31.29
28.67
28.31
21.91
13.58
f1 (ppm)