# Synthesis of Pyrazolo-azepinone Derivatives *via* Morita-Baylis-Hillman Chemistry as Potent Antimicrobial Agents

Nisha Devi,[a*] Virender Singh*[b] and Arun Singh Pathania[c]

Address: [a]Department of Chemistry, DAV University, Jalandhar - Pathankot National Highway (NH 44), Jalandhar - 144012, Punjab, India

[b]Department of Chemistry, School of Basic Sciences, Central University of Punjab, Bathinda

[c]Department of Biotechnology, DAV University, Jalandhar - Pathankot National Highway (NH 44), Jalandhar - 144012, Punjab, India

*Email ID: nisha.nitj@gmail.com, virender.singh@cup.edu.in

***Supporting Information***

**Table of Contents**

# I. General procedure for antimicrobial screening of derivatives 13

The antibacterial and antifungal activities are done using broth microdilution susceptibility test. Among gram positive bacteria, *Staphylococcus aureus* and *Staphylococcus epidermidis* and among gram negative *Escherichia coli* and *Pseudomonas aerugenosa* were used. For antifungal study, *Candida albicans* and *Aspergillus niger* were used. Ciprofloxacin and fluconazole were used as standard drugs for the antibacterial and antifungal studies, respectively. A broth microdilution susceptibility test was carried out in a 96 well microtitre plate by adding 240 µL of sterile media and 30 µL of metal complexes solutions ranging from 1.95 µg $mL^{-1}$ to 1000 µg $mL^{-1}$ using appropriate blanks and controls in each well. The sample solution of all the test compounds (**13**) was prepared by dissolving dry test compound in 1 mL of dimethylsulfoxide (DMSO), and DMSO was used as control for all the test compounds. Then 30 µL bacterial and fungal inocula (organism $10^{-7}$ cells per mL) was poured to each well under sterilized condition and incubated at 30 ºC for 48 hours at 150 rpm in an incubator shaker. The growth in wells was observed in the form of turbidity visualized with naked eyes under light background by comparing the clarity of blank media and the turbidity of the controls. The Minimum Inhibitory Concentration (MICs) of the derivatives (**13**) was recorded as the lowest concentration where no turbidity due to viability of bacteria and fungus was observed in the wells after incubation of 48 h. The growth of the bacteria and fungi was measured by observing the minimum inhibitory concentration.

**II.** $^{1}$H- and $^{13}$C- NMR spectra of the pyrazole MBH adducts **5**

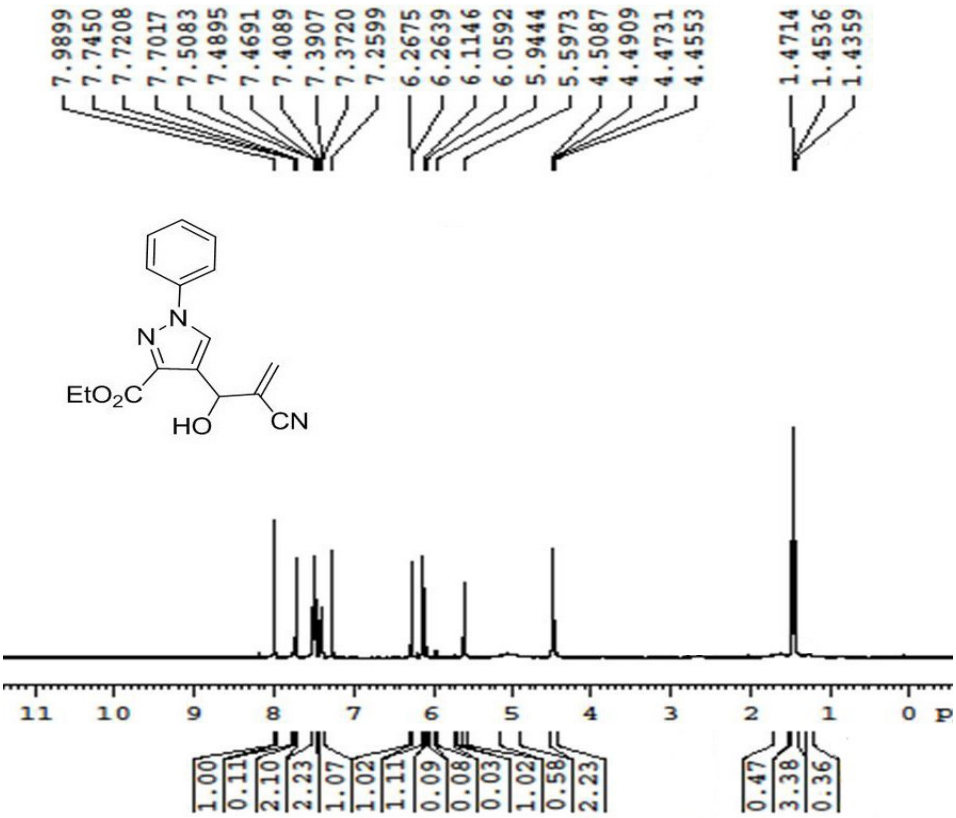


**Fig. S 1.** $^{1}$H-NMR of ethyl 4-(2-cyano-1-hydroxyallyl)-1-phenyl-1*H*-pyrazole-3-carboxylate **(5aA).**

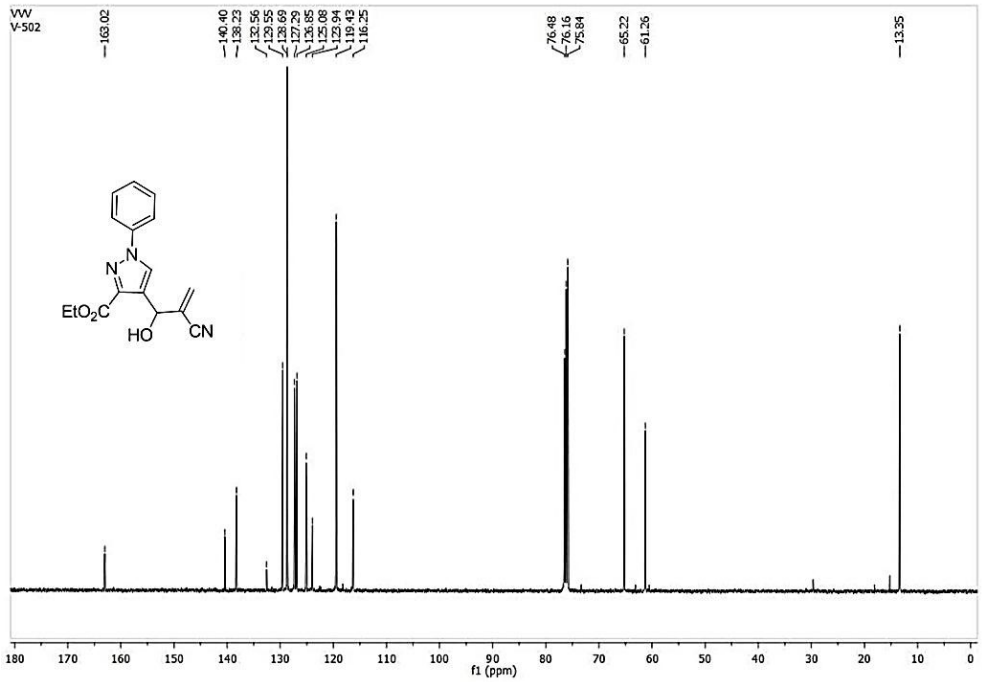


**Fig. S 2.** $^{13}$C-NMR of ethyl 4-(2-cyano-1-hydroxyallyl)-1-phenyl-1*H*-pyrazole-3-carboxylate **(5aA).**

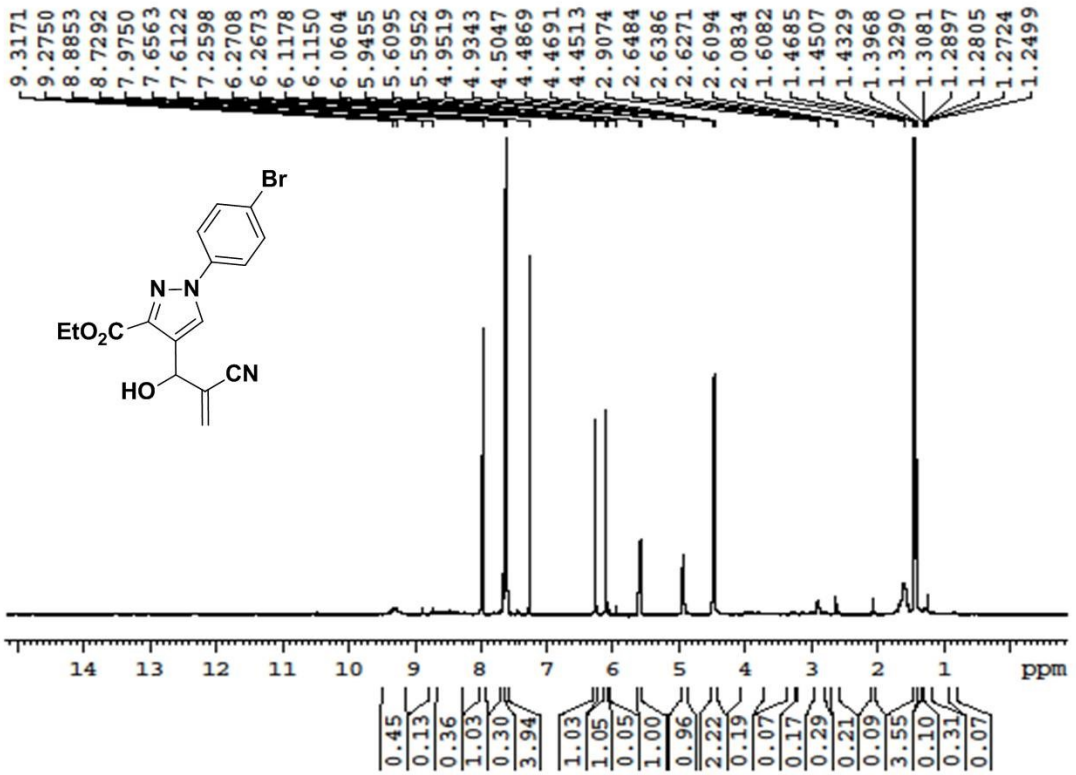


**Fig. S 3.** [1]H-NMR of ethyl 1-(4-bromophenyl)-4-(2-cyano-1-hydroxyallyl)-1*H*-pyrazole-3-carboxylate **(5cA).**

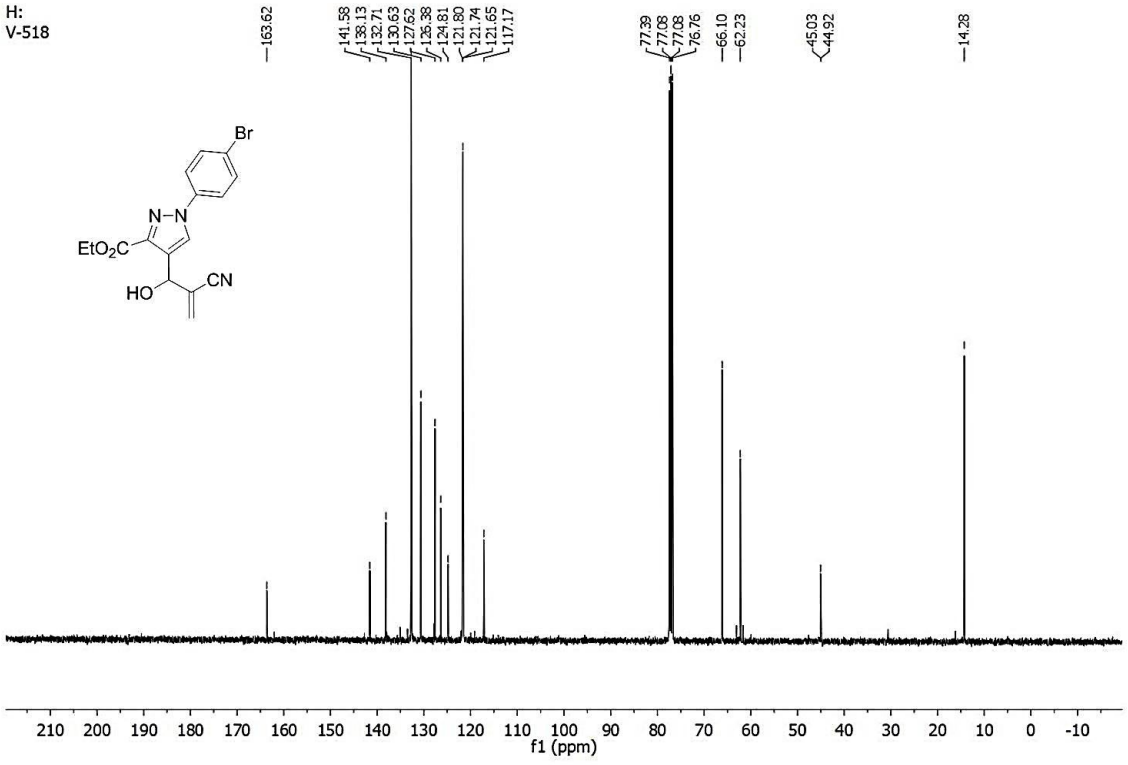


**Fig. S 4.** [13]C-NMR of ethyl 1-(4-bromophenyl)-4-(2-cyano-1-hydroxyallyl)-1*H*-pyrazole-3-carboxylate **(5cA).**

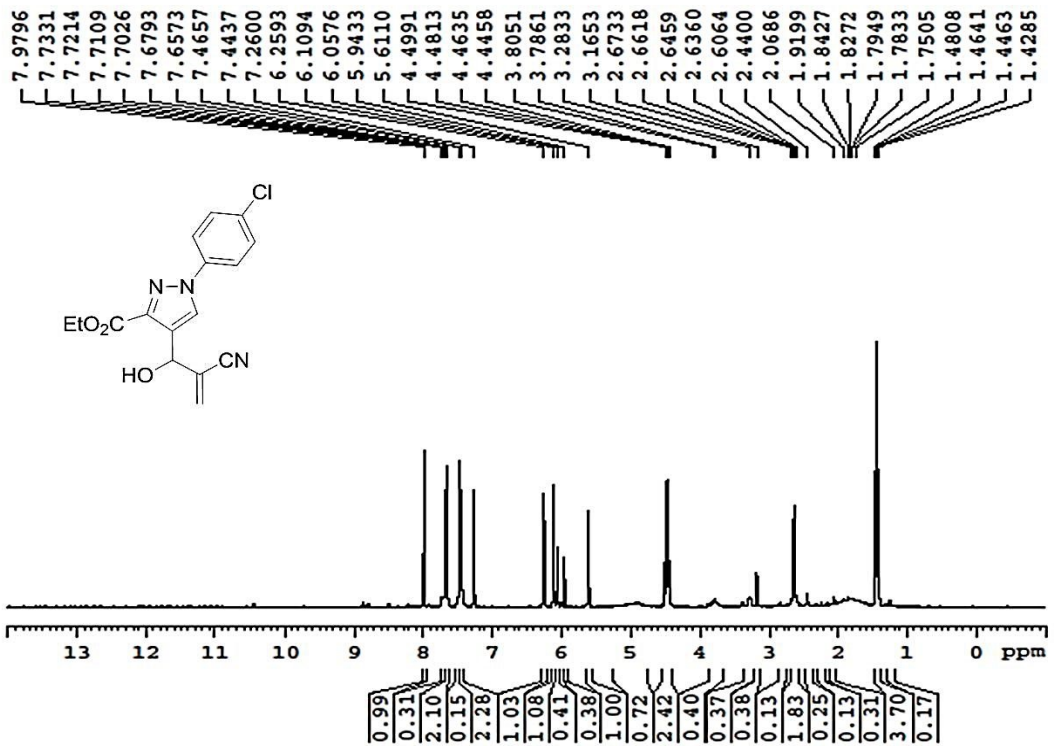


**Fig. S 5.** [1]H-NMR of ethyl 1-(4-chlorophenyl)-4-(2-cyano-1-hydroxyallyl)-1*H*-pyrazole-3-carboxylate **(5dA).**

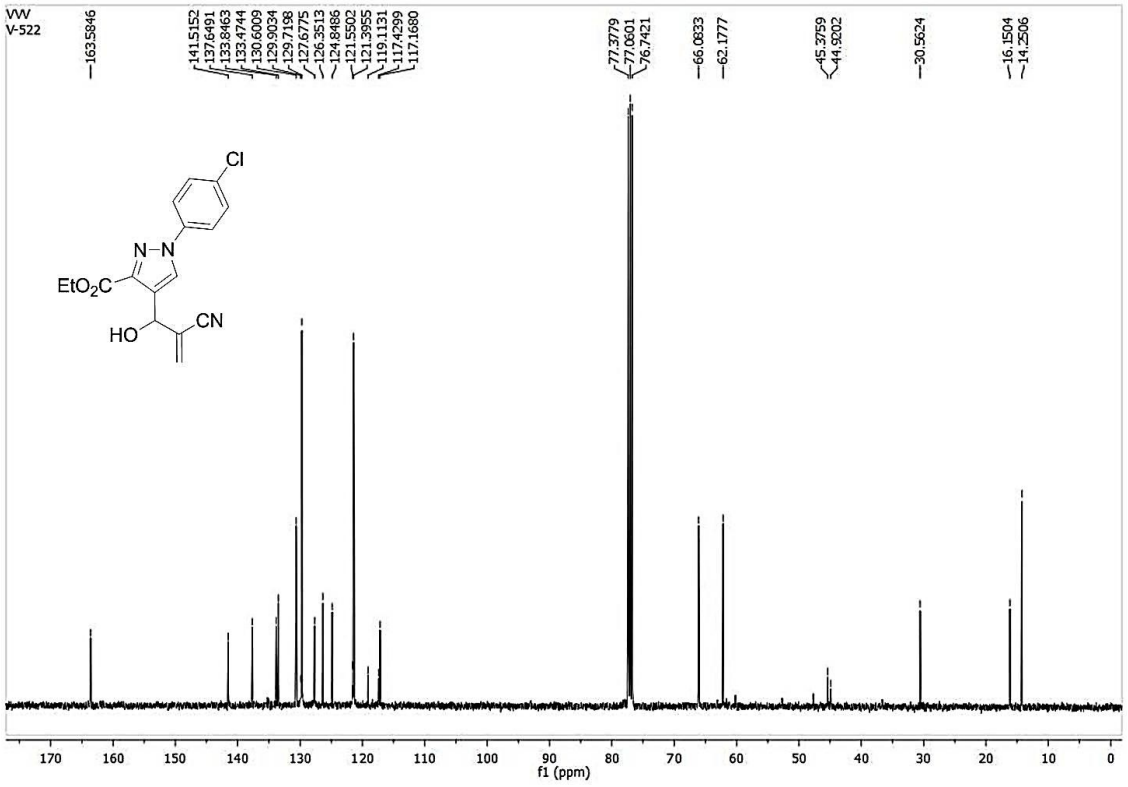


**Fig. S 6.** [13]C-NMR of ethyl 1-(4-chlorophenyl)-4-(2-cyano-1-hydroxyallyl)-1*H*-pyrazole-3-carboxylate **(5dA).**

**III.** $^{1}$H- and $^{13}$C- NMR spectra of the pyrazole MBH acetates **6**

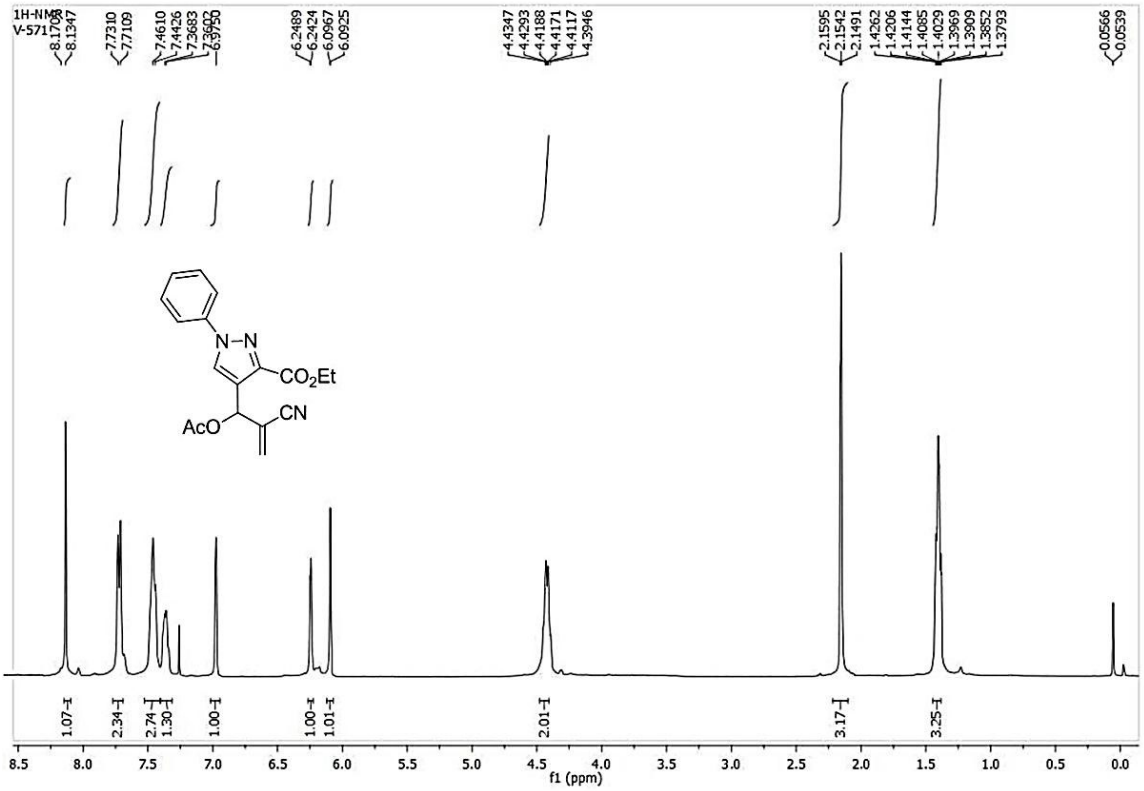


**Fig. S 7.** $^{1}$H-NMR of ethyl 4-(1-acetoxy-2-cyanoallyl)-1-phenyl-1*H*-pyrazole-3-carboxylate **(6aA)**.

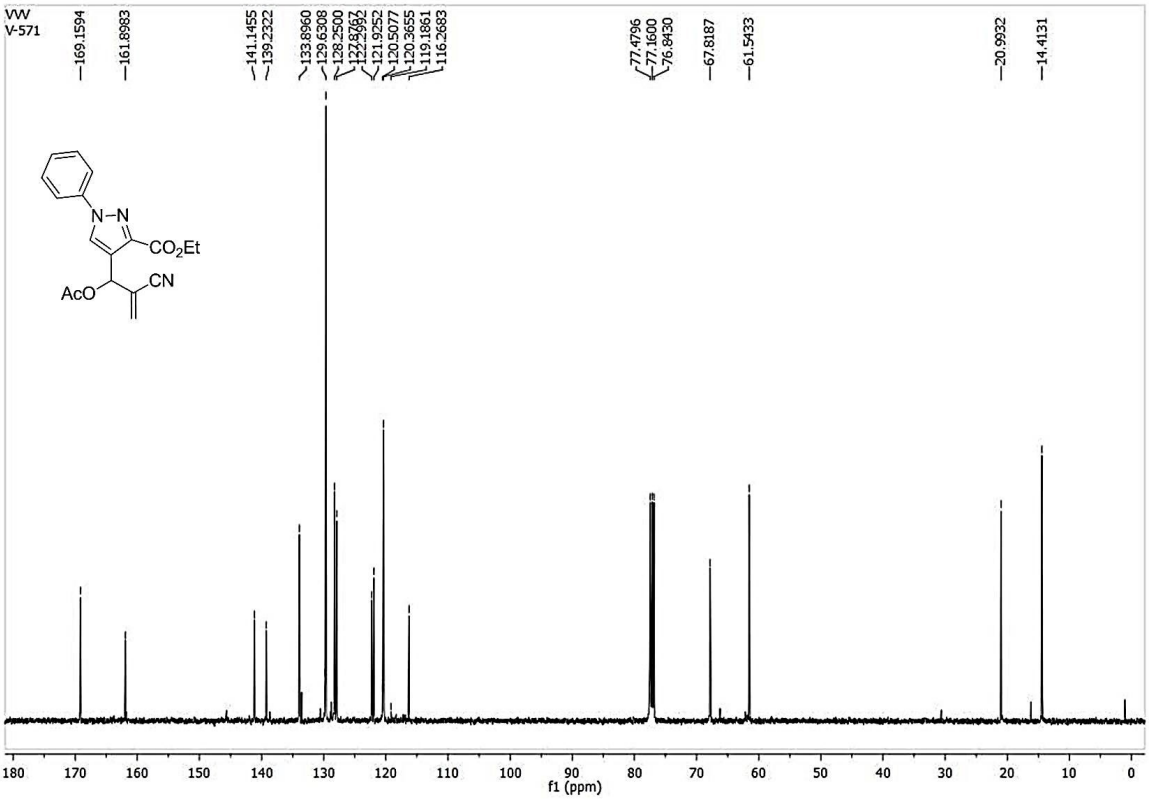


**Fig. S 8.** $^{13}$C-NMR of ethyl 4-(1-acetoxy-2-cyanoallyl)-1-phenyl-1*H*-pyrazole-3-carboxylate **(6aA)**.

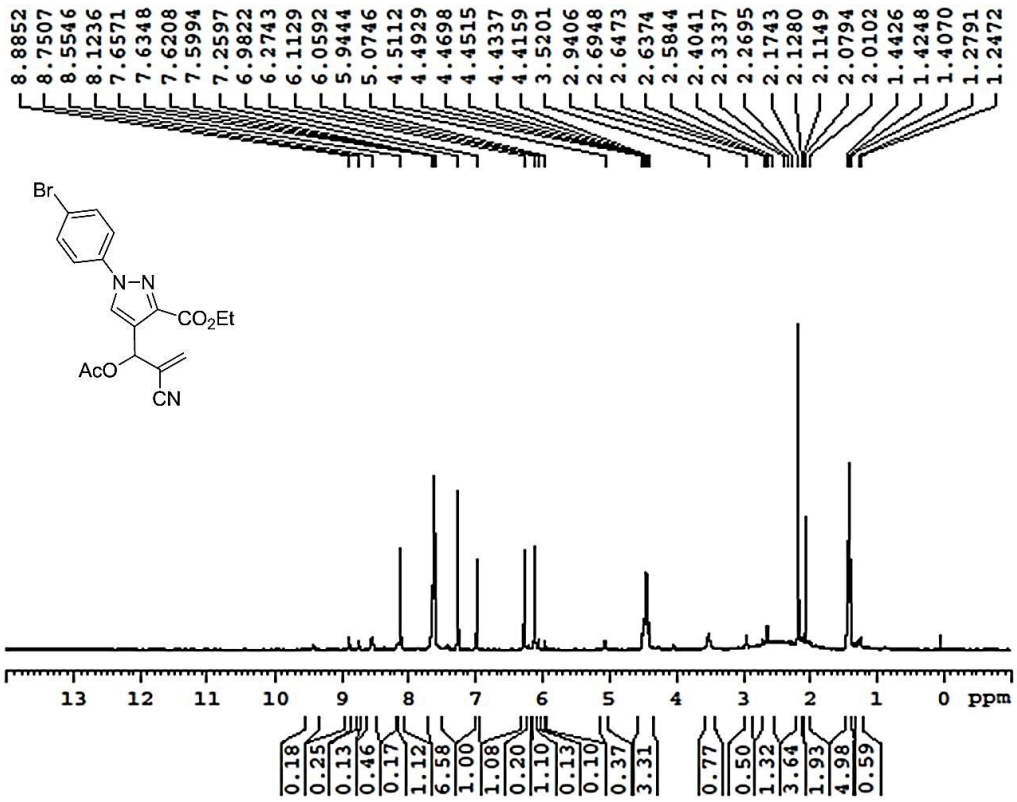


**Fig. S 9.** [1]H-NMR of ethyl 4-(1-acetoxy-2-cyanoallyl)-1-(4-bromophenyl)-1*H*-pyrazole-3-carboxylate **(6cA).**

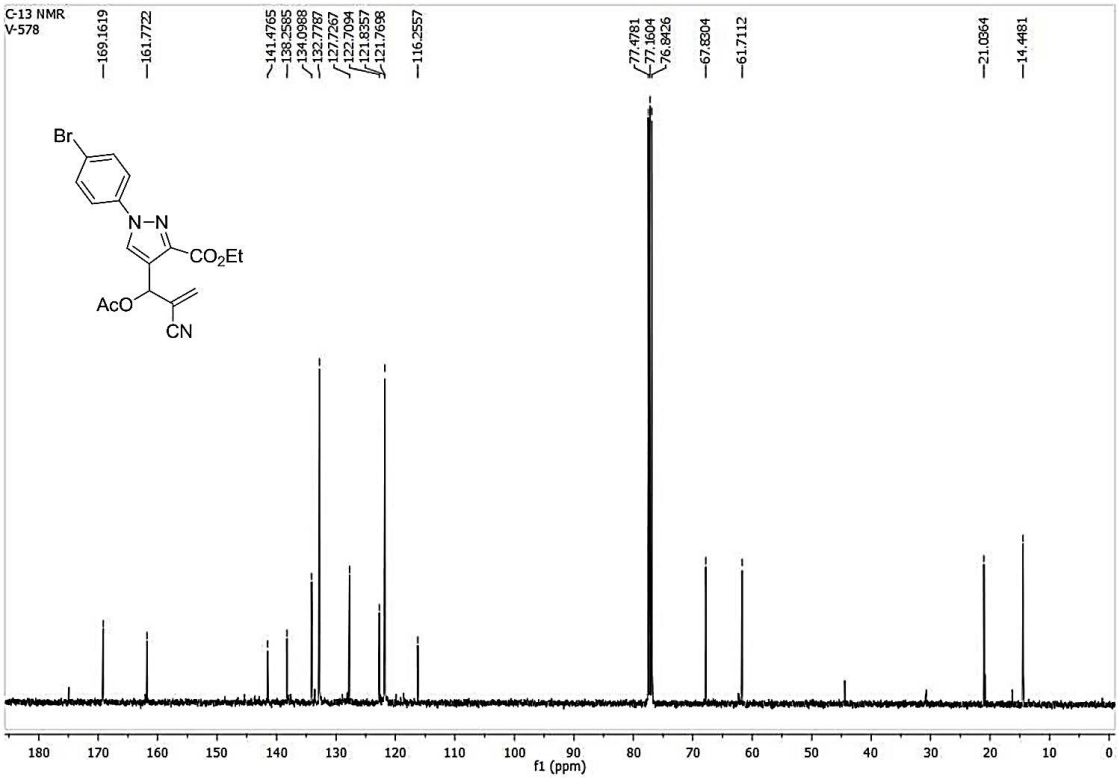


**Fig. S 10.** [13]C-NMR of ethyl 4-(1-acetoxy-2-cyanoallyl)-1-(4-bromophenyl)-1*H*-pyrazole-3-carboxylate **(6cA)**.

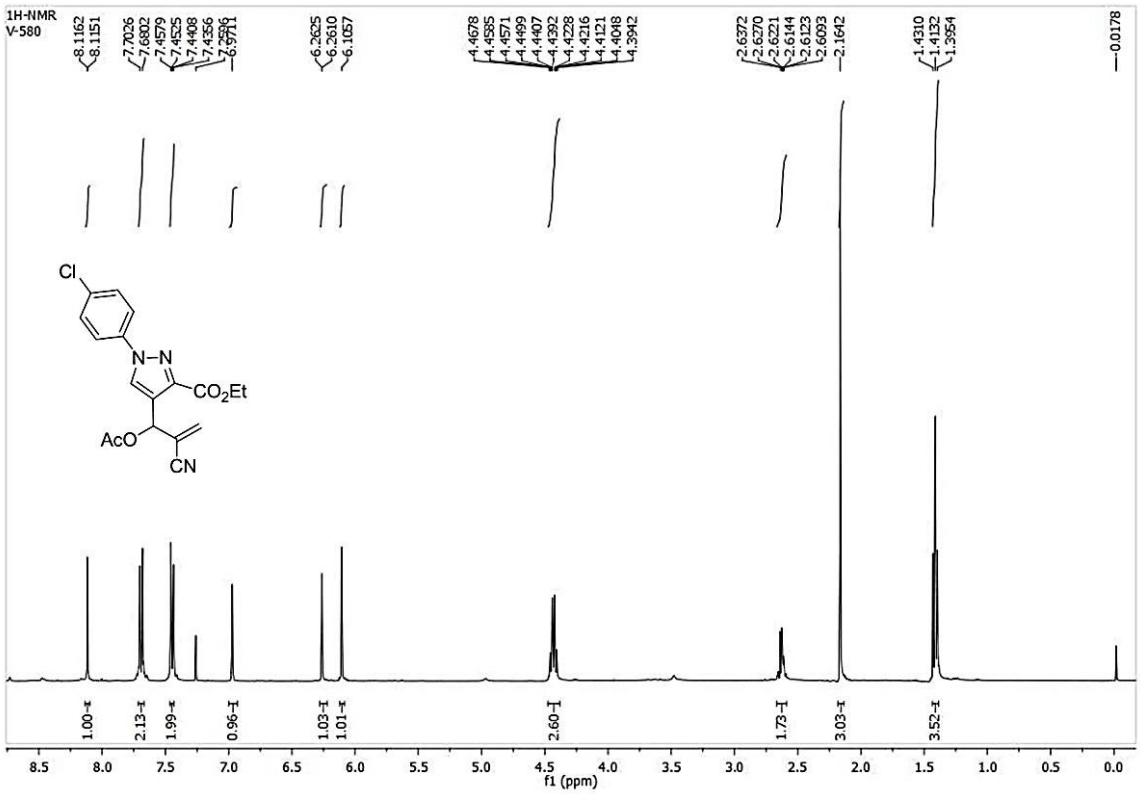


**Fig. S 11.** [1]H-NMR of ethyl 4-(1-acetoxy-2-cyanoallyl)-1-(4-chlorophenyl)-1*H*-pyrazole-3-carboxylate **(6dA).**

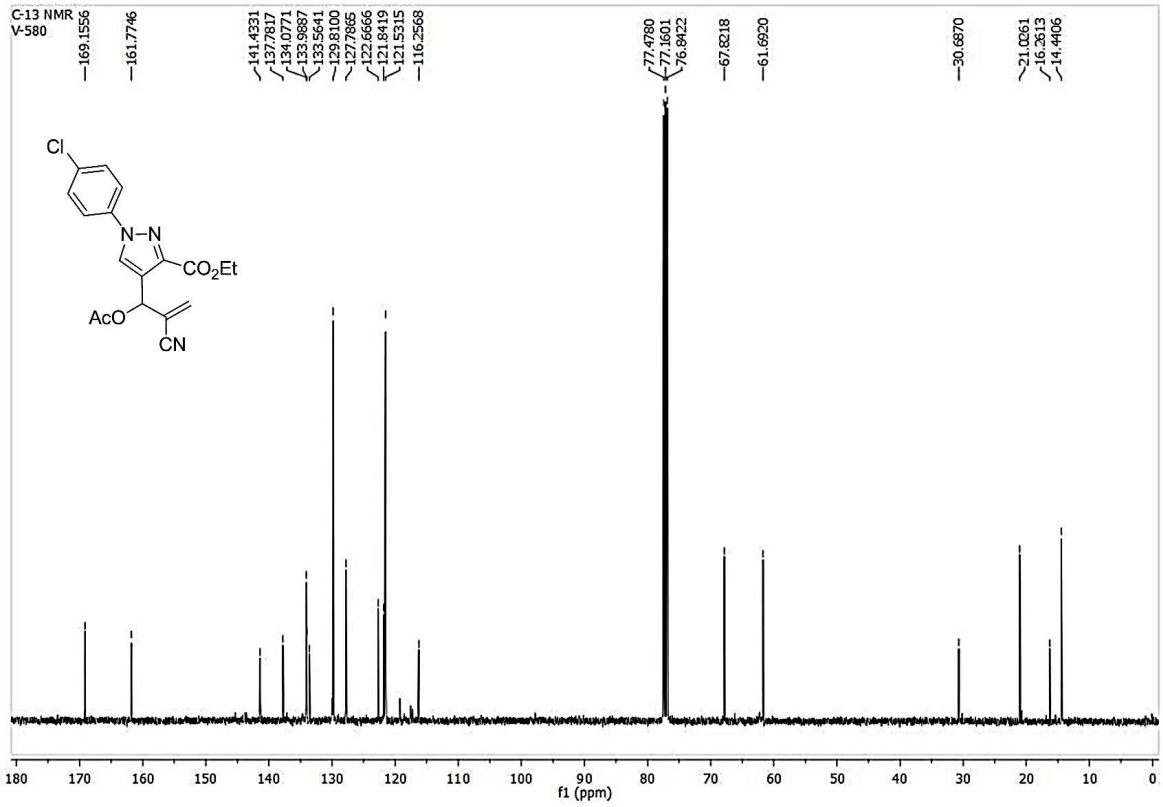


**Fig. S 12.** [13]C-NMR of ethyl 4-(1-acetoxy-2-cyanoallyl)-1-(4-chlorophenyl)-1*H*-pyrazole-3-carboxylate **(6dA).**

**IV.** $^{1}$H- and $^{13}$C- NMR spectra of the new pyrazole products **10**

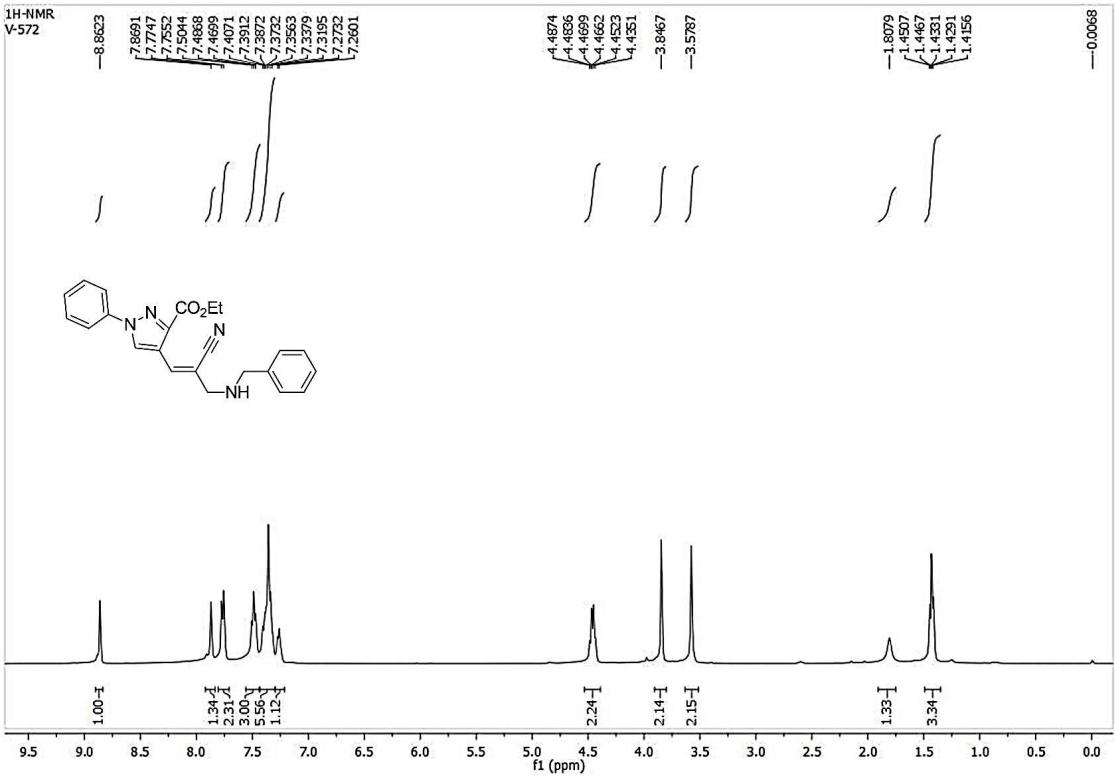


**Fig. S 13.** $^{1}$H-NMR of (*Z*)-ethyl 4-(3-(benzylamino)-2-cyanoprop-1-en-1-yl)-1-phenyl-1*H*-pyrazole-3-carboxylate **(10aAV)**.

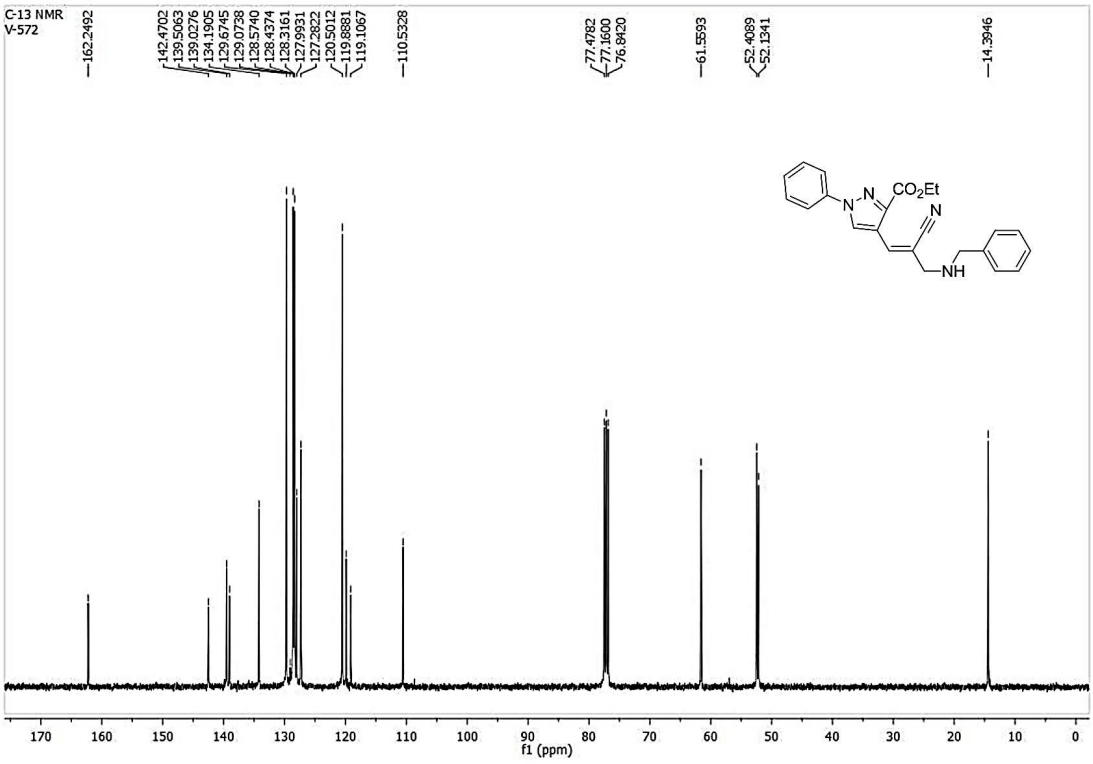


**Fig. S 14.** $^{13}$C-NMR of (*Z*)-ethyl 4-(3-(benzylamino)-2-cyanoprop-1-en-1-yl)-1-phenyl-1*H*-pyrazole-3-carboxylate **(10aAV)**.

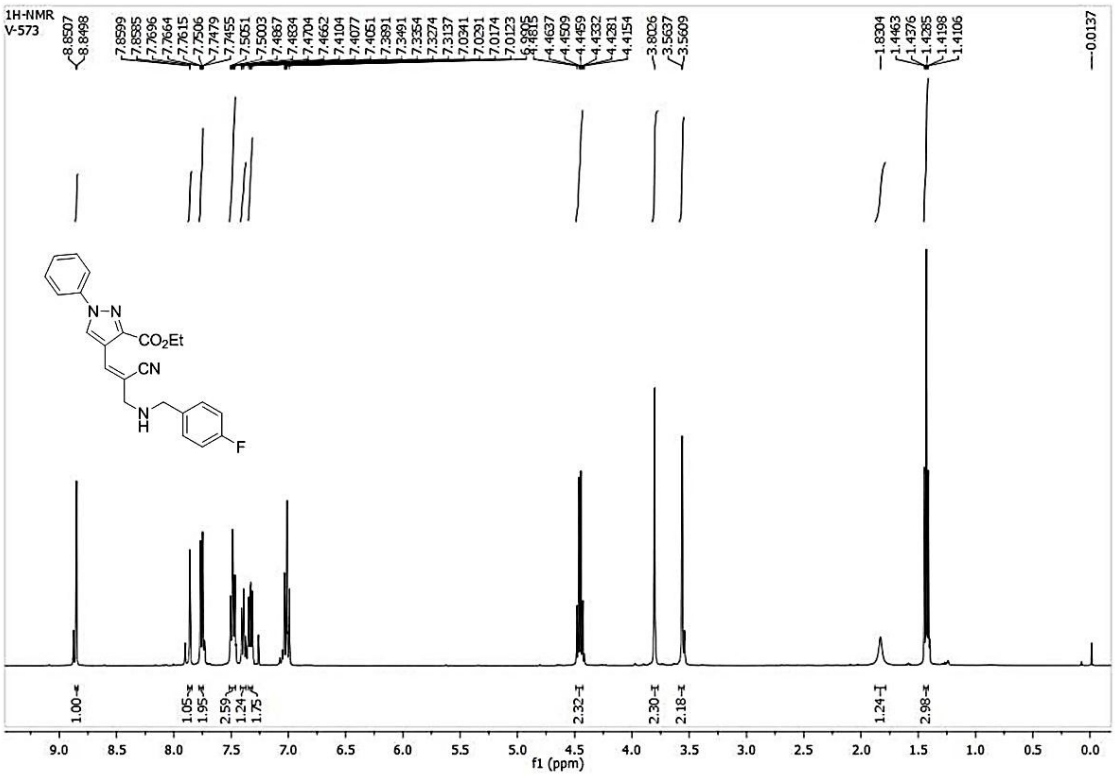


**Fig. S 15.** $^{1}$H-NMR of (*Z*)-ethyl 4-(2-cyano-3-((4-fluorobenzyl)amino)prop-1-en-1-yl)-1-phenyl-1*H*-pyrazole-3-carboxylate **(10aAY).**

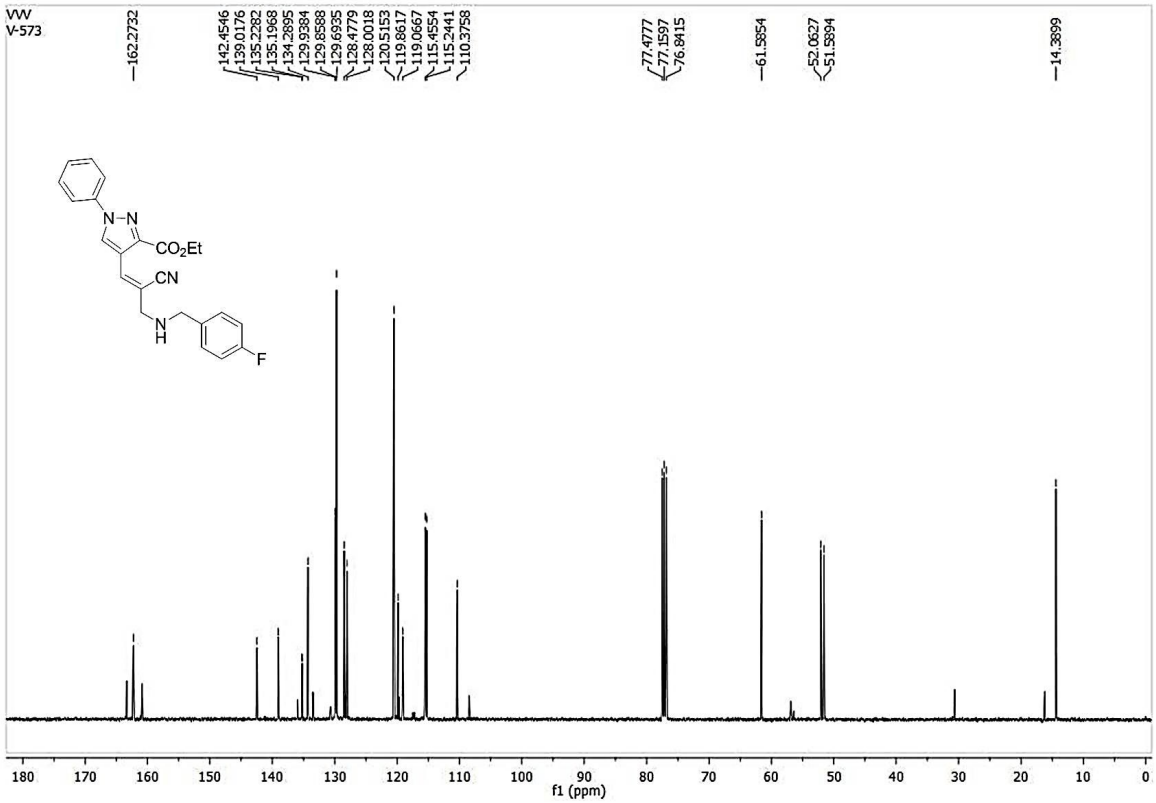


**Fig. S 16.** $^{13}$C-NMR of (*Z*)-ethyl 4-(2-cyano-3-((4-fluorobenzyl)amino)prop-1-en-1-yl)-1-phenyl-1*H*-pyrazole-3-carboxylate **(10aAY).**

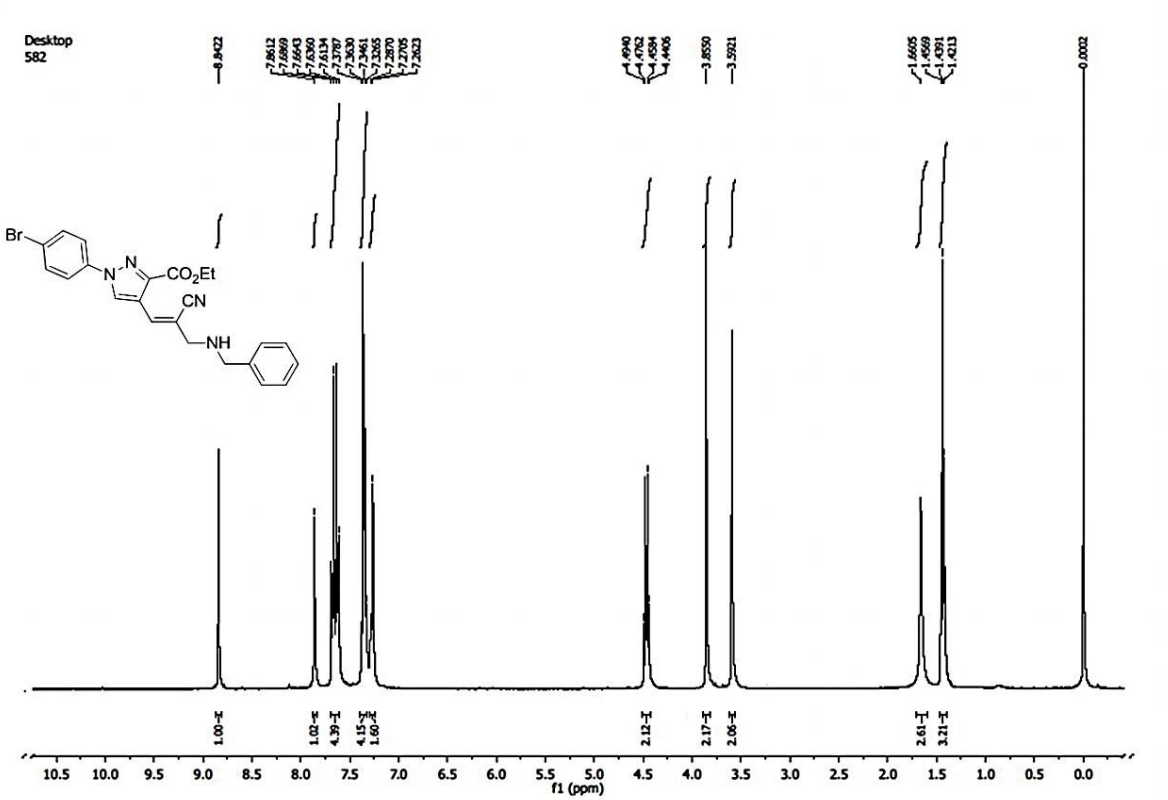


**Fig. S 17.** $^{1}$H-NMR of (*Z*)-ethyl 4-(3-(benzylamino)-2-cyanoprop-1-en-1-yl)-1-(4-bromophenyl)-1*H*-pyrazole-3-carboxylate **(10cAV).**

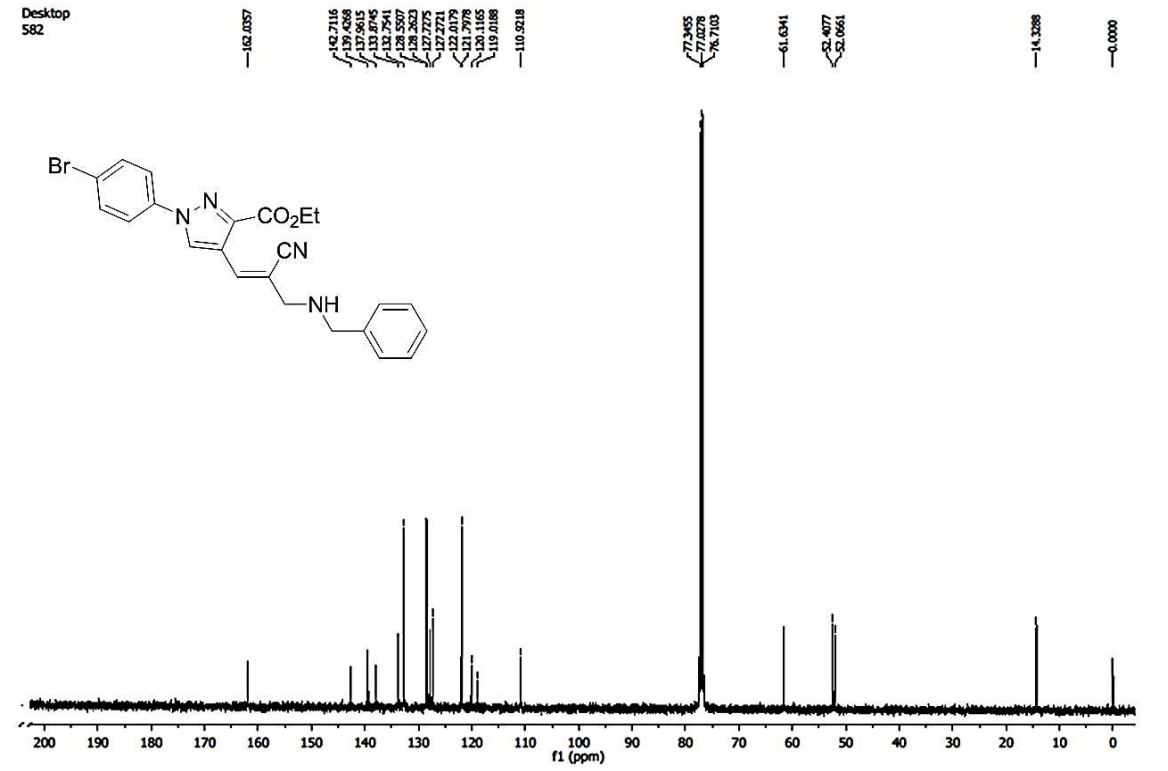


**Fig. S 18.** $^{13}$C-NMR of (*Z*)-ethyl 4-(3-(benzylamino)-2-cyanoprop-1-en-1-yl)-1-(4-bromophenyl)-1*H*-pyrazole-3-carboxylate **(10cAV).**

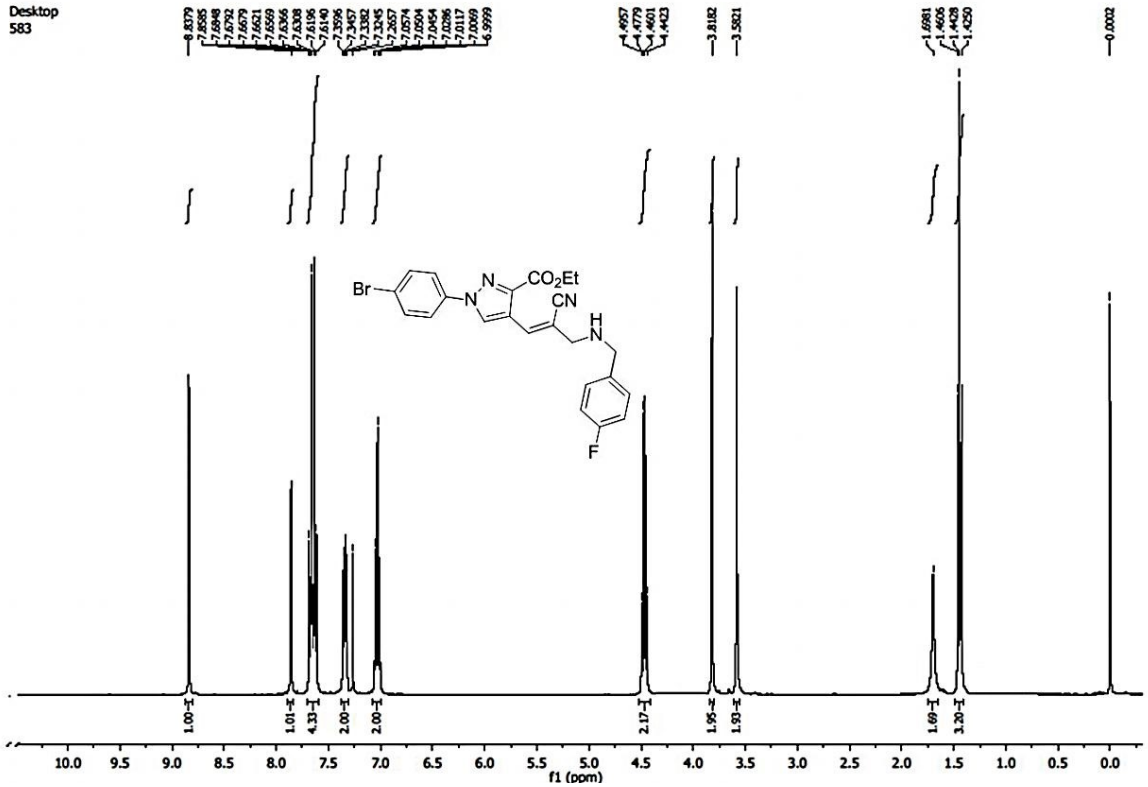


**Fig. S 19.** $^{1}$H-NMR of (*Z*)-ethyl 1-(4-bromophenyl)-4-(2-cyano-3-((4-fluorobenzyl)amino)prop-1-en-1-yl)-1*H*-pyrazole-3-carboxylate **(10cAY).**

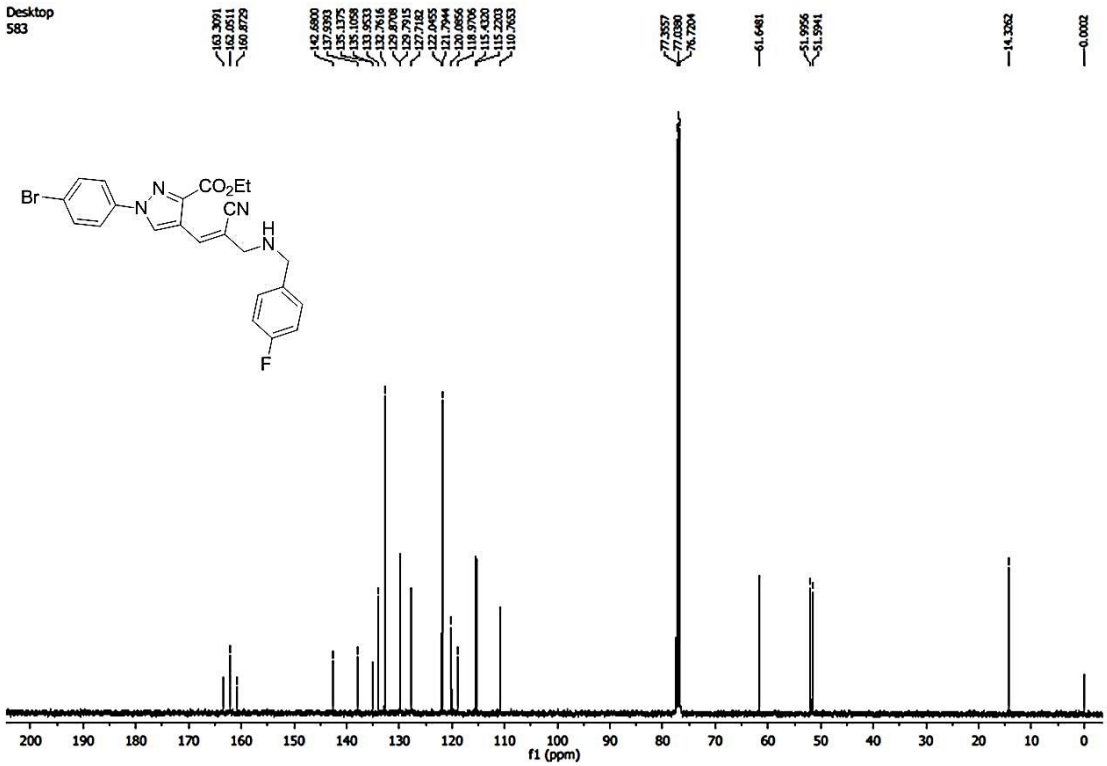


**Fig. S 20.** $^{13}$C-NMR of (*Z*)-ethyl 1-(4-bromophenyl)-4-(2-cyano-3-((4-fluorobenzyl)amino)prop-1-en-1-yl)-1*H*-pyrazole-3-carboxylate **(10cAY).**

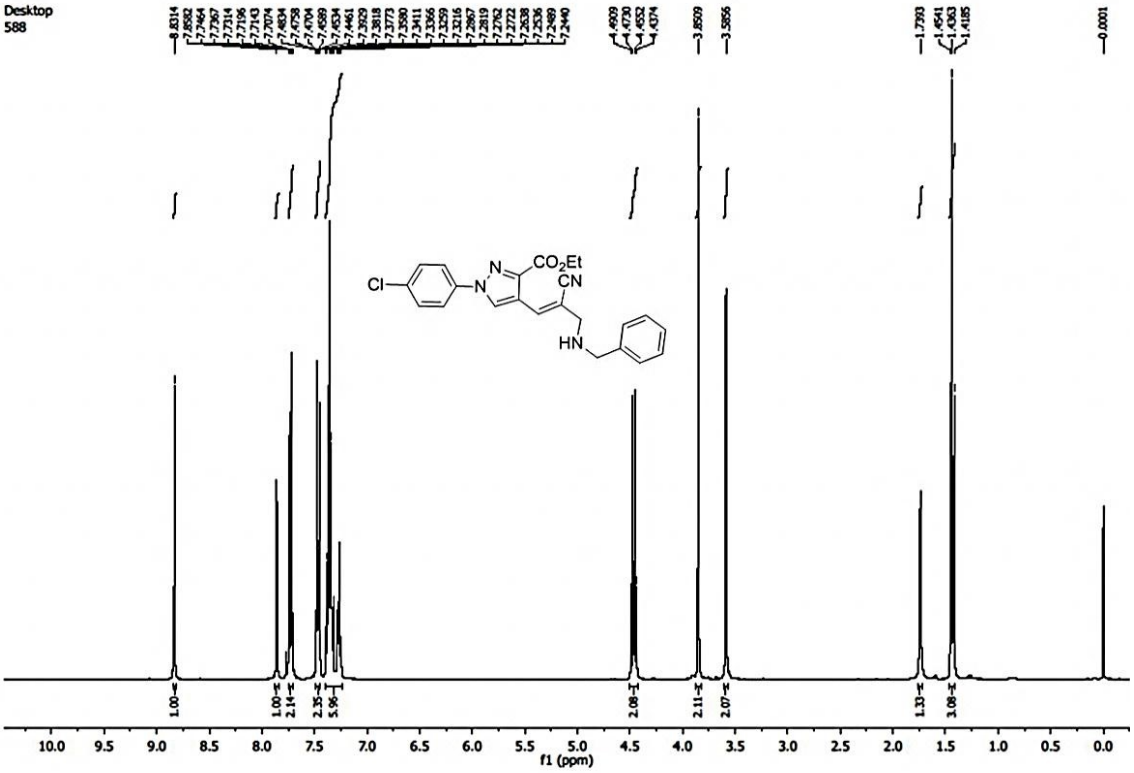


**Fig. S 21.** $^{1}$H-NMR of (*Z*)-ethyl 4-(3-(benzylamino)-2-cyanoprop-1-en-1-yl)-1-(4-chlorophenyl)-1*H*-pyrazole-3-carboxylate **(10dAV).**

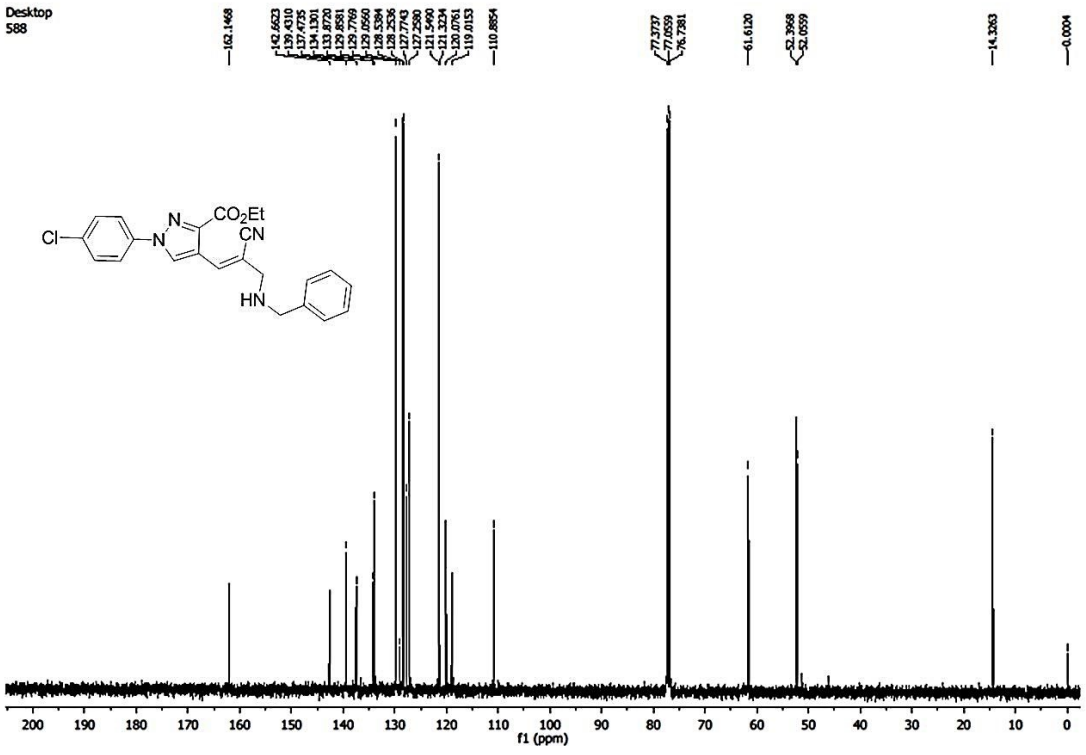


**Fig. S 22.** $^{13}$C-NMR of (*Z*)-ethyl 4-(3-(benzylamino)-2-cyanoprop-1-en-1-yl)-1-(4-chlorophenyl)-1*H*-pyrazole-3-carboxylate **(10dAV).**

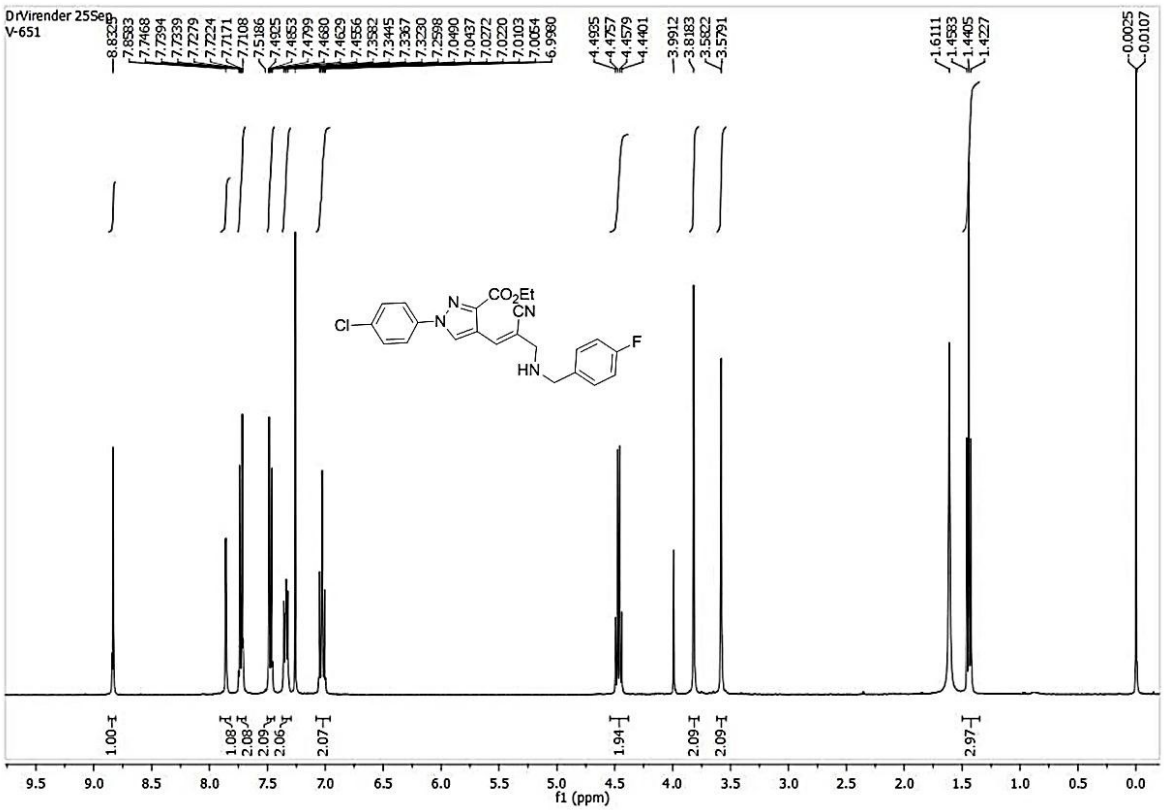


**Fig. S 23.** $^{1}$H-NMR of (*Z*)-ethyl 1-(4-chlorophenyl)-4-(2-cyano-3-((4-fluorobenzyl)amino)prop-1-en-1-yl)-1*H*-pyrazole-3-carboxylate **(10dAY).**

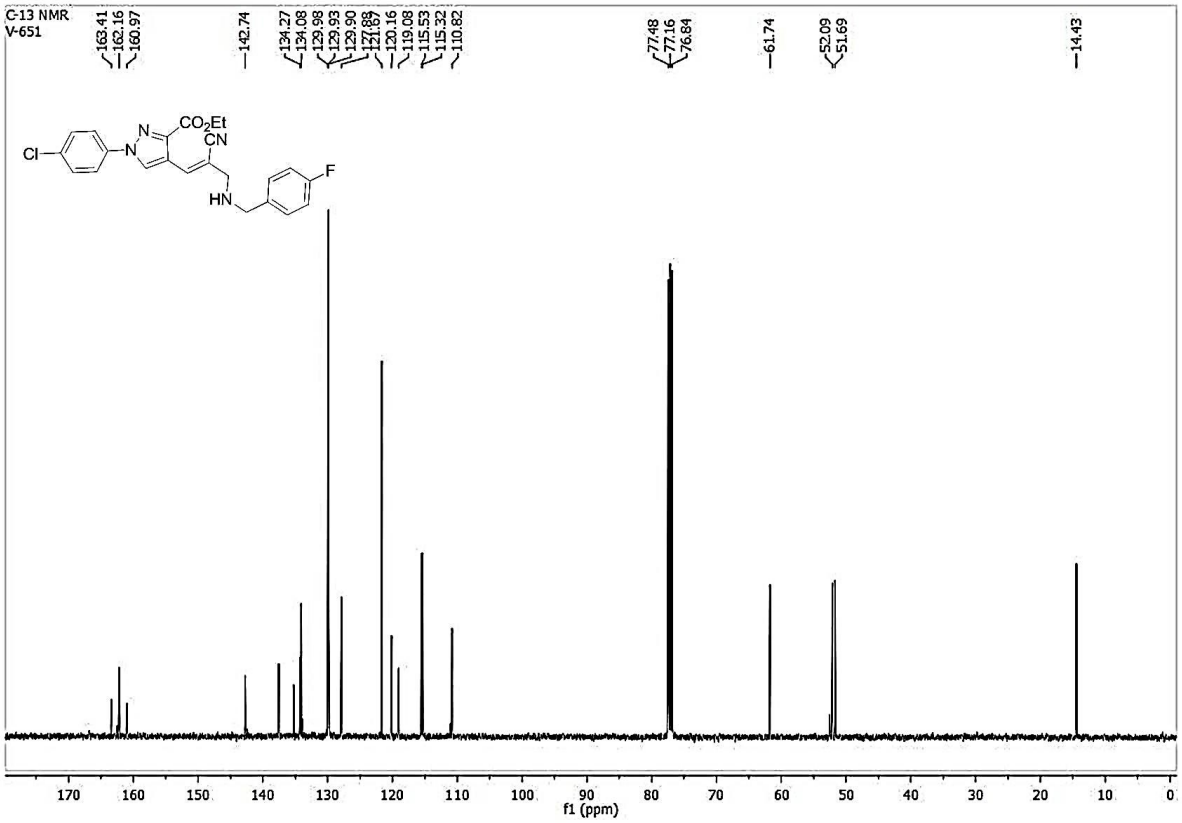


**Fig. S 24.** $^{13}$C-NMR of (*Z*)-ethyl 1-(4-chlorophenyl)-4-(2-cyano-3-((4-fluorobenzyl)amino)prop-1-en-1-yl)-1*H*-pyrazole-3-carboxylate **(10dAY).**

**V.** $^{1}$H- and $^{13}$C- NMR spectra of the new pyrazole MBH adducts **7** and **9**

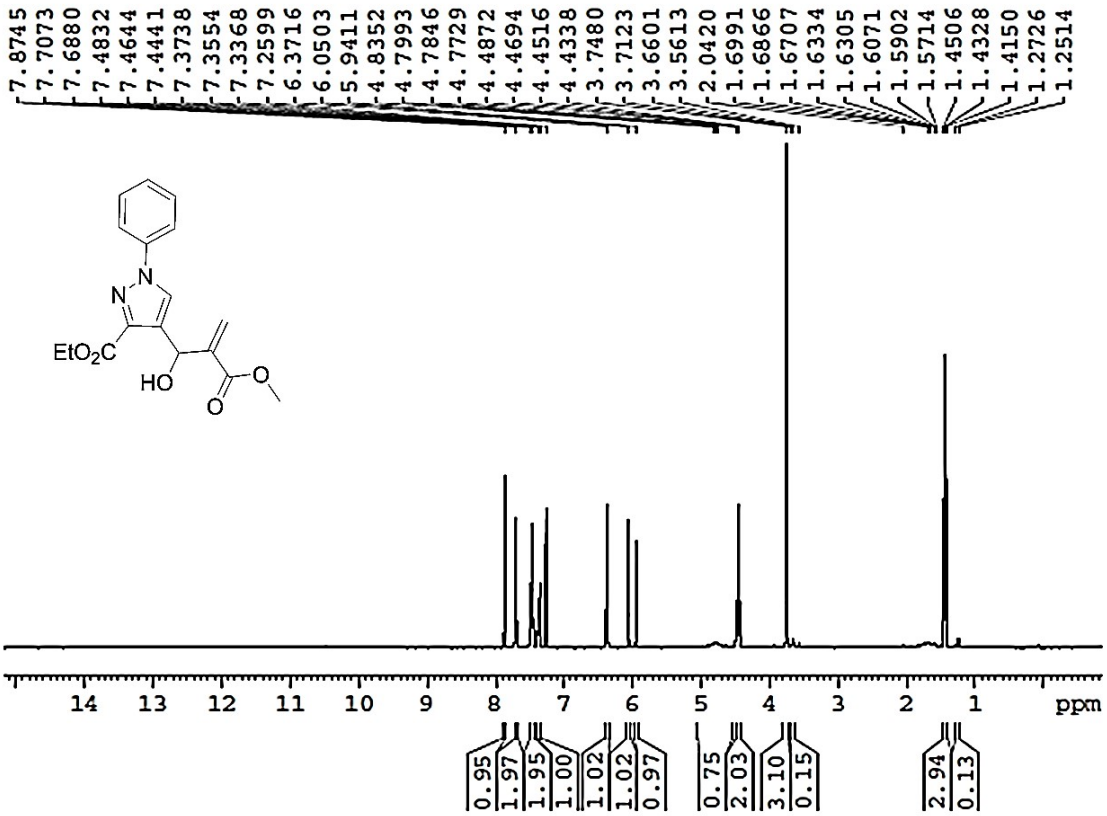


**Fig. S 25.** $^{1}$H-NMR of ethyl 4-(1-hydroxy-2-(methoxycarbonyl)allyl)-1-phenyl-1*H*-pyrazole-3-carboxylate **(7aB).**

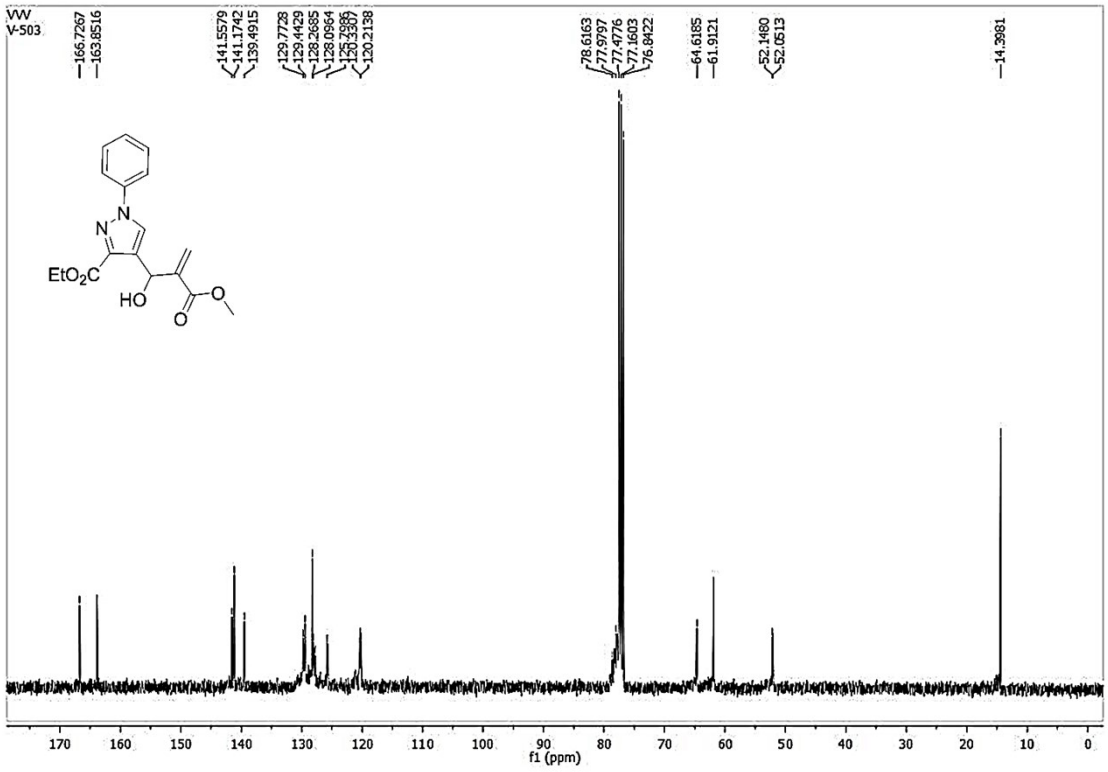


**Fig. S 26.** $^{13}$C-NMR of ethyl 4-(1-hydroxy-2-(methoxycarbonyl)allyl)-1-phenyl-1*H*-pyrazole-3-carboxylate **(7aB).**

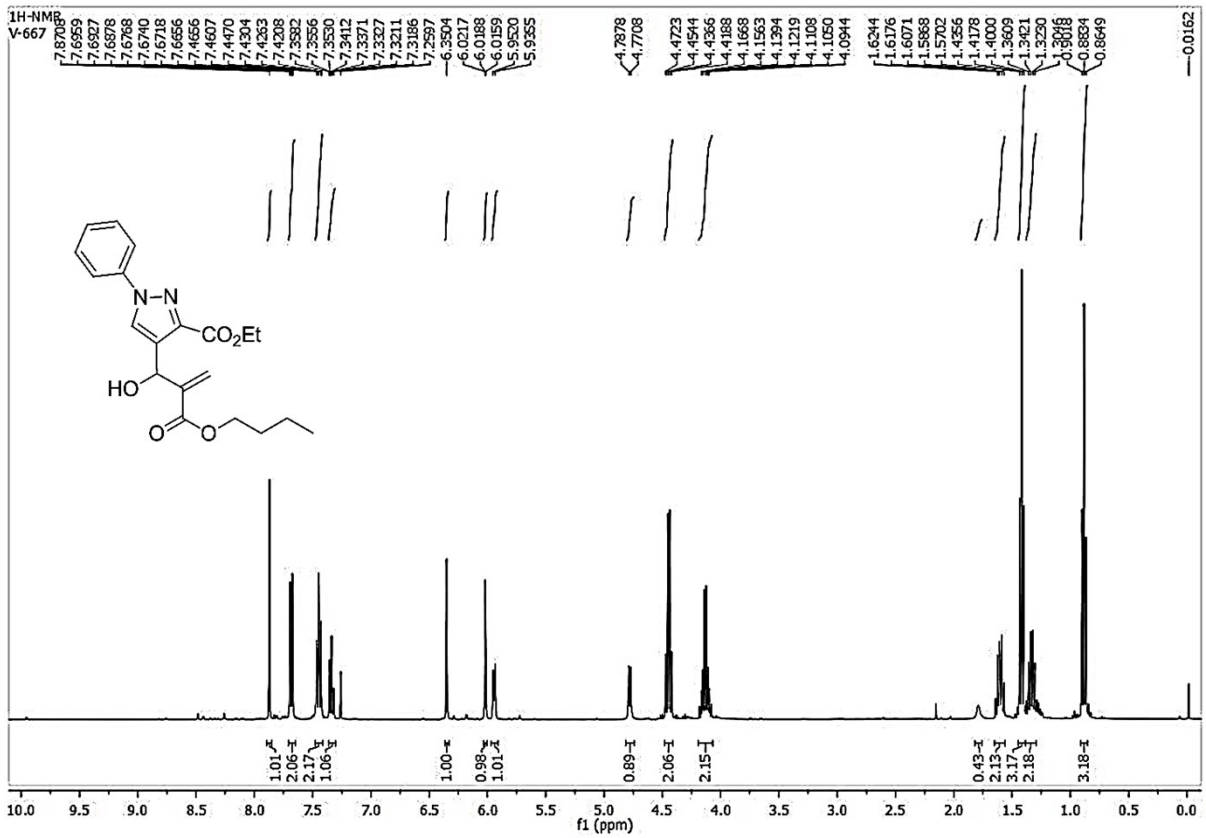


**Fig. S 27.** $^{1}$H-NMR of ethyl 4-(2-(butoxycarbonyl)-1-hydroxyallyl)-1-phenyl-1*H*-pyrazole-3-carboxylate **(7aC).**

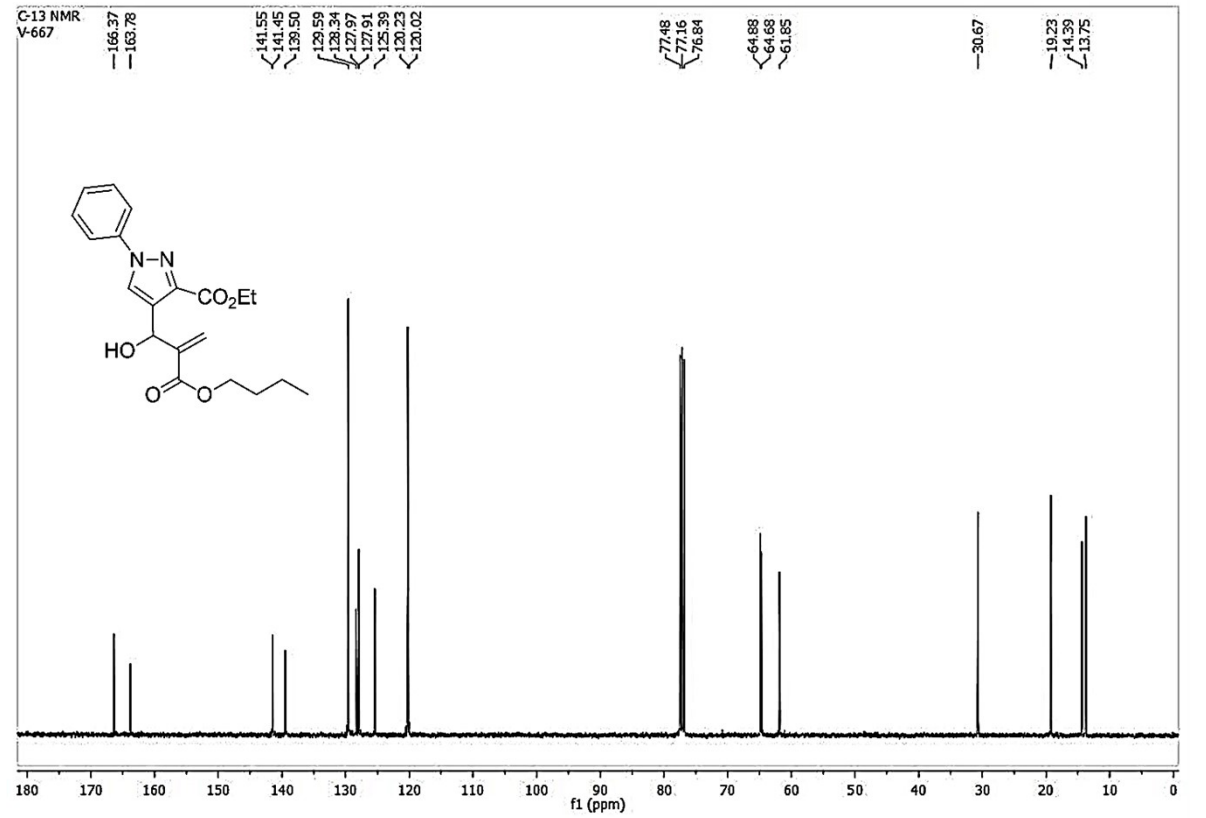


**Fig. S 28.** $^{13}$C-NMR of ethyl 4-(2-(butoxycarbonyl)-1-hydroxyallyl)-1-phenyl-1*H*-pyrazole-3-carboxylate **(7aC).**

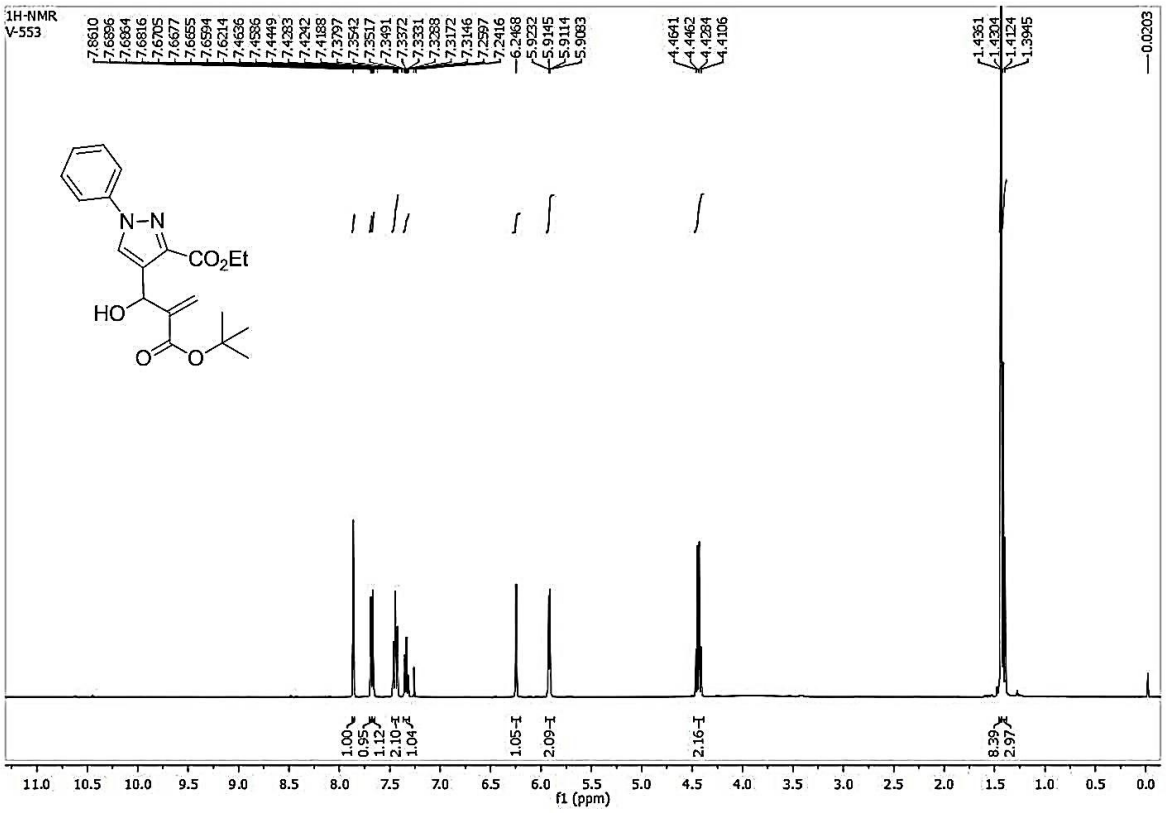


**Fig. S 29.** $^{1}$H-NMR of ethyl 4-(2-(*tert*-butoxycarbonyl)-1-hydroxyallyl)-1-phenyl-1*H*-pyrazole-3-carboxylate **(7aD).**

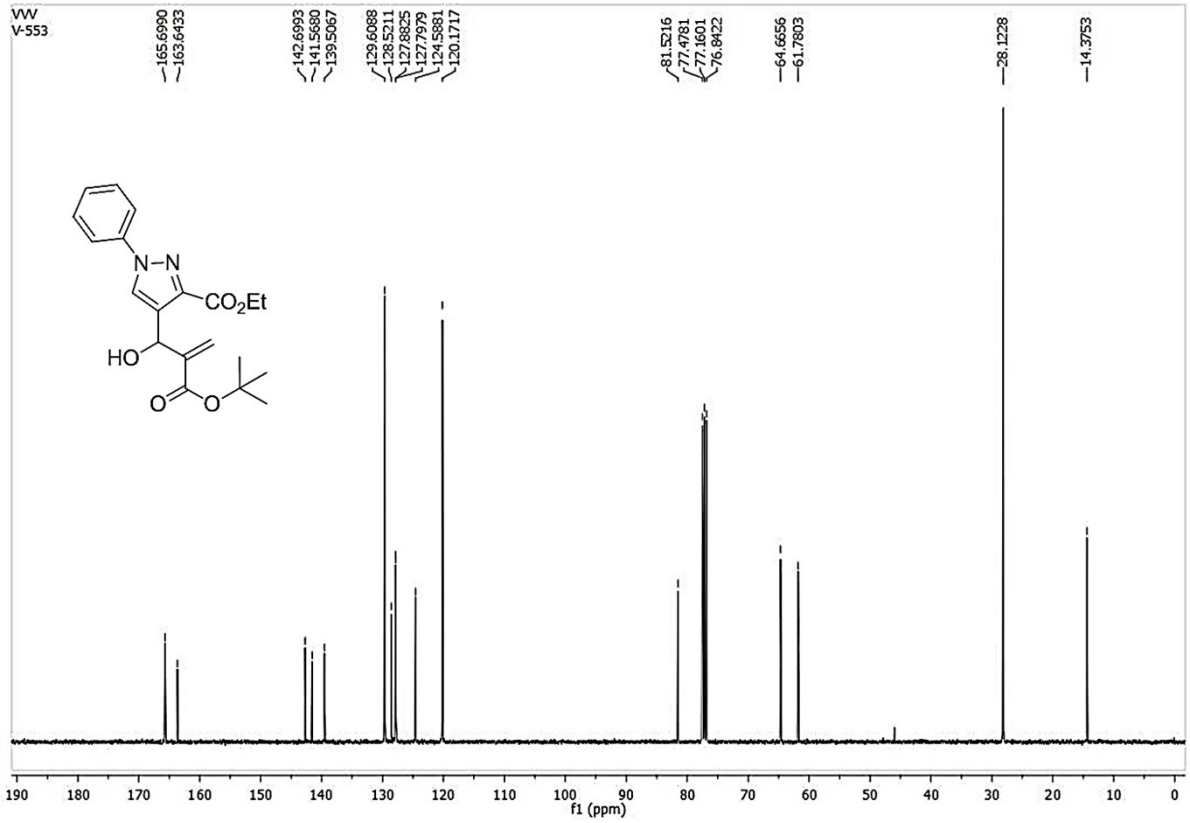


**Fig. S 30.** $^{13}$C-NMR of ethyl 4-(2-(*tert*-butoxycarbonyl)-1-hydroxyallyl)-1-phenyl-1*H*-pyrazole-3-carboxylate **(7aD).**

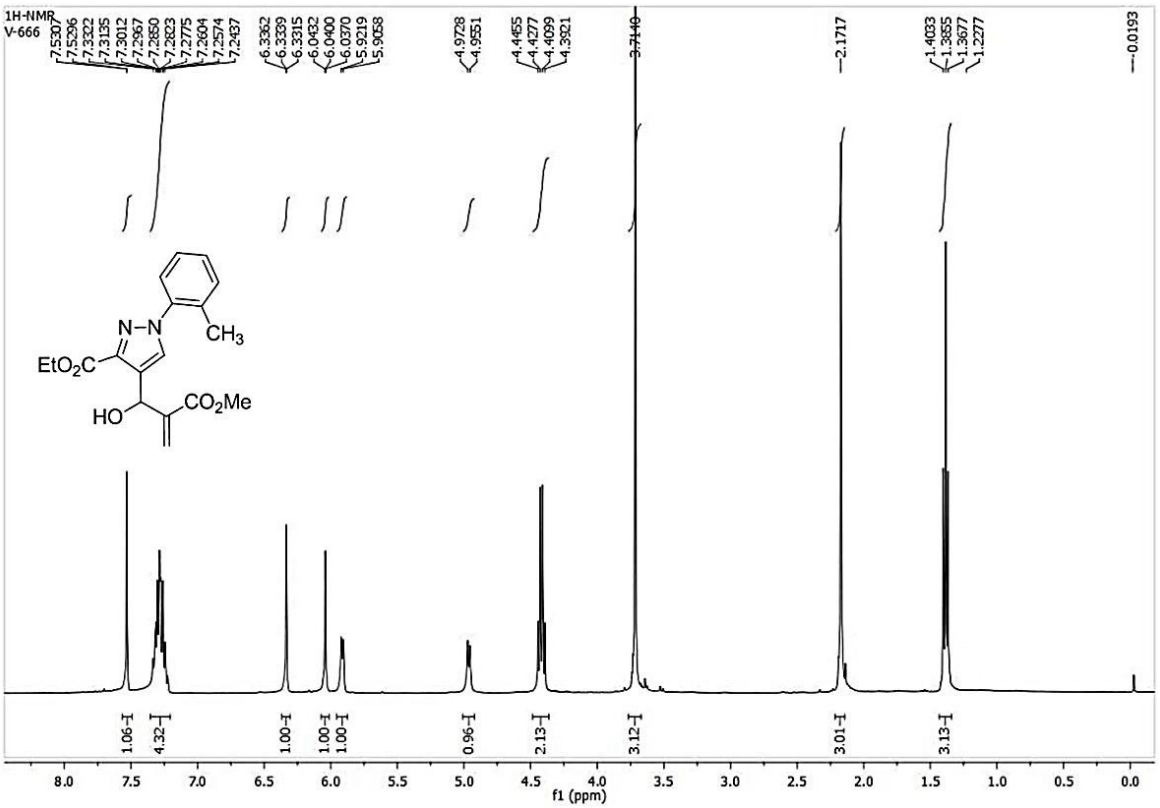


**Fig. S 33.** $^{1}$H-NMR of ethyl 4-(2-cyano-1-hydroxyallyl)-1-(*o*-tolyl)-1*H*-pyrazole-3-carboxylate **(7bB).**

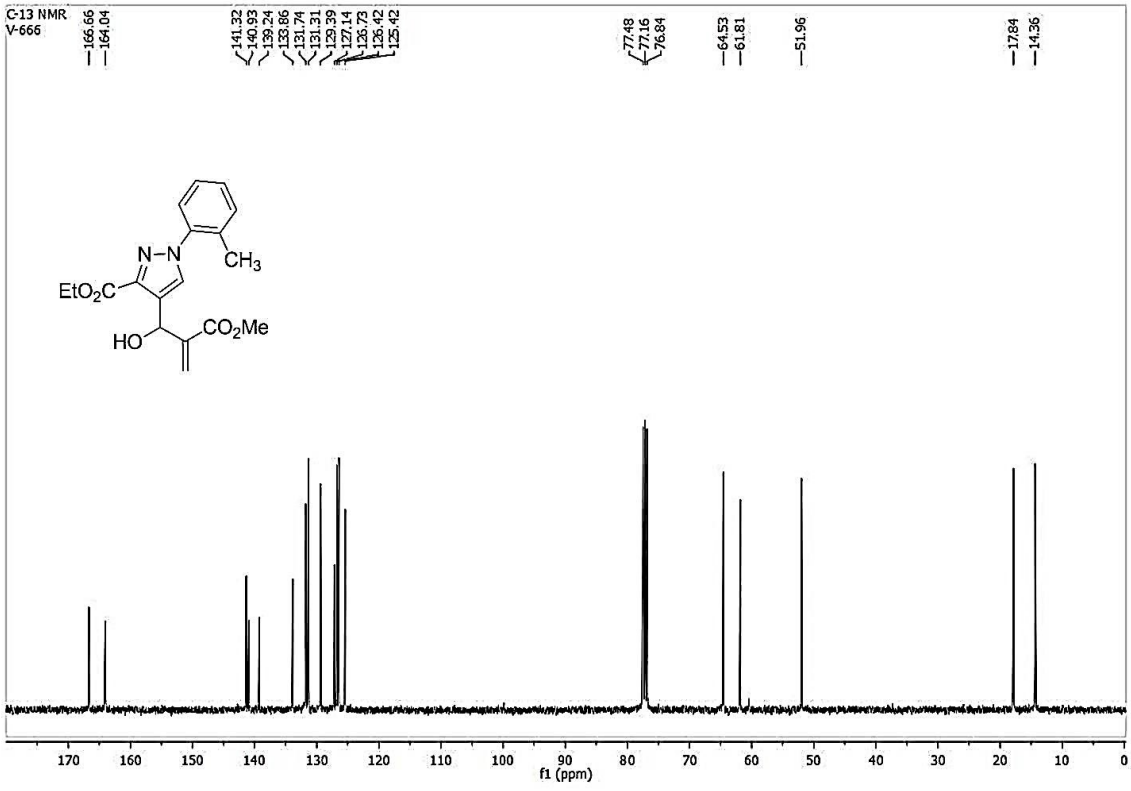


**Fig. S 34.** $^{13}$C-NMR of ethyl 4-(2-cyano-1-hydroxyallyl)-1-(*o*-tolyl)-1*H*-pyrazole-3-carboxylate **(7bB).**

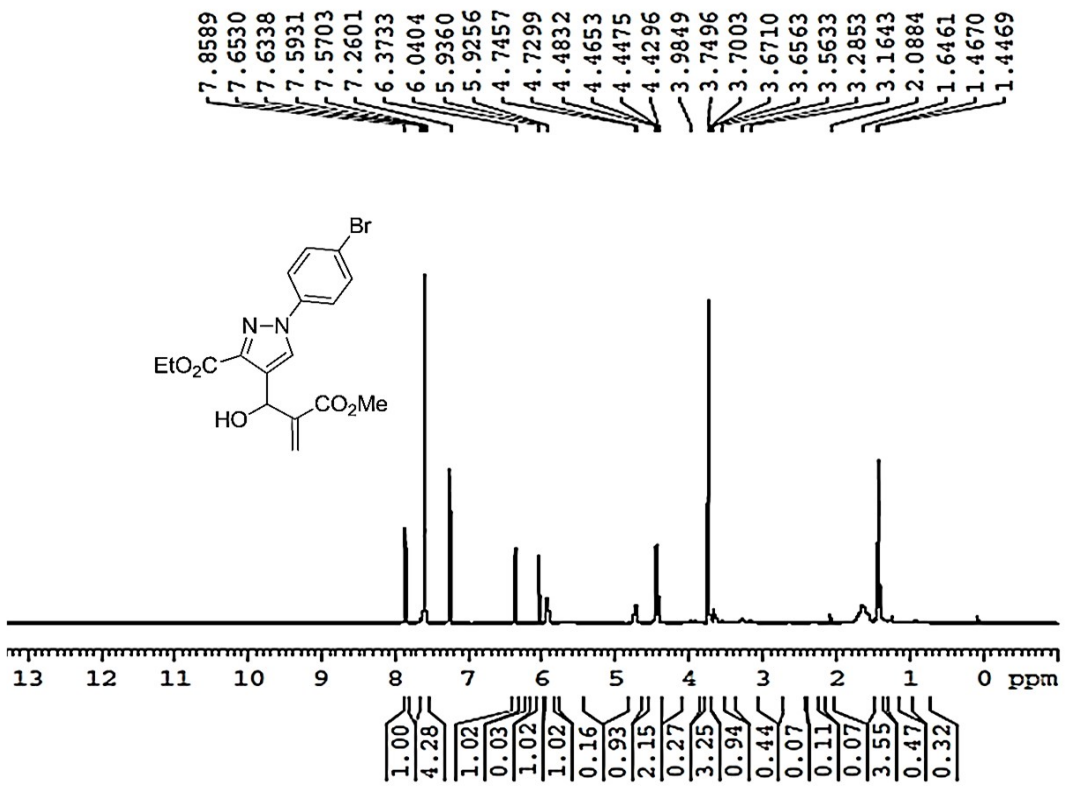


**Fig. S 35.** $^{1}$H-NMR of ethyl 1-(4-bromophenyl)-4-(1-hydroxy-2-(methoxycarbonyl)allyl)-1*H*-pyrazole-3-carboxylate **(7cB).**

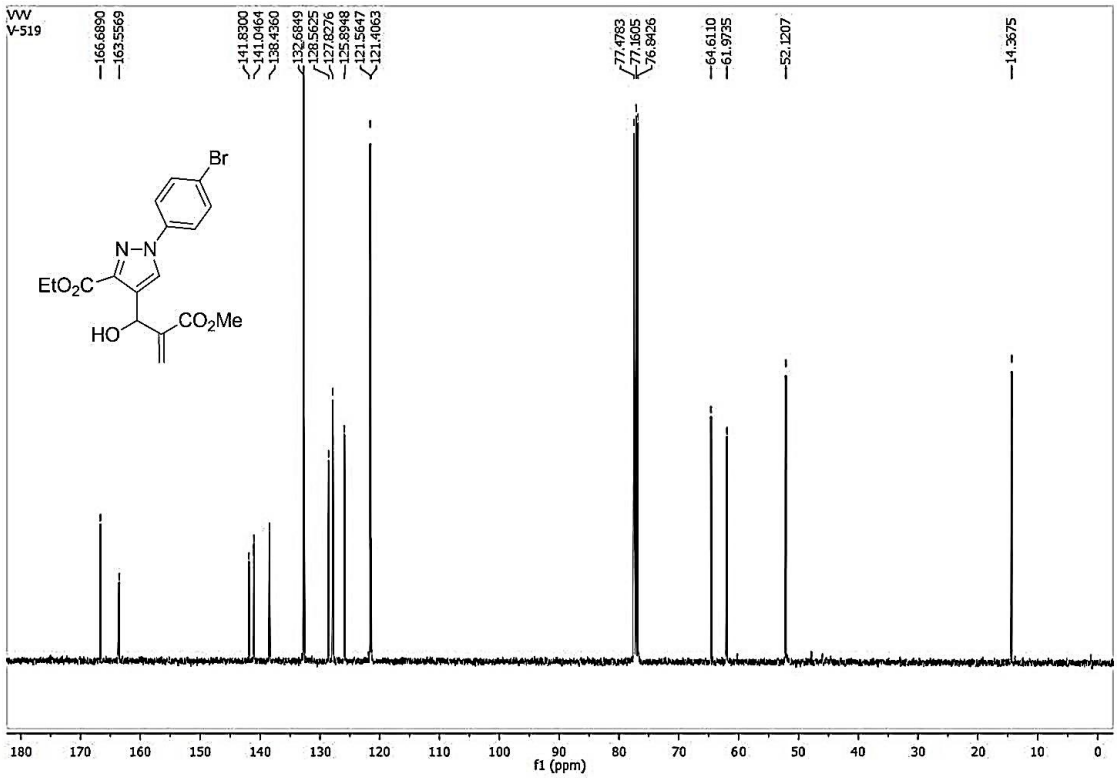


**Fig. S 36.** $^{13}$C-NMR of ethyl 1-(4-bromophenyl)-4-(1-hydroxy-2-(methoxycarbonyl)allyl)-1*H*-pyrazole-3-carboxylate **(7cB).**

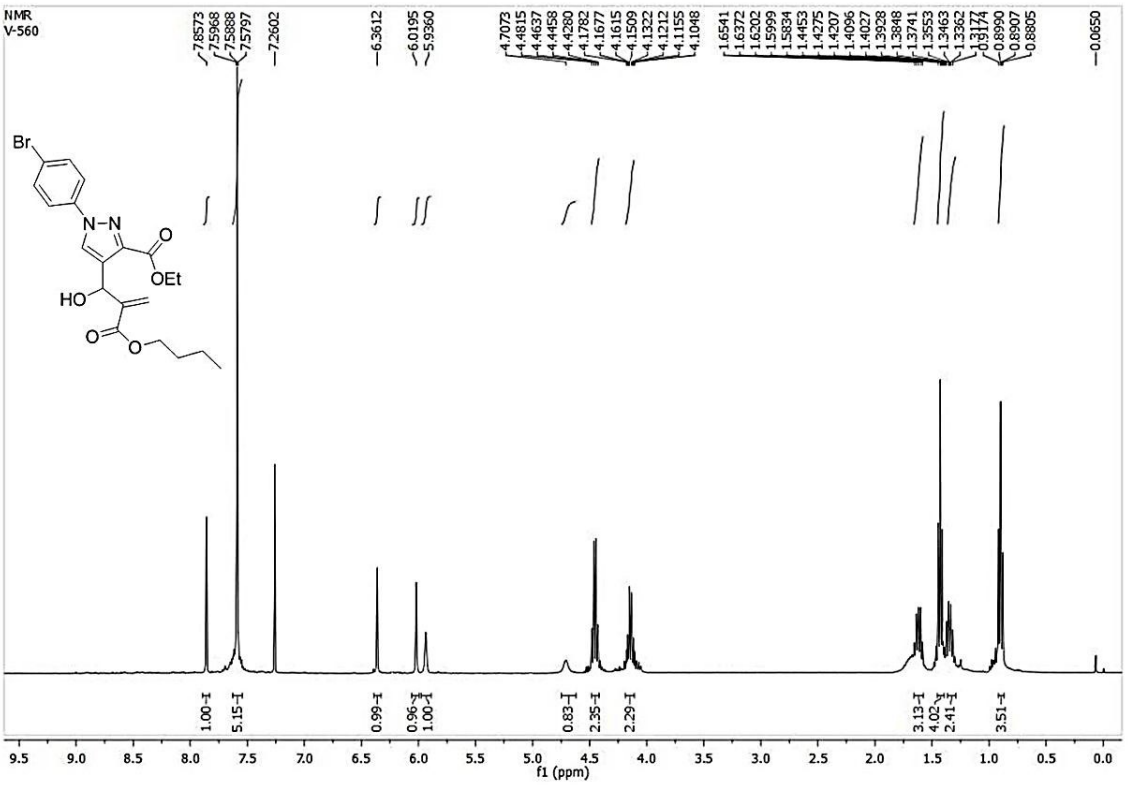


**Fig. S 37.** $^{1}$H-NMR of ethyl 1-(4-bromophenyl)-4-(2-(butoxycarbonyl)-1-hydroxyallyl)-1*H*-pyrazole-3-carboxylate **(7cC).**

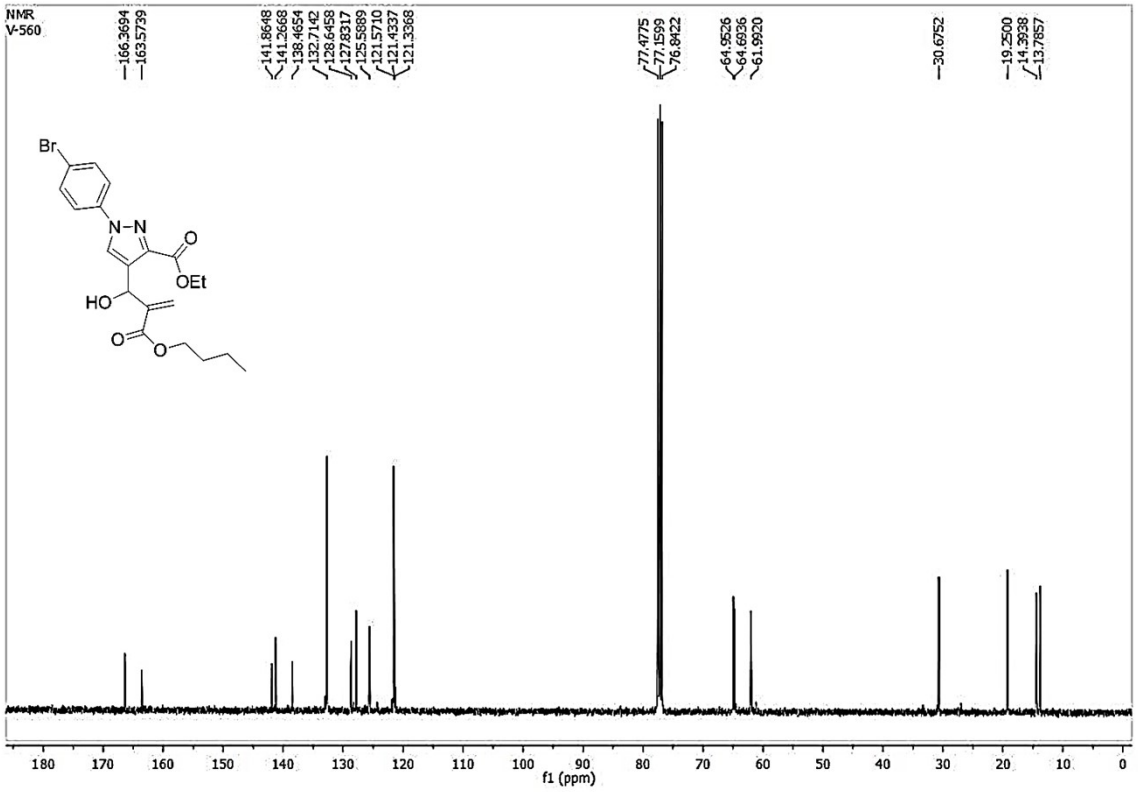


**Fig. S 38.** $^{13}$C-NMR of ethyl 1-(4-bromophenyl)-4-(2-(butoxycarbonyl)-1-hydroxyallyl)-1*H*-pyrazole-3-carboxylate **(7cC).**

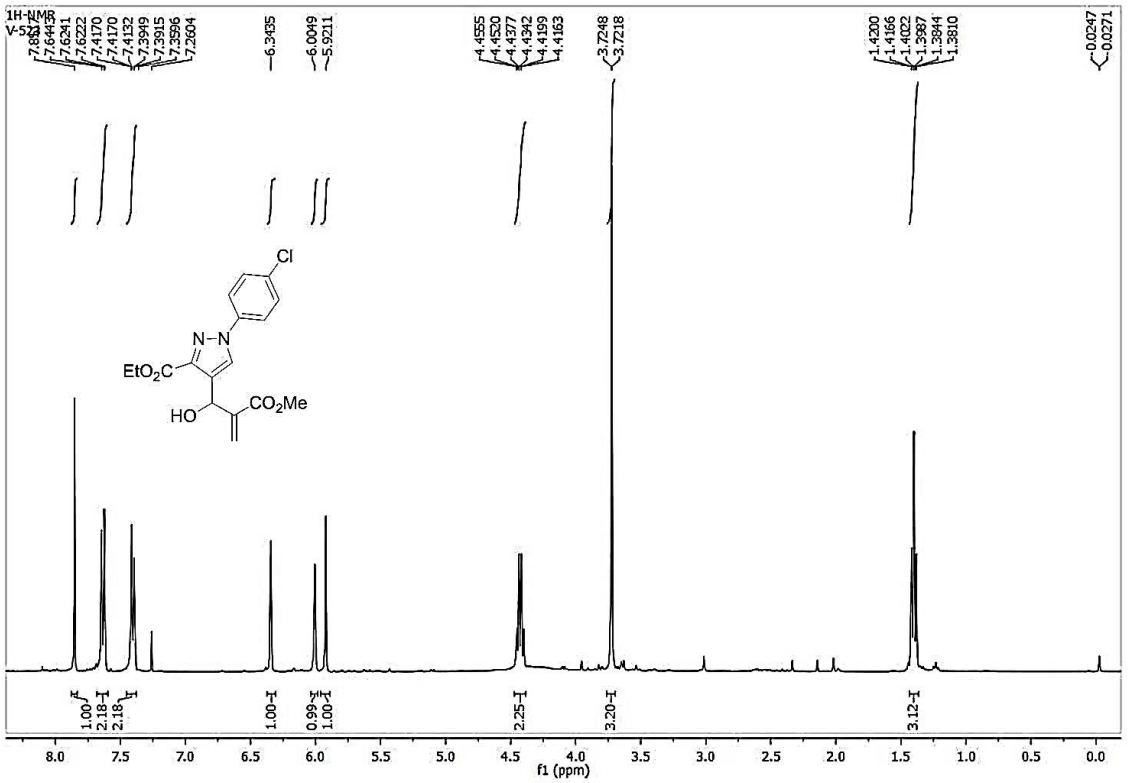


**Fig. S 39.** $^{1}$H-NMR of ethyl 1-(4-chlorophenyl)-4-(1-hydroxy-2-(methoxycarbonyl)allyl)-1*H*-pyrazole-3-carboxylate **(7dB).**

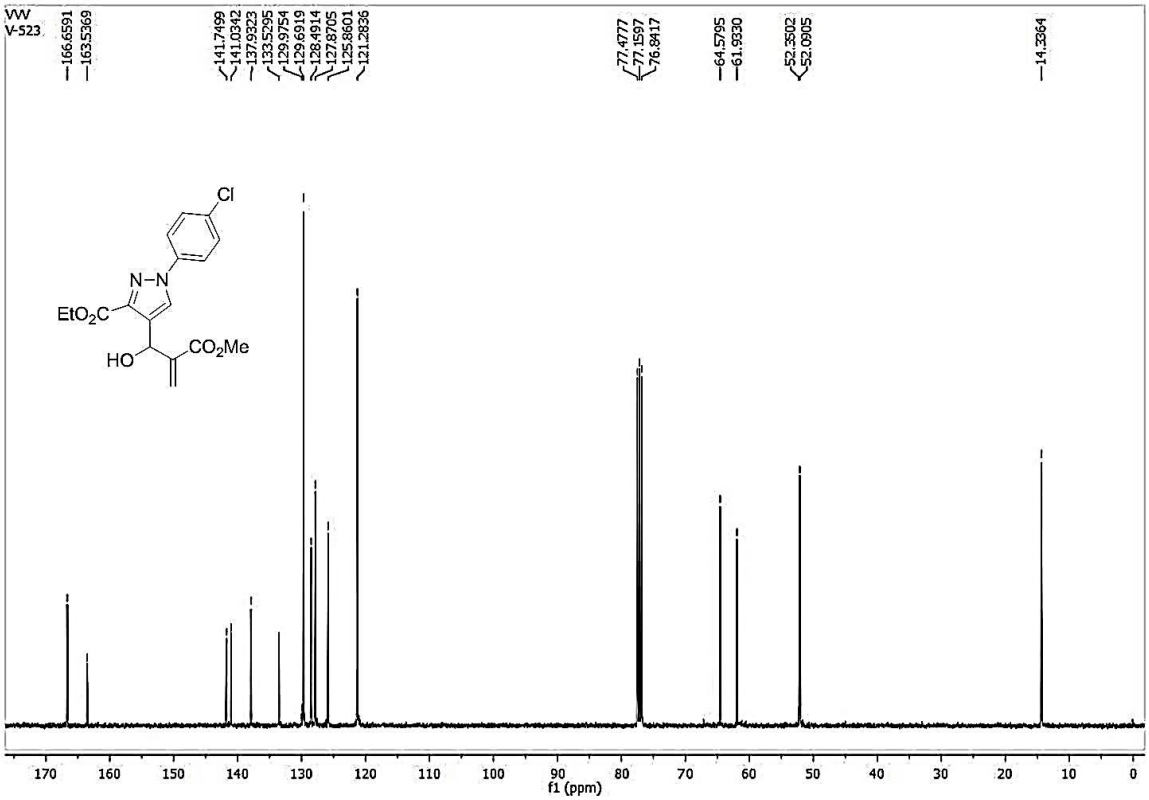


**Fig. S 40**. $^{13}$C-NMR of ethyl 1-(4-chlorophenyl)-4-(1-hydroxy-2-(methoxycarbonyl)allyl)-1*H*-pyrazole-3-carboxylate **(7dB).**

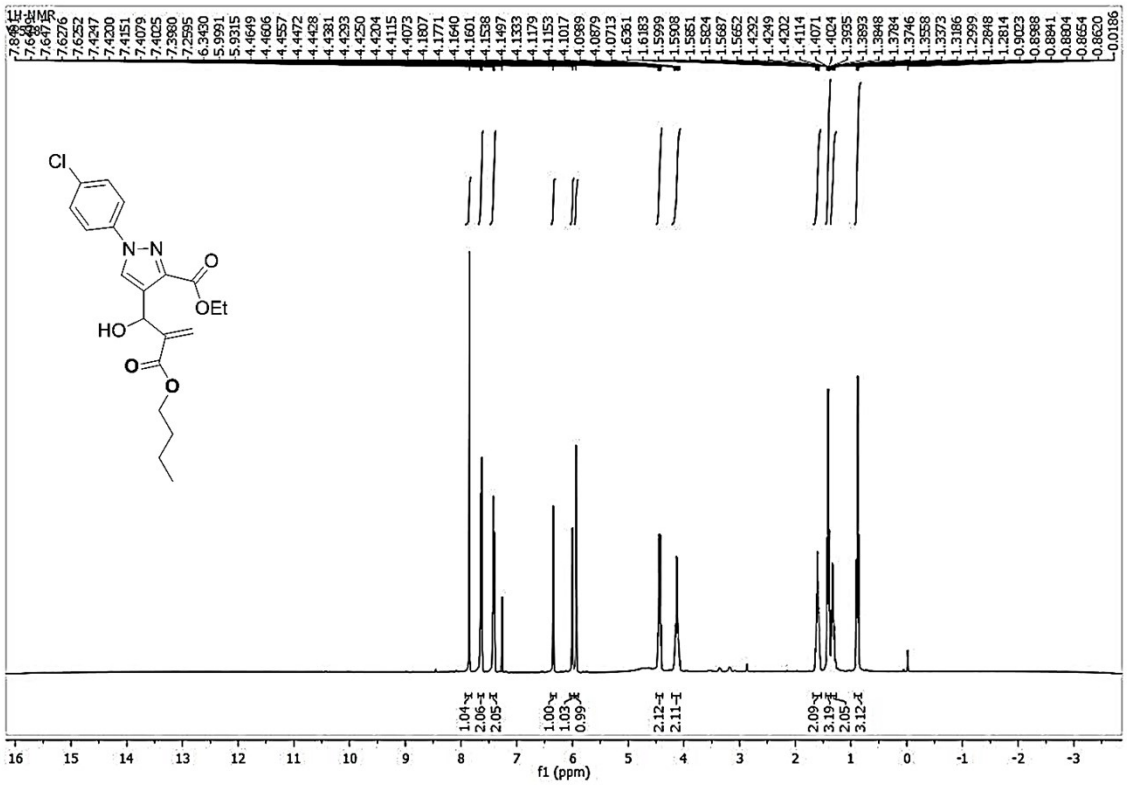


**Fig. S 41.** $^{1}$H-NMR of ethyl 4-(2-(butoxycarbonyl)-1-hydroxyallyl)-1-(4-chlorophenyl)-1*H*-pyrazole-3-carboxylate **(7dC).**

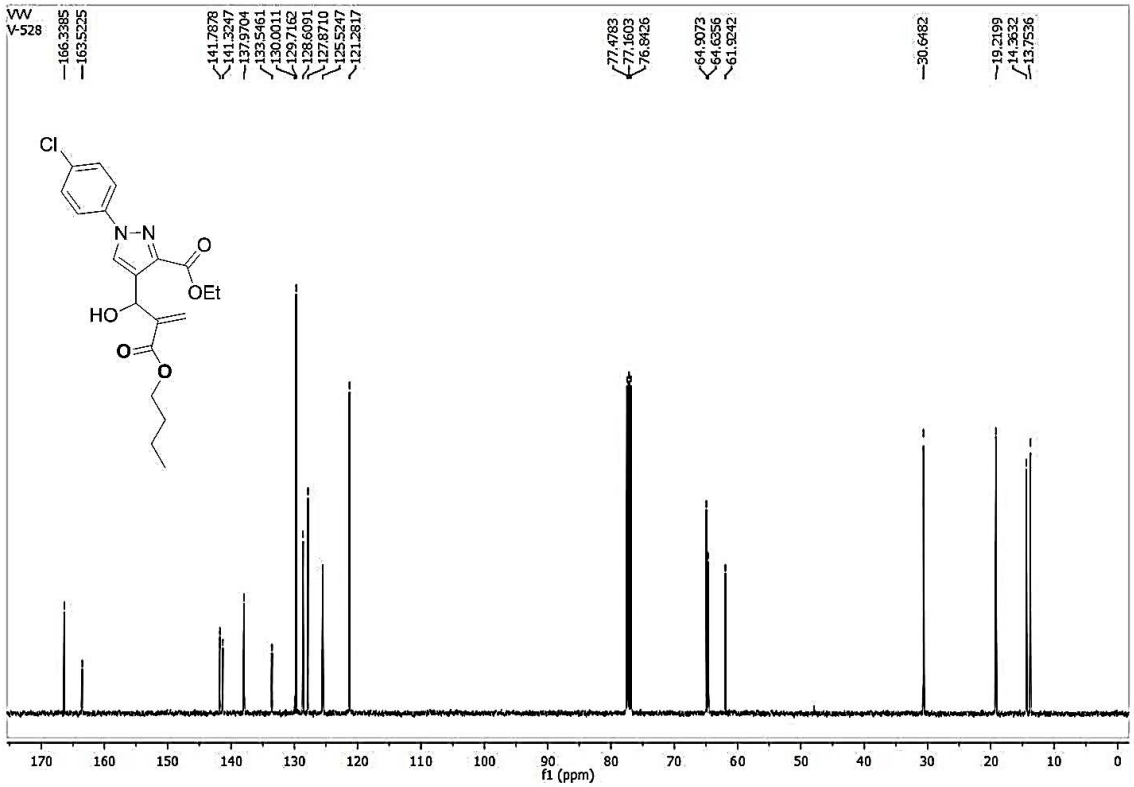


**Fig. S 42.** $^{13}$C-NMR of ethyl 4-(2-(butoxycarbonyl)-1-hydroxyallyl)-1-(4-chlorophenyl)-1*H*-pyrazole-3-carboxylate **(7dC).**

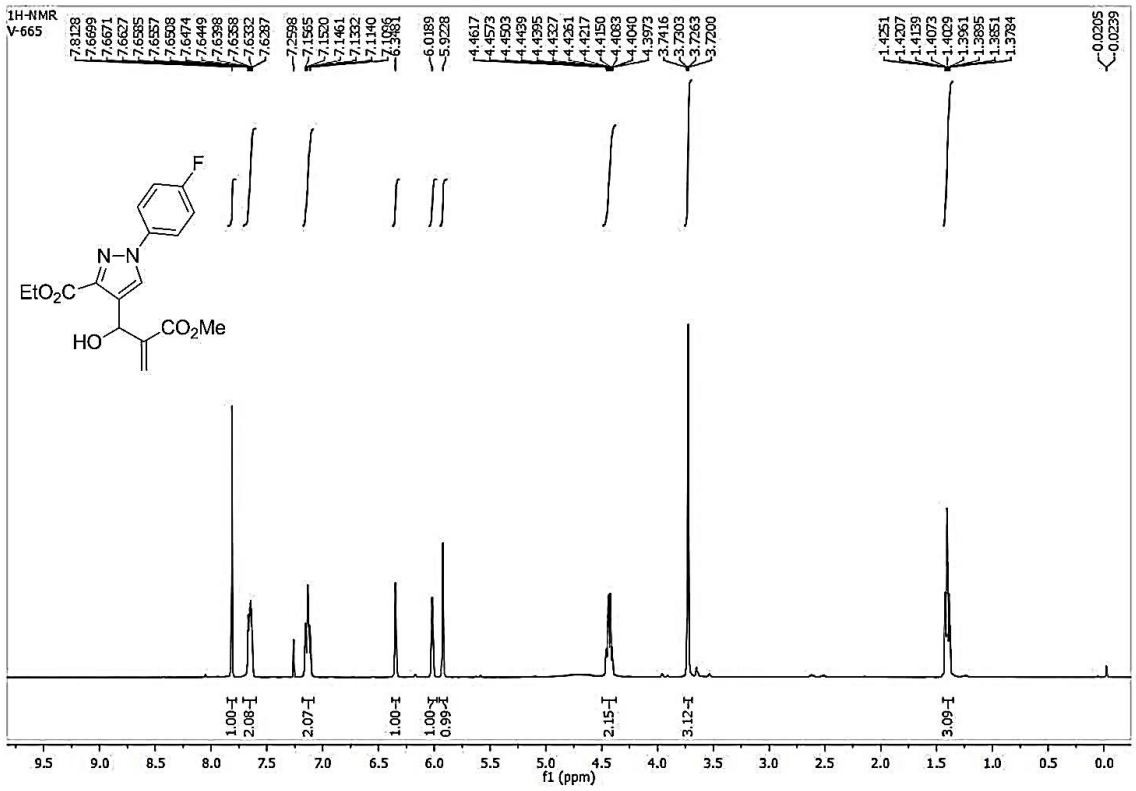


**Fig. S 43.** $^{1}$H-NMR of ethyl 1-(4-fluorophenyl)-4-(1-hydroxy-2-(methoxycarbonyl)allyl)-1*H*-pyrazole-3-carboxylate **(7eB).**

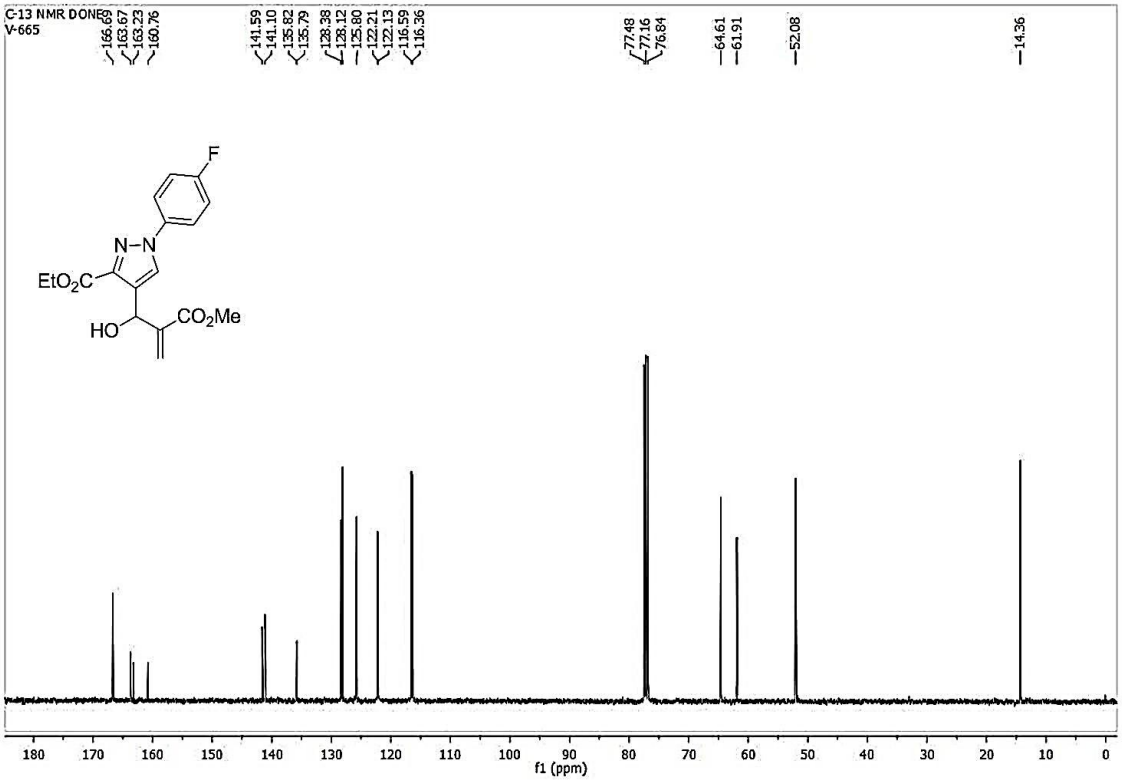


**Fig. S 44.** $^{13}$C-NMR of ethyl 1-(4-fluorophenyl)-4-(1-hydroxy-2-(methoxycarbonyl)allyl)-1*H*-pyrazole-3-carboxylate **(7eB).**

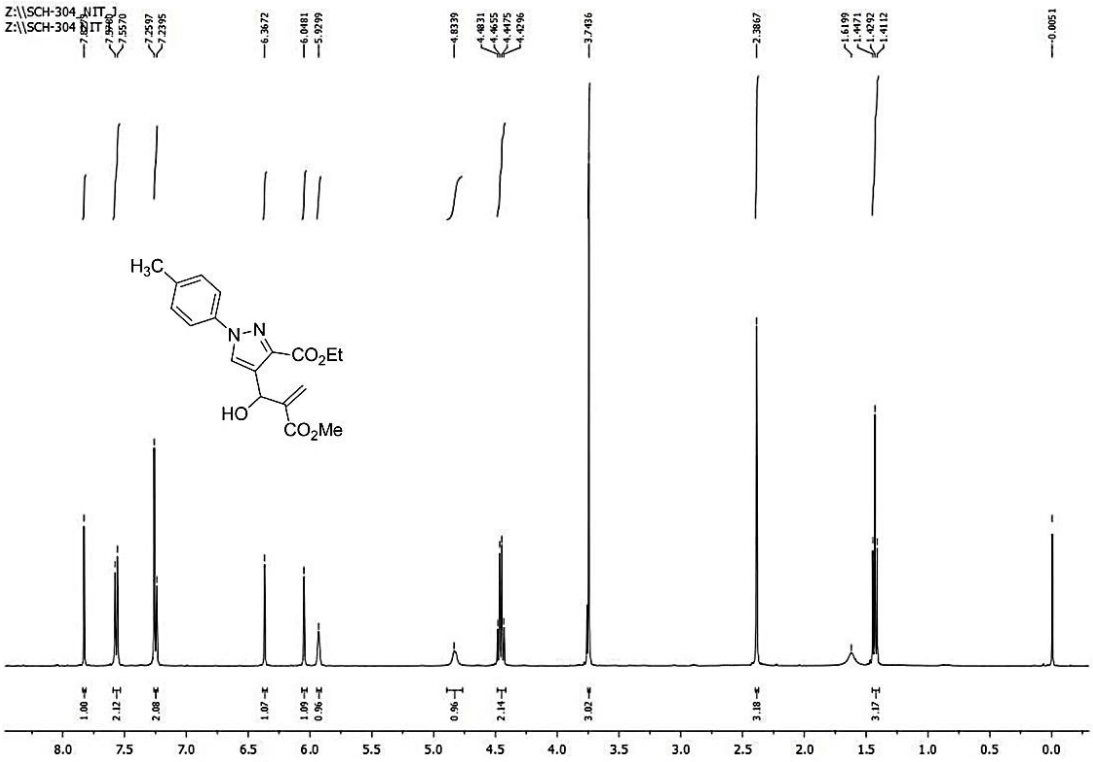


**Fig. S 45. $^{1}$H-NMR of** ethyl 4-(1-hydroxy-2-(methoxycarbonyl)allyl)-1-(p-tolyl)-1H-pyrazole-3-carboxylate **(7Fb).**

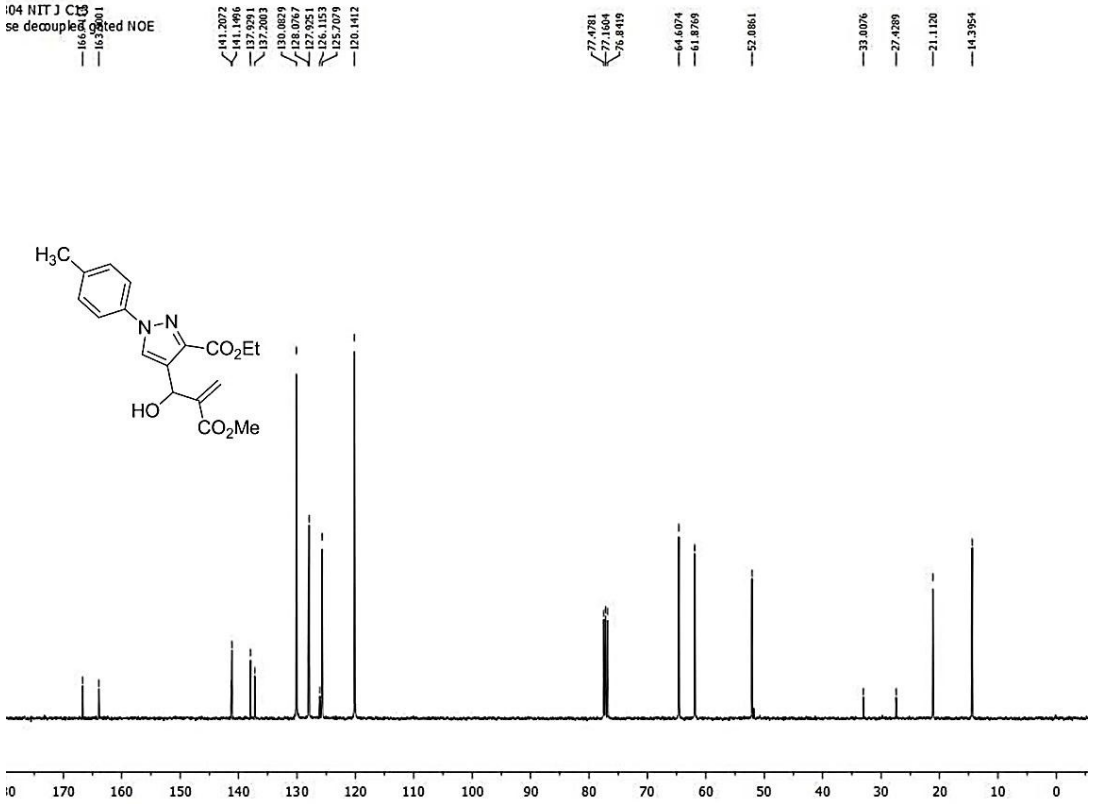


**Fig. S 46.** $^{13}$C-NMR of ethyl 4-(1-hydroxy-2-(methoxycarbonyl)allyl)-1-(p-tolyl)-1H-pyrazole-3-carboxylate **(7Fb).**

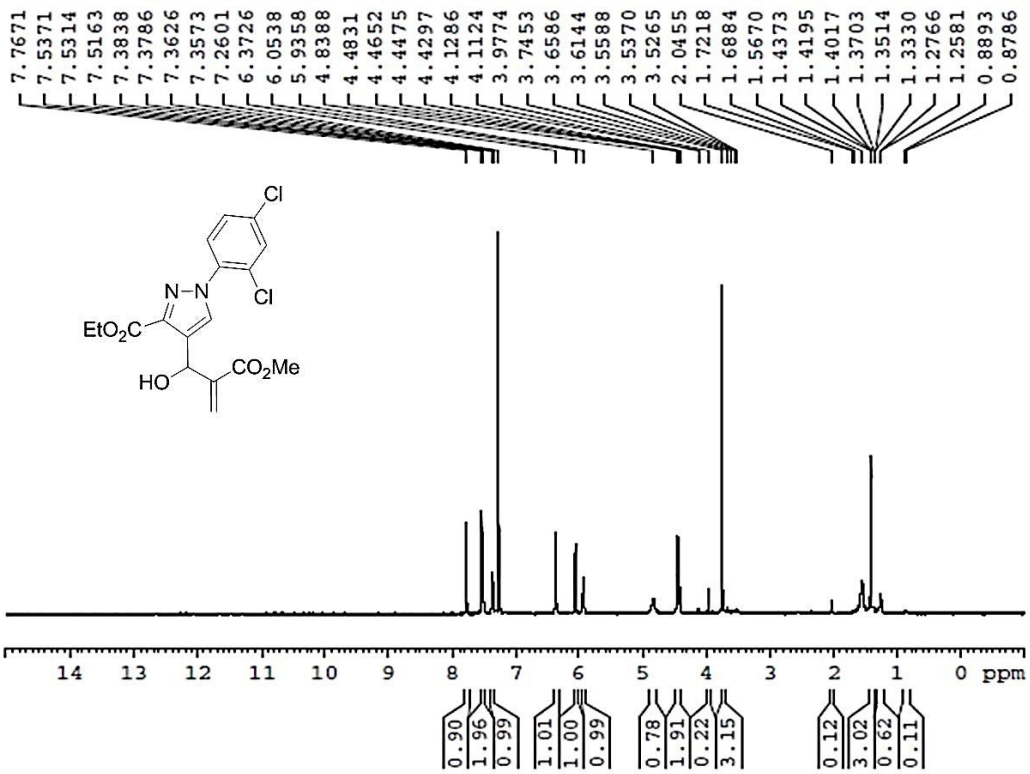


**Fig. S 47.** [1]H-NMR of ethyl 1-(2,4-dichlorophenyl)-4-(1-hydroxy-2-(methoxycarbonyl)allyl)-1*H*-pyrazole-3-carboxylate **(7gB).**

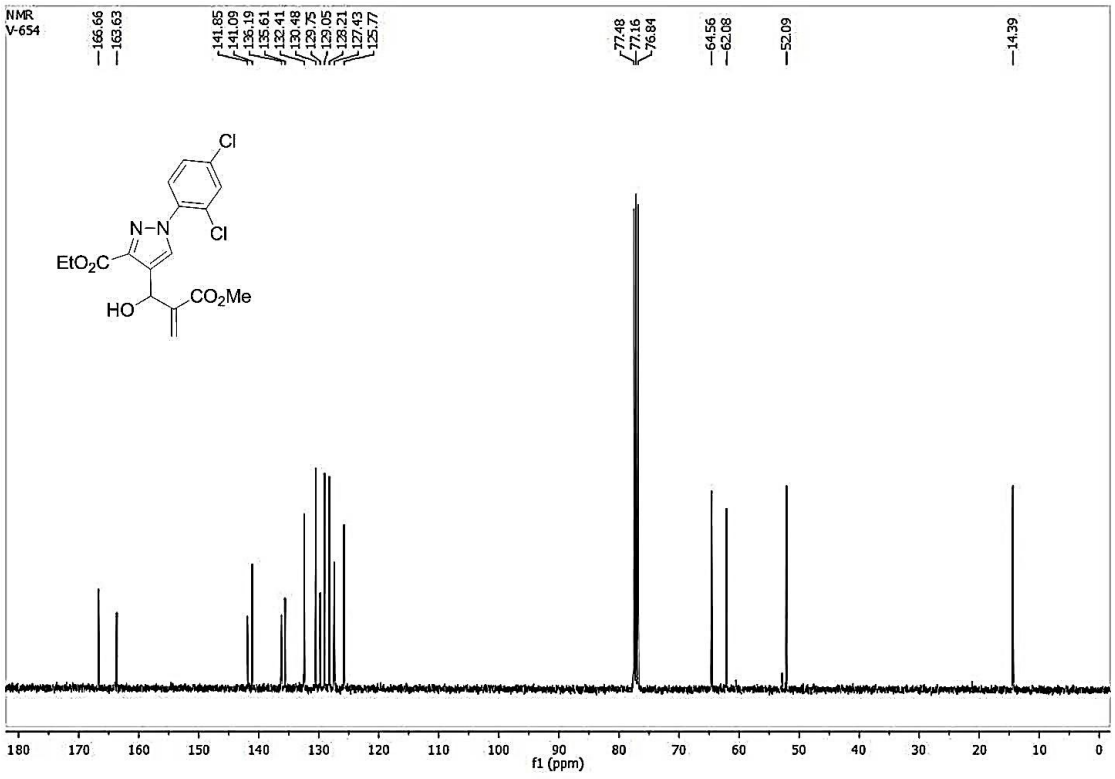


**Fig. S 48.** [13]C-NMR of ethyl 1-(2,4-dichlorophenyl)-4-(1-hydroxy-2-(methoxycarbonyl)allyl)-1*H*-pyrazole-3-carboxylate **(7gB).**

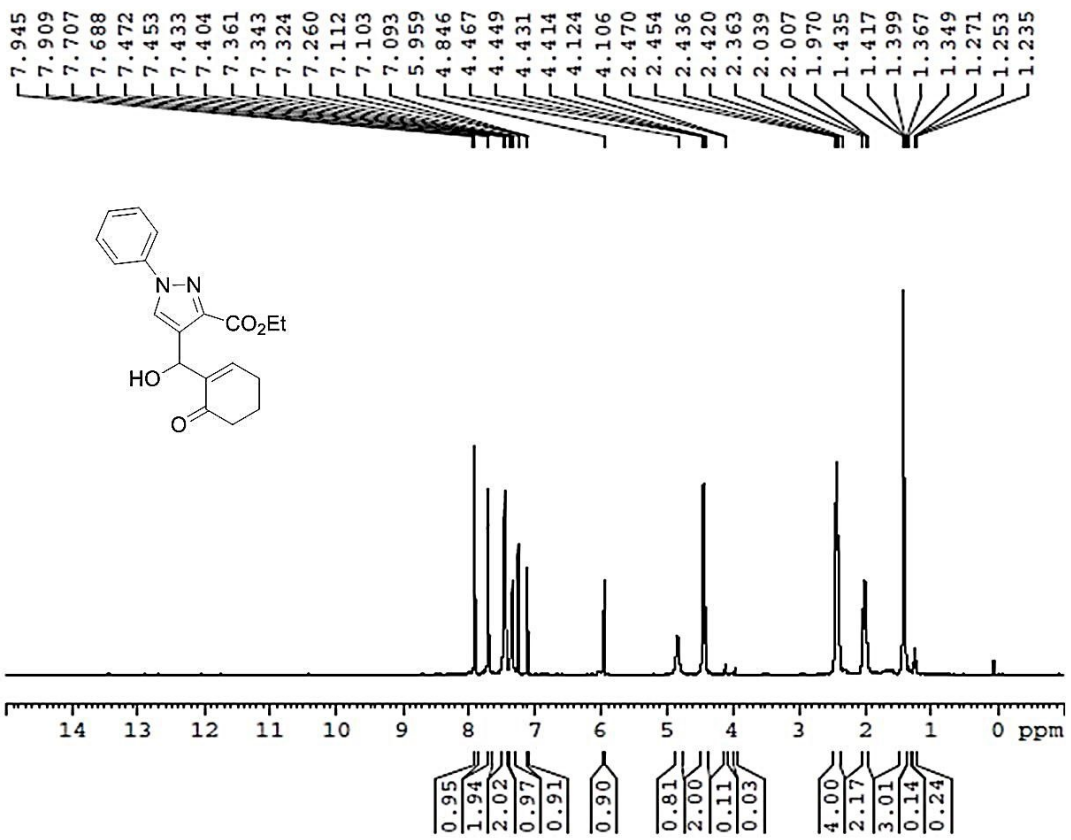


**Fig. S 31.** [1]H-NMR of ethyl 4-(hydroxy(6-oxocyclohex-1-en-1-yl)methyl)-1-phenyl-1*H*-pyrazole-3-carboxylate **(9aE).**

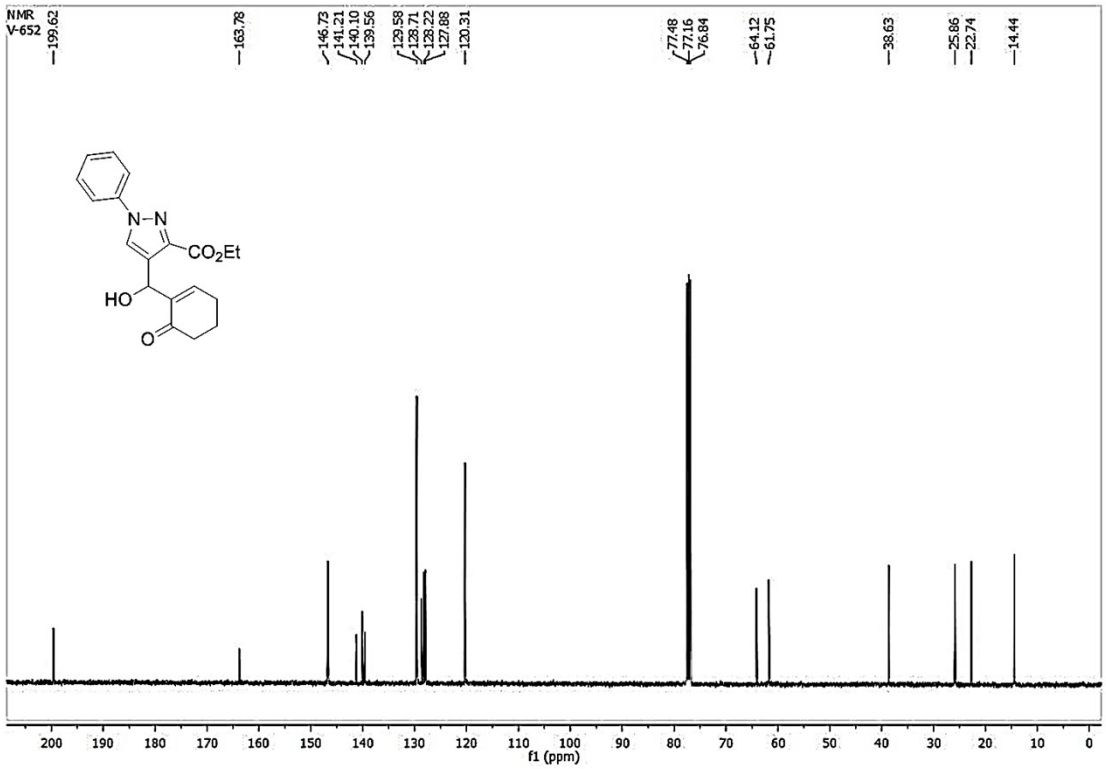


**Fig. S 32.** [13]C-NMR of ethyl 4-(hydroxy(6-oxocyclohex-1-en-1-yl)methyl)-1-phenyl-1*H*-pyrazole-3-carboxylate **(9aE).**

**VI.** $^{1}$H- and $^{13}$C- NMR spectra of the new pyrazole MBH acetates **8**

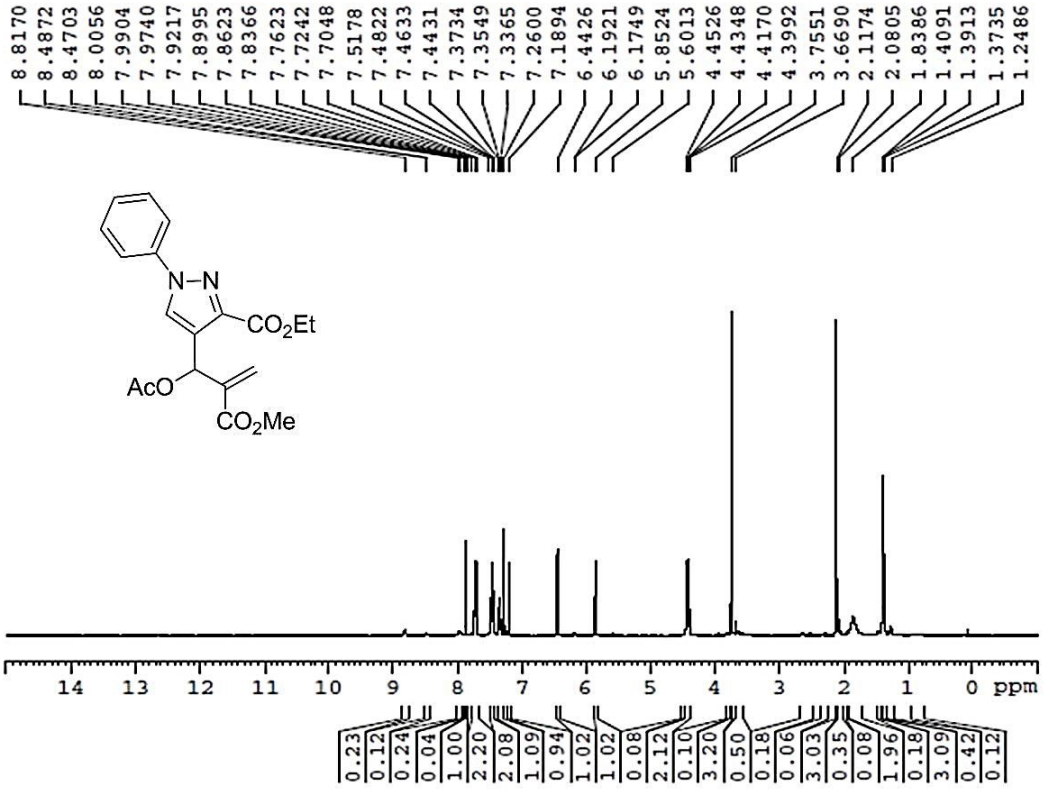


**Fig. S 49.** $^{1}$H-NMR of ethyl 4-(1-acetoxy-2-(methoxycarbonyl)allyl)-1-phenyl-1*H*-pyrazole-3-carboxylate **(8aB).**

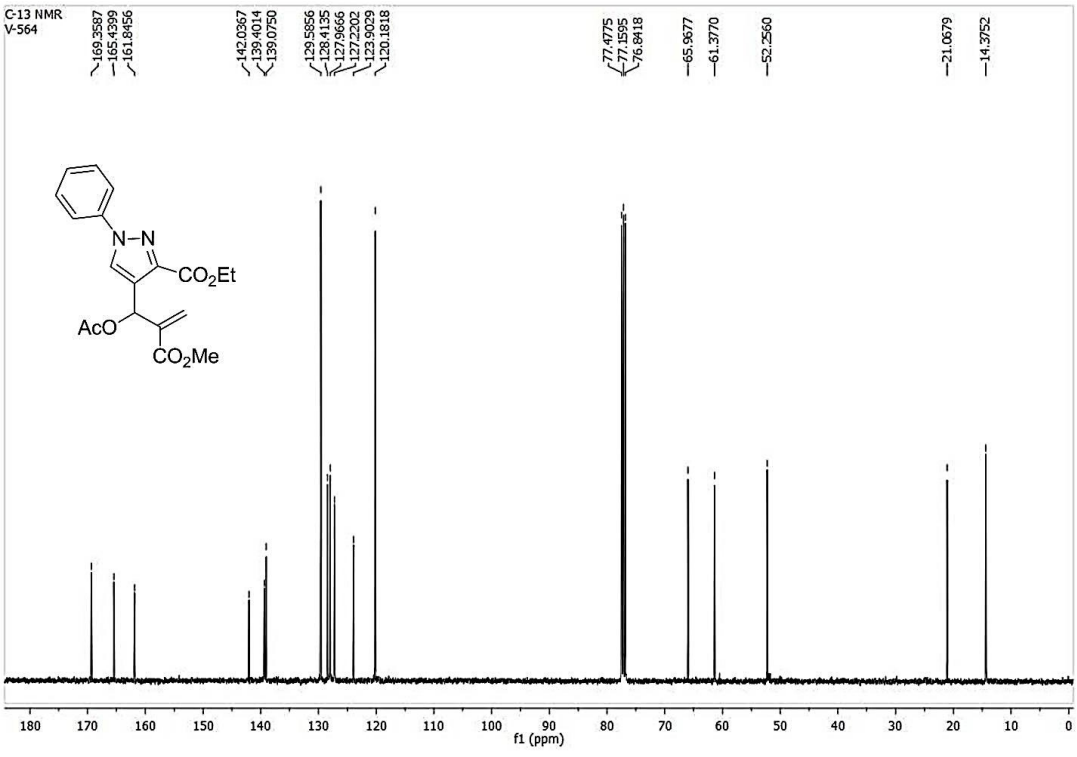


**Fig. S 50.** $^{13}$C-NMR of ethyl 4-(1-acetoxy-2-(methoxycarbonyl)allyl)-1-phenyl-1*H*-pyrazole-3-carboxylate **(8aB).**

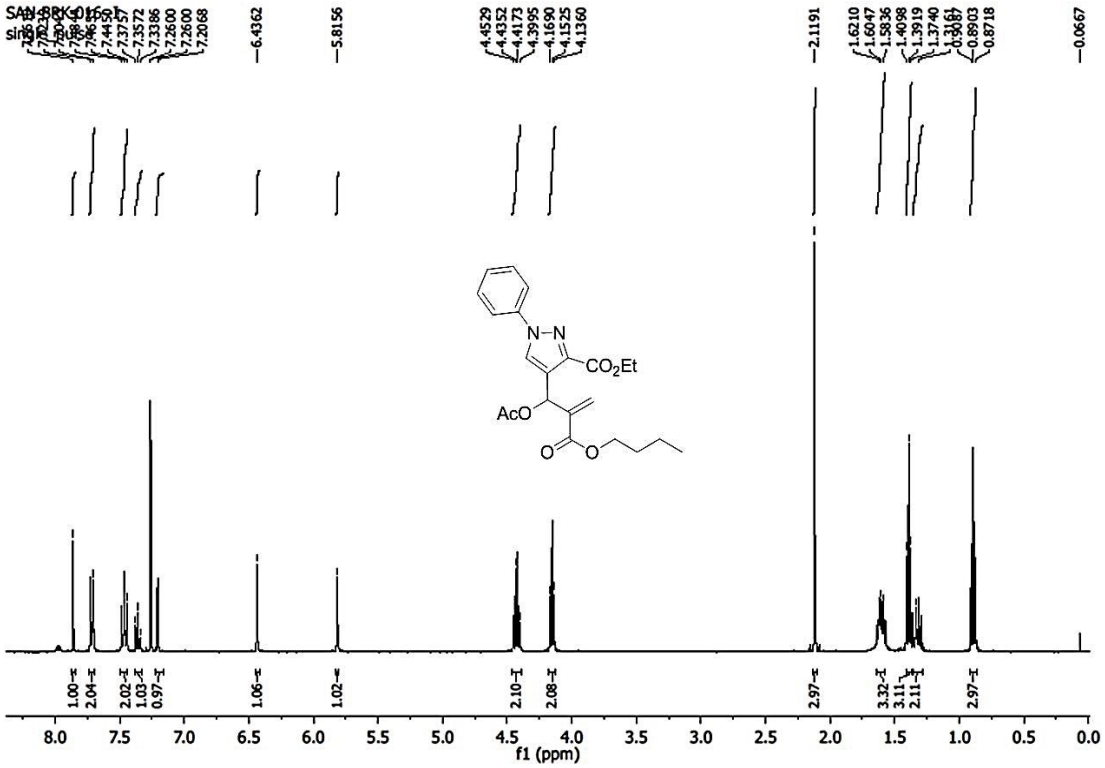


**Fig. S 51.** [1]H-NMR of ethyl 4-(1-acetoxy-2-(butoxycarbonyl)allyl)-1-phenyl-1*H*-pyrazole-3-carboxylate **(8aC).**

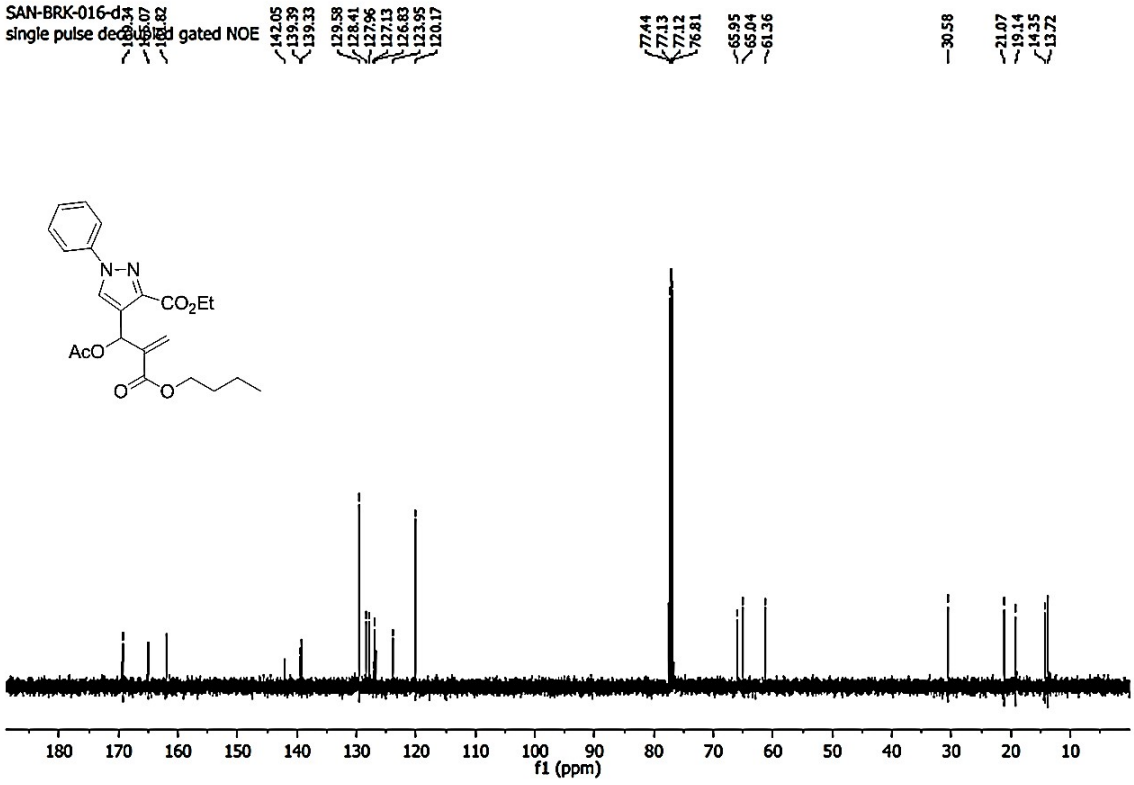


**Fig. S 52.** [13]C-NMR of ethyl 4-(1-acetoxy-2-(butoxycarbonyl)allyl)-1-phenyl-1*H*-pyrazole-3-carboxylate **(8aC).**

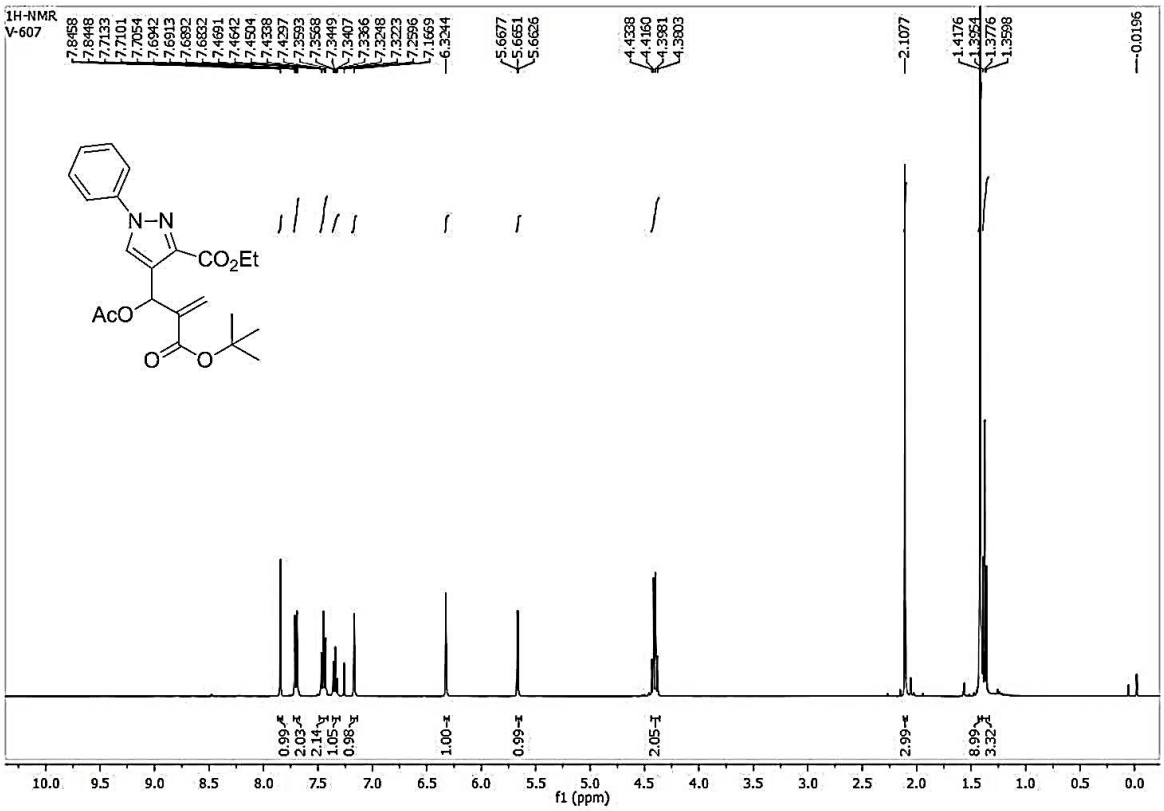


**Fig. S 53.** $^{1}$H-NMR of ethyl 4-(1-acetoxy-2-(*tert*-butoxycarbonyl)allyl)-1-phenyl-1*H*-pyrazole-3-carboxylate **(8aD).**

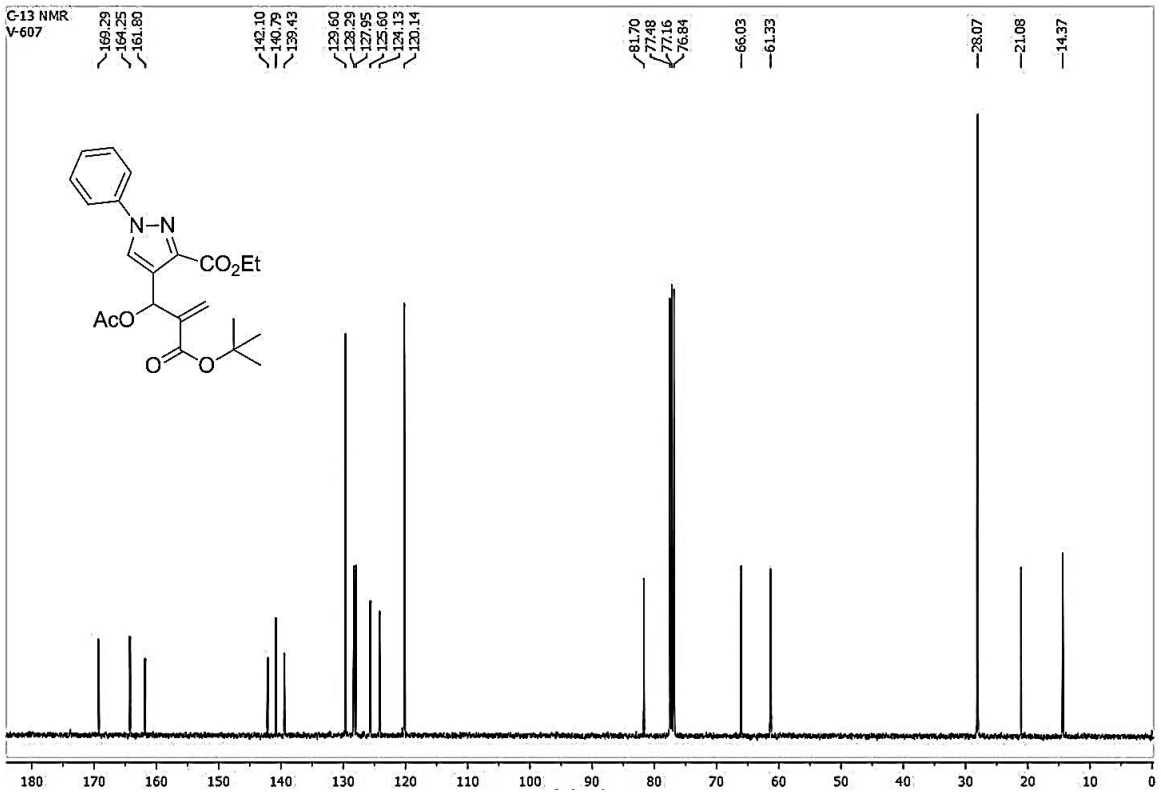


**Fig. S 54.** $^{13}$C-NMR of ethyl 4-(1-acetoxy-2-(*tert*-butoxycarbonyl)allyl)-1-phenyl-1*H*-pyrazole-3-carboxylate **(8aD).**

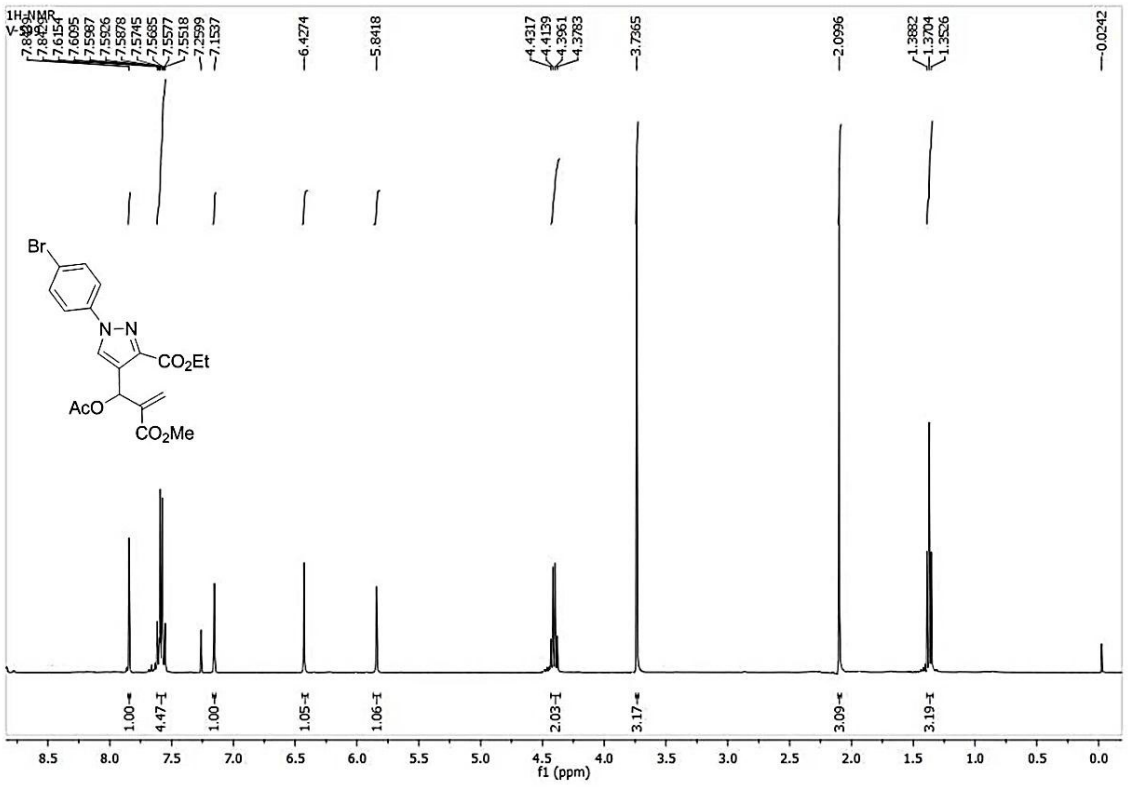


**Fig. S 55.** $^{1}$H-NMR of ethyl 4-(1-acetoxy-2-(methoxycarbonyl)allyl)-1-(4-bromophenyl)-1*H*-pyrazole-3-carboxylate **(8cB).**

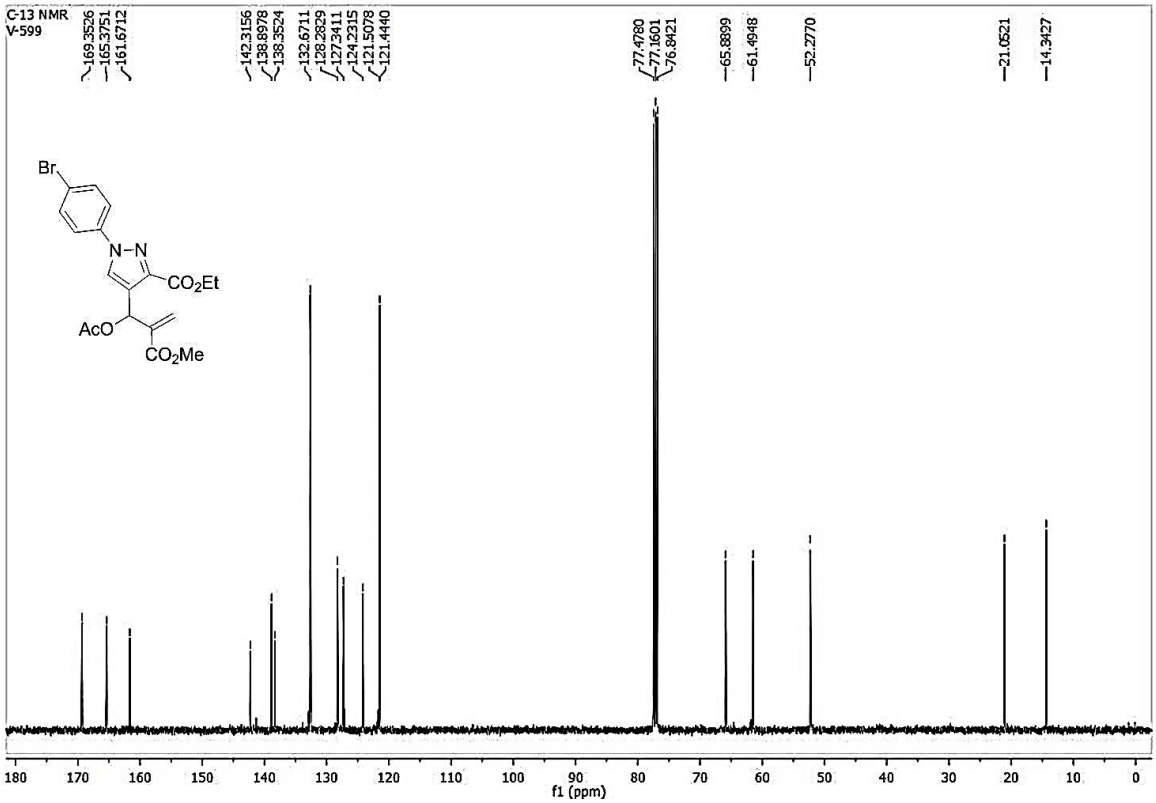


**Fig. S 56.** $^{13}$C-NMR of ethyl 4-(1-acetoxy-2-(methoxycarbonyl)allyl)-1-(4-bromophenyl)-1*H*-pyrazole-3-carboxylate **(8cB).**

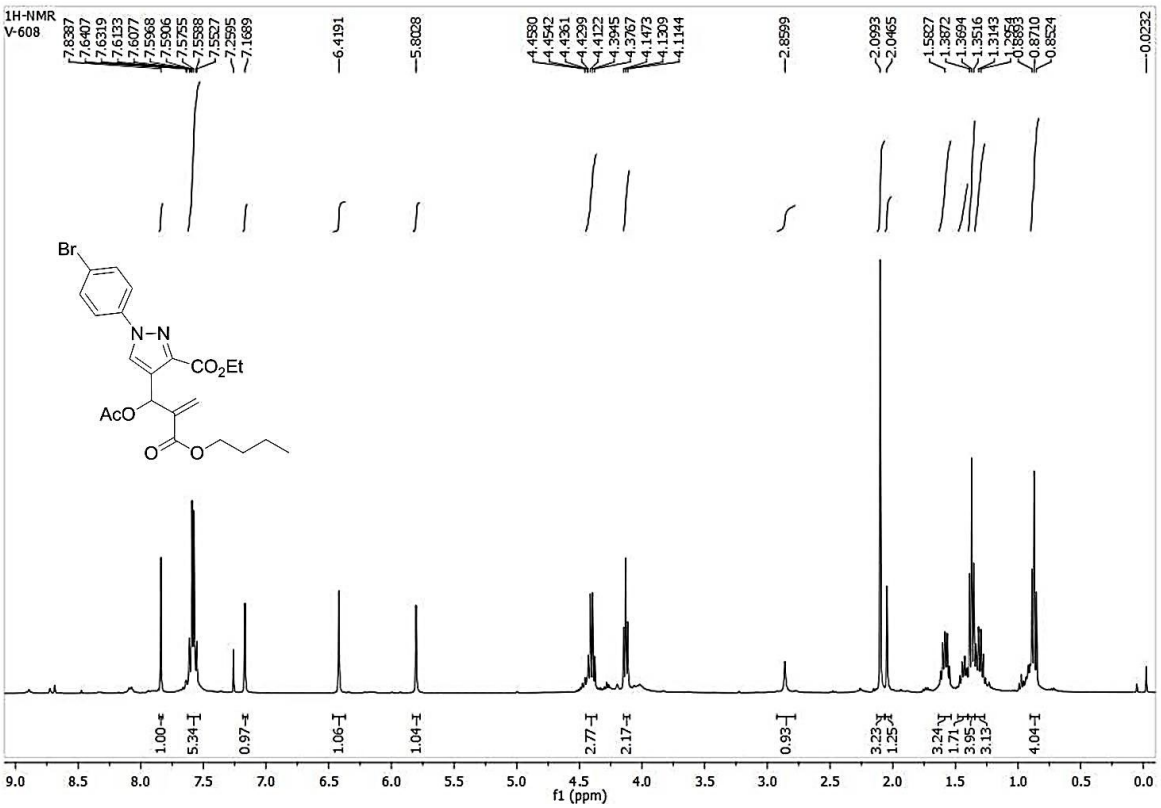


**Fig. S 57.** $^{1}$H-NMR of ethyl 4-(1-acetoxy-2-(butoxycarbonyl)allyl)-1-(4-bromophenyl)-1*H*-pyrazole-3-carboxylate **(8cC).**

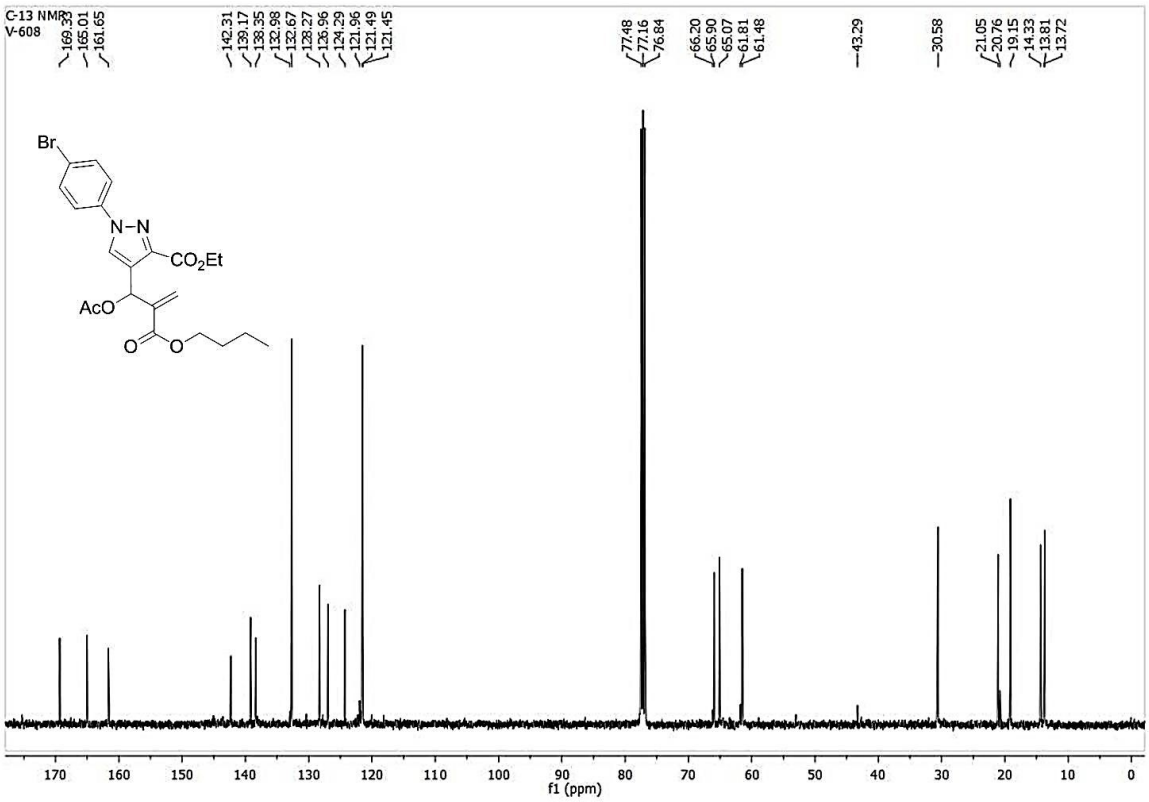


**Fig. S 58.** $^{13}$C-NMR of ethyl 4-(1-acetoxy-2-(butoxycarbonyl)allyl)-1-(4-bromophenyl)-1*H*-pyrazole-3-carboxylate **(8cC).**

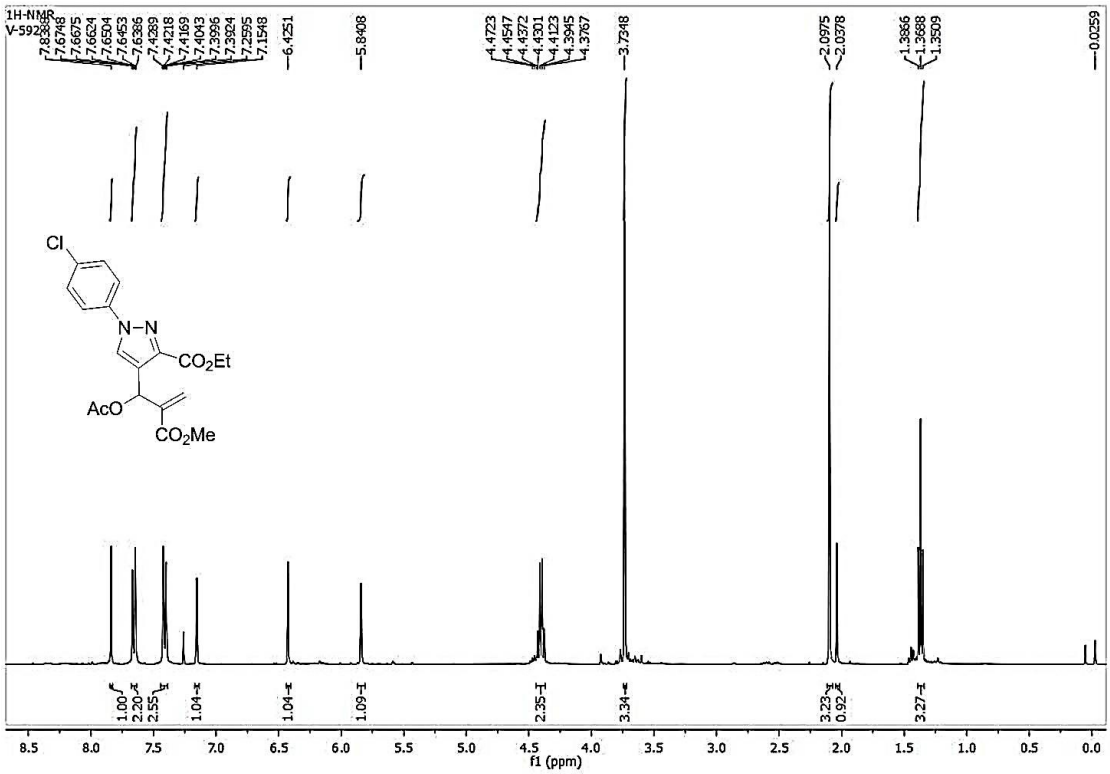


**Fig. S 59.** $^{1}$H-NMR of ethyl 4-(1-acetoxy-2-(methoxycarbonyl)allyl)-1-(4-chlorophenyl)-1*H*-pyrazole-3-carboxylate **(8dB).**

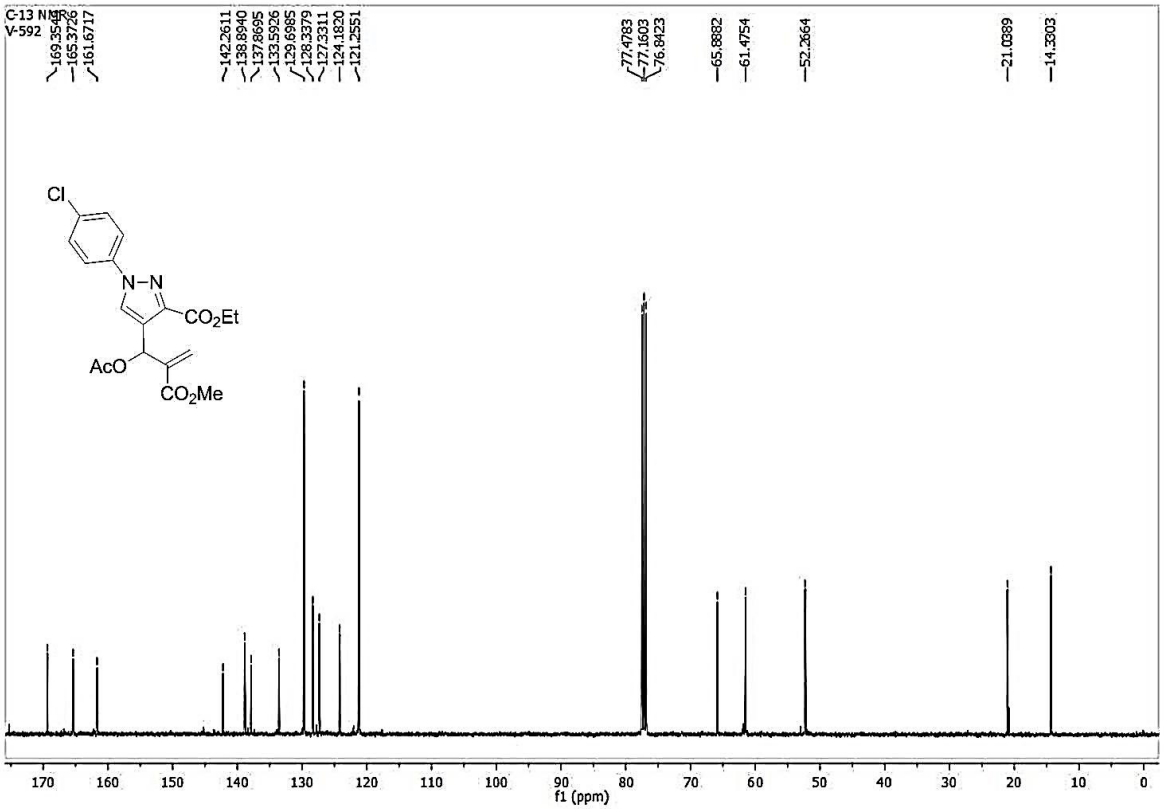


**Fig. S 60.** $^{13}$C-NMR of ethyl 4-(1-acetoxy-2-(methoxycarbonyl)allyl)-1-(4-chlorophenyl)-1*H*-pyrazole-3-carboxylate **(8dB).**

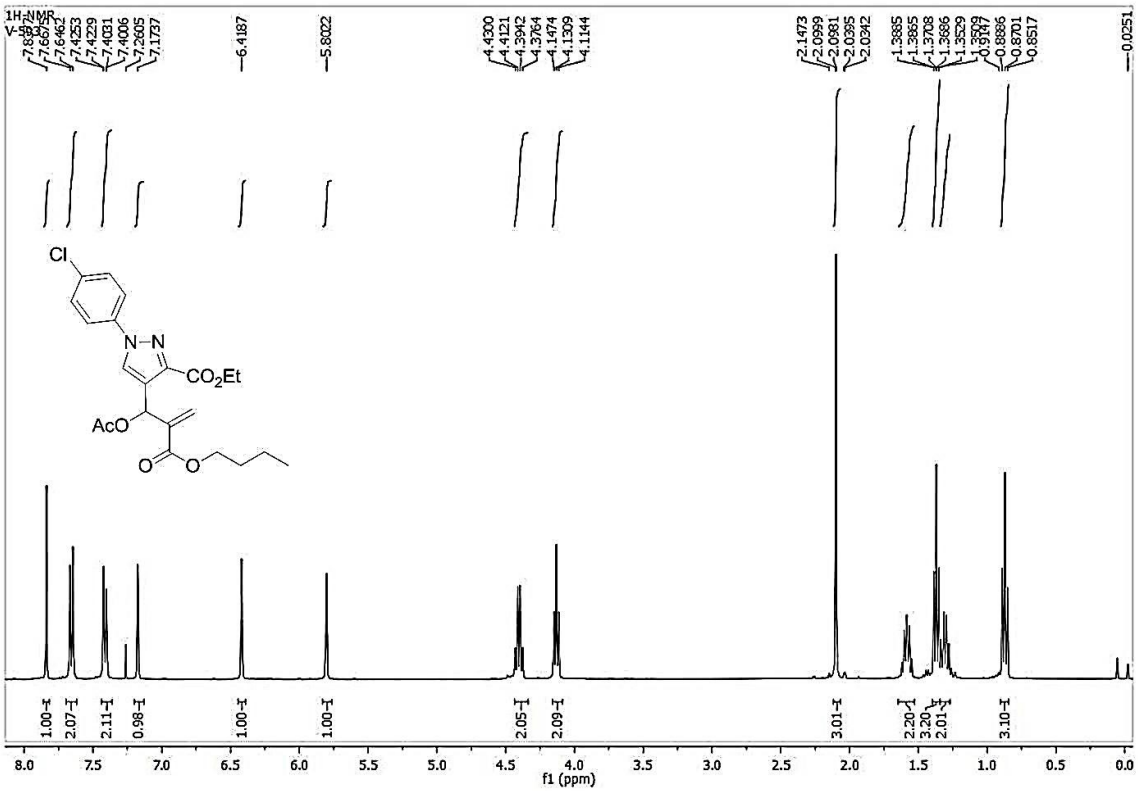


**Fig. S 61.** $^{1}$H-NMR of ethyl 4-(1-acetoxy-2-(butoxycarbonyl)allyl)-1-(4-chlorophenyl)-1*H*-pyrazole-3-carboxylate **(8dC).**

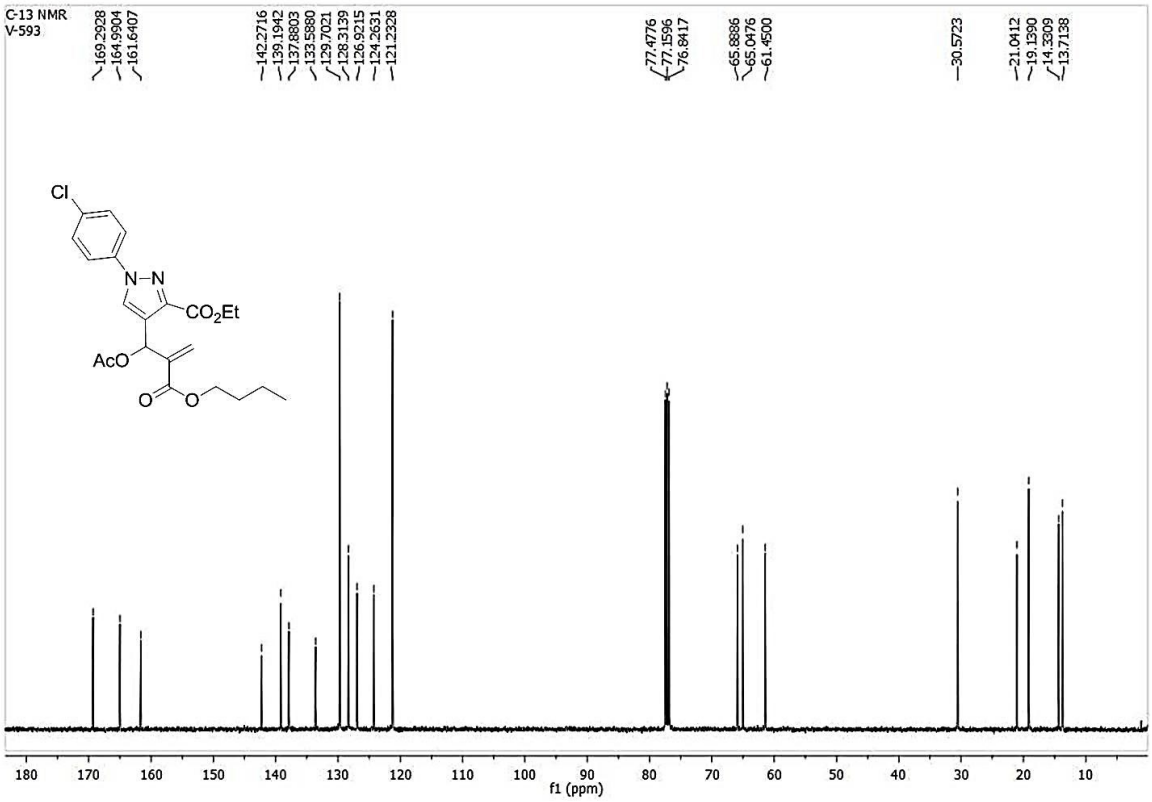


**Fig. S 62.** $^{13}$C-NMR of ethyl 4-(1-acetoxy-2-(butoxycarbonyl)allyl)-1-(4-chlorophenyl)-1*H*-pyrazole-3-carboxylate **(8dC).**

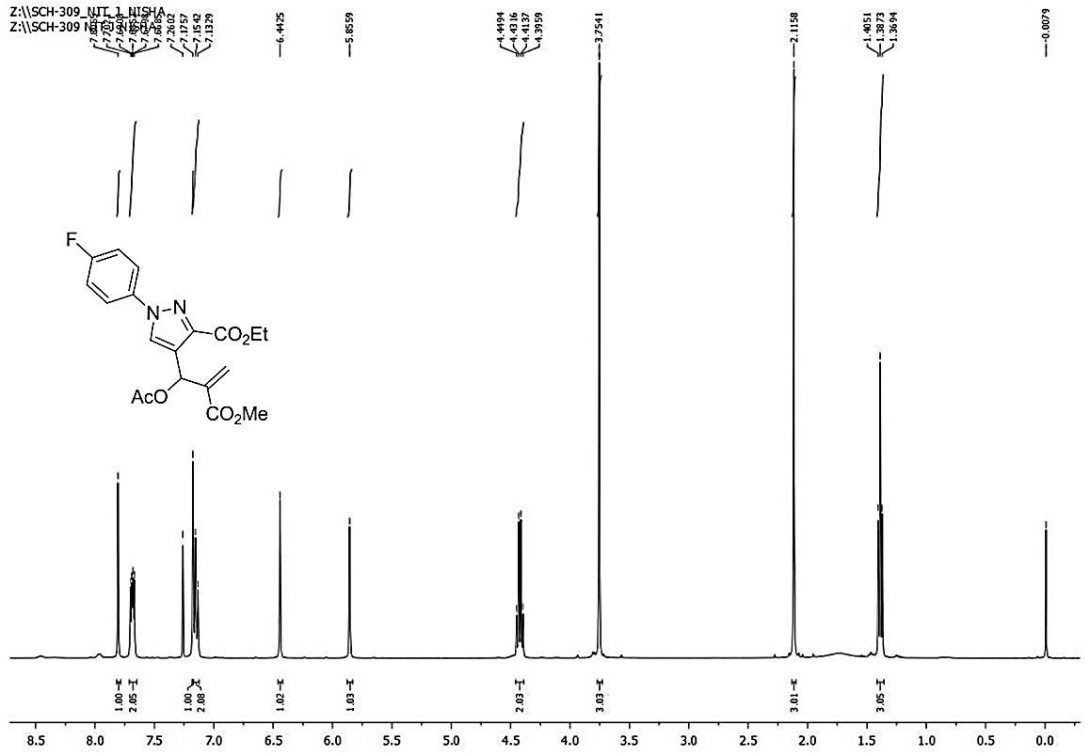


**Fig. S 63.** $^{1}$H-NMR of ethyl 4-(1-acetoxy-2-(methoxycarbonyl)allyl)-1-(4-fluorophenyl)-1*H*-pyrazole-3-carboxylate **(8eB).**

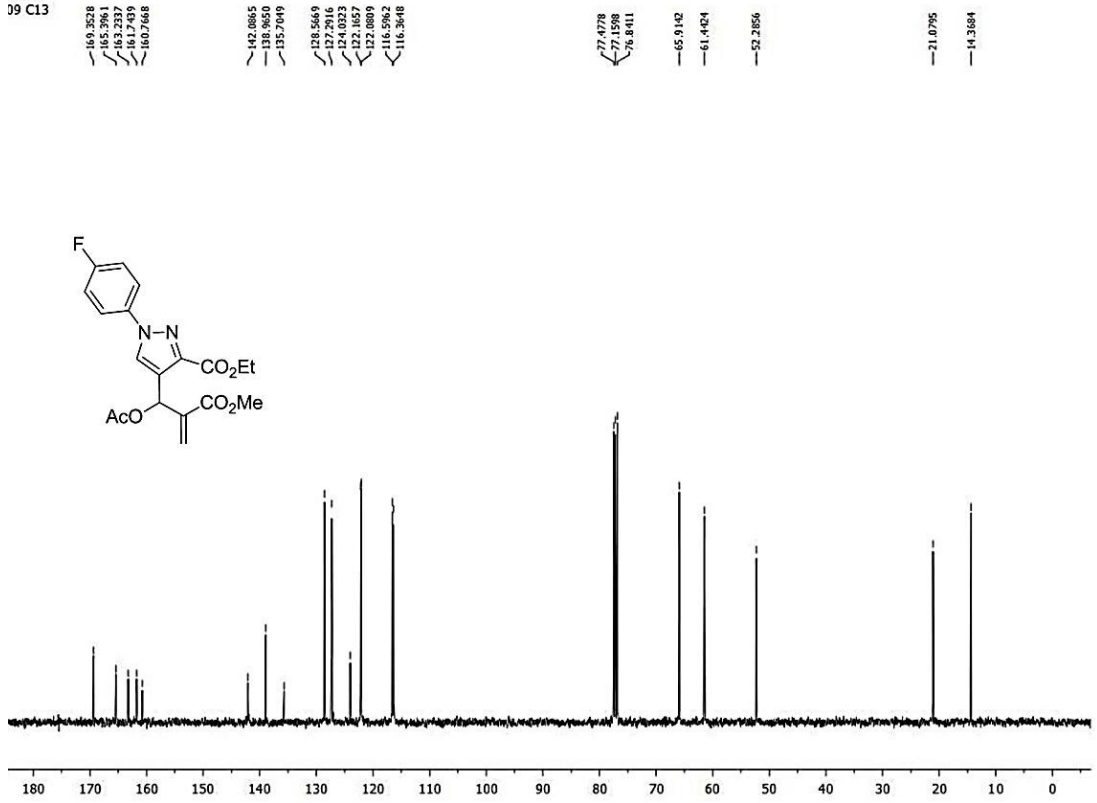


**Fig. S 64.** $^{13}$C-NMR of ethyl 4-(1-acetoxy-2-(methoxycarbonyl)allyl)-1-(4-fluorophenyl)-1*H*-pyrazole-3-carboxylate **(8eB).**

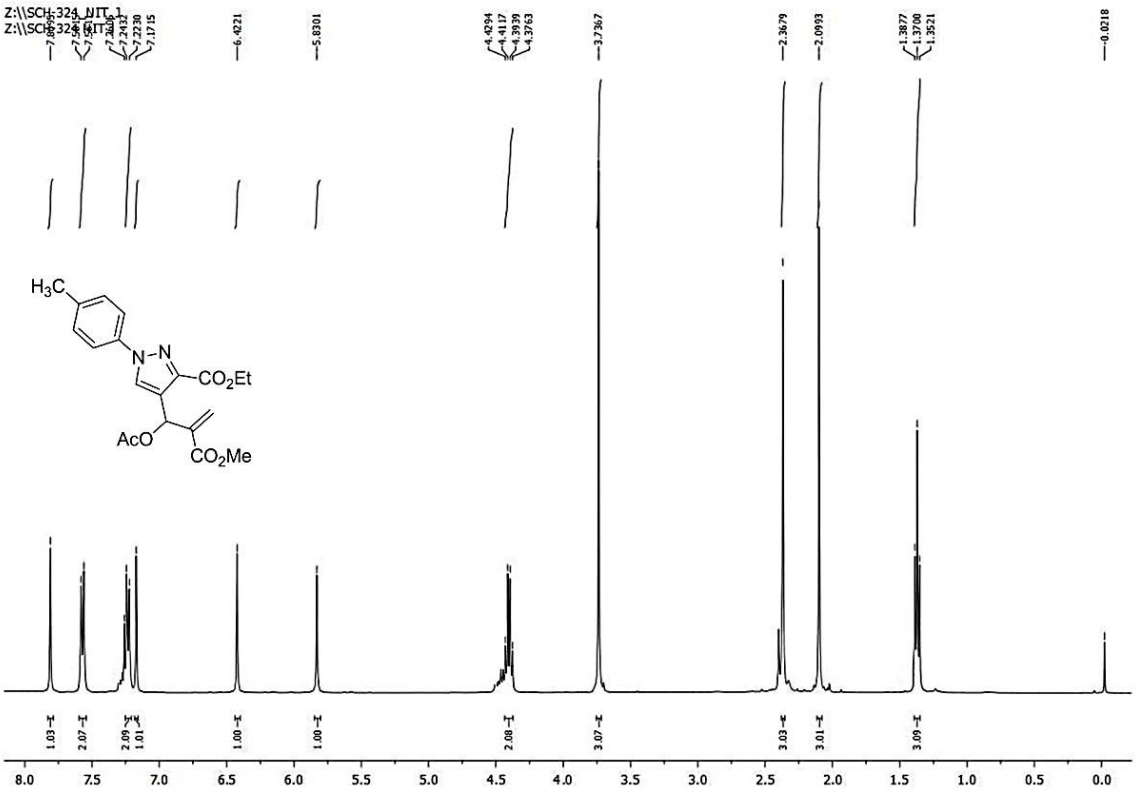


**Fig. S 65.** [1]H-NMR of ethyl 4-(1-acetoxy-2-(methoxycarbonyl)allyl)-1-(*p*-tolyl)-1*H*-pyrazole-3-carboxylate **(8fB).**

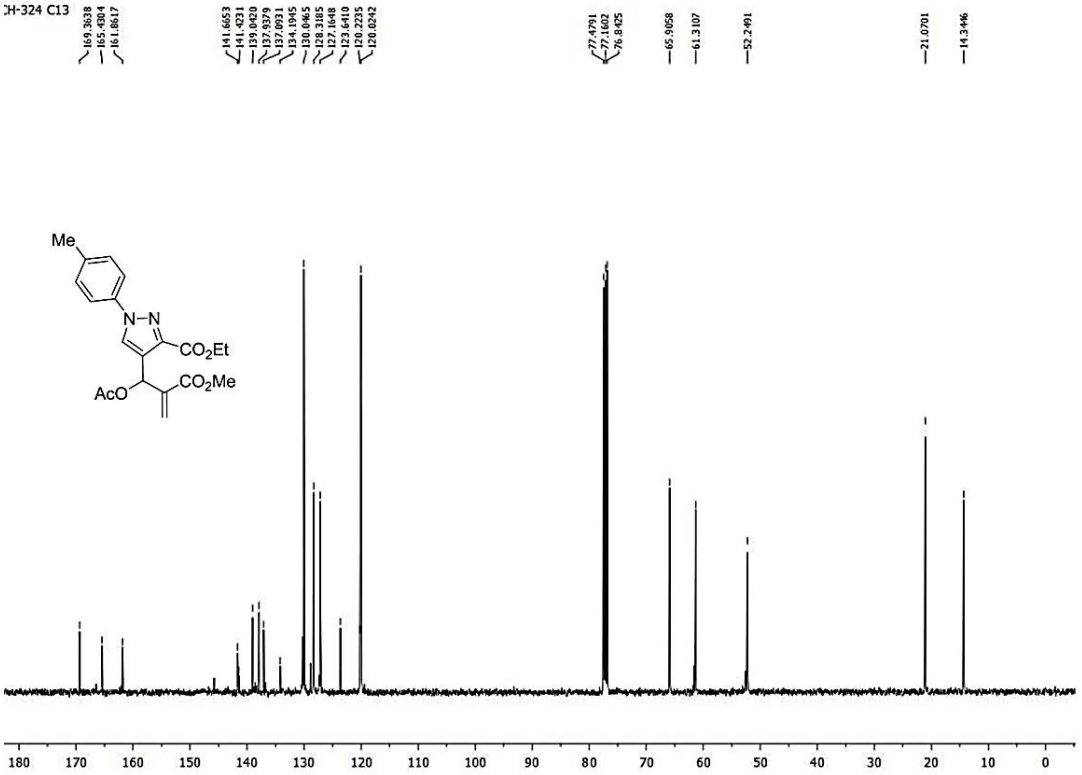


**Fig. S 66.** [13]C-NMR of ethyl 4-(1-acetoxy-2-(methoxycarbonyl)allyl)-1-(*p*-tolyl)-1*H*-pyrazole-3-carboxylate **(8fB).**

**VII.** $^{1}$H- and $^{13}$C- NMR spectra of the new Pyrazolo-azepinone **13**

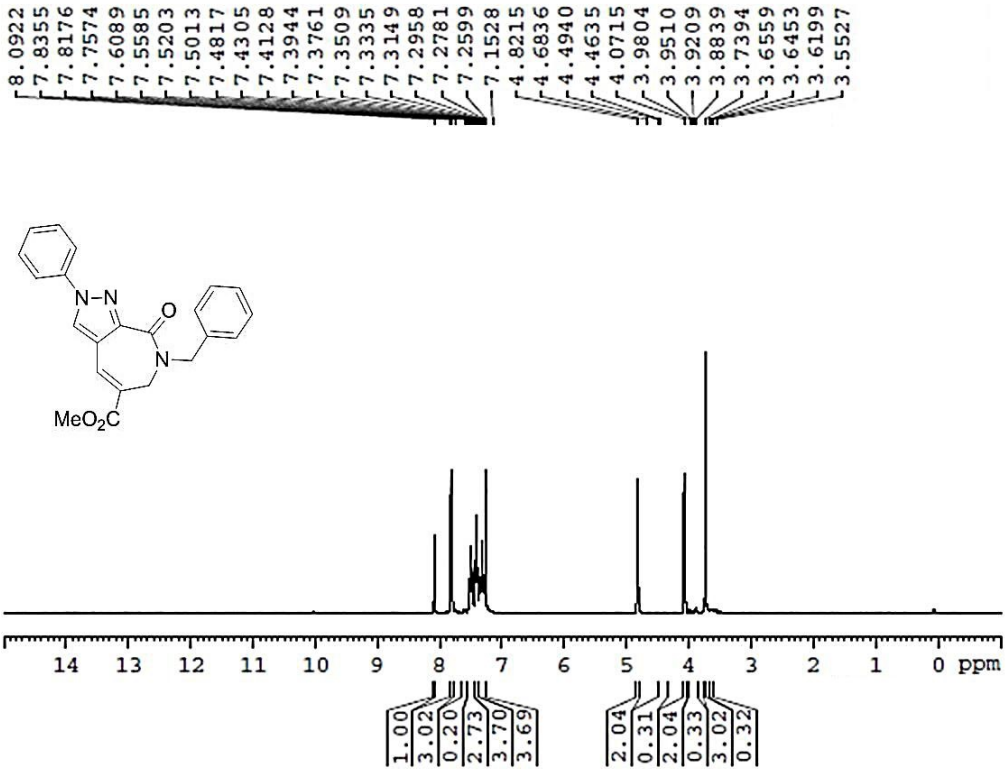


**Fig. S 67.** $^{1}$H-NMR of methyl 7-benzyl-8-oxo-2-phenyl-2,6,7,8-tetrahydropyrazolo[3,4-*c*]azepine-5-carboxylate **(13aBV).**

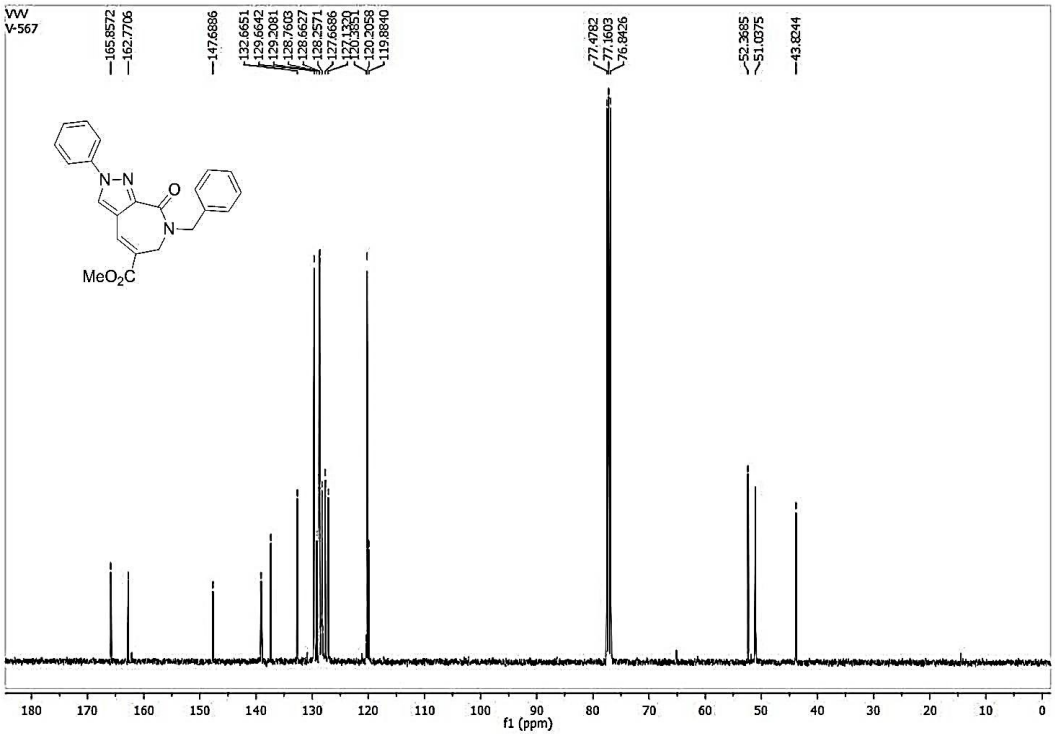


**Fig. S 68.** $^{13}$C-NMR of methyl 7-benzyl-8-oxo-2-phenyl-2,6,7,8-tetrahydropyrazolo[3,4-*c*]azepine-5-carboxylate **(13aBV).**

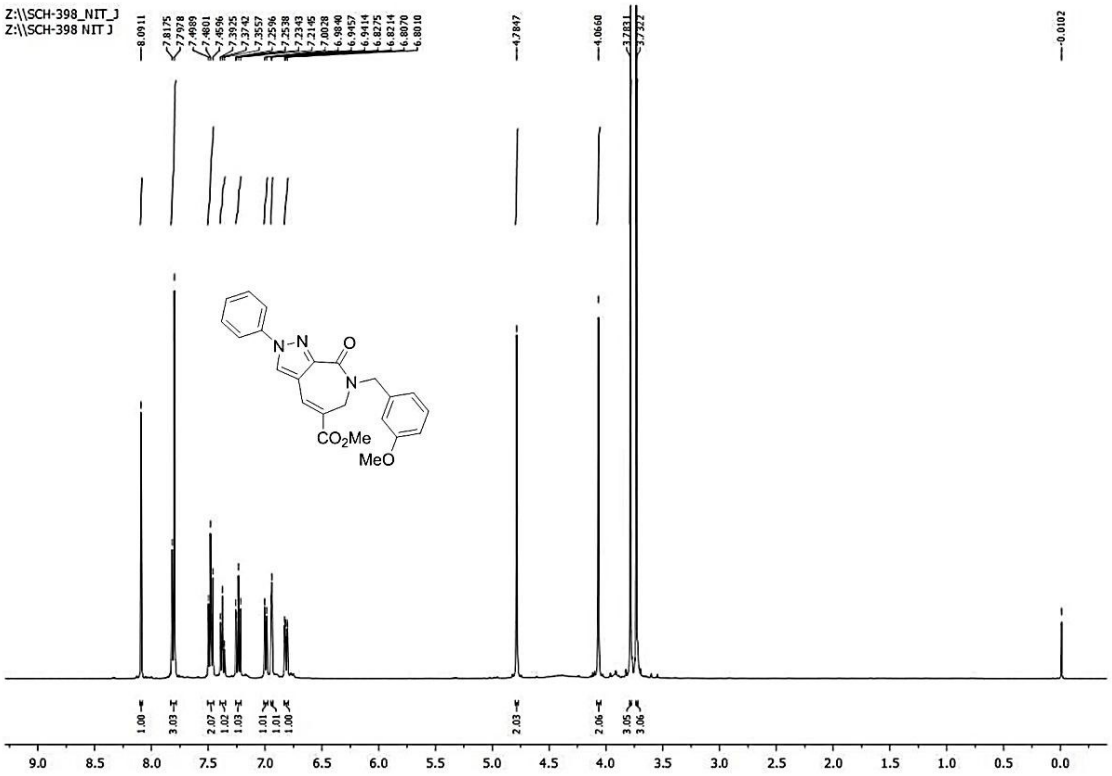


**Fig. S 69.** $^{1}$H-NMR of methyl 7-(3-methoxybenzyl)-8-oxo-2-phenyl-2,6,7,8-tetrahydropyrazolo[3,4-*c*]azepine-5-carboxylate **(13aBW).**

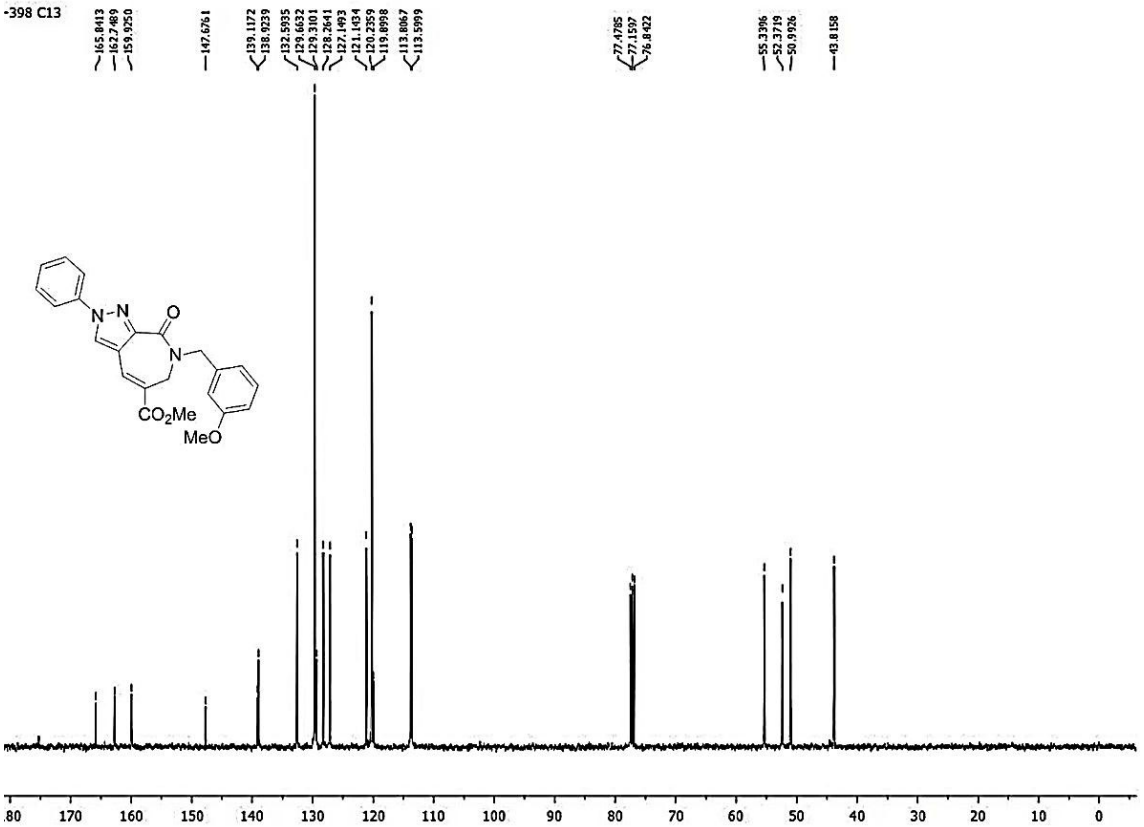


**Fig. S 70.** $^{13}$C-NMR of methyl 7-(3-methoxybenzyl)-8-oxo-2-phenyl-2,6,7,8-tetrahydropyrazolo[3,4-*c*]azepine-5-carboxylate **(13aBW).**

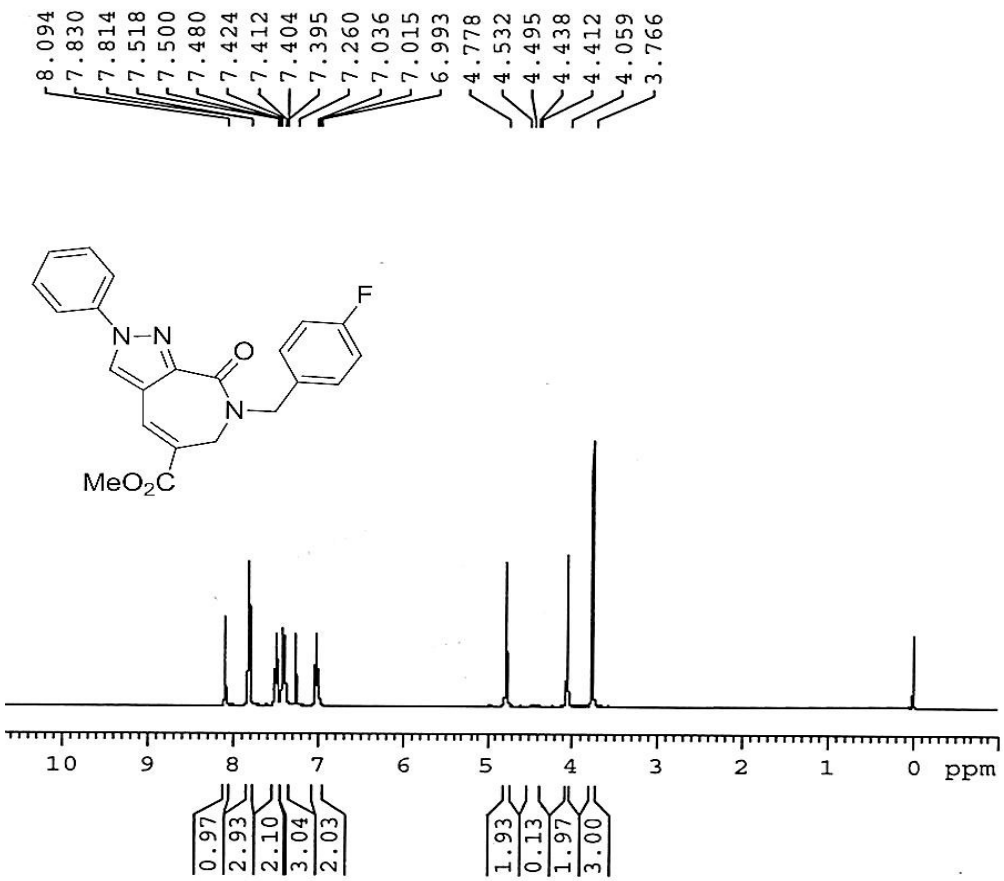


**Fig. S 71.** [1]H-NMR of methyl 7-(4-fluorobenzyl)-8-oxo-2-phenyl-2,6,7,8-tetrahydropyrazolo[3,4-*c*]azepine-5-carboxylate **(13aBX).**

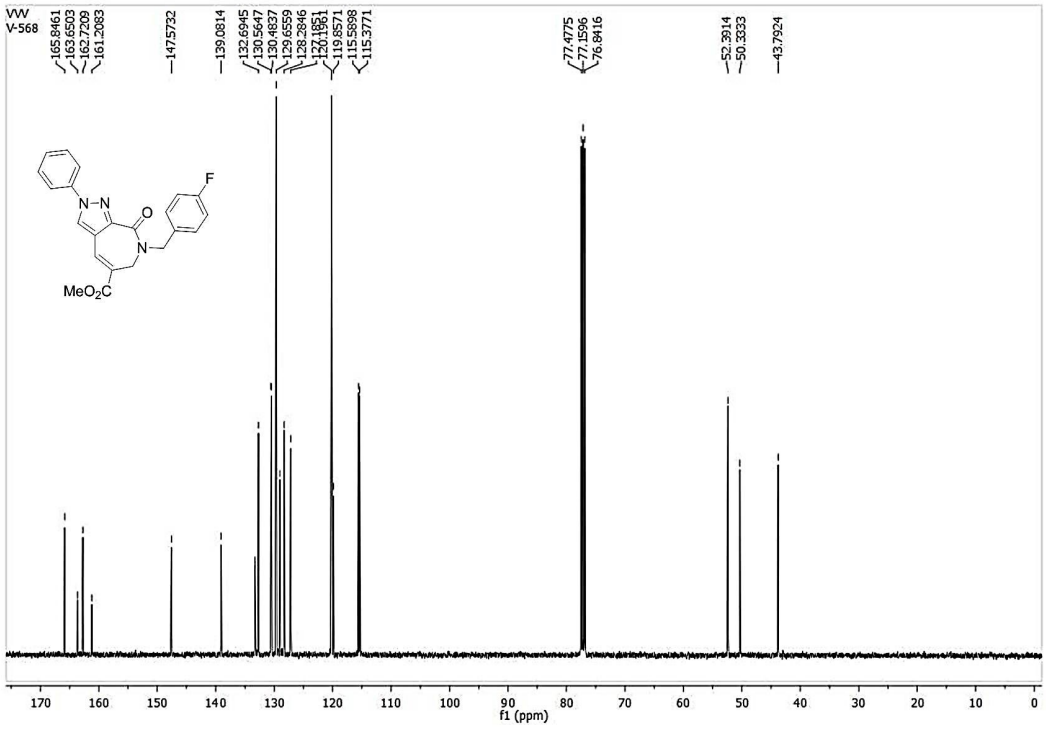


**Fig. S 72.** [13]C-NMR of methyl 7-(4-fluorobenzyl)-8-oxo-2-phenyl-2,6,7,8-tetrahydropyrazolo[3,4-*c*]azepine-5-carboxylate **(13aBX).**

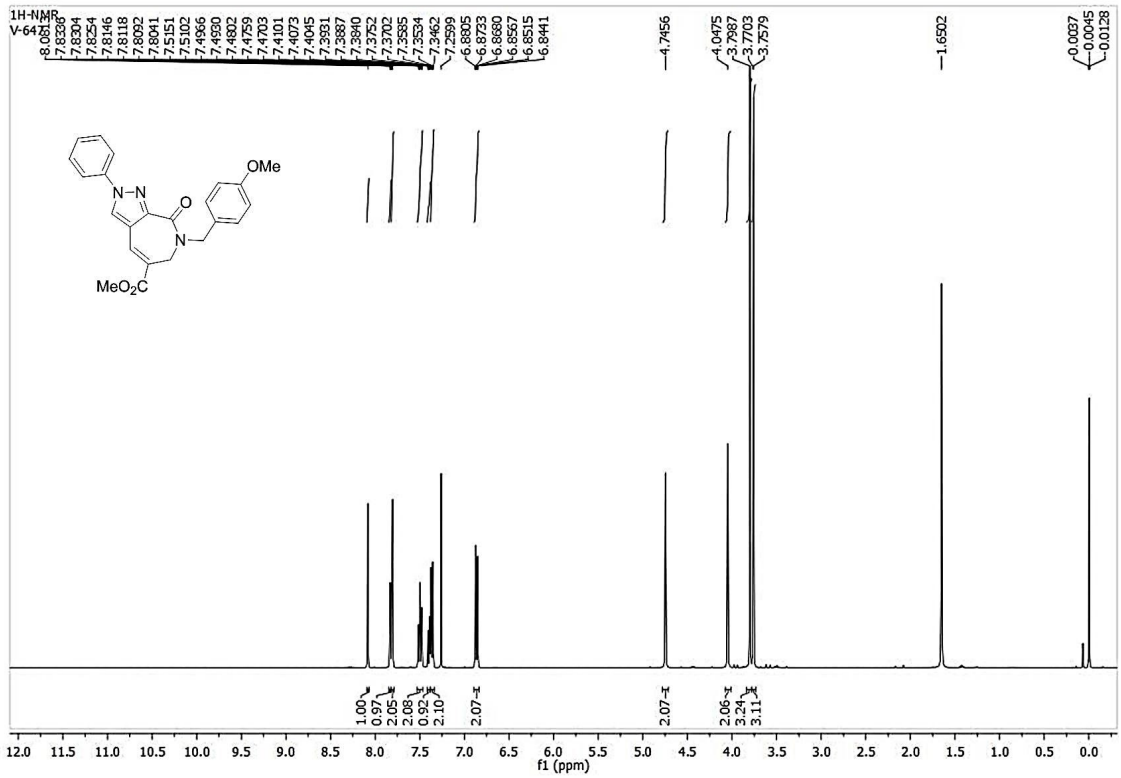


**Fig. S 73.** $^{1}$H-NMR of methyl 7-(4-methoxybenzyl)-8-oxo-2-phenyl-2,6,7,8-tetrahydropyrazolo[3,4-*c*]azepine-5-carboxylate **(13aBY).**

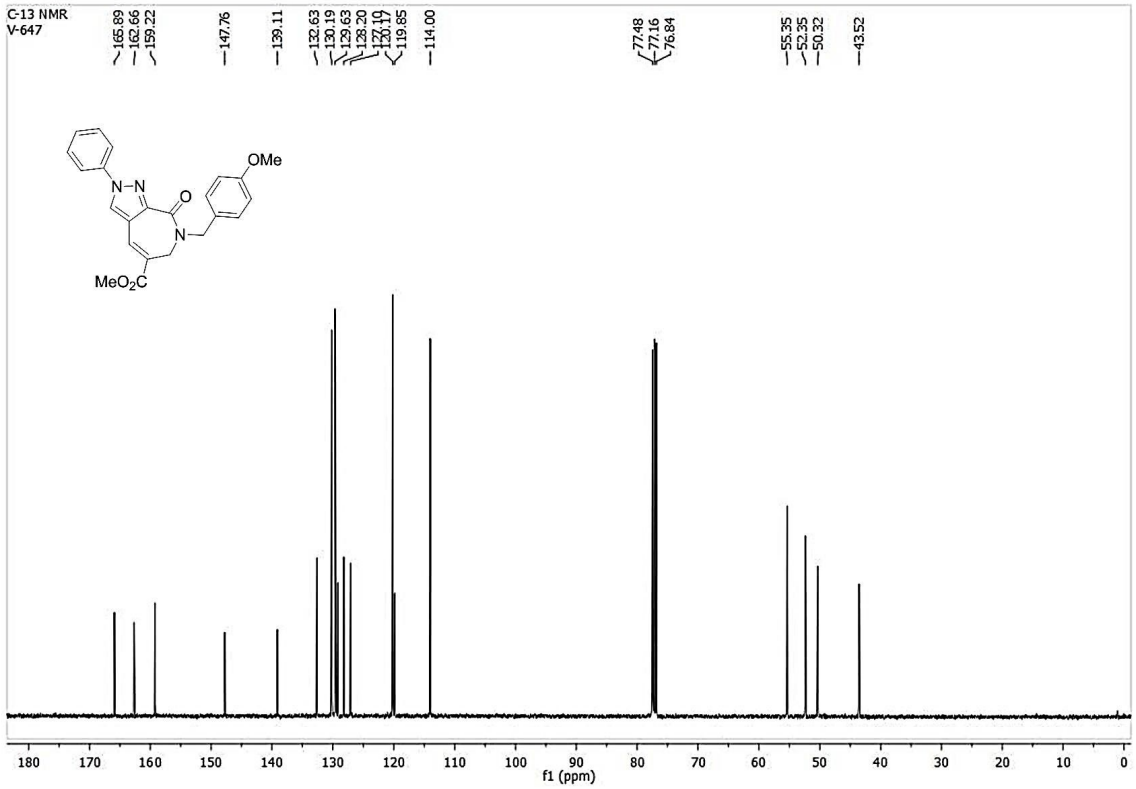


**Fig. S 74.** $^{13}$C-NMR of methyl 7-(4-methoxybenzyl)-8-oxo-2-phenyl-2,6,7,8-tetrahydropyrazolo[3,4-*c*]azepine-5-carboxylate **(13aBY).**

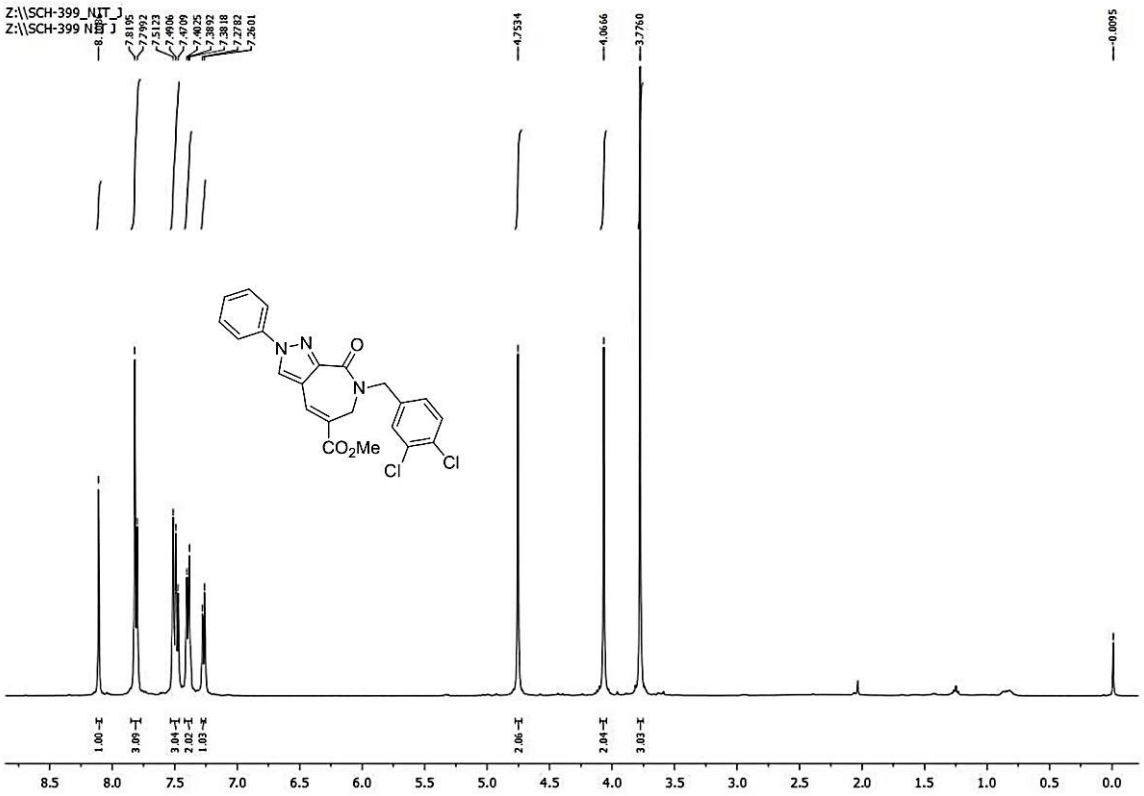


**Fig. S 75.** $^{1}$H-NMR of methyl 7-(3,4-dichlorobenzyl)-8-oxo-2-phenyl-2,6,7,8-tetrahydropyrazolo[3,4-*c*]azepine-5-carboxylate **(13aBZ).**

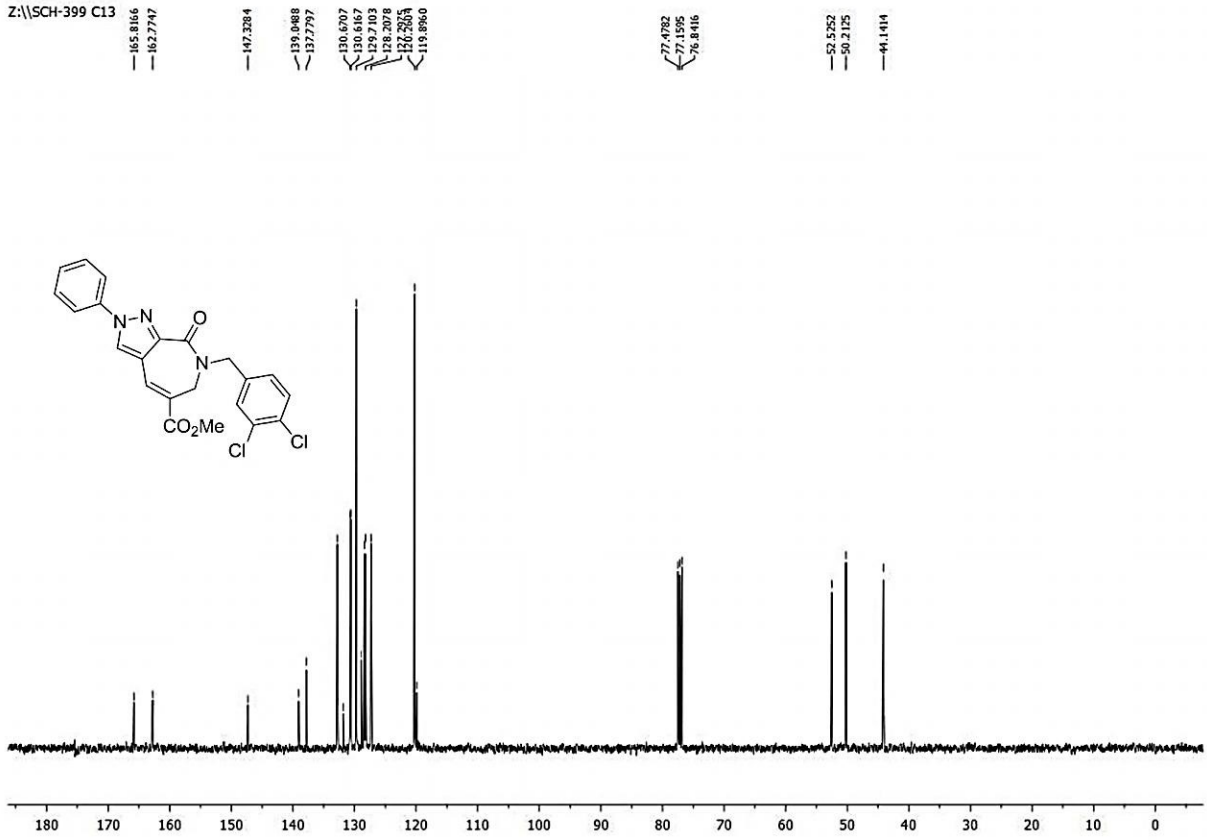


**Fig. S 76.** $^{13}$C-NMR of methyl 7-(3,4-dichlorobenzyl)-8-oxo-2-phenyl-2,6,7,8-tetrahydropyrazolo[3,4-*c*]azepine-5-carboxylate **(13aBZ).**

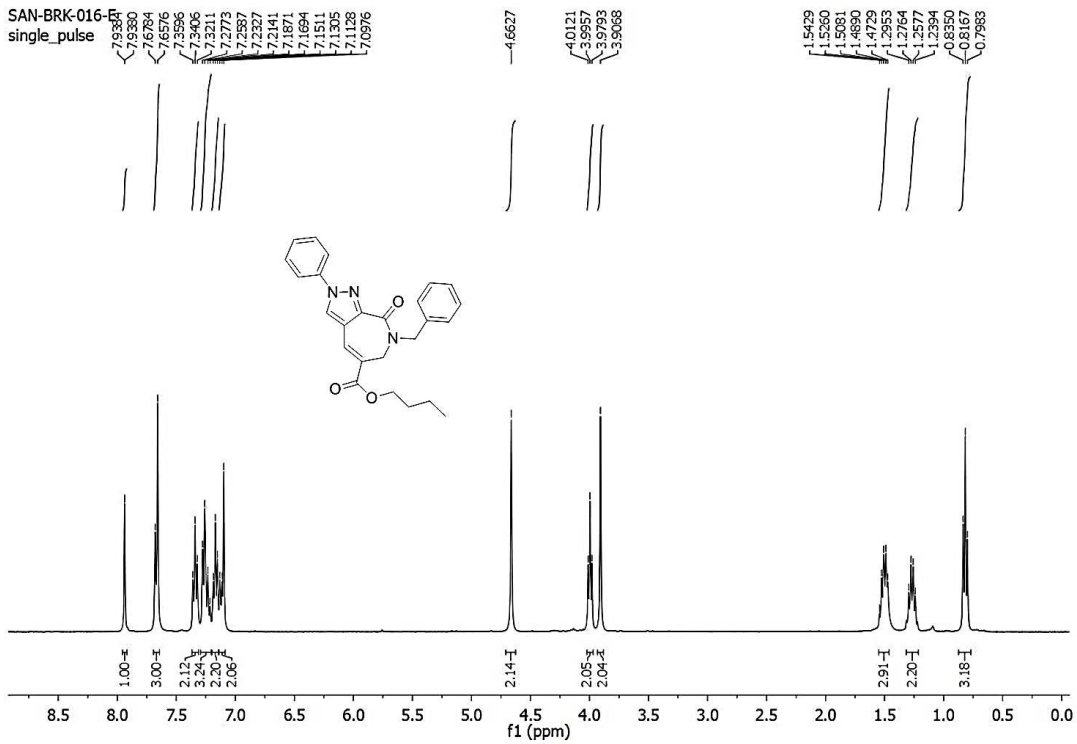


**Fig. S 77.** $^{1}$H-NMR of butyl 7-benzyl-8-oxo-2-phenyl-2,6,7,8-tetrahydropyrazolo[3,4-*c*]azepine-5-carboxylate **(13aCV).**

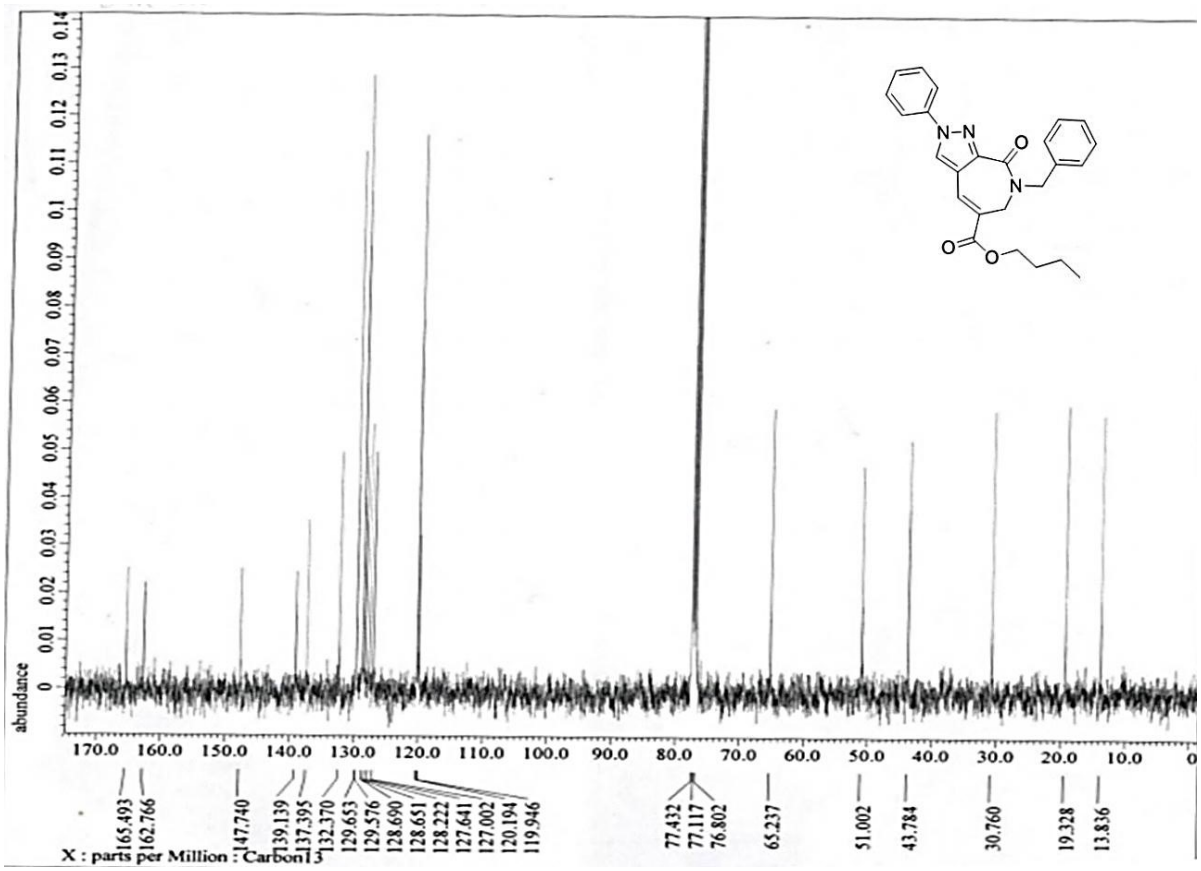


**Fig. S 78.** $^{13}$C-NMR of butyl 7-benzyl-8-oxo-2-phenyl-2,6,7,8-tetrahydropyrazolo[3,4-*c*]azepine-5-carboxylate **(13aCV).**

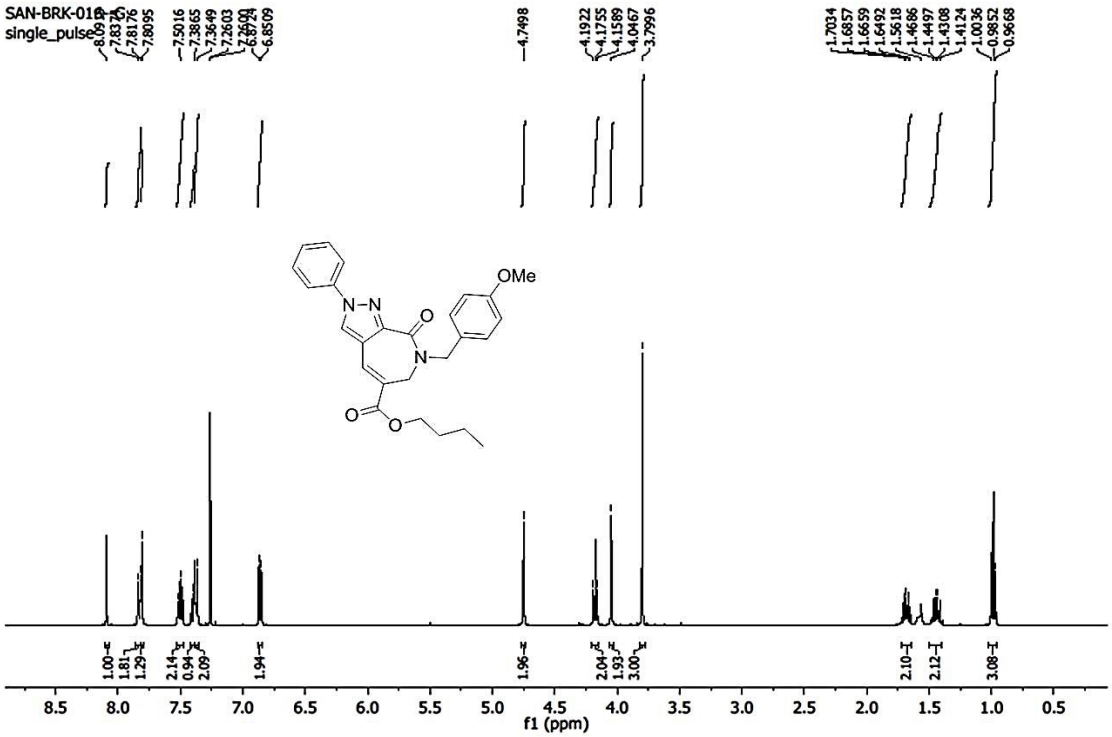


**Fig. S 79.** $^{1}$H-NMR of butyl 7-(4-methoxybenzyl)-8-oxo-2-phenyl-2,6,7,8-tetrahydropyrazolo[3,4-*c*]azepine-5-carboxylate **(13aCY).**

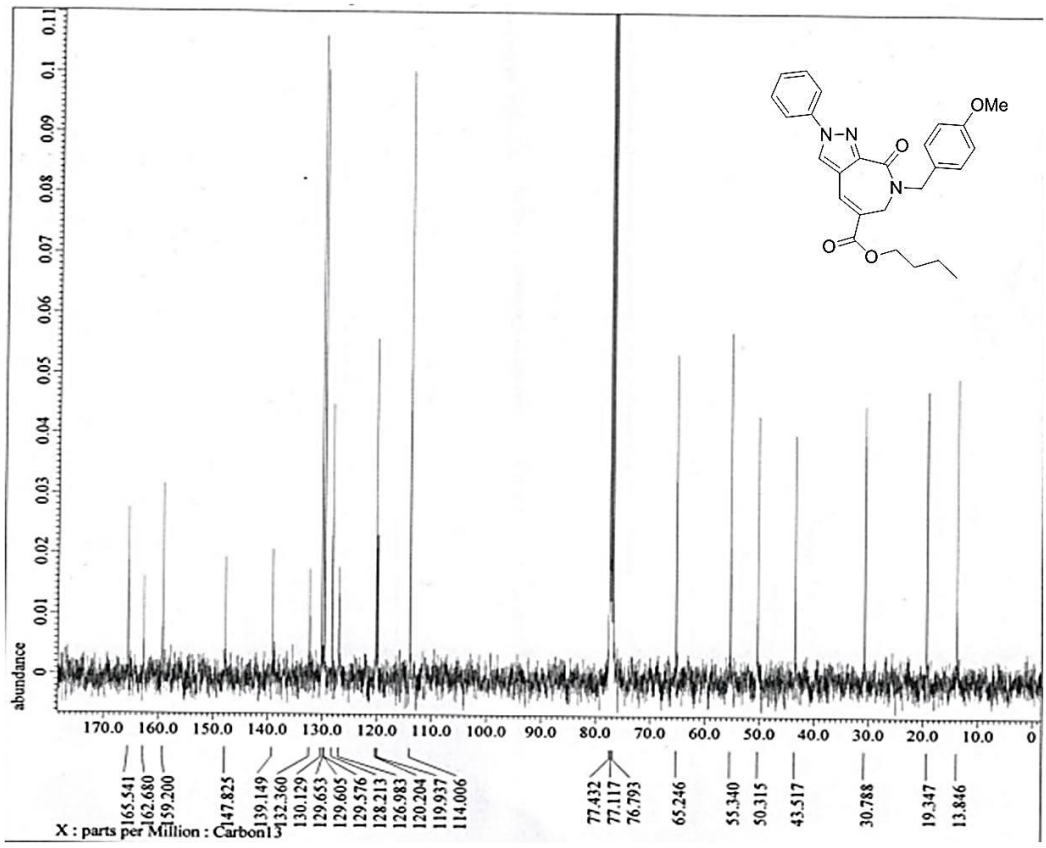


**Fig. S 80.** $^{13}$C-NMR of butyl 7-(4-methoxybenzyl)-8-oxo-2-phenyl-2,6,7,8-tetrahydropyrazolo[3,4-*c*]azepine-5-carboxylate **(13aCY).**

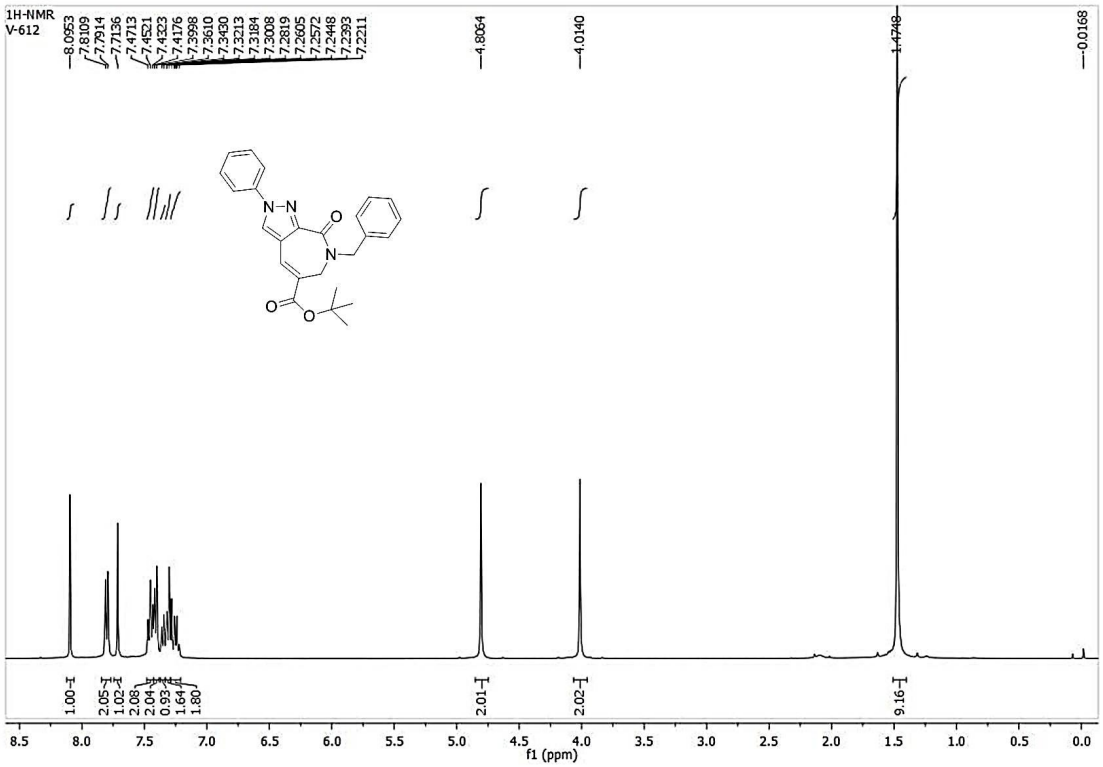


**Fig. S 81.** [1]H-NMR of *tert*-butyl 7-benzyl-8-oxo-2-phenyl-2,6,7,8-tetrahydropyrazolo[3,4-*c*]azepine-5-carboxylate **(13aDV).**

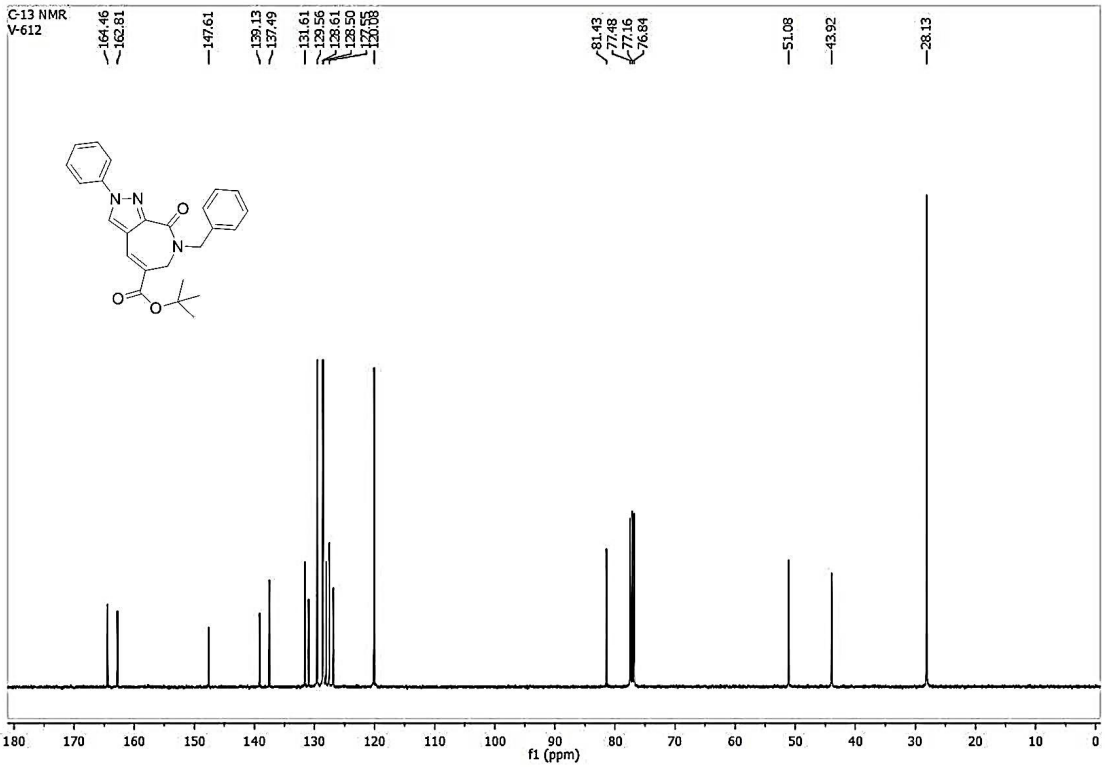


**Fig. S 82.** [13]C-NMR of *tert*-butyl 7-benzyl-8-oxo-2-phenyl-2,6,7,8-tetrahydropyrazolo[3,4-*c*]azepine-5-carboxylate **(13aDV).**

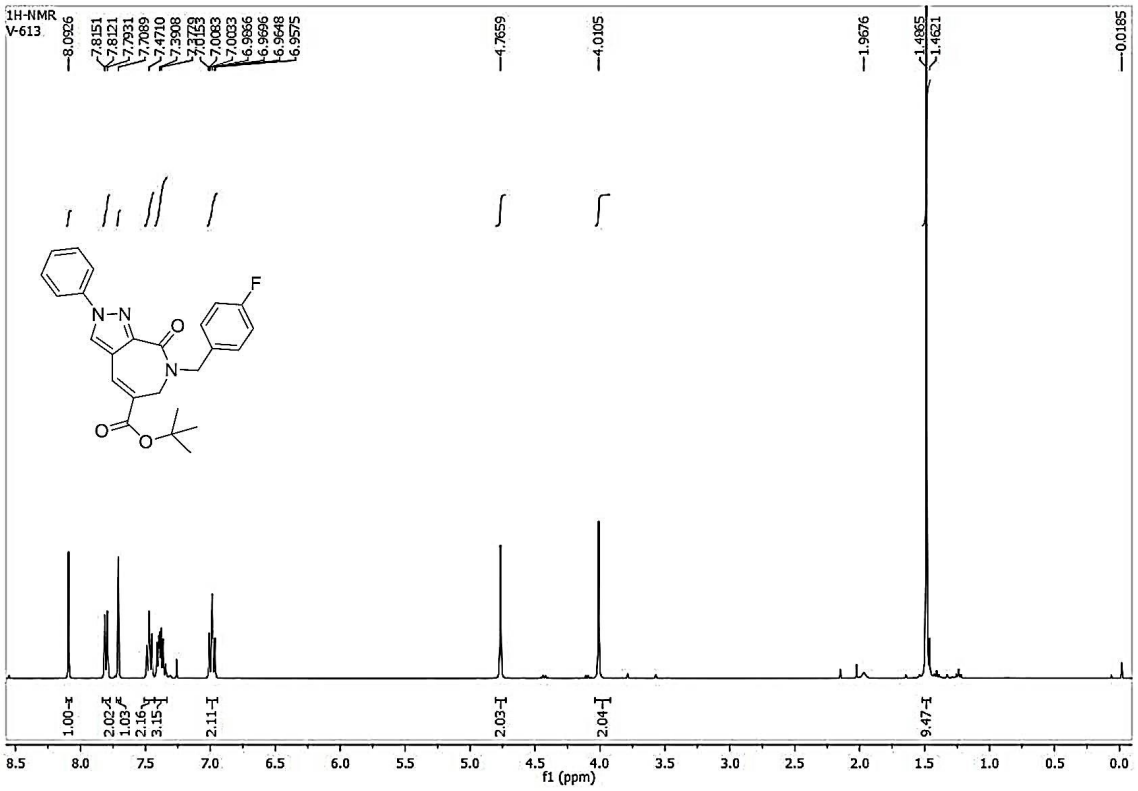


**Fig. S 83.** $^{1}$H-NMR of *tert*-butyl 7-(4-fluorobenzyl)-8-oxo-2-phenyl-2,6,7,8-tetrahydropyrazolo[3,4-*c*]azepine-5-carboxylate **(13aDX).**

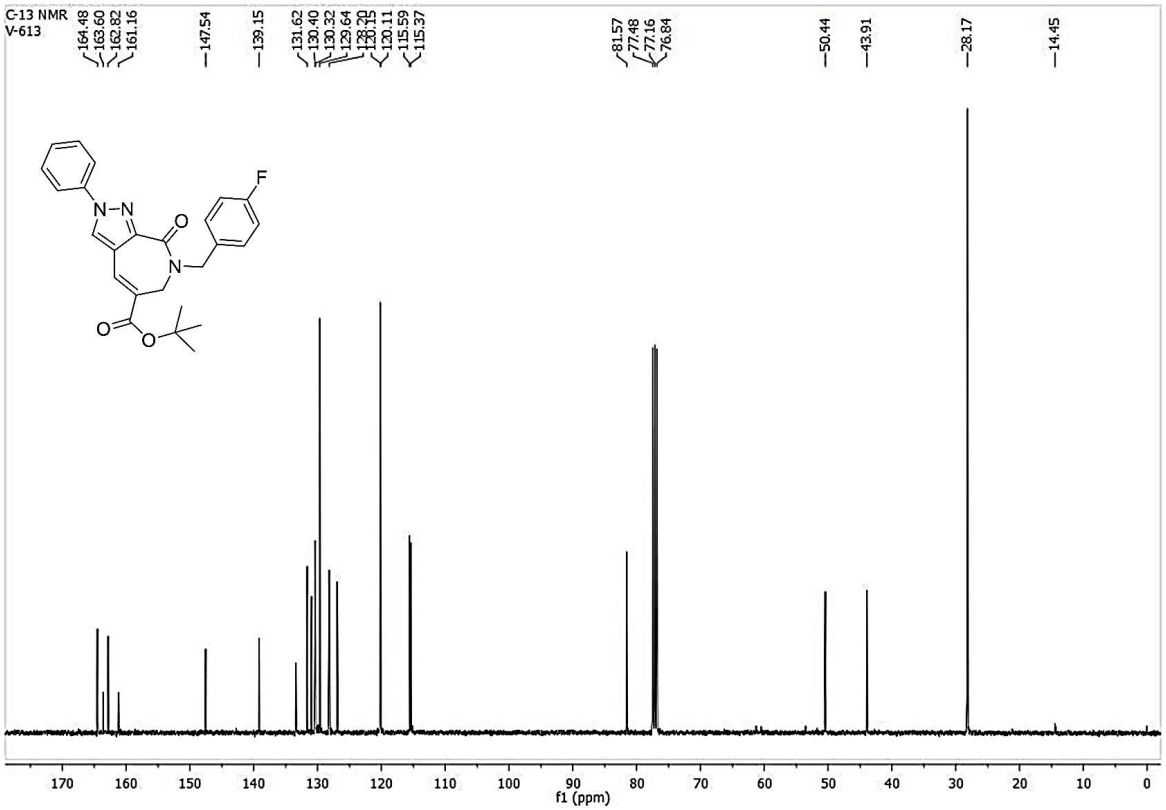


**Fig. S 84.** $^{13}$C-NMR of *tert*-butyl 7-(4-fluorobenzyl)-8-oxo-2-phenyl-2,6,7,8-tetrahydropyrazolo[3,4-*c*]azepine-5-carboxylate **(13aDX).**

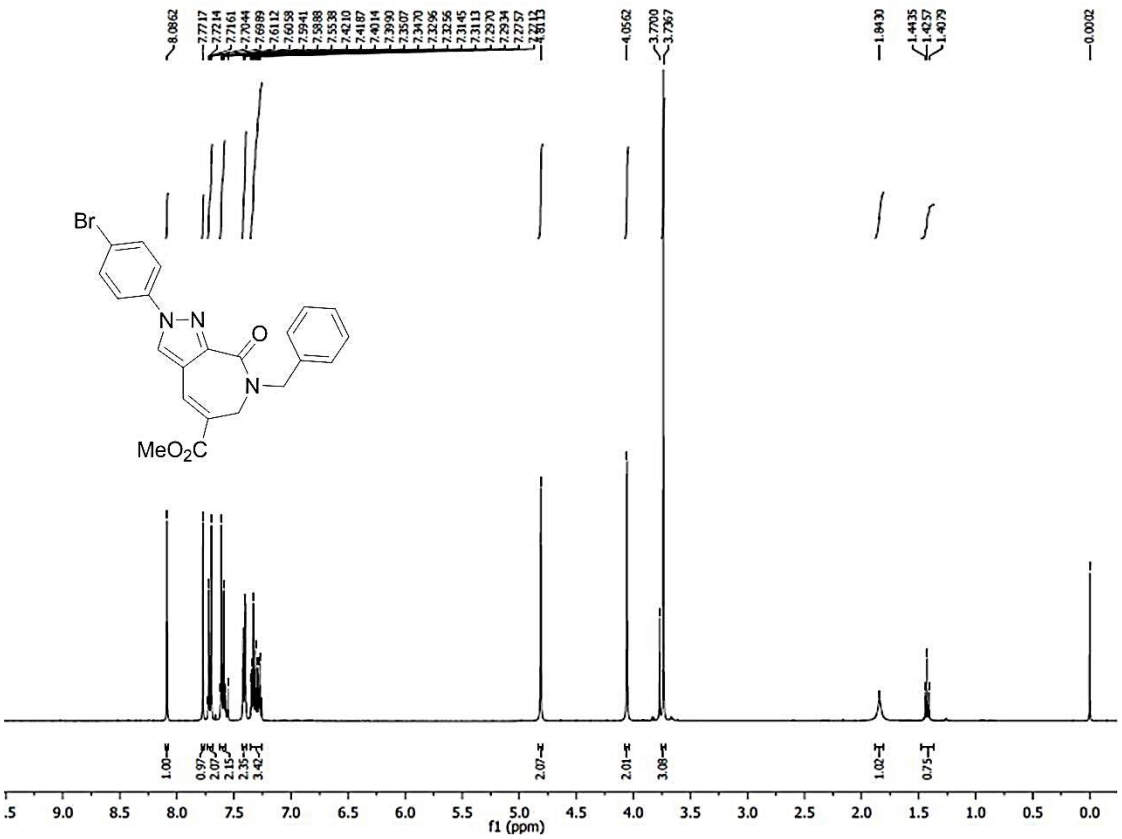


**Fig. S 85.** $^{1}$H-NMR of methyl 7-benzyl-2-(4-bromophenyl)-8-oxo-2,6,7,8-tetrahydropyrazolo[3,4-*c*]azepine-5-carboxylate **(13cBV).**

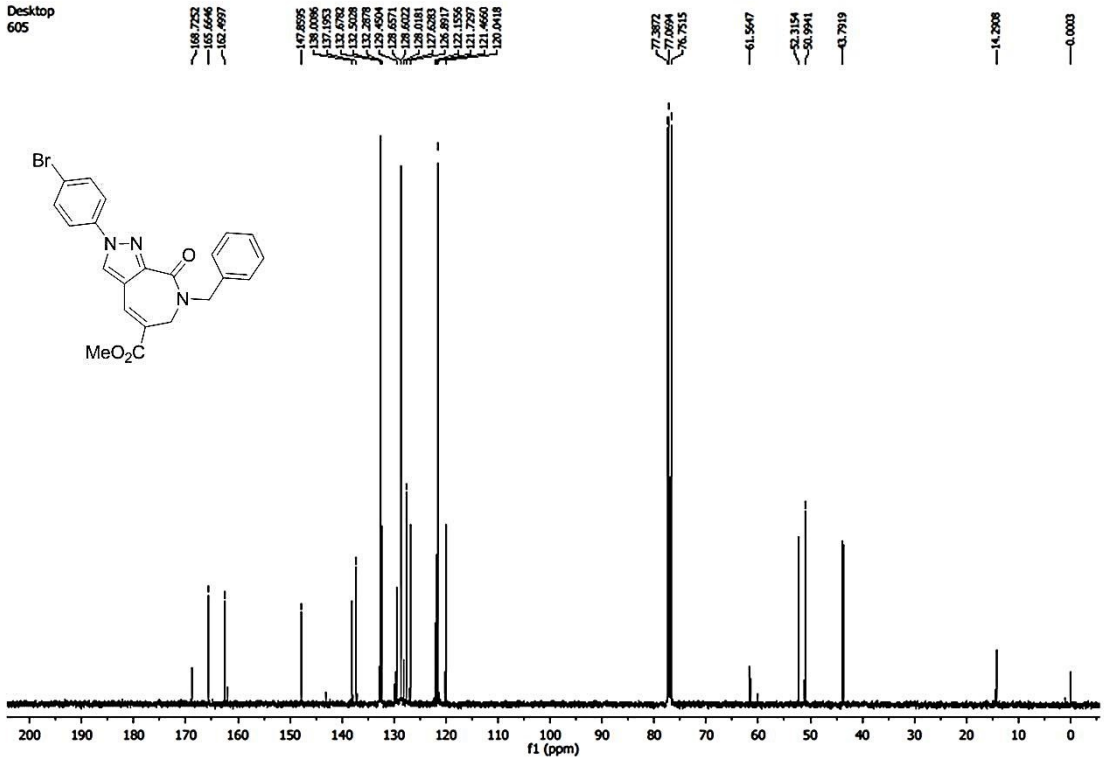


**Fig. S 86.** $^{13}$C-NMR of methyl 7-benzyl-2-(4-bromophenyl)-8-oxo-2,6,7,8-tetrahydropyrazolo[3,4-*c*]azepine-5-carboxylate **(13cBV).**

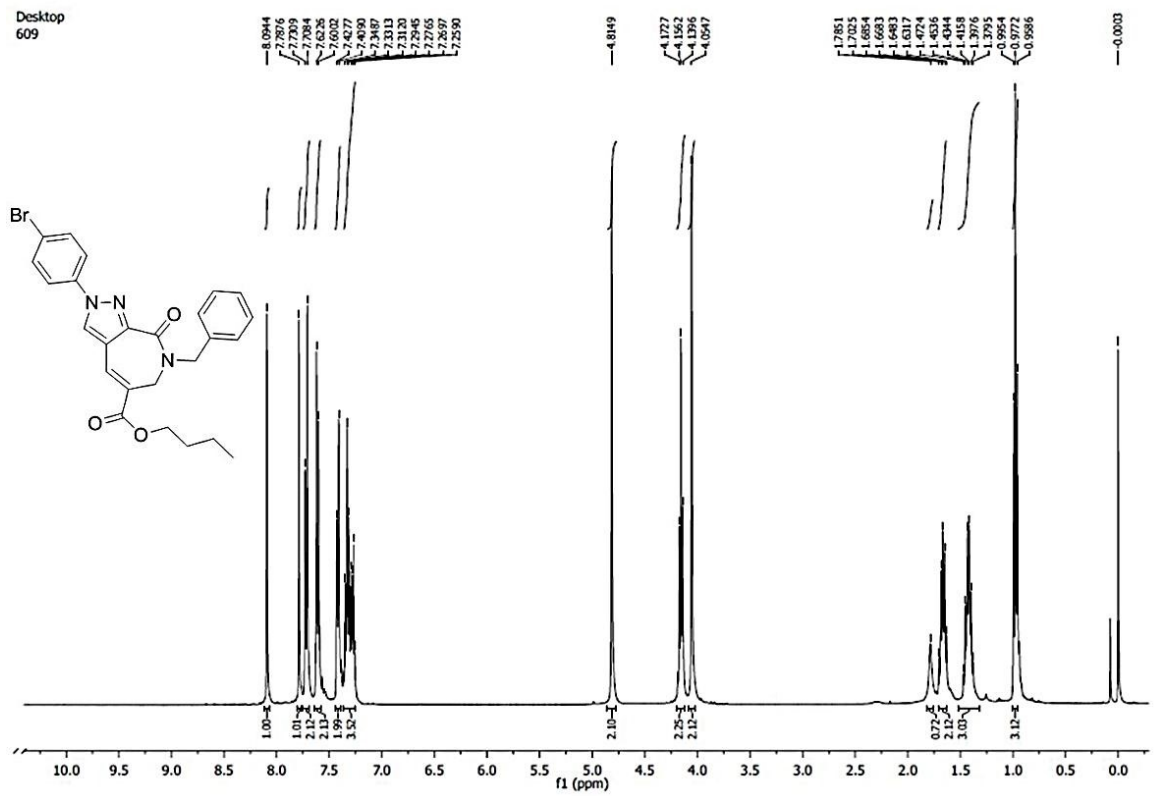


**Fig. S 87.** $^{1}$H-NMR of butyl 7-benzyl-2-(4-bromophenyl)-8-oxo-2,6,7,8-tetrahydropyrazolo[3,4-*c*]azepine-5-carboxylate **(13cCV).**

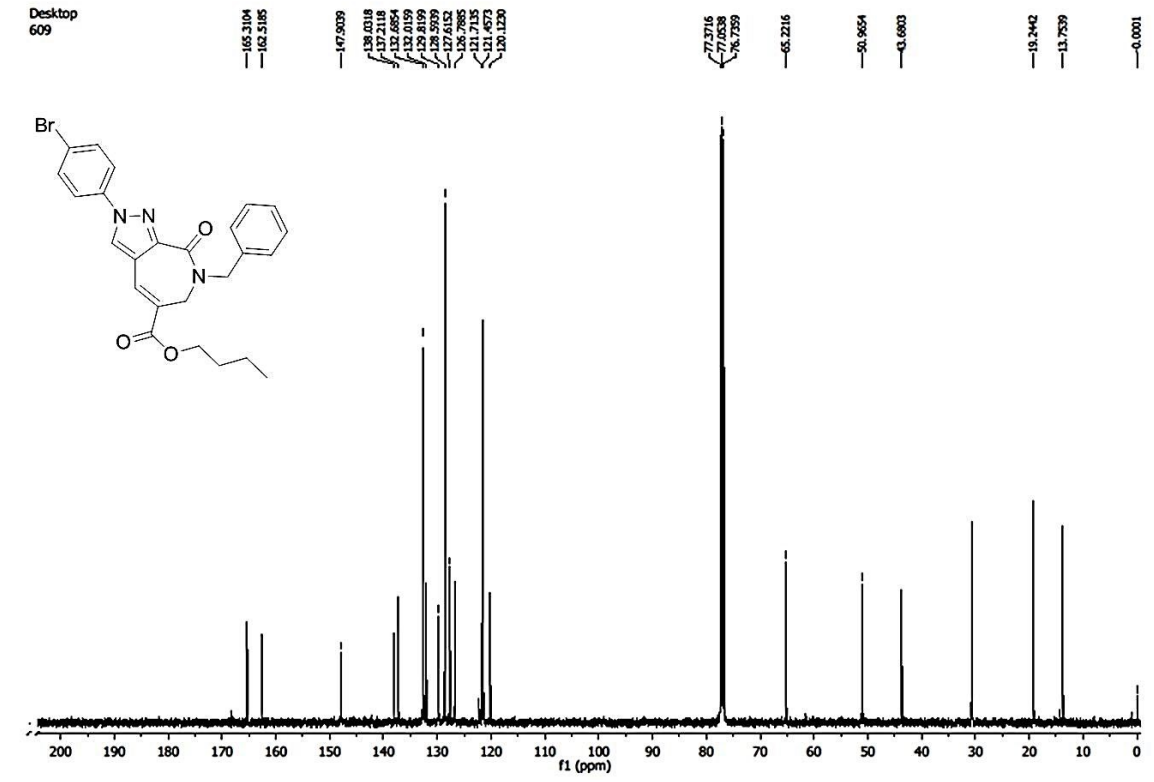


**Fig. S 88.** $^{13}$C-NMR of butyl 7-benzyl-2-(4-bromophenyl)-8-oxo-2,6,7,8-tetrahydropyrazolo[3,4-*c*]azepine-5-carboxylate **(13cCV).**

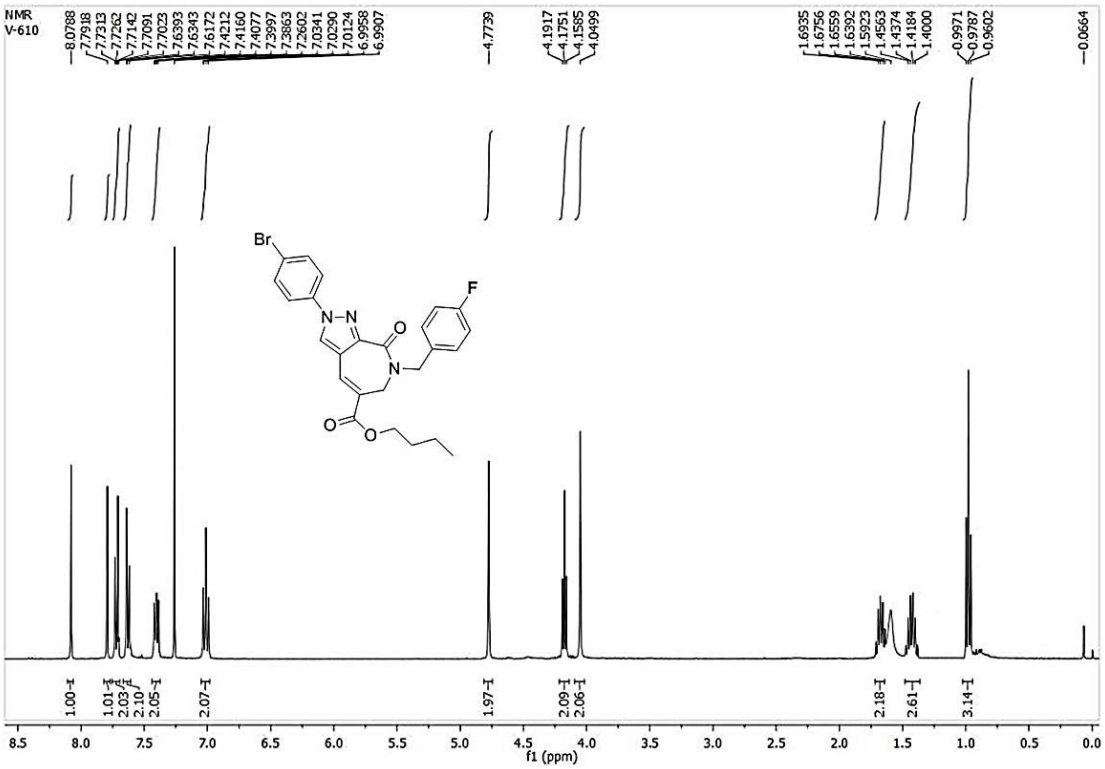


**Fig. S 89.** $^{1}$H-NMR of butyl 2-(4-bromophenyl)-7-(4-fluorobenzyl)-8-oxo-2,6,7,8-tetrahydropyrazolo[3,4-*c*]azepine-5-carboxylate **(13cCX).**

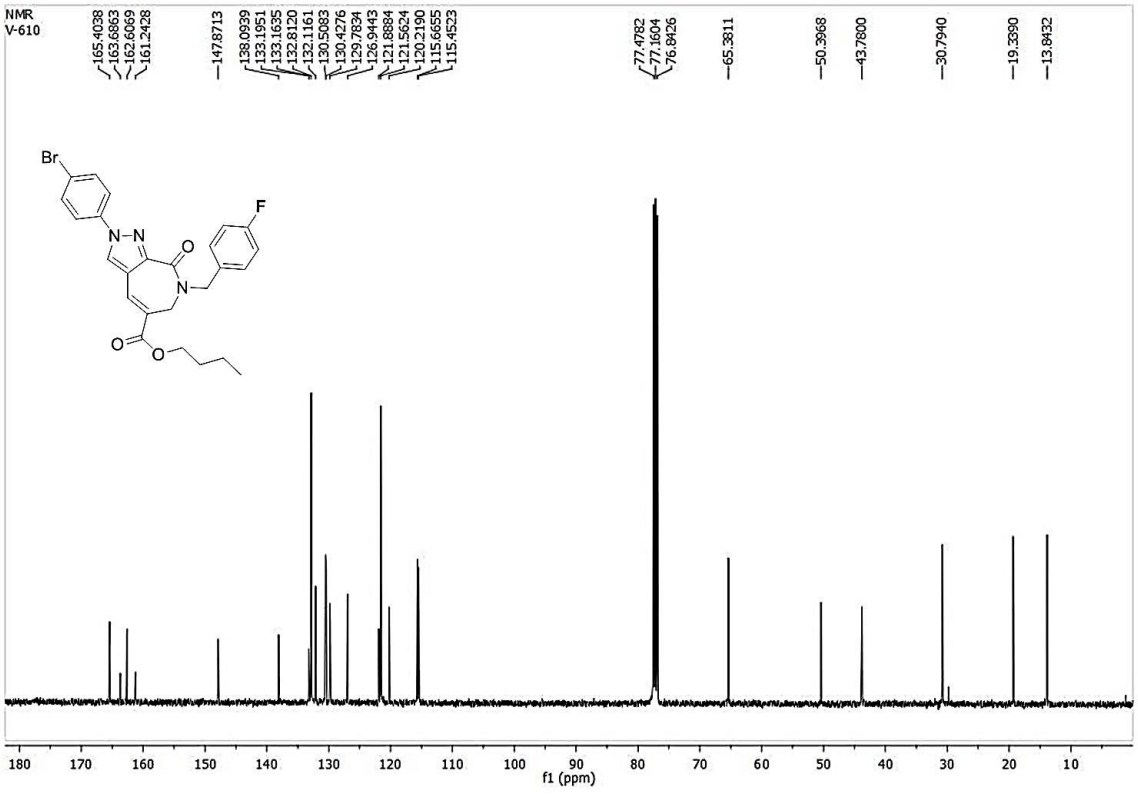


**Fig. S 90.** $^{13}$C-NMR of butyl 2-(4-bromophenyl)-7-(4-fluorobenzyl)-8-oxo-2,6,7,8-tetrahydropyrazolo[3,4-*c*]azepine-5-carboxylate **(13cCX).**

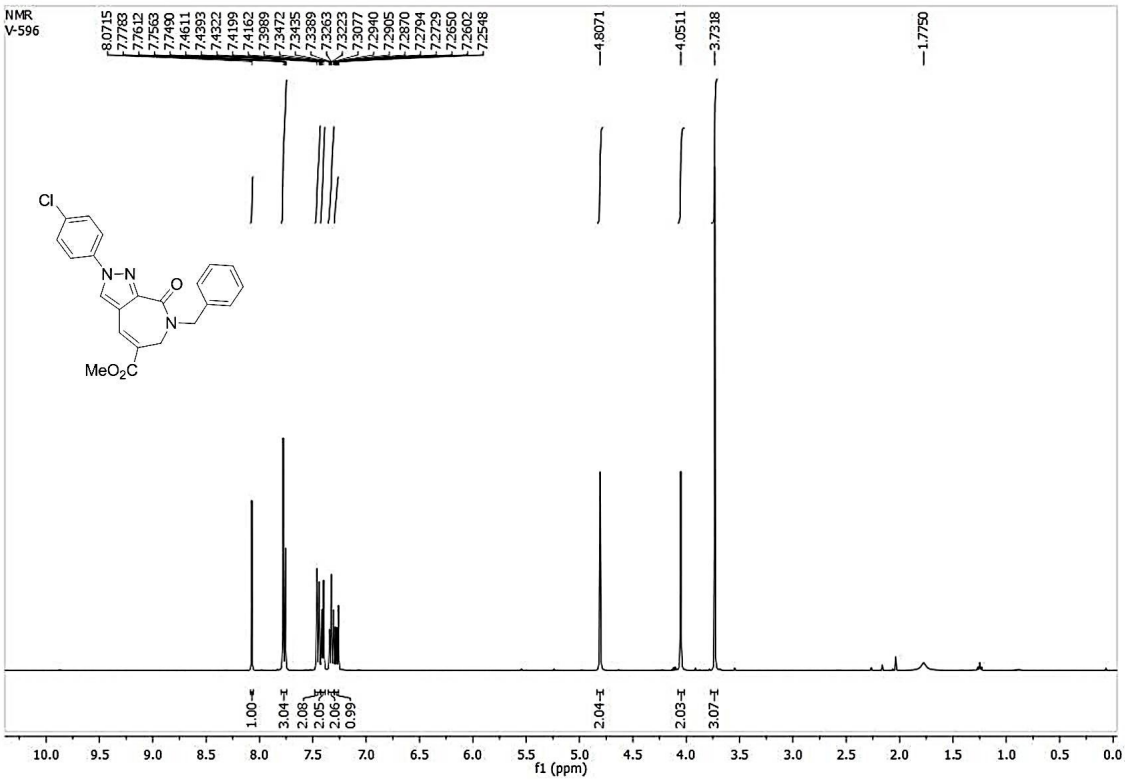


**Fig. S 91.** $^{1}$H-NMR of methyl 7-benzyl-2-(4-chlorophenyl)-8-oxo-2,6,7,8-tetrahydropyrazolo[3,4-*c*]azepine-5-carboxylate **(13dBV).**

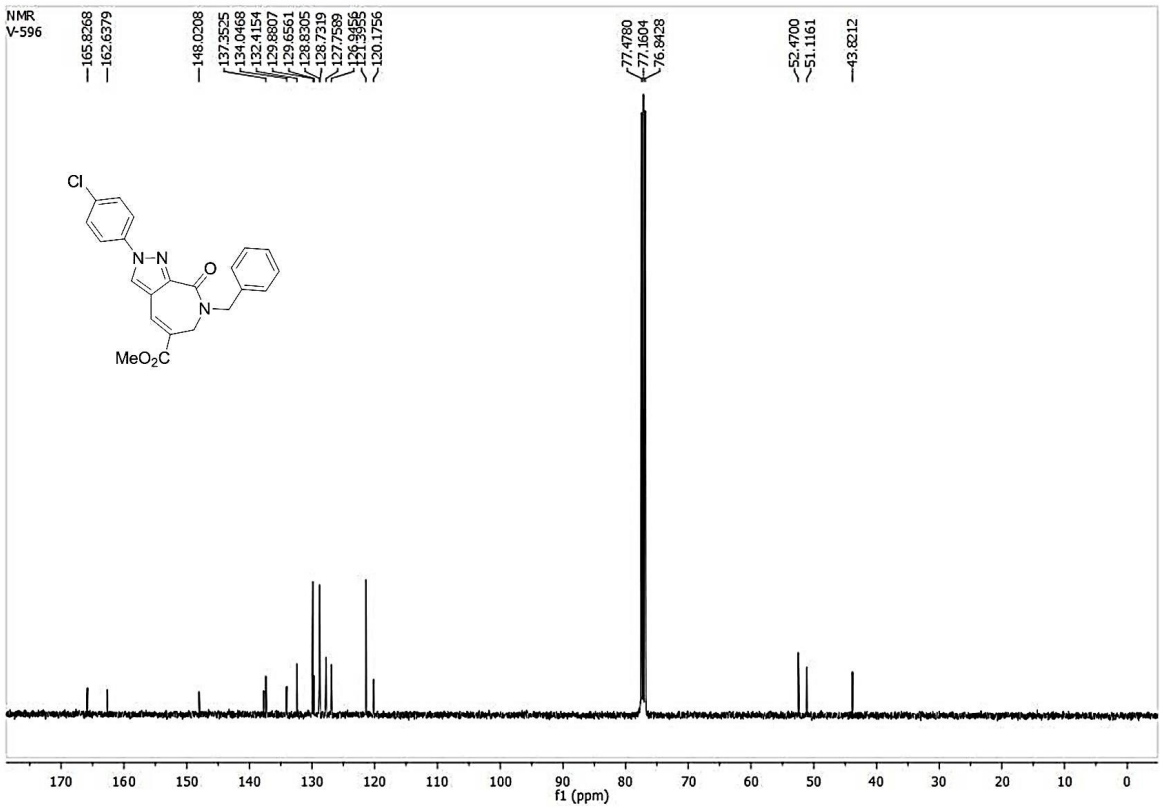


**Fig. S 92.** $^{13}$C-NMR of methyl 7-benzyl-2-(4-chlorophenyl)-8-oxo-2,6,7,8-tetrahydropyrazolo[3,4-*c*]azepine-5-carboxylate **(13dBV).**

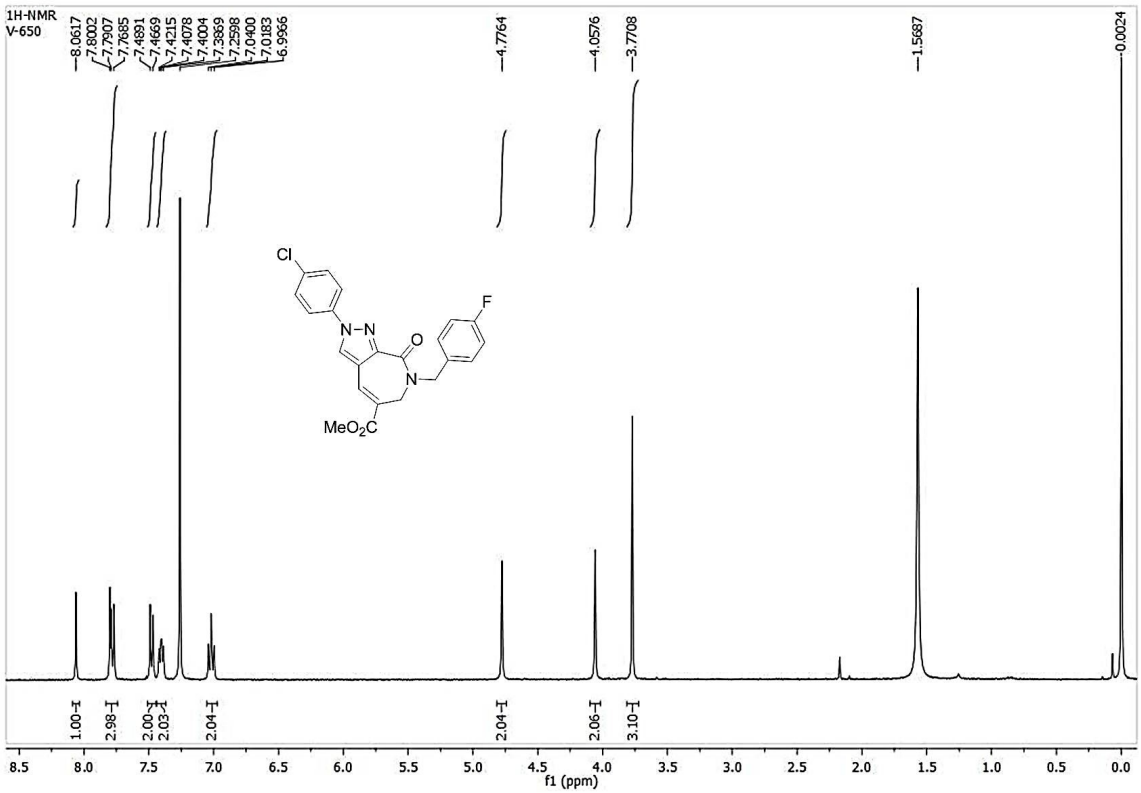


**Fig. S 93.** $^{1}$H-NMR of methyl 2-(4-chlorophenyl)-7-(4-fluorobenzyl)-8-oxo-2,6,7,8-tetrahydropyrazolo[3,4-*c*]azepine-5-carboxylate **(13dBX).**

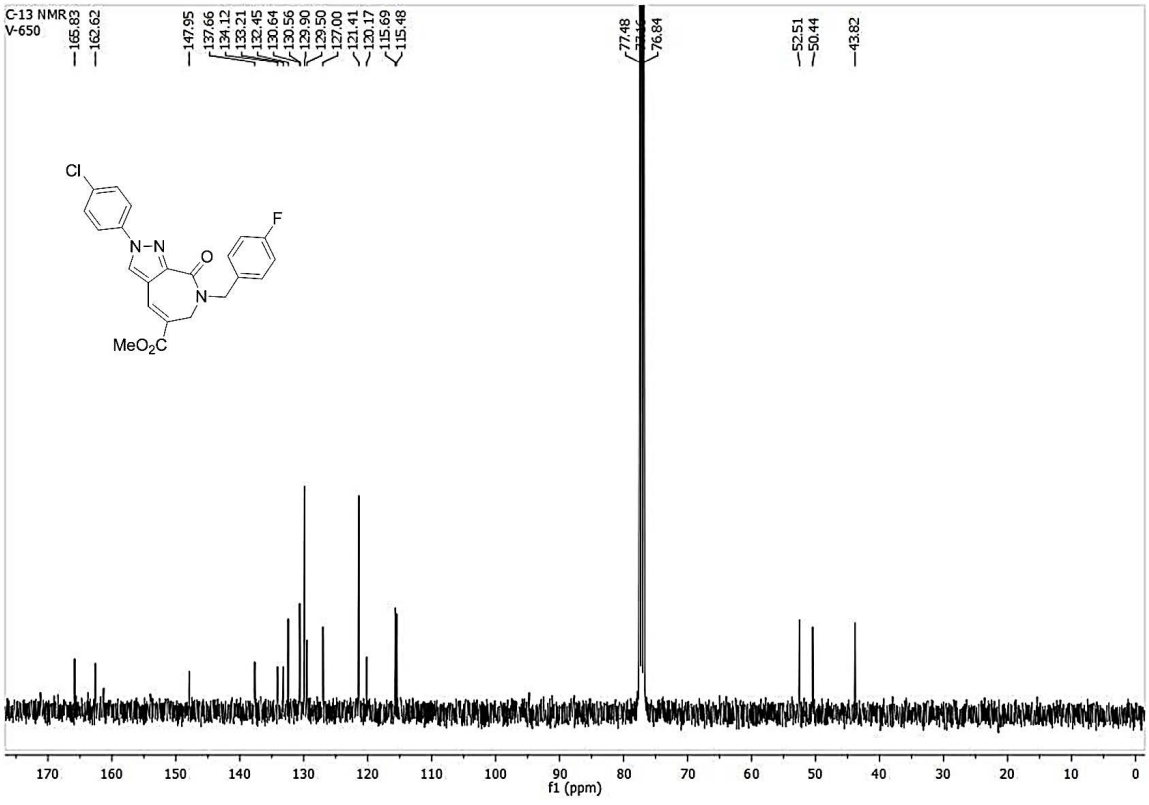


**Fig. S 94.** $^{13}$C-NMR of methyl 2-(4-chlorophenyl)-7-(4-fluorobenzyl)-8-oxo-2,6,7,8-tetrahydropyrazolo[3,4-*c*]azepine-5-carboxylate **(13dBX).**

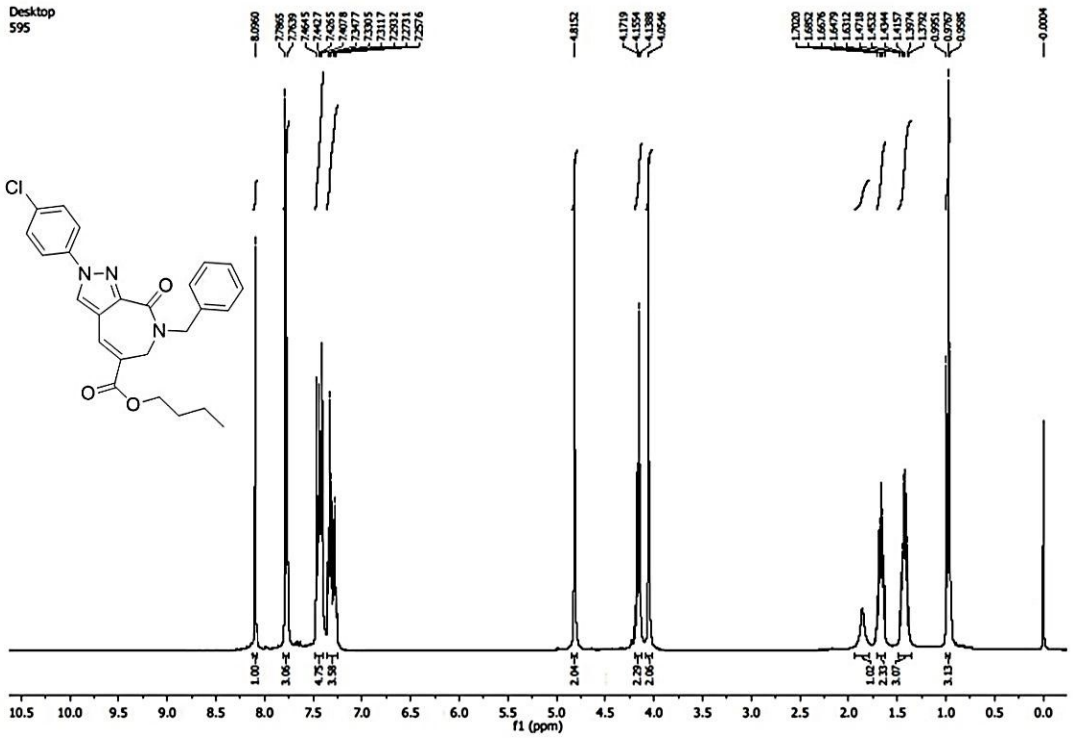


**Fig. S 95.** $^{1}$H-NMR of butyl 7-benzyl-2-(4-chlorophenyl)-8-oxo-2,6,7,8-tetrahydropyrazolo[3,4-*c*]azepine-5-carboxylate **(13dCV).**

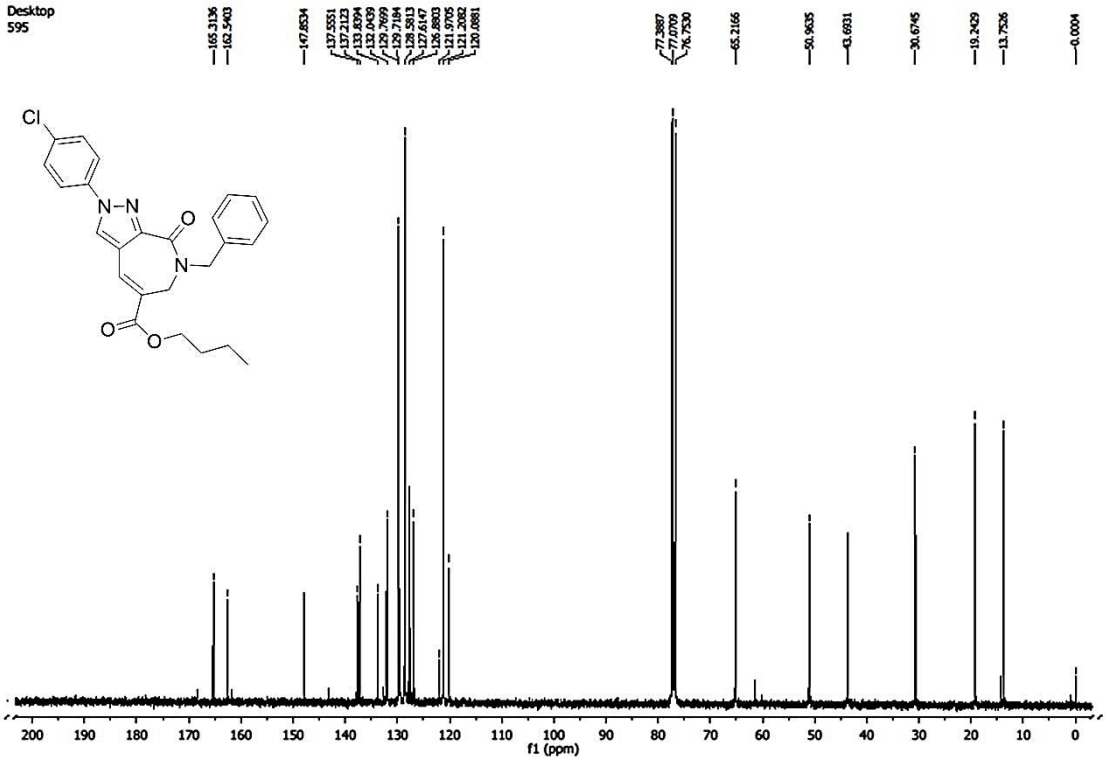


**Fig. S 96.** $^{13}$C-NMR of butyl 7-benzyl-2-(4-chlorophenyl)-8-oxo-2,6,7,8-tetrahydropyrazolo[3,4-*c*]azepine-5-carboxylate **(13dCV).**

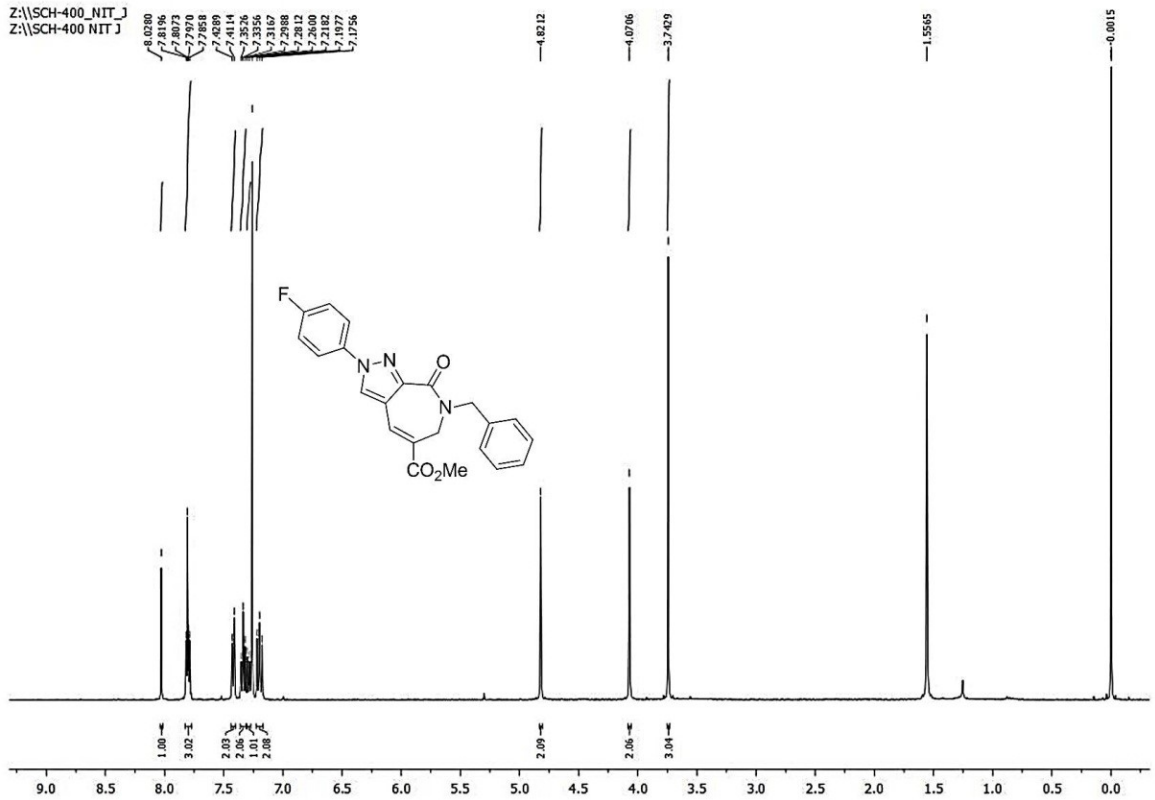


**Fig. S 97.** $^{1}$H-NMR of methyl 7-benzyl-2-(4-fluorophenyl)-8-oxo-2,6,7,8-tetrahydropyrazolo[3,4-*c*]azepine-5-carboxylate **(13eBV).**

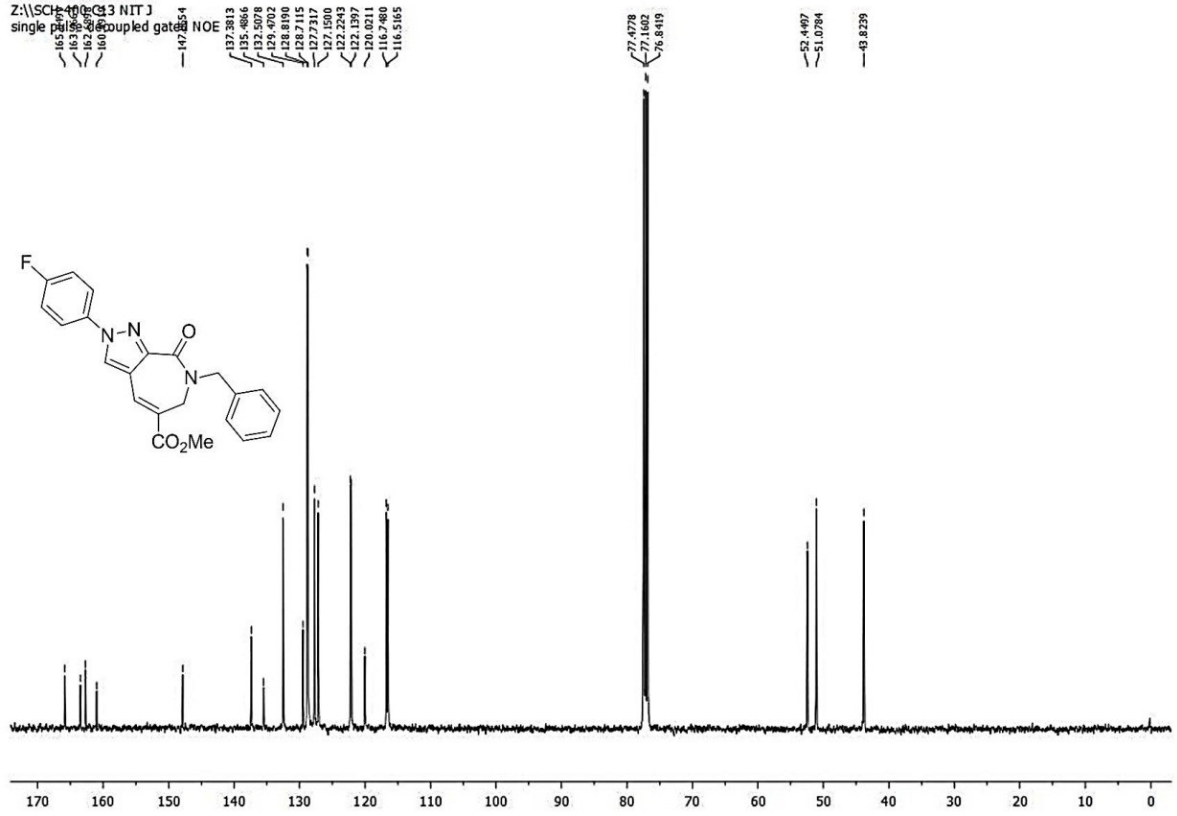


**Fig. S 98.** $^{13}$C-NMR of methyl 7-benzyl-2-(4-fluorophenyl)-8-oxo-2,6,7,8-tetrahydropyrazolo[3,4-*c*]azepine-5-carboxylate **(13eBV).**

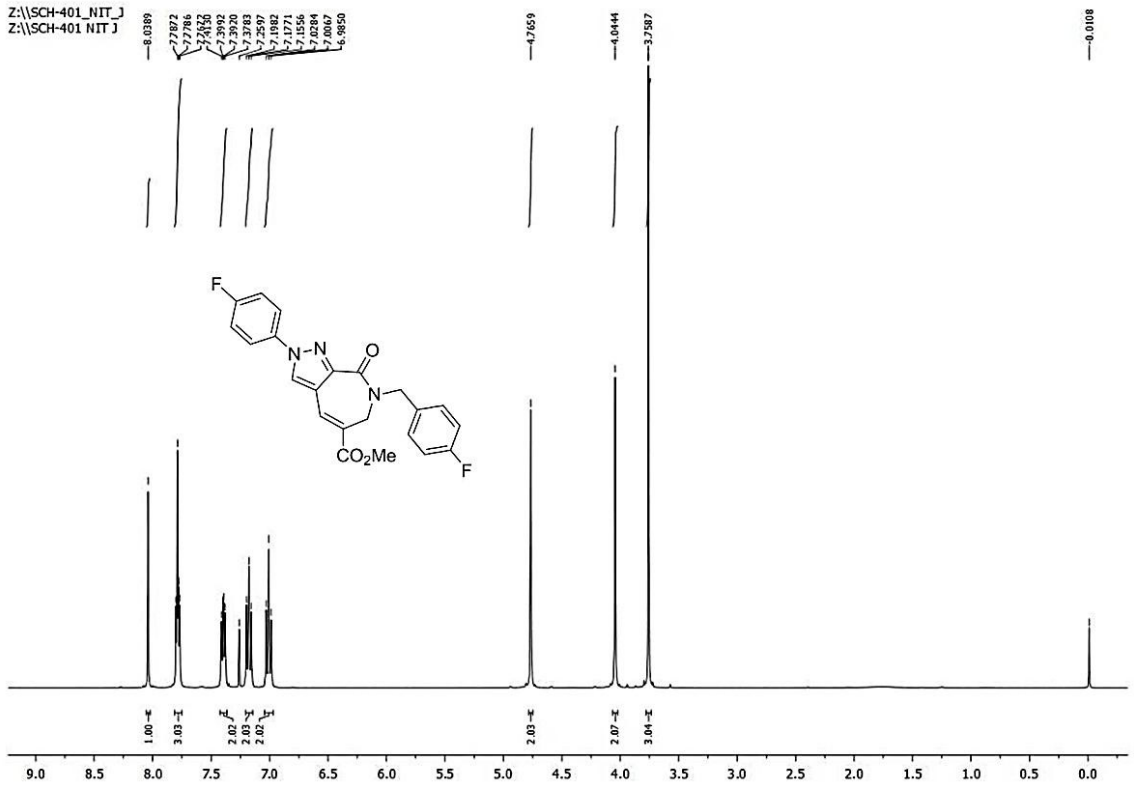


**Fig. S 99.** $^{1}$H-NMR of methyl 7-(4-fluorobenzyl)-2-(4-fluorophenyl)-8-oxo-2,6,7,8-tetrahydropyrazolo[3,4-*c*]azepine-5-carboxylate **(13eBX).**

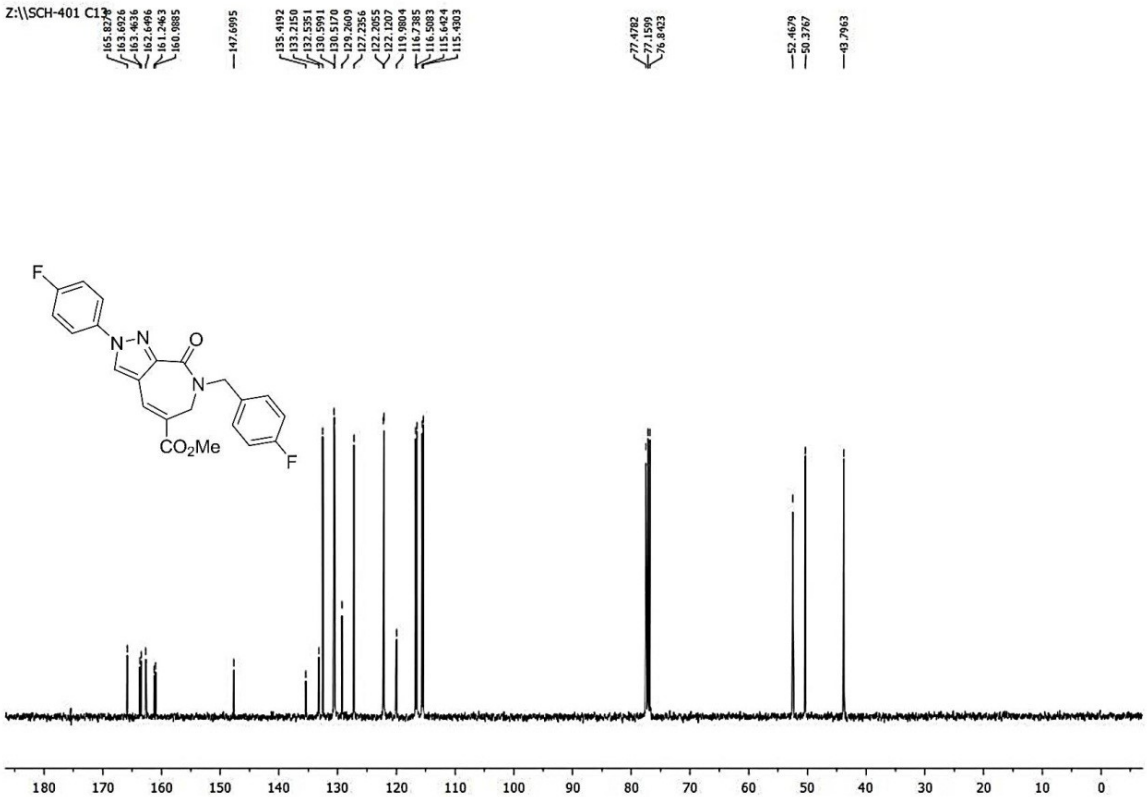


**Fig. S 100.** $^{13}$C-NMR of methyl 7-(4-fluorobenzyl)-2-(4-fluorophenyl)-8-oxo-2,6,7,8-tetrahydropyrazolo[3,4-*c*]azepine-5-carboxylate **(13eBX).**

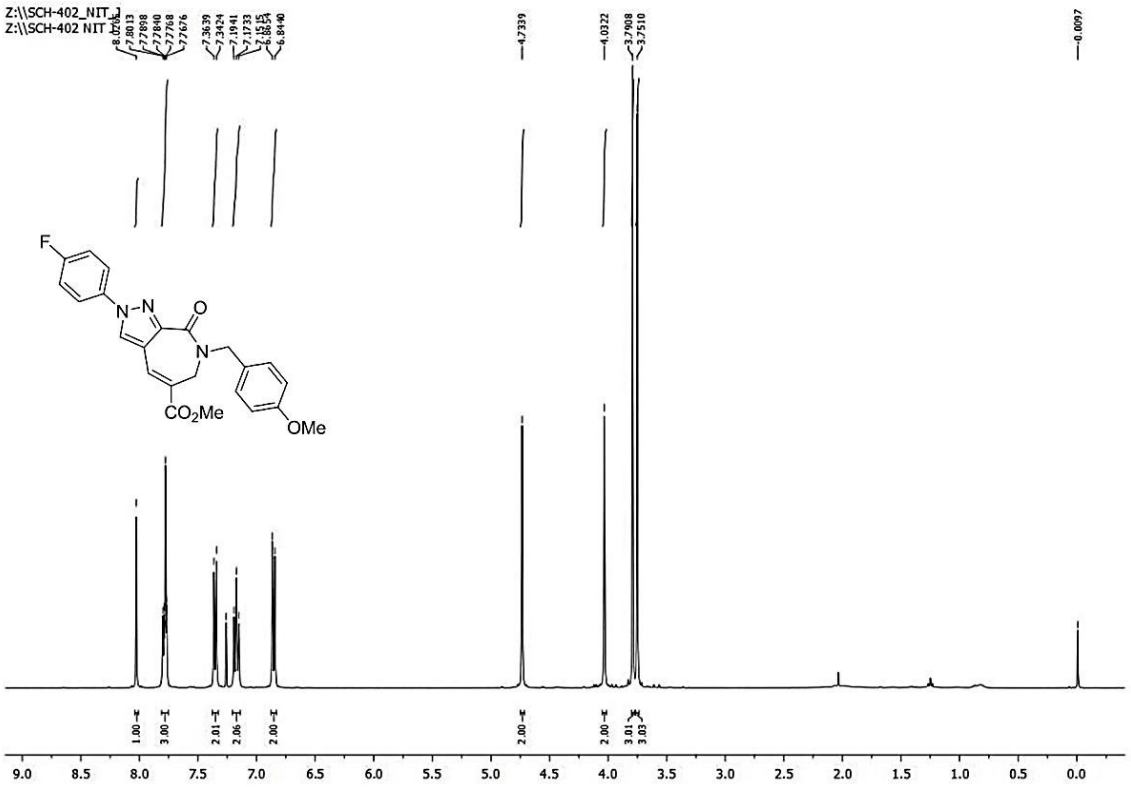


**Fig. S 101.** [1]H-NMR of methyl 2-(4-fluorophenyl)-7-(4-methoxybenzyl)-8-oxo-2,6,7,8-tetrahydropyrazolo[3,4-*c*]azepine-5-carboxylate **(13eBY).**

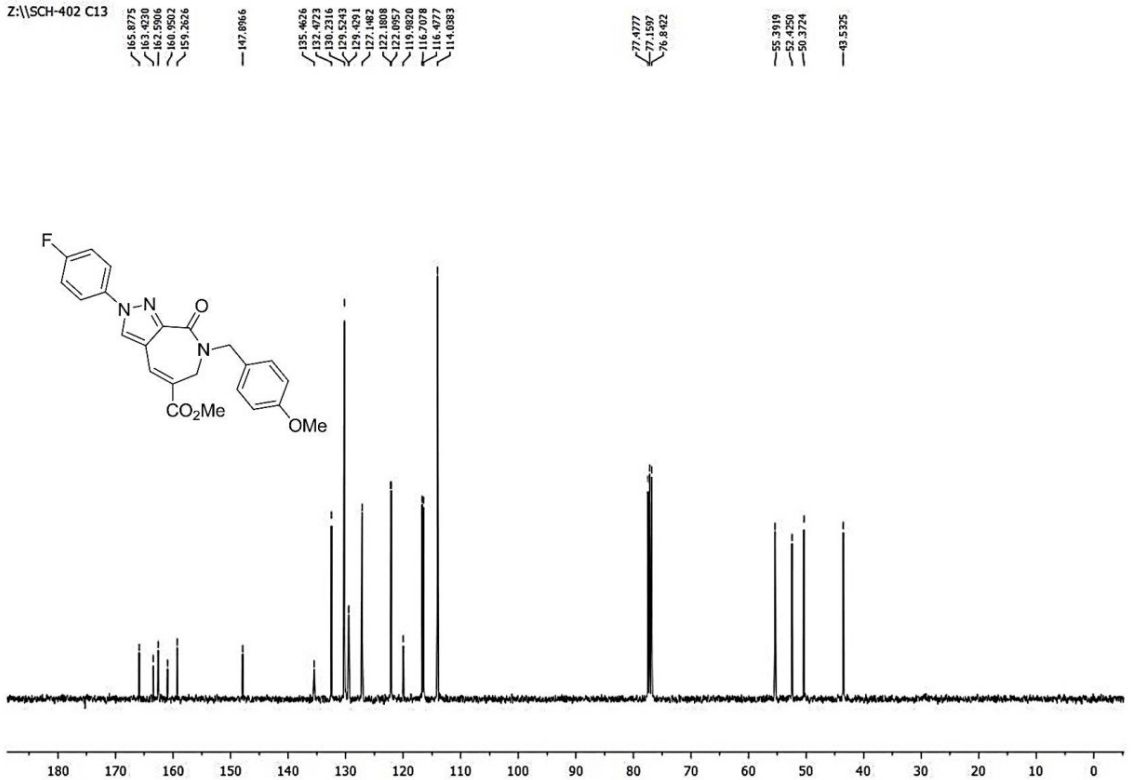


**Fig. S 102.** [13]C-NMR of methyl 2-(4-fluorophenyl)-7-(4-methoxybenzyl)-8-oxo-2,6,7,8-tetrahydropyrazolo[3,4-*c*]azepine-5-carboxylate **(13eBY).**

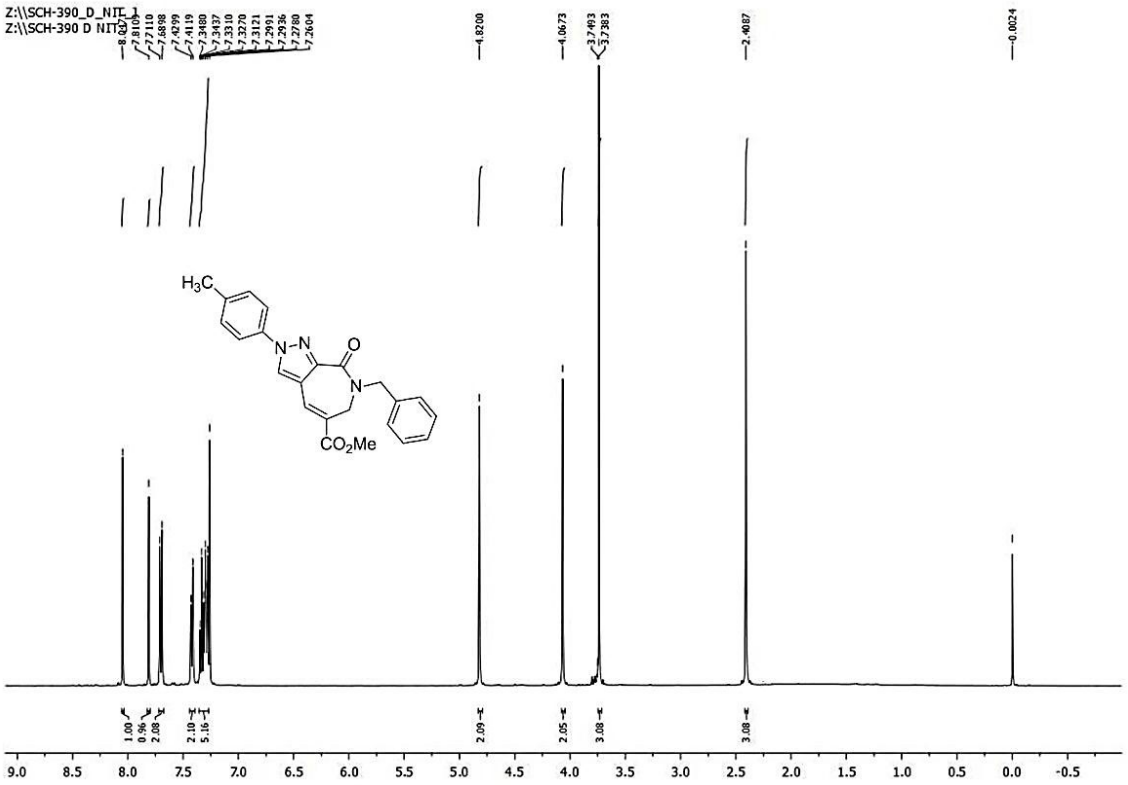

**Fig. S 103.** [1]H-NMR of methyl 7-benzyl-8-oxo-2-(*p*-tolyl)-2,6,7,8-tetrahydropyrazolo[3,4-*c*]azepine-5-carboxylate **(13fBV).**

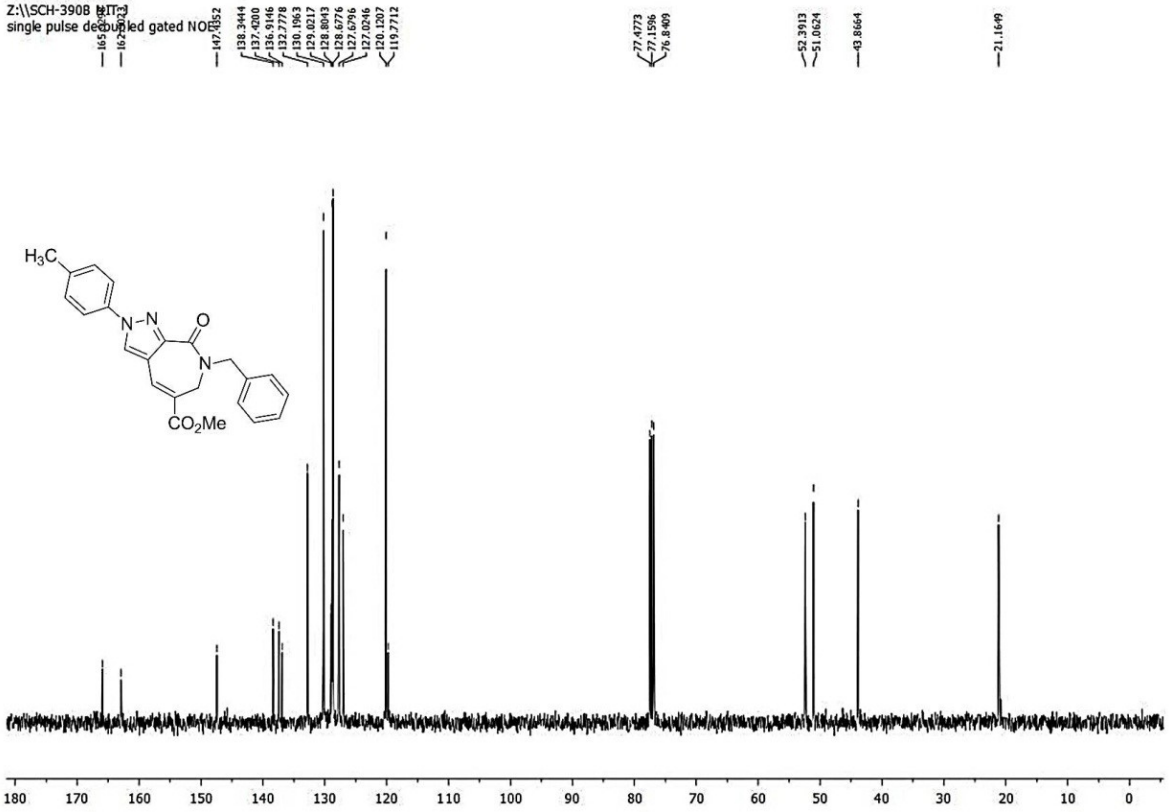

**Fig. S 104.** [13]C-NMR of methyl 7-benzyl-8-oxo-2-(*p*-tolyl)-2,6,7,8-tetrahydropyrazolo[3,4-*c*]azepine-5-carboxylate **(13fBV).**

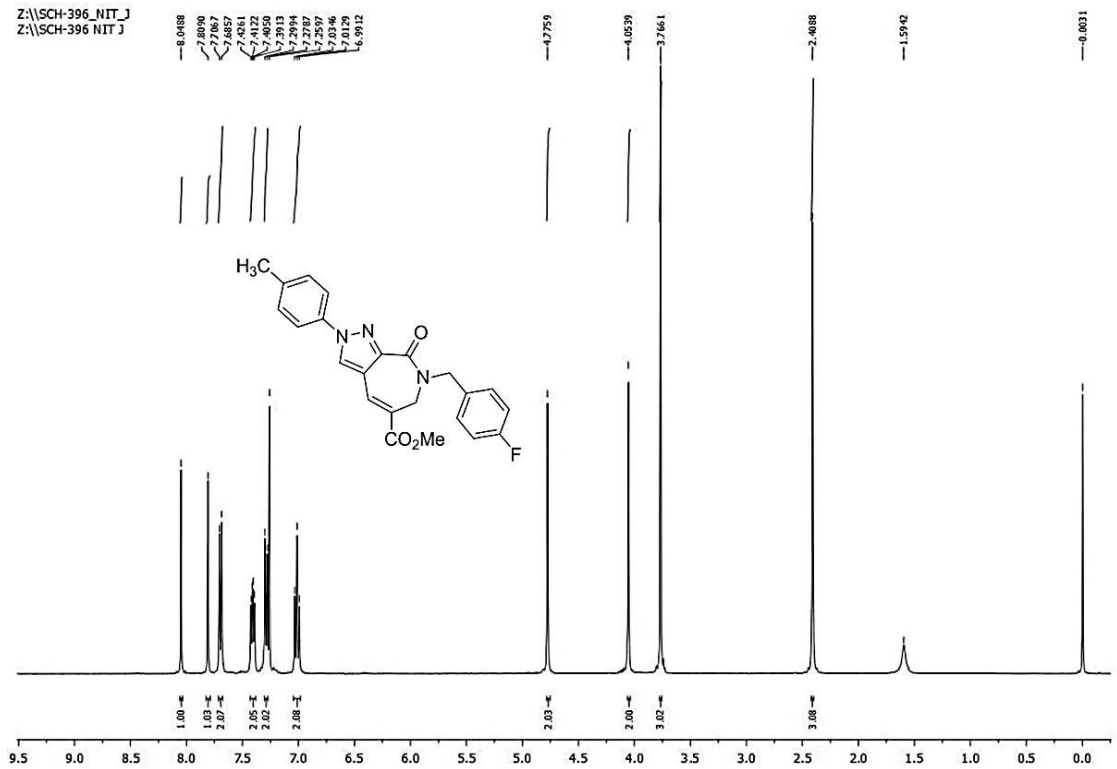


**Fig. S 105.** $^{1}$H-NMR of methyl 7-(4-fluorobenzyl)-8-oxo-2-(*p*-tolyl)-2,6,7,8-tetrahydropyrazolo[3,4-*c*]azepine-5-carboxylate **(13fBX).**

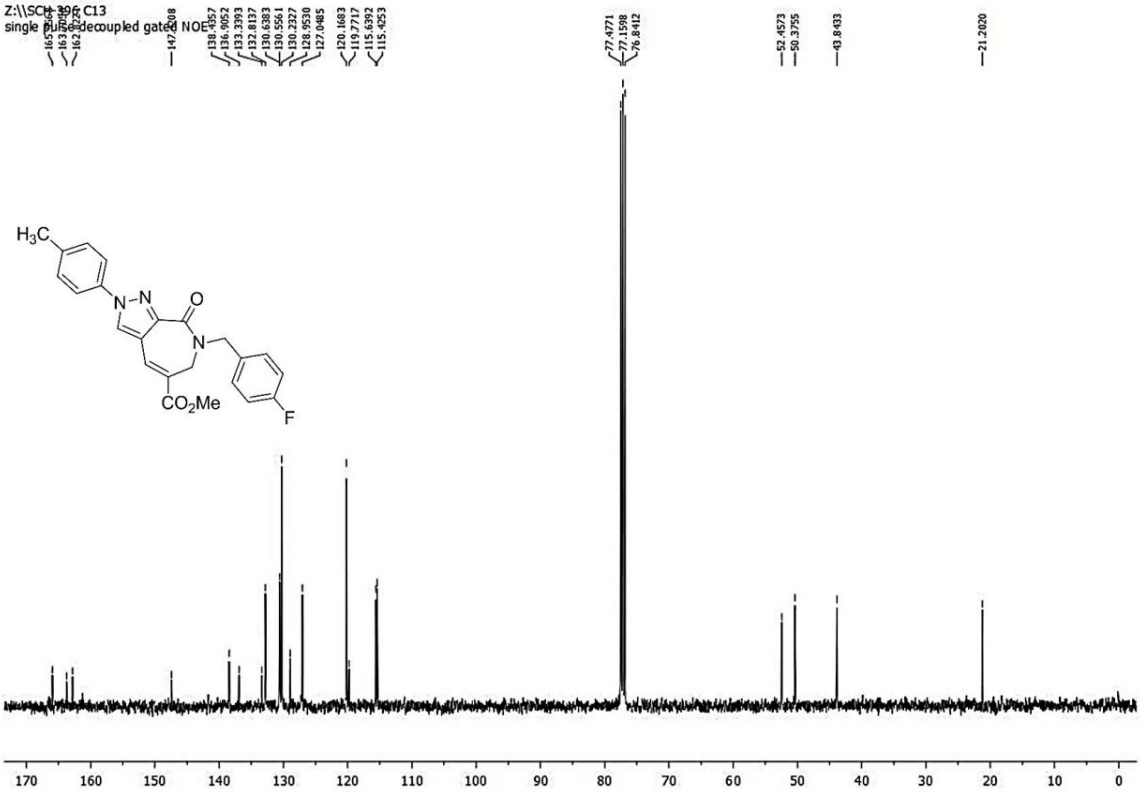


**Fig. S 106.** $^{13}$C-NMR of methyl 7-(4-fluorobenzyl)-8-oxo-2-(*p*-tolyl)-2,6,7,8-tetrahydropyrazolo[3,4-*c*]azepine-5-carboxylate **(13fBX).**

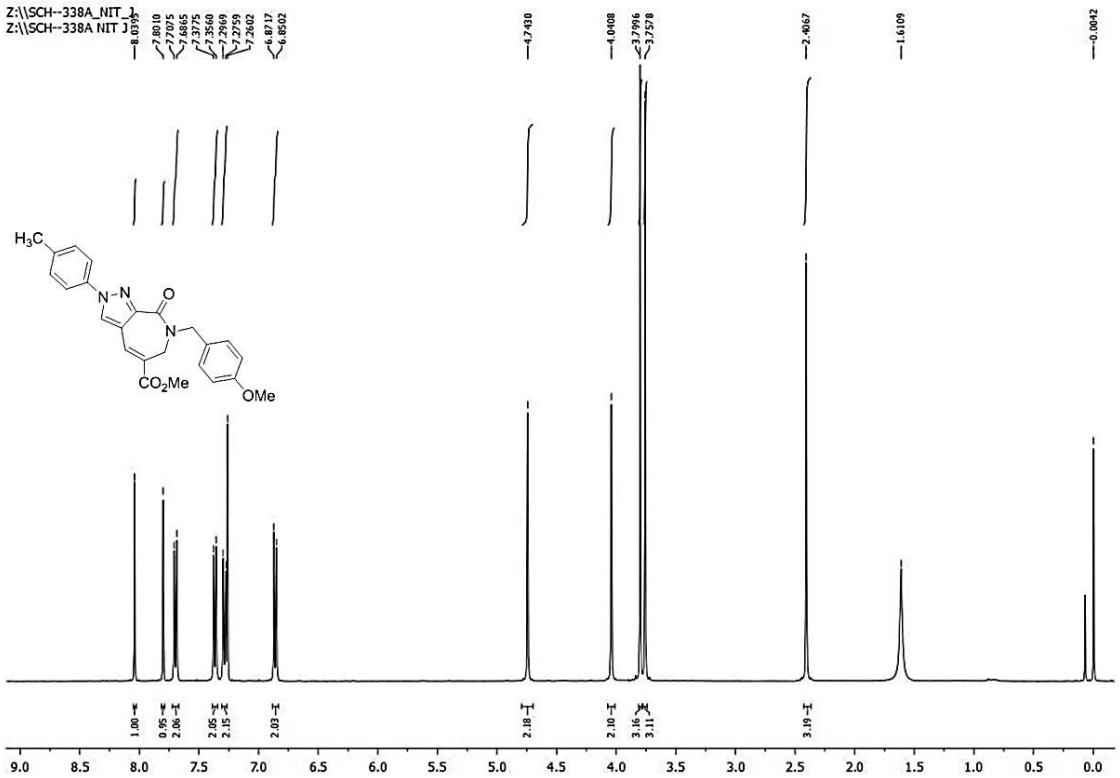

**Fig. S 107.** $^{1}$H-NMR of methyl 7-(4-methoxybenzyl)-8-oxo-2-(*p*-tolyl)-2,6,7,8-tetrahydropyrazolo[3,4-*c*]azepine-5-carboxylate **(13fBY).**

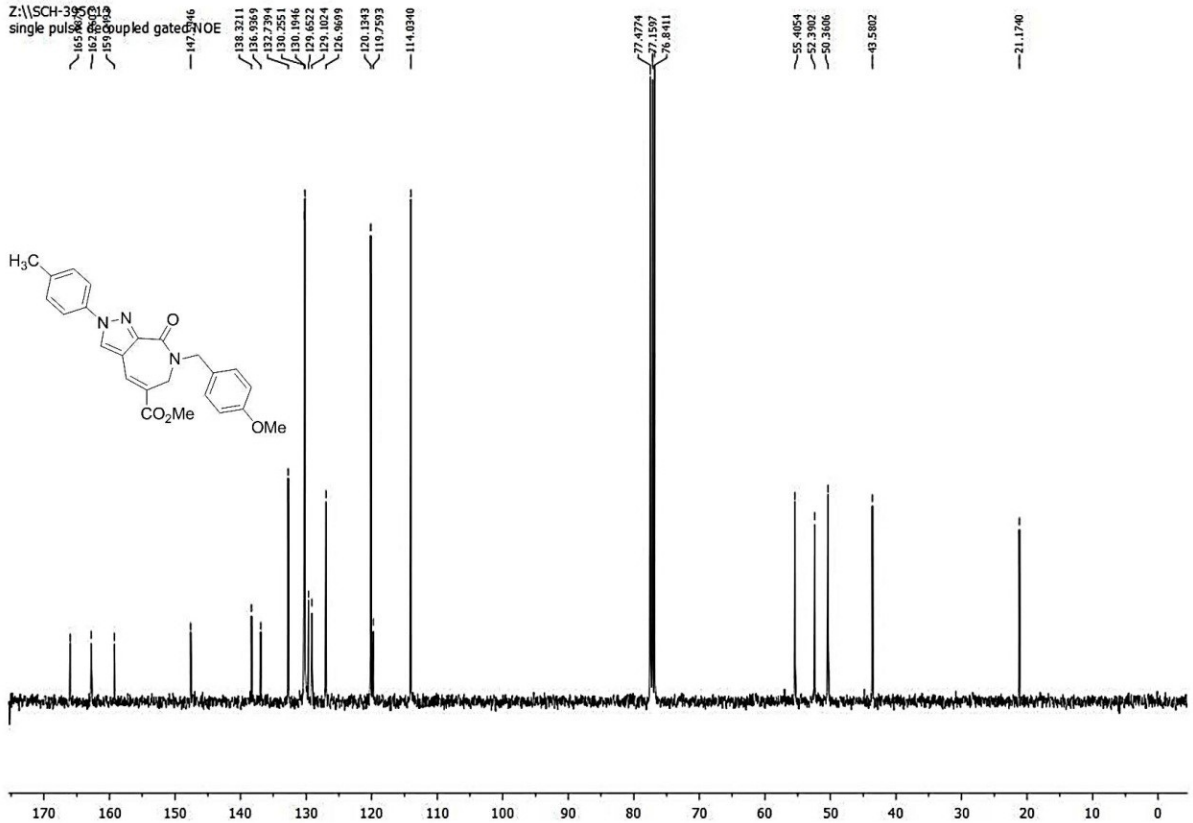

**Fig. S 108.** $^{13}$C-NMR of methyl 7-(4-methoxybenzyl)-8-oxo-2-(*p*-tolyl)-2,6,7,8-tetrahydropyrazolo[3,4-*c*]azepine-5-carboxylate **(13fBY).**

**VIII.** $^{1}$H- and $^{13}$C- NMR spectra of the new pyrazole products **14**

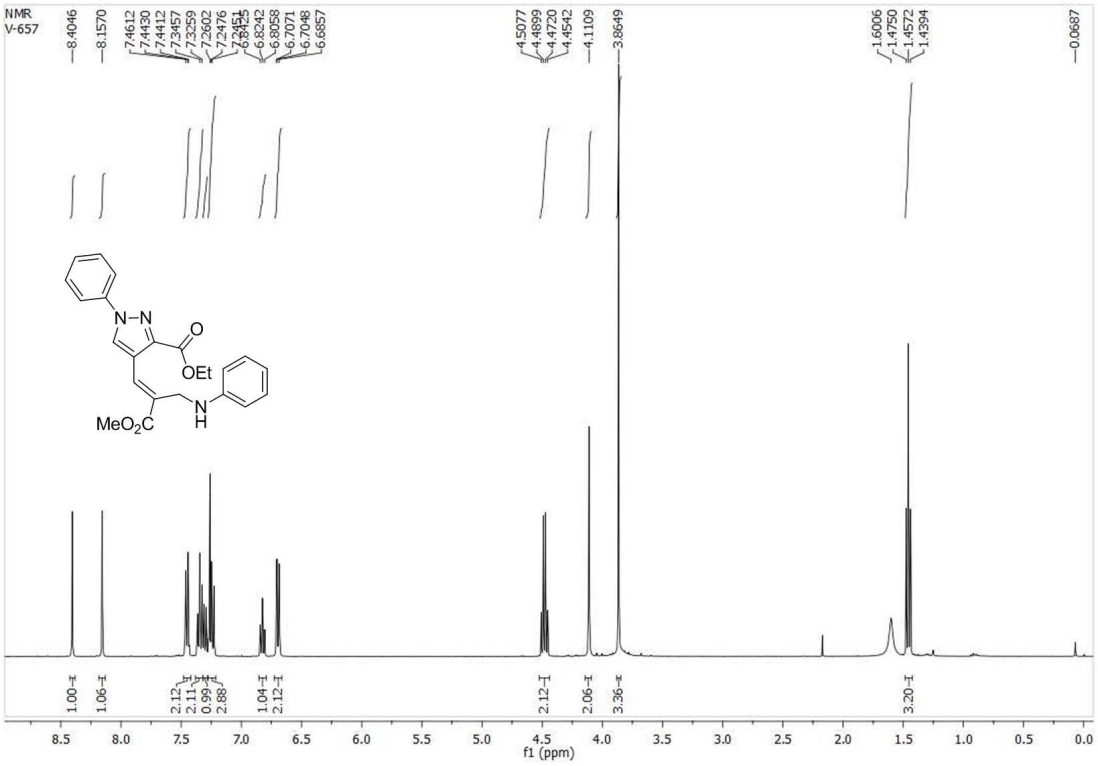


**Fig. S 109.** $^{1}$H-NMR of (*E*)-Ethyl 4-(3-methoxy-3-oxo-2-((phenylamino)methyl)prop-1-en-1-yl)-1-phenyl-1*H*-pyrazole-3-carboxylate **(14aBX')**.

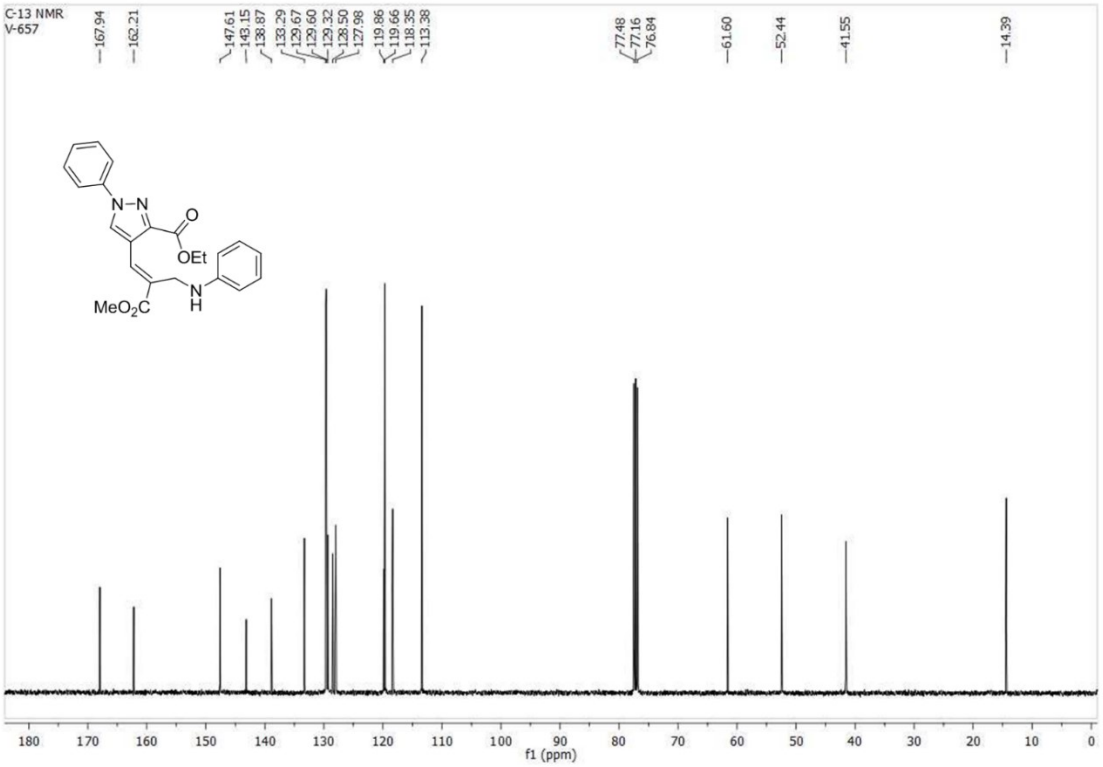


**Fig. S 110.** $^{13}$C-NMR of (*E*)-Ethyl 4-(3-methoxy-3-oxo-2-((phenylamino)methyl)prop-1-en-1-yl)-1-phenyl-1*H*-pyrazole-3-carboxylate **(14aBX')**.

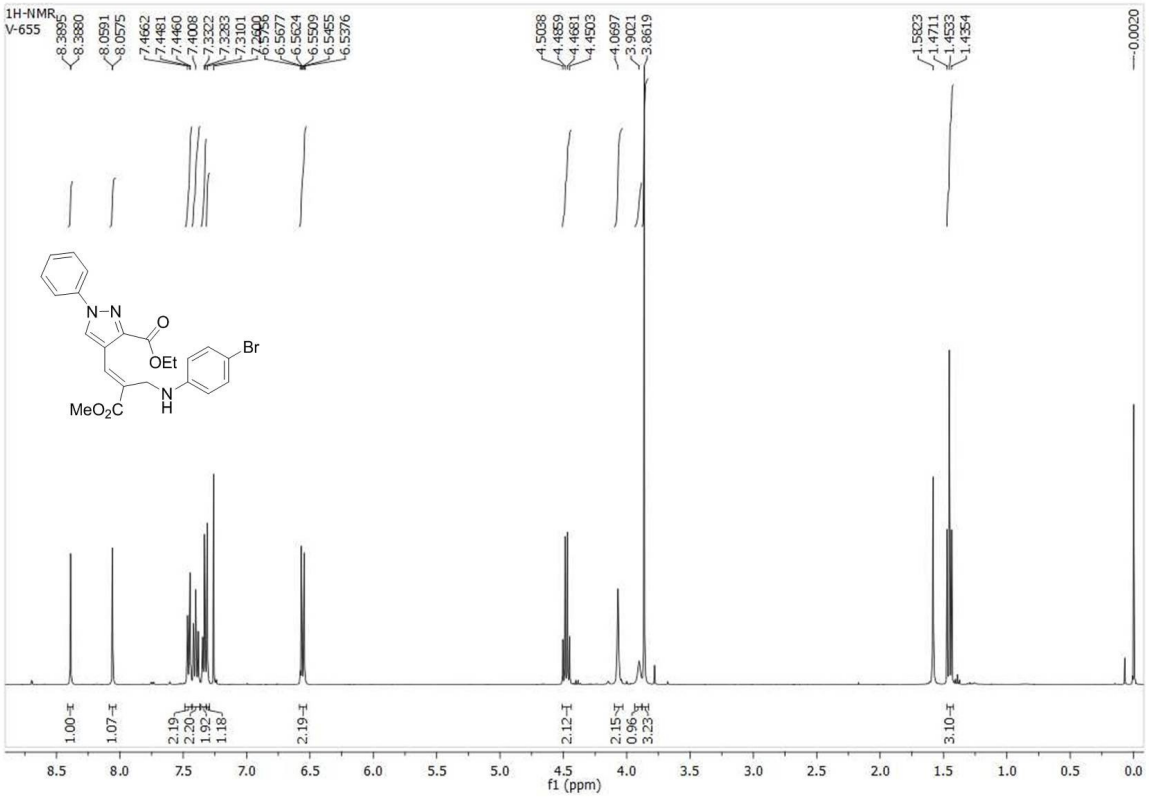


**Fig. S 111.** $^{1}$H-NMR of (*E*)-Ethyl 4-(2-(((4-bromophenyl)amino)methyl)-3-methoxy-3-oxoprop-1-en-1-yl)-1-phenyl-1*H*-pyrazole-3-carboxylate **(14aBY')**.

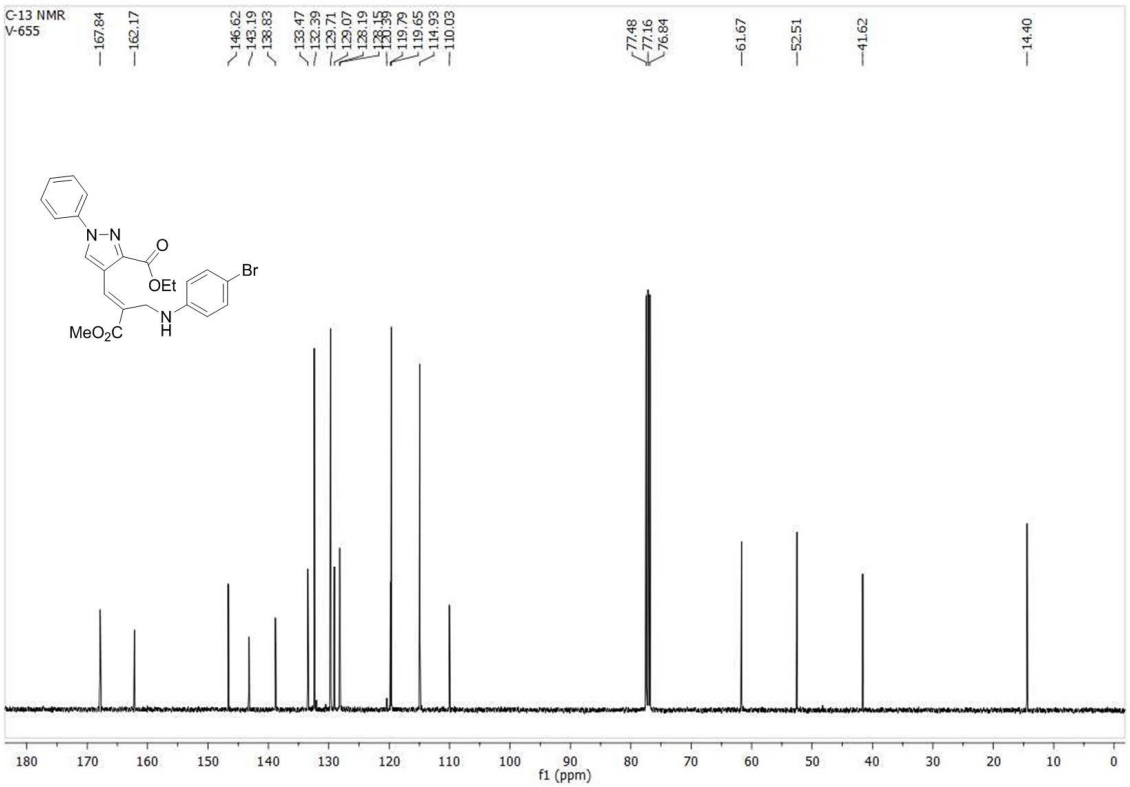


**Fig. S 112.** $^{13}$C-NMR of (*E*)-Ethyl 4-(2-(((4-bromophenyl)amino)methyl)-3-methoxy-3-oxoprop-1-en-1-yl)-1-phenyl-1*H*-pyrazole-3-carboxylate **(14aBY')**.

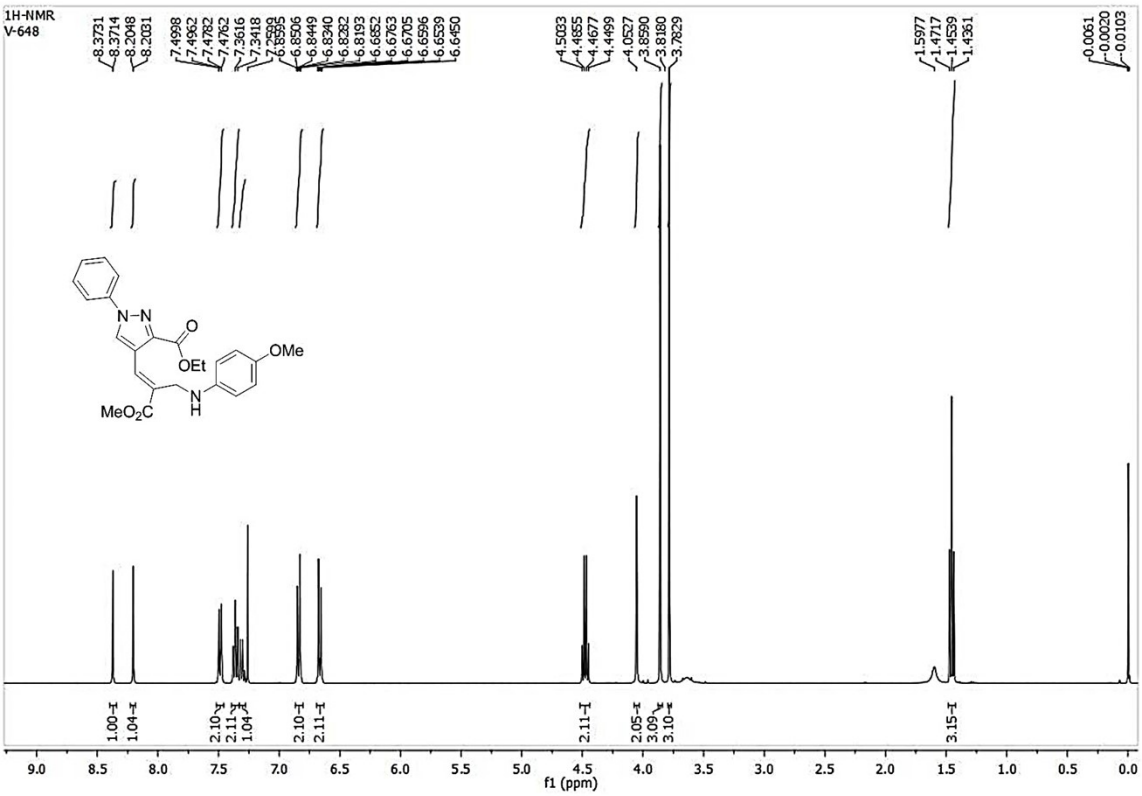


**Fig. S 113.** $^{1}$H-NMR of (*E*)-Ethyl 4-(3-methoxy-2-(((4-methoxyphenyl)amino)methyl)-3-oxoprop-1-en-1-yl)-1-phenyl-1*H*-pyrazole-3-carboxylate **(14aBZ')**.

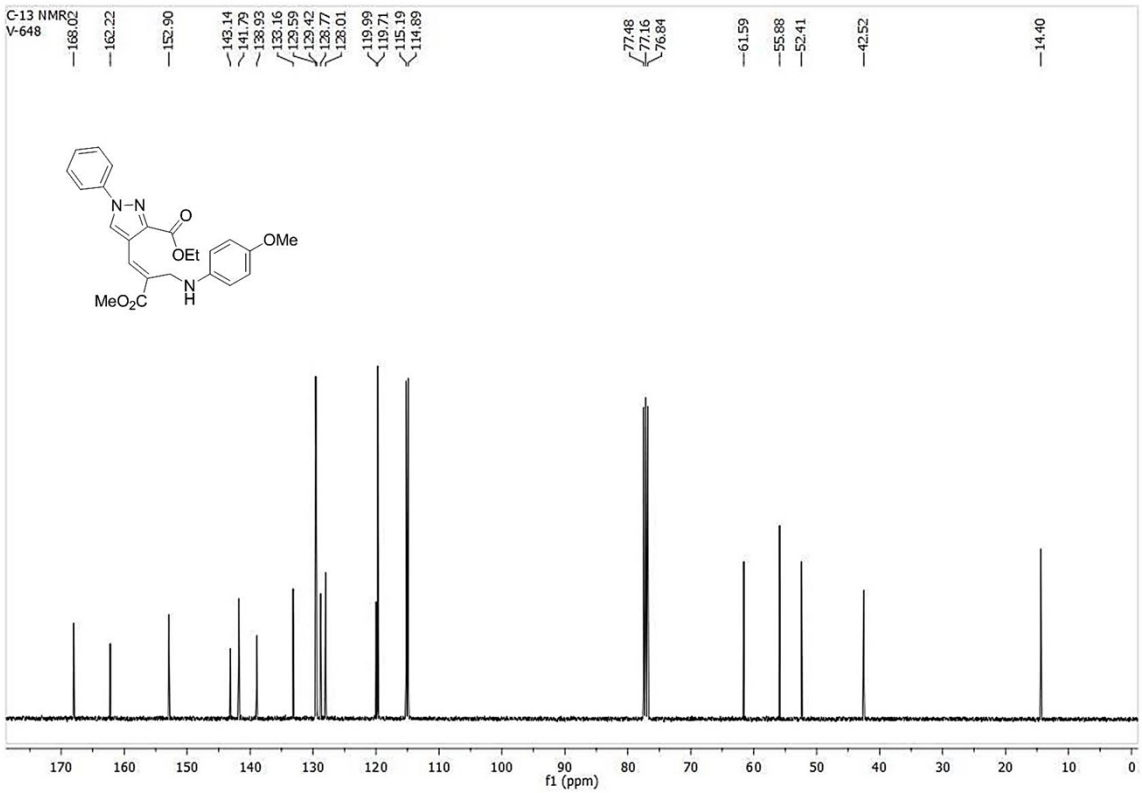


**Fig. S 114.** $^{13}$C-NMR of (*E*)-Ethyl 4-(3-methoxy-2-(((4-methoxyphenyl)amino)methyl)-3-oxoprop-1-en-1-yl)-1-phenyl-1*H*-pyrazole-3-carboxylate **(14aBZ')**.