Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Synthesis of Pyrazolo[5,1-*a*]isoquinolines through Copper-Catalyzed Regioselective Bicyclization of *N*-Propargylic Sulfonylhydrazones

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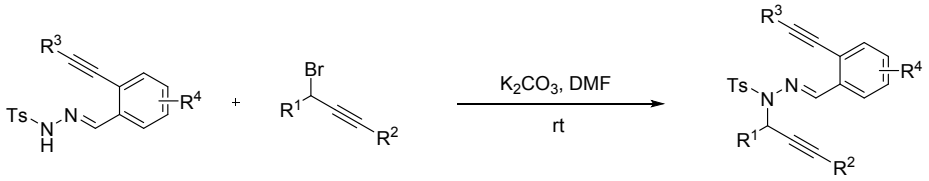
Content

General Information

Unless otherwise noted, all reagents and solvents were obtained commercially and used without further purification. *N*-sulfonylhydrazones **1** were prepared according to our previous work. Column chromatography on silica gel (300-400 mesh) was carried out using technical grade 60-90 ^{o}C petroleum ether (distillated prior to use) and analytical grade EtOAc (without further purification). ^{1}H and ^{13}C spectra were recorded on a 500 MHz or 400 MHz spectrometer. Chemical shifts were reported in ppm. ^{1}H NMR spectra were referenced to $CDCl_3$ (7.26 ppm), and ^{13}C-NMR spectra were referenced to $CDCl_3$ (77.0 ppm). Peak multiplicities were designated by the following abbreviations: s, singlet; d, doublet; t, triplet; m, multiplet; brs, broad singlet and J, coupling constant in Hz.[1] IR spectra were recorded on an FTIR spectrometer as thin film. Absorptions were given in wavenumbers (cm^{-1}). HRMS spectra were recorded with Micromass QTOF2 Quadrupole/Time-of-Flight Tandem mass spectrometer using electron spray ionization.

General procedure for synthesis of *N*-propargylic sulfonylhydrazones 1 and pyrazolo[5,1-*a*]isoquinolines 2

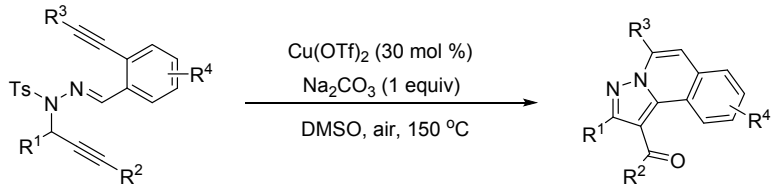
General procedure for synthesis of *N*-propargylic sulfonylhydrazones **1**



5 **6** **1**

To a solution of *N*-sulfonylhydrazone **5** (2 mmol) and propargyl bromide **6** (2.2 mmol) in DMF (10 mL), K_2CO_3 (2.2 mmol) were slowly added. The reaction mixture was stirred at room temperature, and the reaction progress monitored by TLC. Upon completion, the mixture was filtered off and water (20 mL) was added. The aqueous phase was extracted with CH_2Cl_2 (3×10 mL). The combined organic layers were washed with brine, dried over Na_2SO_4. The solvent was removed under vacuum, and then the residue was further purified by silica gel column chromatography (petroleum ether and ethyl acetate) to afford propargylic hydrazone **1**.

General procedure for synthesis pyrazolo[5,1-*a*]isoquinolines **2**



1 **2**

To a solution of *N*-propargylic sulfonylhydrazone **1** (0.5 mmol) and Na_2CO_3 (0.5 mmol) in DMSO (5 mL), $Cu(OTf)_2$ (0.15 mmol) was added and the mixture was stirred at 150 °C in air. When the reaction was completed (30 min - 1 h, monitored by TLC), water was added to the mixture. The aqueous phase was extracted with CH_2Cl_2 (3×10 mL). The combined organic layers were washed with brine, dried over Na_2SO_4. The solvent was removed under vacuum, and then the residue was further purified by silica gel column chromatography (petroleum ether and ethyl acetate) to afford product **2**.

Single crystal X-ray structure for 2i

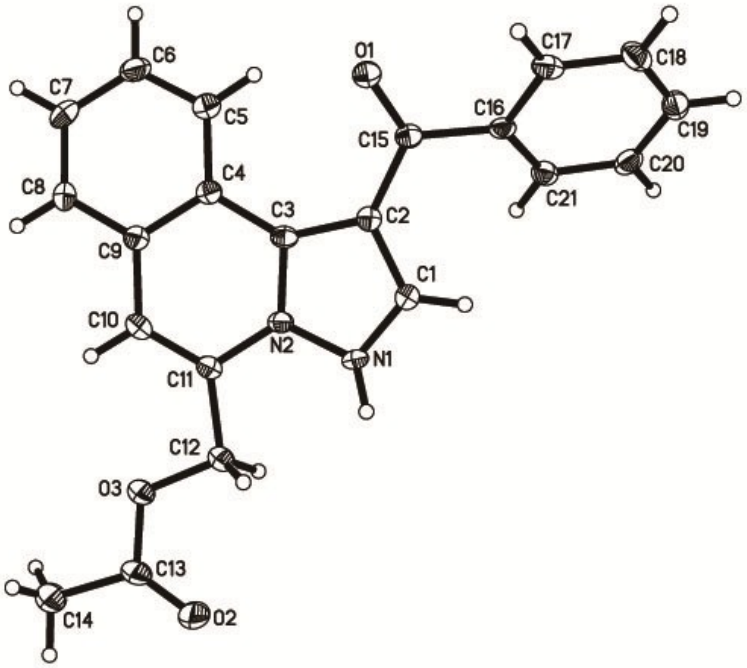


Figure S1. Single crystal X-ray structure for **2i** (drawn with 30% probability).

checkCIF/PLATON report

You have not supplied any structure factors. As a result the full set of tests cannot be run.

THIS REPORT IS FOR GUIDANCE ONLY. IF USED AS PART OF A REVIEW PROCEDURE FOR PUBLICATION, IT SHOULD NOT REPLACE THE EXPERTISE OF AN EXPERIENCED CRYSTALLOGRAPHIC REFEREE.

No syntax errors found. CIF dictionary Interpreting this report

Datablock: tht160623-1

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Cell:            a=11.0348(7)     b=21.2718(12)     c=7.2221(6)
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Temperature:     184 K

                Calculated               Reported
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Hall group      P 2c -2ac                ?
Moiety formula  C21 H17 N2 O3            ?
Sum formula     C21 H17 N2 O3            C21 H16 N2 O3
Mr              345.37                   344.36
Dx,g cm-3       1.353                    1.349
Z               4                        4
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Correction method= # Reported T Limits: Tmin=3.510 Tmax=*****
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S = 1.200                 Npar= 235
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The following ALERTS were generated. Each ALERT has the format
test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.

Alert level C

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ABSTY02_ALERT_1_C  An _exptl_absorpt_correction_type has been given without
           a literature citation. This should be contained in the
           _exptl_absorpt_process_details field.
           Absorption correction given as multi-scan
STRVA01_ALERT_2_C           Chirality of atom sites is inverted?
          From the CIF: _refine_ls_abs_structure_Flack    2.000
          From the CIF: _refine_ls_abs_structure_Flack_su    2.000
PLAT041_ALERT_1_C Calc. and Reported SumFormula    Strings  Differ     Please Check
PLAT043_ALERT_1_C Calculated and Reported Mol. Weight Differ by ..       1.01 Check
PLAT068_ALERT_1_C Reported F000 Differs from Calcd (or Missing)...     Please Check
PLAT089_ALERT_3_C Poor Data / Parameter Ratio (Zmax < 18) ........       7.00 Note
PLAT220_ALERT_2_C Non-Solvent Resd 1   C   Ueq(max)/Ueq(min) Range        3.3 Ratio
PLAT242_ALERT_2_C Low    'MainMol' Ueq as Compared to Neighbors of        C13 Check
PLAT250_ALERT_2_C Large U3/U1 Ratio for Average U(i,j) Tensor ....        2.2 Note
PLAT340_ALERT_3_C Low Bond Precision on  C-C Bonds ..............    0.00467 Ang.
PLAT420_ALERT_2_C D-H Without Acceptor       N1     --  H1A    ...     Please Check
PLAT907_ALERT_2_C Flack x > 0.5, Structure needs to be Inverted? .       2.00 Check
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Alert level G

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           Atom count from _chemical_formula_sum:C21 H16 N2 O3
           Atom count from the _atom_site data:  C21 H17 N2 O3
CELLZ01_ALERT_1_G Difference between formula and atom_site contents detected.
CELLZ01_ALERT_1_G ALERT: Large difference may be due to a
           symmetry error - see SYMMG tests
          From the CIF: _cell_formula_units_Z    4
          From the CIF: _chemical_formula_sum  C21 H16 N2 O3
          TEST: Compare cell contents of formula and atom_site data

          atom    Z*formula  cif sites diff
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          H         64.00     68.00   -4.00
          N          8.00      8.00    0.00
          O         12.00     12.00    0.00
PLAT005_ALERT_5_G No Embedded Refinement Details found  in the CIF     Please Do !
PLAT007_ALERT_5_G Number of Unrefined Donor-H Atoms ..............          1 Report
PLAT032_ALERT_4_G Std. Uncertainty on Flack Parameter Value High .      2.000 Report
PLAT093_ALERT_1_G No s.u.'s on H-positions, Refinement Reported as      mixed Check
PLAT380_ALERT_4_G Incorrectly? Oriented X(sp2)-Methyl Moiety .....        C14 Check
PLAT899_ALERT_4_G SHELXL97   is Deprecated and Succeeded by SHELXL       2014 Note
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   0 ALERT level A = Most likely a serious problem - resolve or explain
   0 ALERT level B = A potentially serious problem, consider carefully
  12 ALERT level C = Check. Ensure it is not caused by an omission or oversight
   9 ALERT level G = General information/check it is not something unexpected

   7 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
   7 ALERT type 2 Indicator that the structure model may be wrong or deficient
   2 ALERT type 3 Indicator that the structure quality may be low
   3 ALERT type 4 Improvement, methodology, query or suggestion
   2 ALERT type 5 Informative message, check
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It is advisable to attempt to resolve as many as possible of the alerts in all categories. Often the minor alerts point to easily fixed oversights, errors and omissions in your CIF or refinement strategy, so attention to these fine details can be worthwhile. In order to resolve some of the more serious problems it may be necessary to carry out additional measurements or structure refinements. However, the purpose of your study may justify the reported deviations and the more serious of these should normally be commented upon in the discussion or experimental section of a paper or in the "special_details" fields of the CIF. checkCIF was carefully designed to identify outliers and unusual parameters, but every test has its limitations and alerts that are not important in a particular case may appear. Conversely, the absence of alerts does not guarantee there are no aspects of the results needing attention. It is up to the individual to critically assess their own results and, if necessary, seek expert advice.

Publication of your CIF in IUCr journals

A basic structural check has been run on your CIF. These basic checks will be run on all CIFs submitted for publication in IUCr journals (*Acta Crystallographica*, *Journal of Applied Crystallography*, *Journal of Synchrotron Radiation*); however, if you intend to submit to *Acta Crystallographica Section C* or *E* or *IUCrData*, you should make sure that full publication checks are run on the final version of your CIF prior to submission.

Publication of your CIF in other journals

Please refer to the *Notes for Authors* of the relevant journal for any special instructions relating to CIF submission.

PLATON version of 11/08/2016; check.def file version of 04/08/2016

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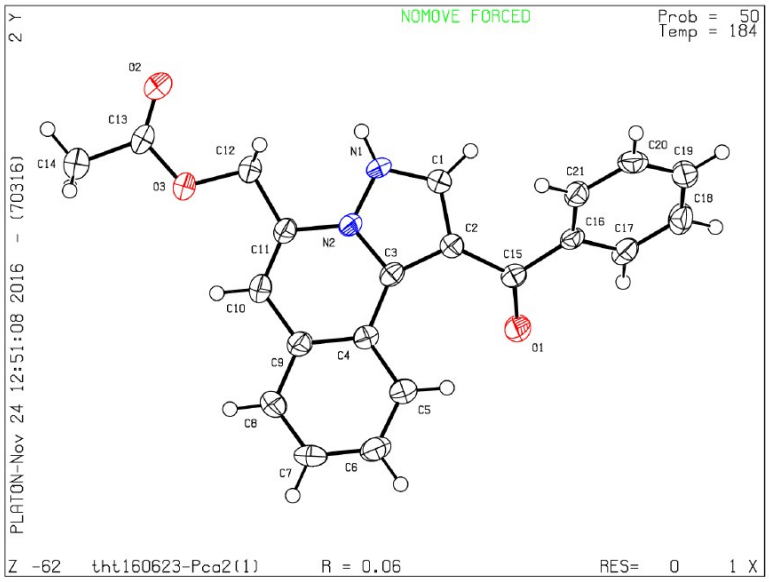
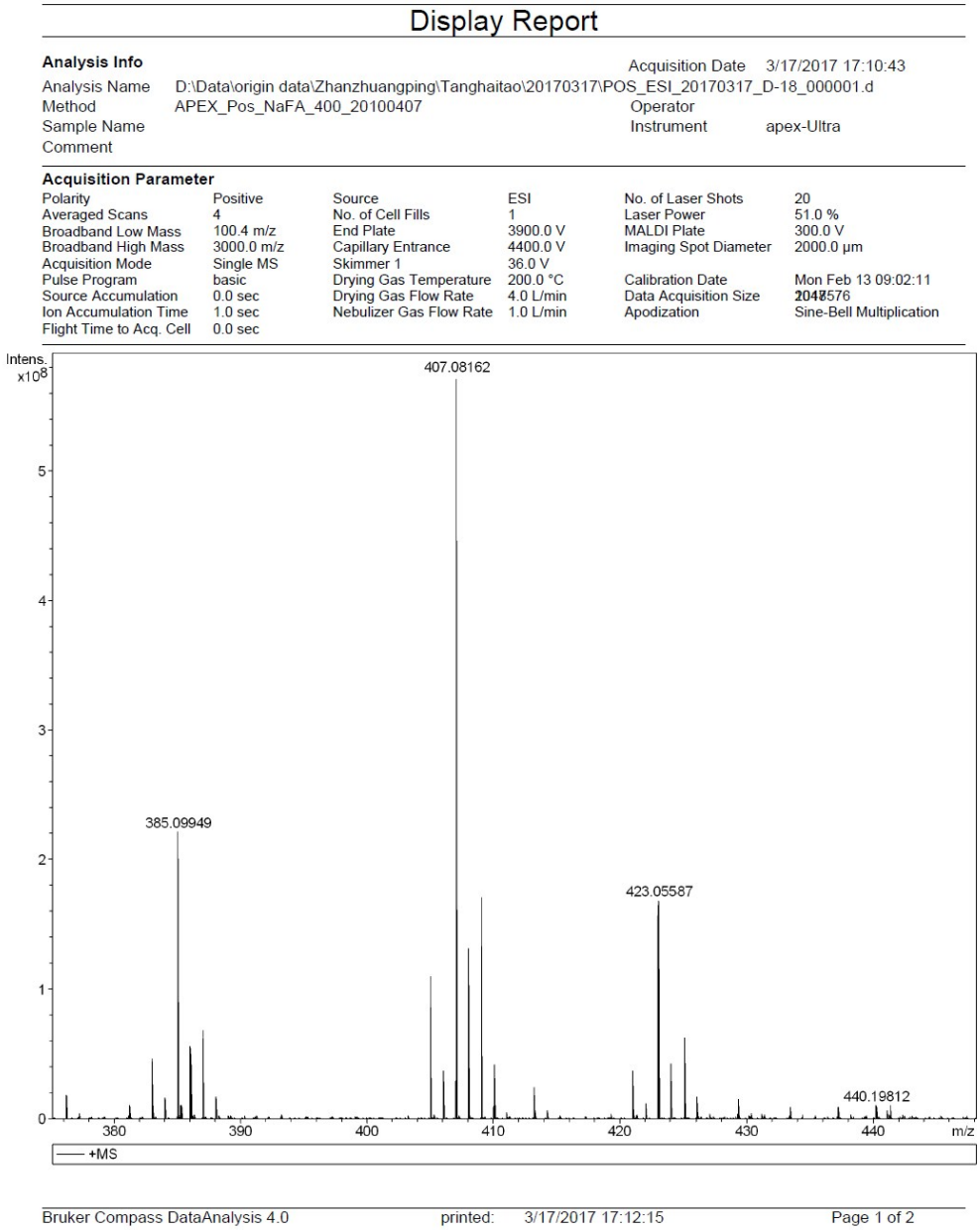


The HRMS of 2n-^{18}O



Display Report

Analysis Info

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Sample Name		Instrument	apex-Ultra
Comment			

Acquisition Parameter

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Broadband High Mass	3000.0 m/z	Capillary Entrance	4400.0 V	Imaging Spot Diameter	2000.0 µm
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Flight Time to Acq. Cell	0.0 sec				

Bruker Compass DataAnalysis 4.0 printed: 3/17/2017 17:12:15 Page 1 of 2

Figure S2. **2n**-^{18}O HRMS (ESI) *m/z* calcd for $C_{24}H_{15}ClN_2{}^{18}O$ $[M+Na]^+$ 407.0808, found: 407.0816.

^{1}H, ^{13}C-NMR, IR, MP and MS Data of 2a-2g, 2i-2s, 2v, 4v

Phenyl(5-phenylpyrazolo[5,1-a]isoquinolin-1-yl)methanone ***(2a).*** A white solid (mp: 182-183 ^{o}C, Rf = 0.6, petroleum ether/ethyl acetate = 6:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (s, 1H), 7.50-7.58 (m, 5H), 7.59-7.64 (m, 1H), 7.65-7.72 (m, 2H), 7.81-7.88 (m, 3H), 7.96 (d, 2H, *J* = 7.38 Hz), 8.16 (s, 1H), 9.45 (d, 1H, *J* = 7.74 Hz); ^{13}C NMR (100 MHz, CDCl3) δ 115.8, 123.9, 126.9, 127.1, 127.7, 128.4, 128.4, 129.5, 129.7, 129.8, 129.8, 130.9, 132.3, 133.4, 138.3, 139.8, 140.2, 146.2, 190.4; IR (film): 3056, 1645, 1519 cm^{-1};HRMS (ESI) *m/z* calcd for $C_{24}H_{16}N_2O$ $[M+Na]^+$ 371.1155, found: 371.1149.

(5-(4-Bromophenyl)pyrazolo[5,1-a]isoquinolin-1-yl)(phenyl)methanone ***(2b).*** A yellow solid (mp: 212-213 ^{o}C, Rf = 0.4, petroleum ether/ethyl acetate = 6:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (s, 1H), 7.50-7.55 (m, 2H), 7.59-7.63 (m, 1H), 7.65-7.71 (m, 4H), 7.72-7.76 (m, 2H), 7.80-7.84 (m, 1H), 7.92-7.97 (m, 2H), 8.14 (s, 1H), 9.42 (d, 1H, *J* = 7.97 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 115.8, 116.0, 123.9, 124.0, 126.9, 127.2, 127.9, 128.4, 129.7, 129.9, 130.7, 131.3, 131.7, 132.2, 132.4, 137.1, 139.8, 140.1, 146.1, 190.3; IR (film): 3058, 1639, 1520 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{24}H_{15}BrN_2O$ $[M+Na]^+$ 449.0260 and 451.0240, found: 449.0258 and 451.0238.

Phenyl(5-(p-tolyl)pyrazolo[5,1-a]isoquinolin-1-yl)methanone ***(2c).*** A white solid (mp: 184-185 ^{o}C, Rf = 0.7, petroleum ether/ethyl acetate = 6:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.46 (s, 3H), δ 7.30 (s, 1H), 7.36 (d, 2H, *J* = 7.92 Hz), 7.49-7.56 (m, 2H), 7.58-7.70 (m, 3H), 7.72-7.76 (m, 2H), 7.79-7.85 (m, 1H), 7.91-8.00 (m, 2H), 8.15 (s, 1H), 9.44 (d, 1H, *J* = 7.90 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4, 115.5, 115.8,

123.8, 126.9, 127.0, 127.5, 128.4, 129.1, 129.6, 129.8, 130.5, 131.0, 132.3, 138.4, 139.6, 139.8, 140.2, 146.2, 190.4; IR (film): 3061, 1642, 1508 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{25}H_{18}N_2O$ $[M+Na]^+$ 385.1311, found: 385.1308.

(5-(4-Methoxyphenyl)pyrazolo[5,1-a]isoquinolin-1-yl)(phenyl)methanone ***(2d).*** A white solid (mp: 195-196 °C, Rf = 0.5, petroleum ether/ethyl acetate = 5:1); ^1H NMR (500 MHz, $CDCl_3$) δ 3.90 (s, 3H), δ 7.05-7.09 (m, 2H), 7.28 (s, 1H), 7.50-7.54 (m, 2H), 7.59-7.70 (m, 3H), 7.78-7.84 (m, 3H), 7.93-7.97 (m, 2H), 8.15 (s, 1H), 9.43 (d, 1H, *J* = 8.15 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.4, 113.9, 115.3, 115.8, 123.8, 125.8, 126.9, 127.0, 127.5, 128.4, 129.8, 131.1, 132.3, 138.2, 139.8, 140.3, 146.2, 160.6, 190.4; IR (film): 3058, 1640, 1511 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{25}H_{18}N_2O_2$ $[M+Na]^+$ 401.1260, found: 401.1256.

(5-(4-Ethylphenyl)pyrazolo[5,1-a]isoquinolin-1-yl)(phenyl)methanone ***(2e).*** A white solid (mp: 179-180 °C, Rf = 0.7, petroleum ether/ethyl acetate = 6:1); ^1H NMR (500 MHz, $CDCl_3$) δ 1.32 (t, 3H, *J* = 7.62 Hz), δ 2.77 (q, 2H, *J* = 7.60 Hz), 7.31 (s, 1H), 7.38-7.41 (m, 2H), 7.50-7.54 (m, 2H), 7.59-7.70 (m, 3H), 7.75-7.79 (m, 2H), 7.80-7.84 (m, 1H), 7.93-7.98 (m, 2H), 8.16 (s, 1H), 9.44 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.3, 28.8, 115.6, 115.8, 123.8, 126.9, 127.0, 127.5, 128.0, 128.4, 129.6, 129.8, 130.7, 131.0, 132.3, 138.4, 139.8, 140.2, 145.9, 146.2, 190.4; IR (film): 3055, 1642, 1508 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{26}H_{20}N_2O$ $[M+Na]^+$ 399.1468, found: 399.1465.

Phenyl(5-(m-tolyl)pyrazolo[5,1-a]isoquinolin-1-yl)methanone ***(2f).*** A white solid (mp:185-186 °C, Rf = 0.6, petroleum ether/ethyl acetate = 6:1); ^1H NMR (400 MHz,

$CDCl_3$) δ 2.47 (s, 3H), 7.30 (s, 1H), 7.32-7.36 (m, 1H), 7.42-7.48 (m, 1H), 7.50-7.55 (m, 2H), 7.58-7.71 (m, 5H), 7.80-7.85 (m, 1H), 7.93-7.98 (m, 2H), 8.15 (s, 1H), 9.45 (d, 1H, *J* = 7.86 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 115.8, 115.8, 123.9, 126.8, 126.9, 127.1, 127.6, 128.3, 128.4, 129.8, 130.2, 130.3, 131.0, 132.3, 133.4, 138.2, 138.5, 139.8, 140.2, 146.3, 190.4; IR (film): 3055, 1643, 1518 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{25}H_{18}N_2O$ $[M+Na]^+$ 385.1311, found: 385.1308.

(Phenyl(5-(thiophen-3-yl)pyrazolo[5,1-a]isoquinolin-1-yl)methanone ***(2g).*** A white solid (mp: 167-168 °C, Rf = 0.6, petroleum ether/ethyl acetate = 5:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48-7.56 (m, 4H), 7.60-7.67 (m, 2H), 7.67-7.71 (m, 1H), 7.72-7.76 (m, 1H), 7.81-7.85 (m, 1H), 7.94-7.97 (m, 2H), 8.20 (s, 1H), 8.26-8.30 (m, 1H), 9.41 (d, 1H, *J* = 8.05 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 114.9, 115.8, 123.6, 125.5, 126.8, 127.0, 127.3, 127.7, 128.2, 128.4, 129.8, 129.8, 130.8, 132.4, 133.3, 133.4, 139.9, 140.2, 146.1, 190.5; IR (film): 3051, 1638, 1507 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{22}H_{14}N_2OS$ $[M+Na]^+$ 377.0719, found: 377.0716.

(1-Benzoylpyrazolo[5,1-a]isoquinolin-5-yl)methyl acetate ***(2i).*** A white solid (mp: 138-139 °C, Rf = 0.5, petroleum ether/ethyl acetate = 5:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.21 (s, 3H), 5.70 (s, 2H), 7.38 (s, 1H), 7.51-7.55 (m, 2H), 7.60-7.72 (m, 3H), 7.81-7.85 (m, 1H), 7.91-7.95 (m, 2H), 8.19 (s, 1H), 9.42 (d, 1H, *J* = 7.81 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.9, 60.8, 114.8, 116.0, 124.2, 127.0, 127.2, 128.1, 128.4, 129.7, 129.8, 130.2, 132.3, 132.7, 139.3, 140.1, 146.4, 170.4, 190.3; IR (film): 3061, 1745, 1642, 1520 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{21}H_{16}N_2O_3$ $[M+Na]^+$ 367.1053, found: 367.1050.

(5-Cyclopropylpyrazolo[5,1-a]isoquinolin-1-yl)(phenyl)methanone ***(2j).*** A white solid (mp: 112-115 ^{o}C, Rf = 0.6, petroleum ether/ethyl acetate = 6:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.94-0.98 (m, 2H), 1.21-1.26 (m, 2H), 2.71-2.79 (m, 1H), 6.93 (s, 1H), 7.50-7.54 (m, 2H), 7.56-7.65 (m, 3H), 7.69-7.73 (m, 1H), 7.92-8.00 (m, 2H), 8.21 (s, 1H), 9.40 (d, 1H, *J* = 8.26 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 7.3, 11.7, 110.3, 115.9, 123.2, 126.4, 126.8, 126.9, 128.3, 129.5, 129.7, 131.0, 132.2, 139.4, 140.3, 140.6, 146.2, 190.4; IR (film): 3058, 2917, 1645, 1514 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{21}H_{16}N_2O$ $[M+Na]^+$ 335.1155, found: 335.1151.

(5-Pentylpyrazolo[5,1-a]isoquinolin-1-yl)(phenyl)methanone ***(2k).*** A yellow solid (mp: 59-60 ^{o}C, Rf = 0.7, petroleum ether/ethyl acetate = 6:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.94 (t, 3H, *J* = 7.14 Hz), 1.40-1.50 (m, 4H), 1.88-1.94 (m, 2H), 3.22 (t, 2H, *J* = 7.68 Hz), 7.09 (s, 1H), 7.50-7.54 (m, 2H), 7.57-7.65 (m, 3H), 7.72-7.75 (m, 1H), 7.92-7.96 (m, 2H), 8.16 (s, 1H), 9.42 (d, 1H, *J* = 8.17 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.0, 22.4, 26.7, 31.2, 31.5, 113.0, 115.7, 123.3, 126.3, 126.8, 126.8, 128.3, 129.5, 129.7, 130.9, 132.1, 139.3, 139.4, 140.3, 146.1, 190.3; IR (film): 3056, 2955, 1648, 1517 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{23}H_{22}N_2O$ $[M+Na]^+$ 365.1624, found: 365.1621.

(2-Methyl-5-phenylpyrazolo[5,1-a]isoquinolin-1-yl)(phenyl)methanone ***(2l).*** A yellow solid (mp: 55-56 ^{o}C, Rf = 0.7, petroleum ether/ethyl acetate = 7:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.28 (s, 3H), 7.16 (s, 1H), 7.36-7.41 (m, 1H), 7.45-7.62 (m, 7H), 7.72-7.77 (m, 1H), 7.90-7.96 (m, 4H), 8.22 (d, 1H, *J* = 8.24 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2, 114.0, 123.0, 125.3, 127.2, 127.2, 128.3, 128.7, 129.4, 129.7, 129.7,

130.5, 133.1, 133.5, 137.9, 138.9, 139.4, 151.1, 193.6; IR (film): 3058, 1642, 1526 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{25}H_{18}N_2O$ $[M+Na]^+$ 385.1311, found: 385.1307.

(2-Ethyl-5-phenylpyrazolo[5,1-a]isoquinolin-1-yl)(phenyl)methanone ***(2m).*** A white solid (mp: 51-52 ^oC, Rf = 0.7, petroleum ether/ethyl acetate = 7:1); ^1H NMR (400 MHz, $CDCl_3$) δ 1.18 (t, 3H, *J* = 7.55 Hz), 2.68 (q, 2H, *J* = 7.54 Hz), 7.15 (s, 1H), 7.32-7.38 (m, 1H), 7.44-7.56 (m, 6H), 7.57-7.62 (m, 1H), 7.71-7.75 (m, 1H), 7.93-7.98 (m, 4H), 8.08 (d, 1H, *J* = 8.30 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 21.5, 113.1, 113.8, 123.1, 125.2, 127.2, 127.2, 128.3, 128.6, 128.7, 129.4, 129.7, 129.8, 130.5, 133.2, 133.6, 138.0, 138.6, 139.3, 156.2, 193.9; IR (film): 3061, 2965, 1649, 1530 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{26}H_{20}N_2O$ $[M+Na]^+$ 399.1468, found: 399.1465.

(9-Chloro-5-phenylpyrazolo[5,1-a]isoquinolin-1-yl)(phenyl)methanone ***(2n).*** A white solid (mp: 199-200 ^oC, Rf = 0.6, petroleum ether/ethyl acetate = 5:1); ^1H NMR (400 MHz, $CDCl_3$) δ 7.27 (s, 1H), 7.50-7.56 (m, 5H), 7.59-7.65 (m, 2H), 7.73-7.77 (m, 1H), 7.82-7.86 (m, 2H), 7.91-7.95 (m, 2H), 8.17 (s, 1H), 9.56 (d, 1H, *J* = 1.66 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 115.1, 116.1, 124.8, 126.3, 128.4, 128.4, 129.2, 129.6, 130.4, 132.4, 133.0, 130.4, 133.6, 138.6, 138.8, 140.0, 146.4, 190.2; IR (film): 3064, 1642, 1517 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{24}H_{15}ClN_2O$ $[M+Na]^+$ 405.0765, found: 405.0761.

(9-Methoxy-5-phenylpyrazolo[5,1-a]isoquinolin-1-yl)(phenyl)methanone ***(2o).*** A white solid (mp: 192-193 ^oC, Rf = 0.5, petroleum ether/ethyl acetate = 5:1); ^1H NMR (400 MHz, $CDCl_3$) δ 4.02 (s, 3H), 7.28 (s, 1H), 7.29-7.34 (m, 1H), 7.48-7.63 (m, 6H),

7.70-7.75 (m, 1H), 7.81-7.95(m, 4H), 8.15 (s, 1H), 9.14 (d, 1H, J = 2.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.8, 107.4, 115.6, 115.7, 121.1, 125.3, 125.3, 128.3, 128.4, 128.4, 129.3, 129.6, 129.7, 132.0, 133.6, 136.1, 139.5, 140.7, 146.8, 159.0, 190.6; IR (film): 3098, 1639, 1520 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{25}H_{18}N_2O_2$ $[M+Na]^+$ 401.1260, found: 401.1256.

(8-Methyl-5-phenylpyrazolo[5,1-a]isoquinolin-1-yl)(phenyl)methanone ***(2p).*** A white solid (mp: 142-143 °C, Rf = 0.7, petroleum ether/ethyl acetate = 6:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.56 (s, 3H), 7.25 (s, 1H), 7.47-7.56 (m, 6H), 7.58-7.63 (m, 2H), 7.81-7.86 (m, 2H), 7.92-7.98(m, 2H), 8.14 (s, 1H), 9.37 (d, 1H, J = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.7, 115.4, 115.6, 121.8, 126.7, 126.9, 128.3, 128.4, 129.4, 129.5, 129.7, 129.7, 131.2, 132.2, 133.5, 138.2, 139.9, 140.2, 140.3, 146.3, 190.3; IR (film): 3058, 1645, 1517 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{25}H_{18}N_2O$ $[M+Na]^+$ 385.1311, found: 385.1308.

Naphthalen-1-yl(5-phenylpyrazolo[5,1-a]isoquinolin-1-yl)methanone ***(2q).*** A white solid (mp: 85-86 °C, Rf = 0.5, petroleum ether/ethyl acetate = 5:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 (s, 1H), 7.51-7.56 (m, 6H), 7.74-7.78 (m, 3H), 7.83-7.88 (m, 3H), 7.94-7.97 (m, 2H), 8.00-8.04 (m, 1H), 8.32-8.38 (m, 1H), 9.98-10.02 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 116.2, 118.0, 124.1, 124.4, 125.7, 126.4, 127.0, 127.2, 127.5, 127.8, 127.8, 128.3, 129.5, 129.7, 130.1, 130.9, 131.1, 131.2, 133.3, 133.8, 138.3, 138.8, 139.9, 147.6, 191.2; IR (film): 3055, 1642, 1514 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{28}H_{18}N_2O$ $[M+Na]^+$ 421.1311, found: 421.1307.

(4-Chlorophenyl)(5-phenylpyrazolo[5,1-a]isoquinolin-1-yl)methanone ***(2r).*** A

white solid (mp: 166-167 °C, Rf = 0.4, petroleum ether/ethyl acetate = 5:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (s, 1H), 7.47-7.51 (m, 2H), 7.52-7.58 (m, 3H), 7.63-7.72 (m, 2H), 7.80-7.90 (m, 5H), 8.12 (s, 1H), 9.40 (d, 1H, *J* = 7.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 115.5, 116.0, 123.8, 126.8, 127.1, 127.7, 128.4, 128.7, 129.6, 129.7, 129.9, 131.0, 131.1, 133.3, 138.3, 138.5, 138.6, 139.8, 145.9, 188.9; IR (film): 3058, 1642, 1517 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{24}H_{15}ClN_2O$ $[M+Na]^+$ 405.0765, found: 405.0761.

(5-Phenylpyrazolo[5,1-a]isoquinolin-1-yl)(p-tolyl)methanone ***(2s).*** A white solid (mp:142-143 °C, Rf = 0.6, petroleum ether/ethyl acetate = 6:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.44 (s, 3H), 7.31 (s, 1H), 7.38-7.44 (m, 2H), 7.52-7.59 (m, 3H), 7.63-7.71 (m, 2H), 7.72-7.79 (m, 2H), 7.81-7.88 (m, 3H), 8.17 (s, 1H), 9.44(d, 1H, *J* = 7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.3, 115.8, 115.9, 123.9, 126.9, 127.1, 127.7, 128.2, 128.4, 129.5, 129.7, 129.8, 130.3, 130.9, 133.1, 138.2, 138.3, 139.7, 140.1, 146.2, 190.6; IR (film): 3055, 1642, 1517 cm^{-1}; HRMS (ESI) *m/z* calcd for $C_{25}H_{18}N_2O$ $[M+Na]^+$ 385.1311, found: 385.1308.

(9-Chloro-5-phenylpyrazolo[5,1-a]isoquinolin-1-yl)(p-tolyl)methanone ***(2v).*** A white solid (mp: 135-136 °C, Rf = 0.5, petroleum ether/ethyl acetate = 5:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.47 (s, 3H), 7.27 (s, 1H), 7.30-7.35 (m, 2H), 7.50-7.59 (m, 3H), 7.61-7.66 (m, 1H), 7.72-7.78 (m, 1H), 7.80-7.88 (m, 4H), 8.17 (s, 1H), 9.48 (d, 1H, *J* = 1.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6, 115.0, 116.3, 124.9, 126.3, 128.4, 128.5, 129.1, 129.6, 129.7, 130.0, 130.3, 133.1, 133.6, 137.3, 138.6, 138.7, 143.3, 146.2, 190.0; IR (film): 3052, 1642, 1524 cm^{-1}; HRMS (ESI) *m/z* calcd for

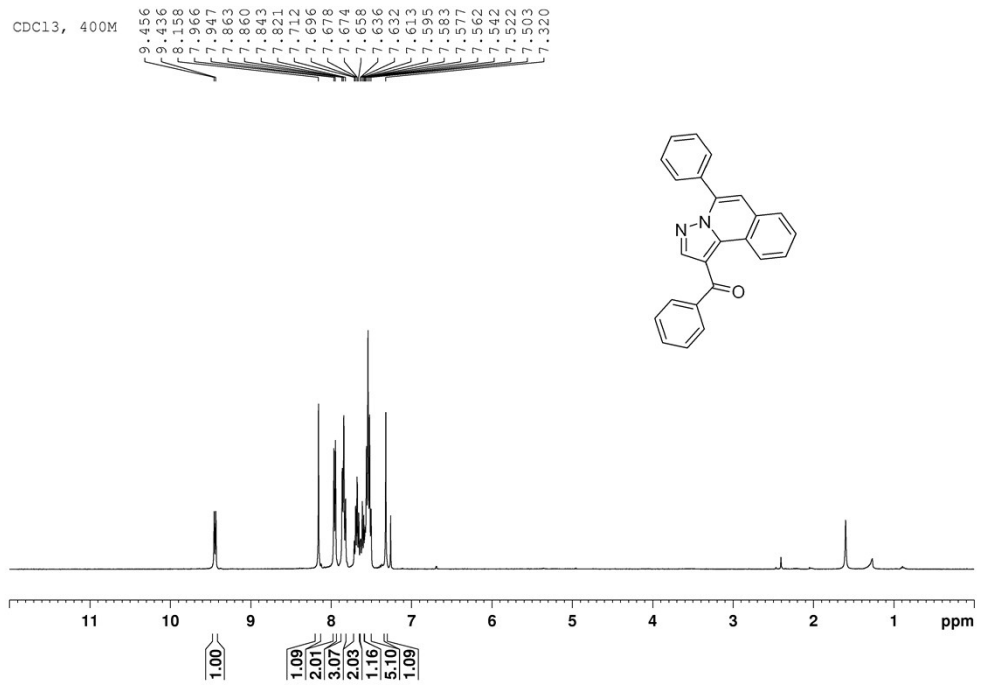
$C_{25}H_{17}ClN_2O$ $[M+Na]^+$ 419.0922, found: 419.0920.

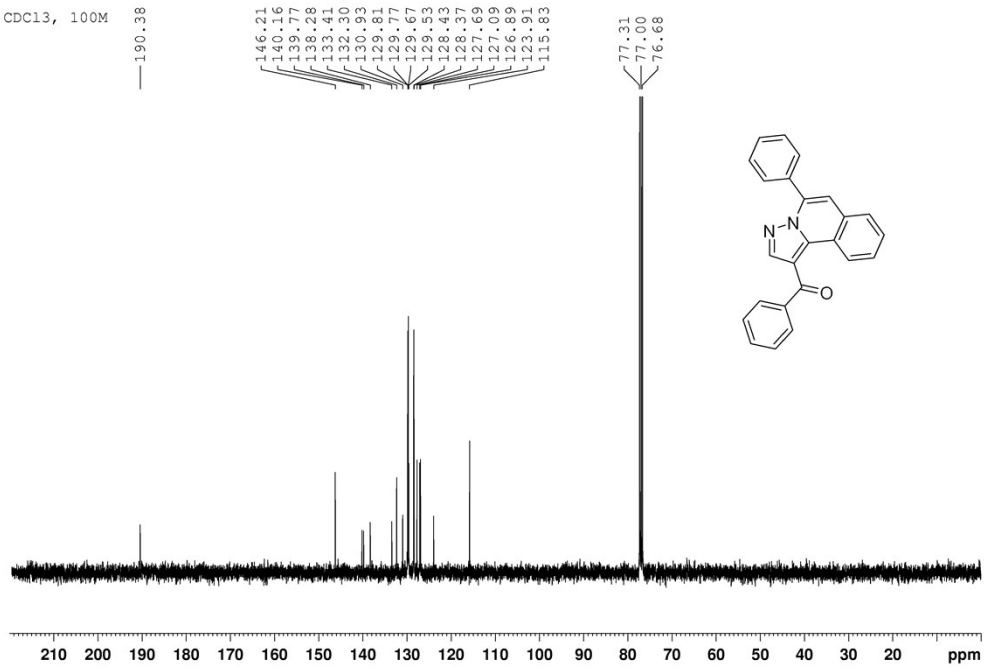
9-Chloro-1-(methoxy(p-tolyl)methyl)-5-phenylpyrazolo[5,1-a]isoquinoline ***(4v)*** A colourless liquid (Rf = 0.4, petroleum ether/ethyl acetate = 5:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.39 (s, 3H), 3.54 (s, 3H), 5.85 (s, 1H), 7.02 (s, 1H), 7.20-7.26 (m, 2H), 7.40-7.44 (m, 2H), 7.46-7.55 (m, 4H), 7.63-7.68 (m, 2H), 7.79-7.88 (m, 2H), 8.30-8.38 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.1, 56.5, 78.3, 112.4, 116.8, 124.7, 125.3, 127.4, 128.0, 128.1, 128.3, 129.2, 129.4, 133.0, 133.5, 134.9, 136.6, 137.7, 138.8, 141.7; IR (film): 3055, 2923, 1598 cm−1; HRMS (ESI) m/z calcd for C26H21ClN2O [M+Na]+ 435.1235, found: 435.1233.

3-phenylisoquinoline ***(12a)*** This compound is known (CAS: 37993-76-3). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43-7.48 (m, 1H), 7.51-7.61 (m, 3H), 7.66-7.74 (m, 1H), 7.85-7.90 (m, 1H), 7.97-8.02 (m, 1H), 8.08 (s, 1H), 8.14-8.20 (m, 2H) 9.37 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 116.4, 126.8, 126.9, 127.0, 127.5, 127.7, 128.4, 128.7, 130.4, 136.6, 139.5, 151.2, 152.3.

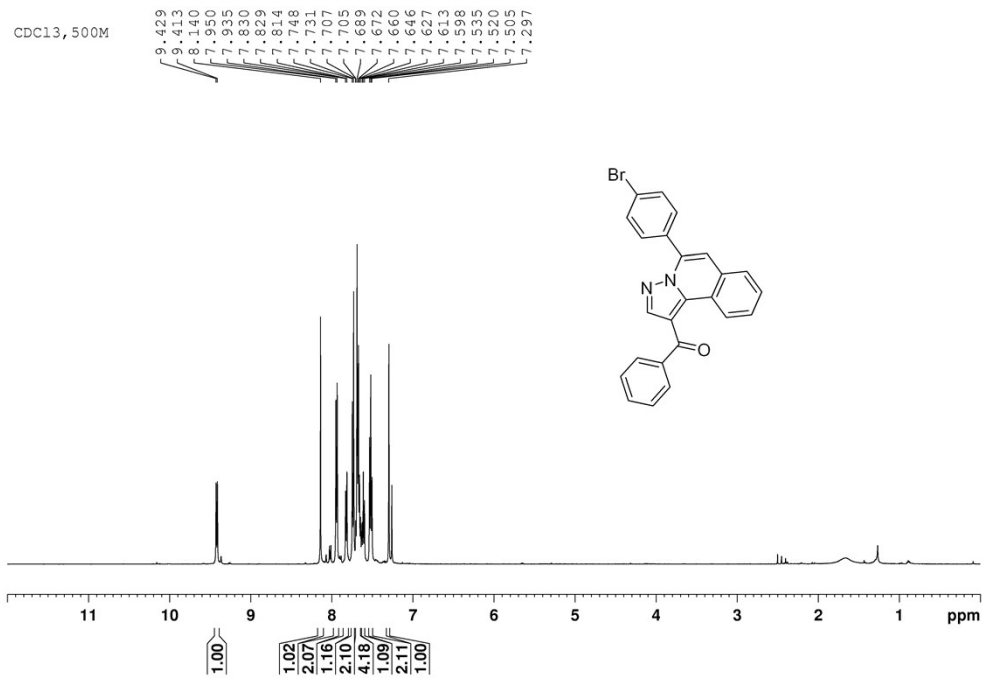
^{1}H, ^{13}C-NMR Spectra of products 2a-2g, 2i-2s, 2v, 4v

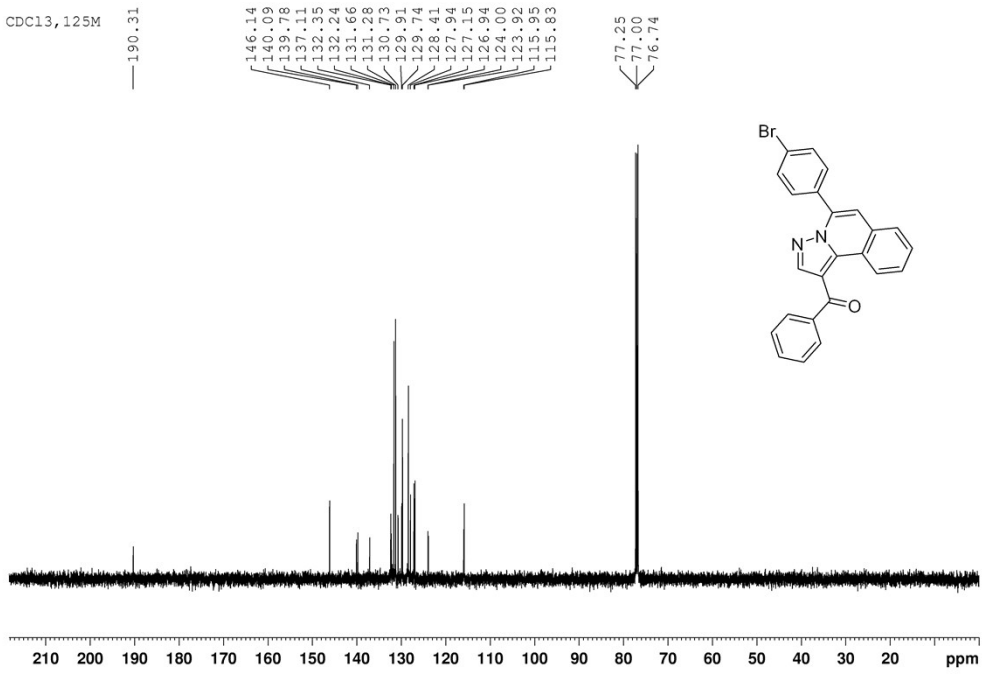
Phenyl(5-phenylpyrazolo[5,1-a]isoquinolin-1-yl)methanone (**2a**)



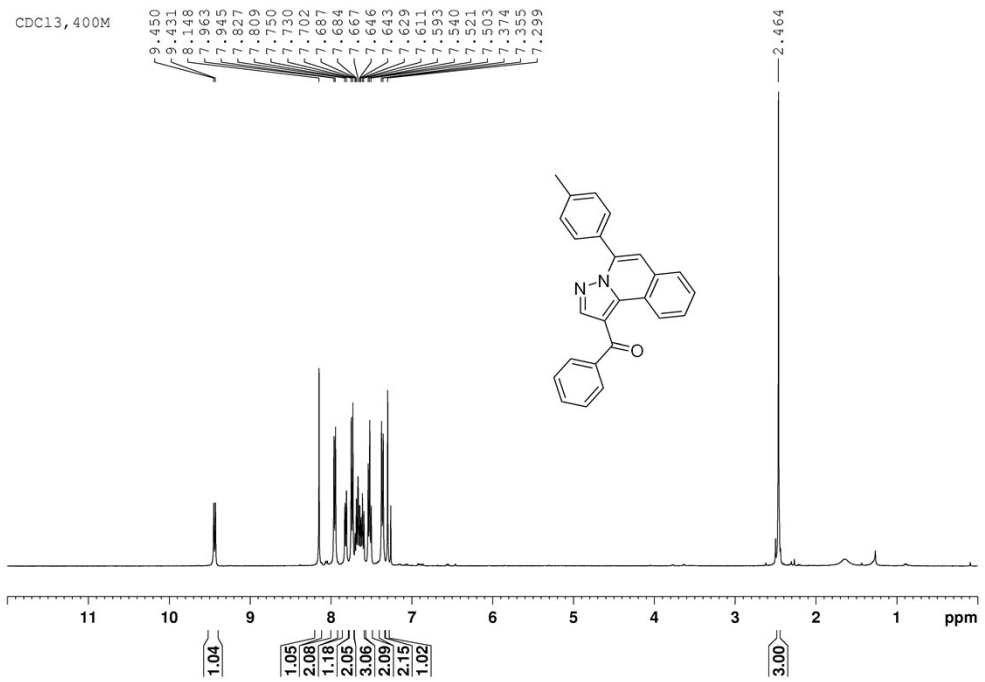


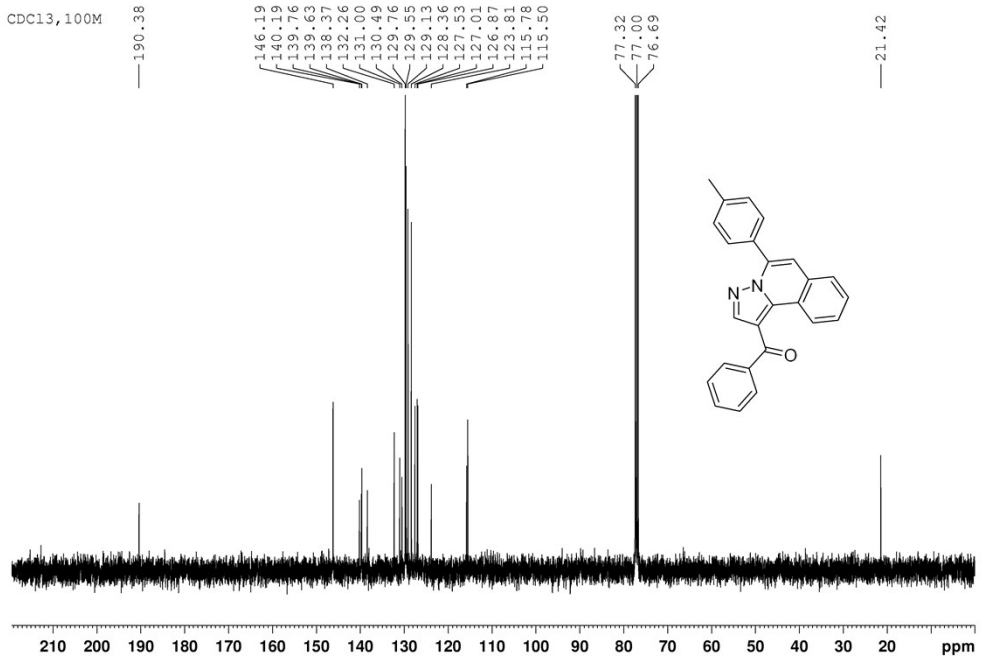
(5-(4-Bromophenyl)pyrazolo[5,1-a]isoquinolin-1-yl)(phenyl)methanone (**2b**)



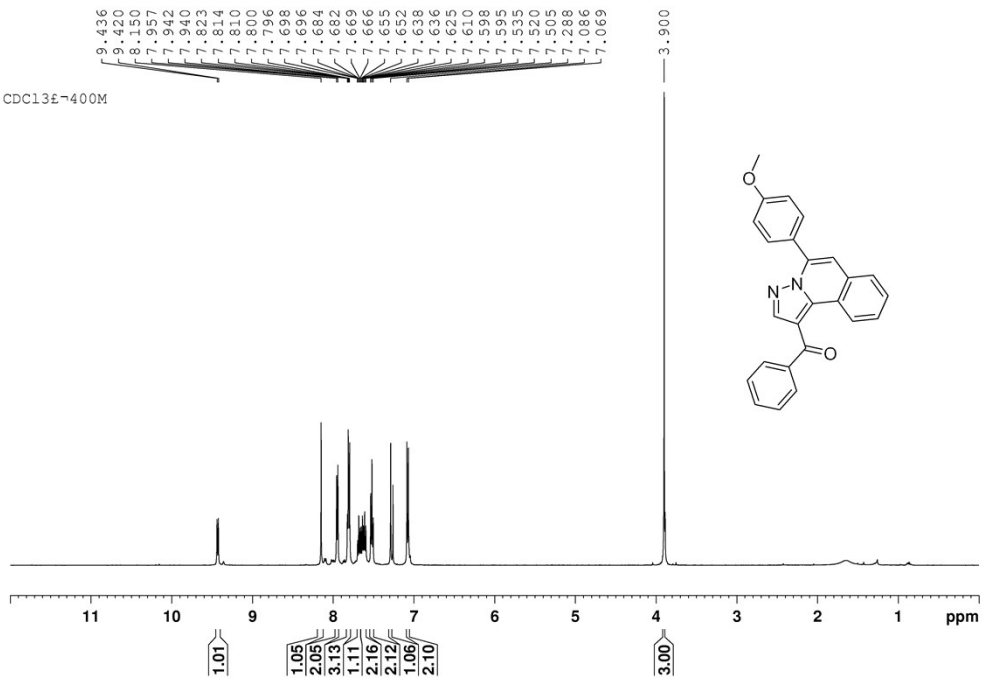


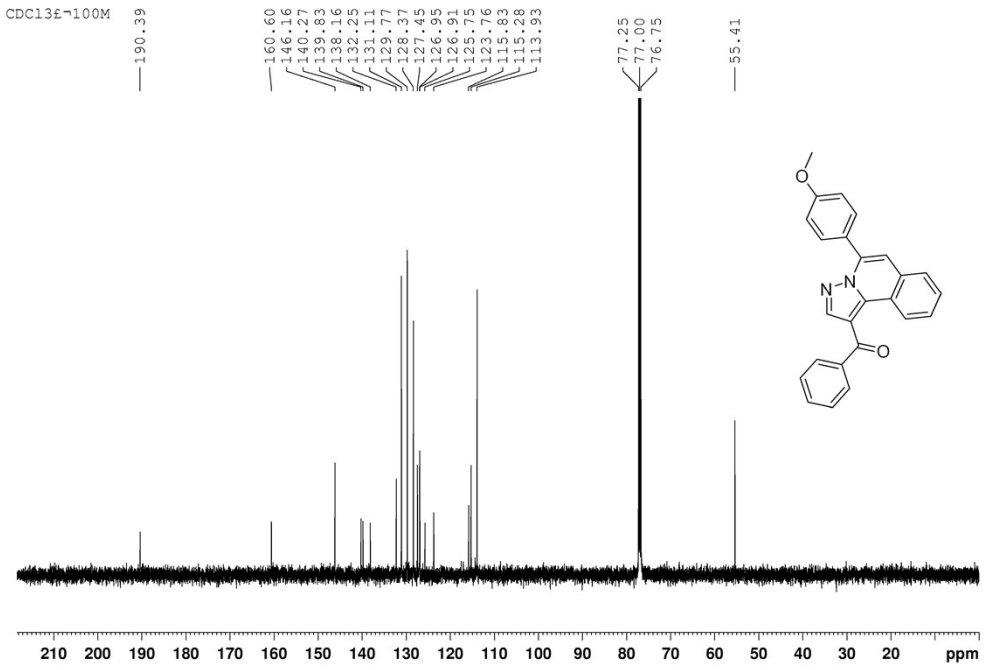
Phenyl(5-(p-tolyl)pyrazolo[5,1-a]isoquinolin-1-yl)methanone (**2c**)



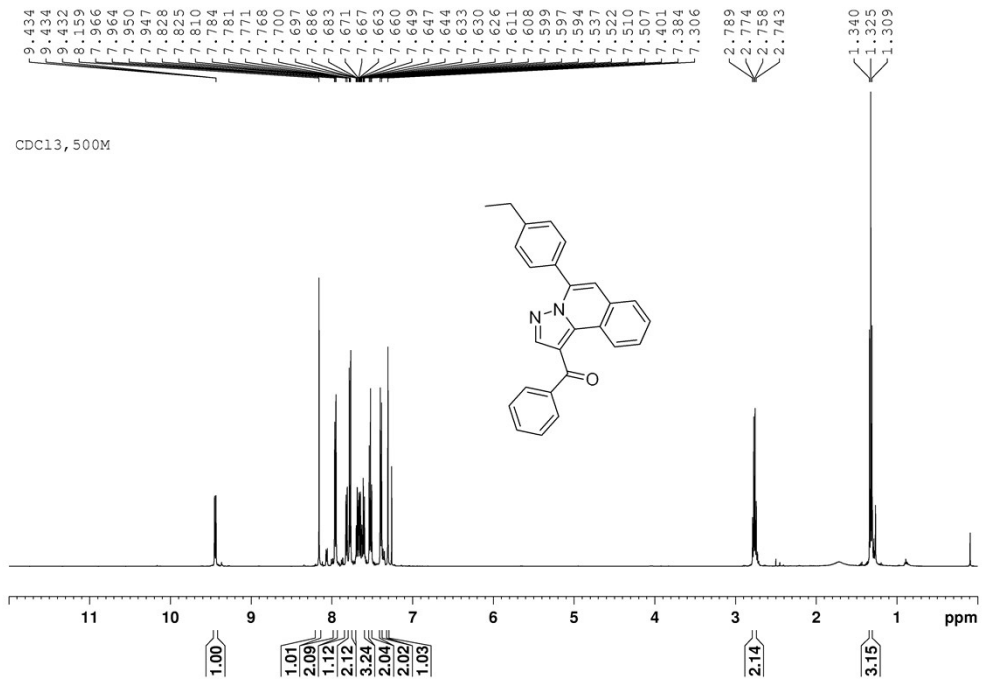


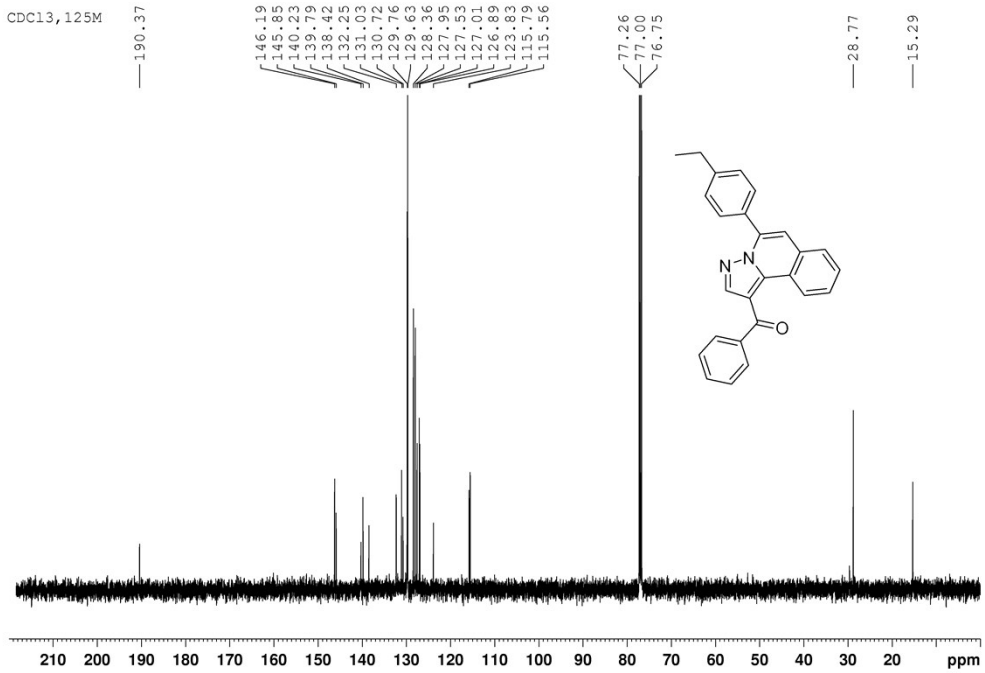
(5-(4-Methoxyphenyl)pyrazolo[5,1-a]isoquinolin-1-yl)(phenyl)methanone (**2d**)



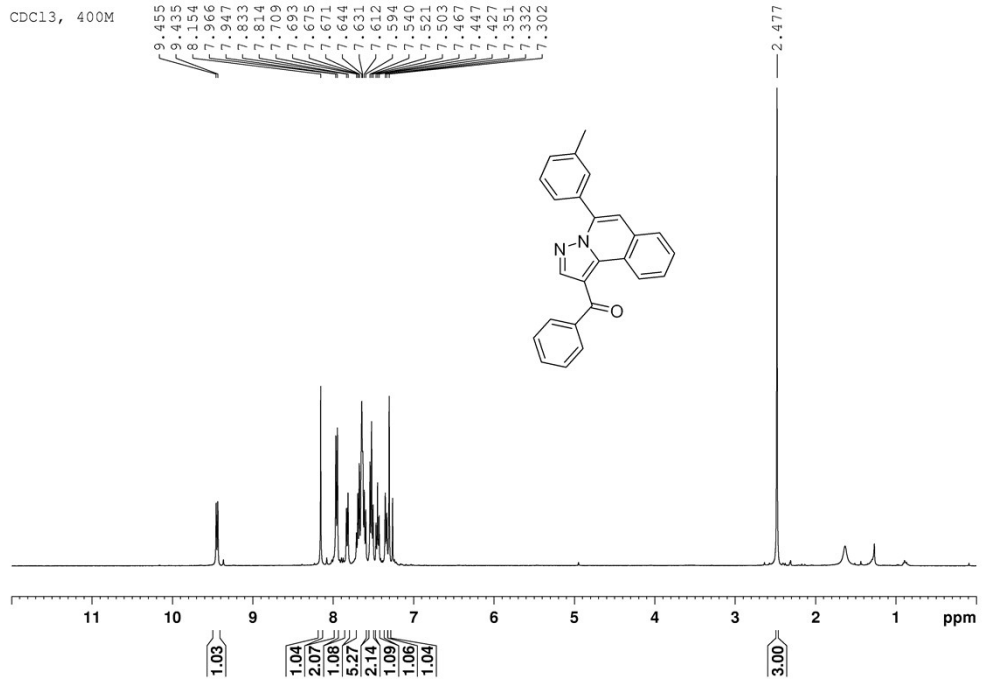


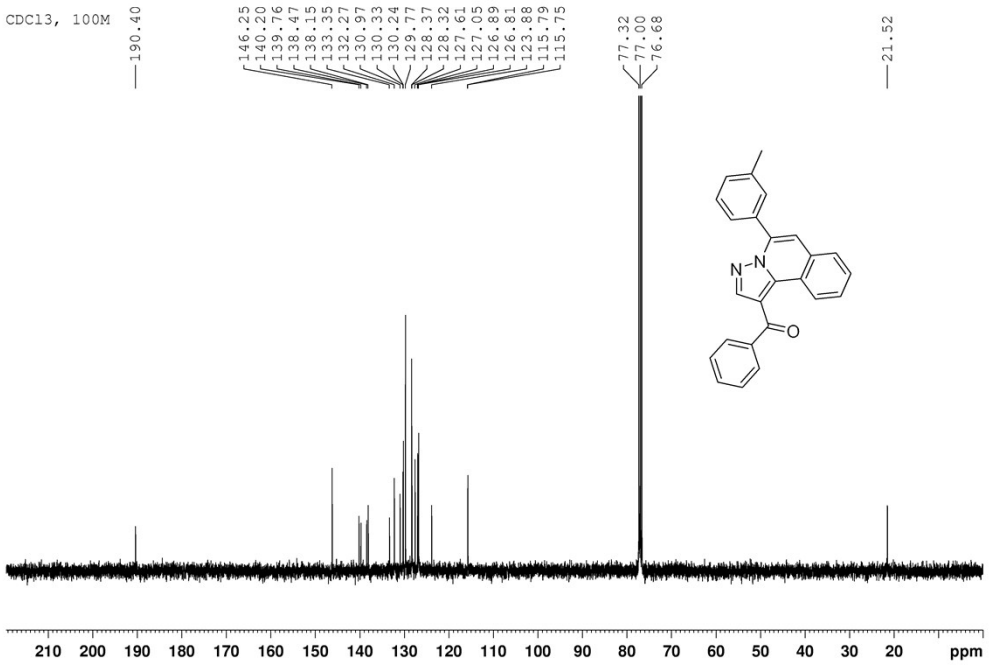
(5-(4-Ethylphenyl)pyrazolo[5,1-a]isoquinolin-1-yl)(phenyl)methanone (**2e**)



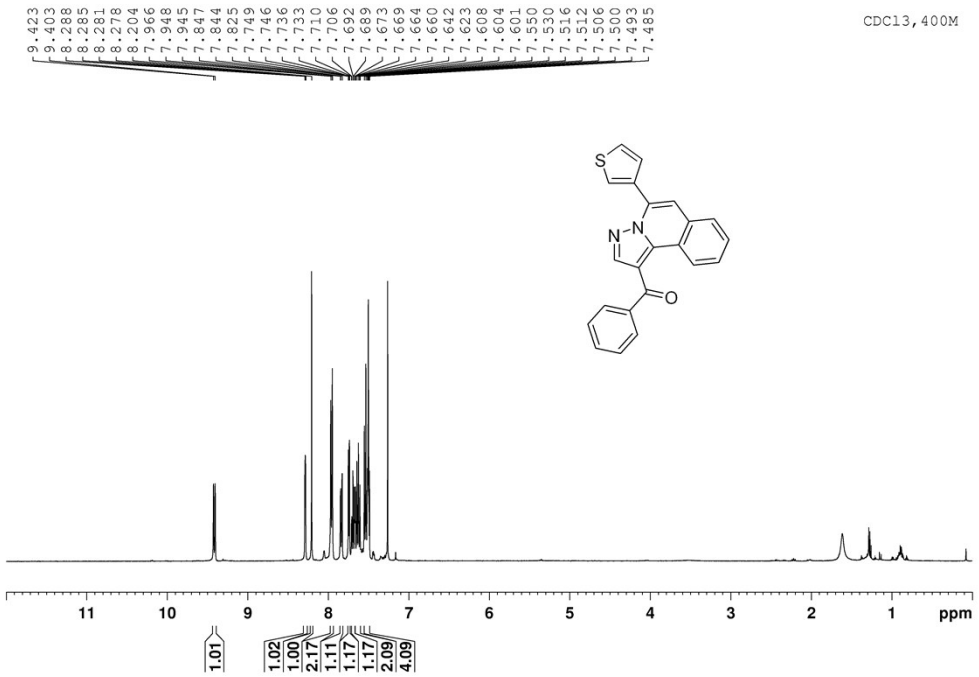


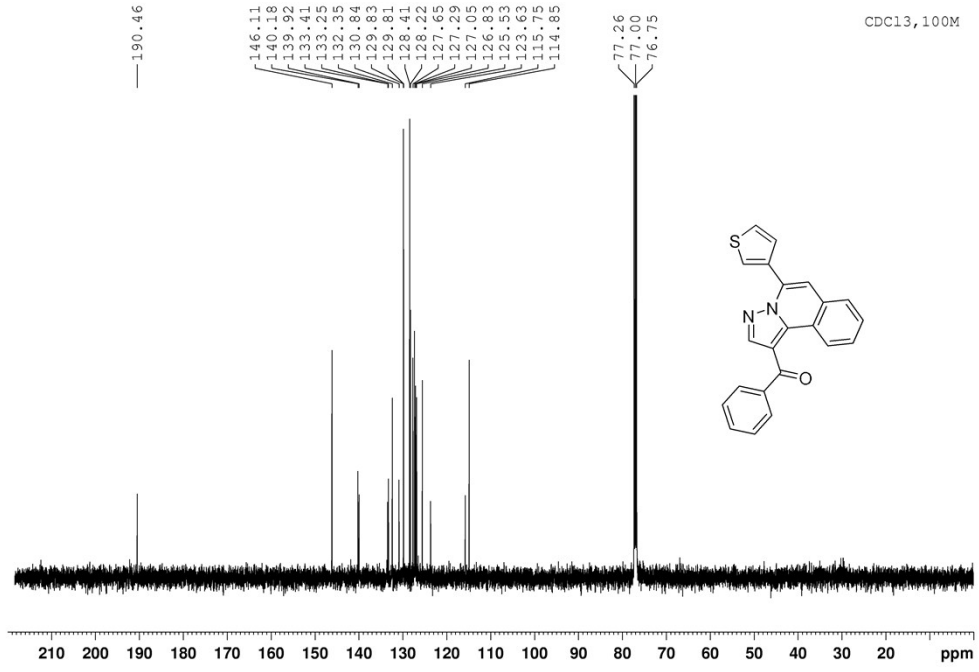
Phenyl(5-(m-tolyl)pyrazolo[5,1-a]isoquinolin-1-yl)methanone (**2f**)



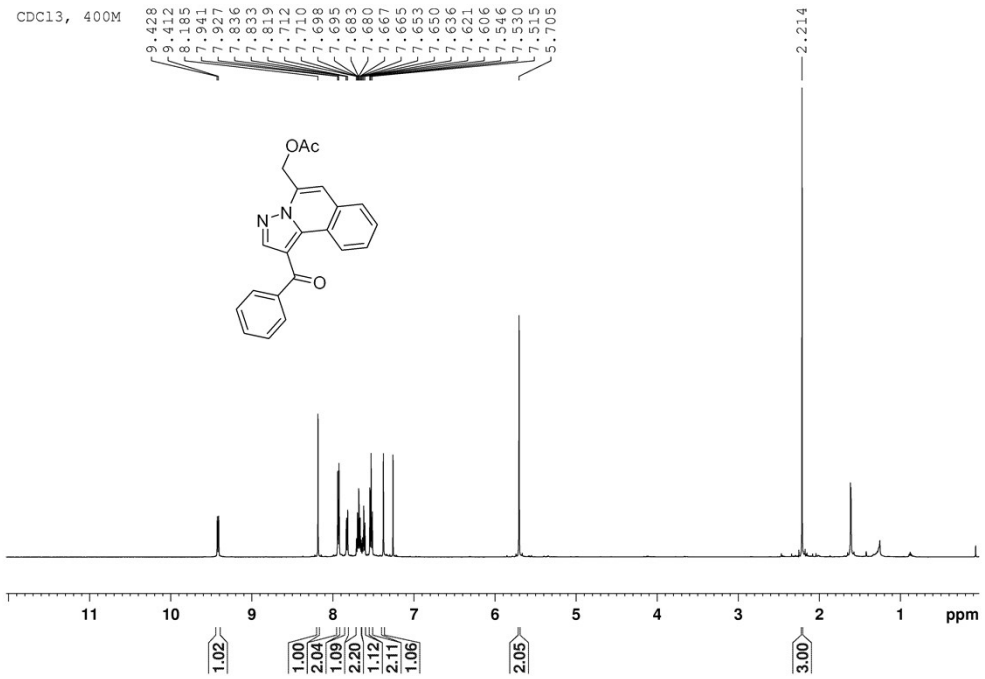


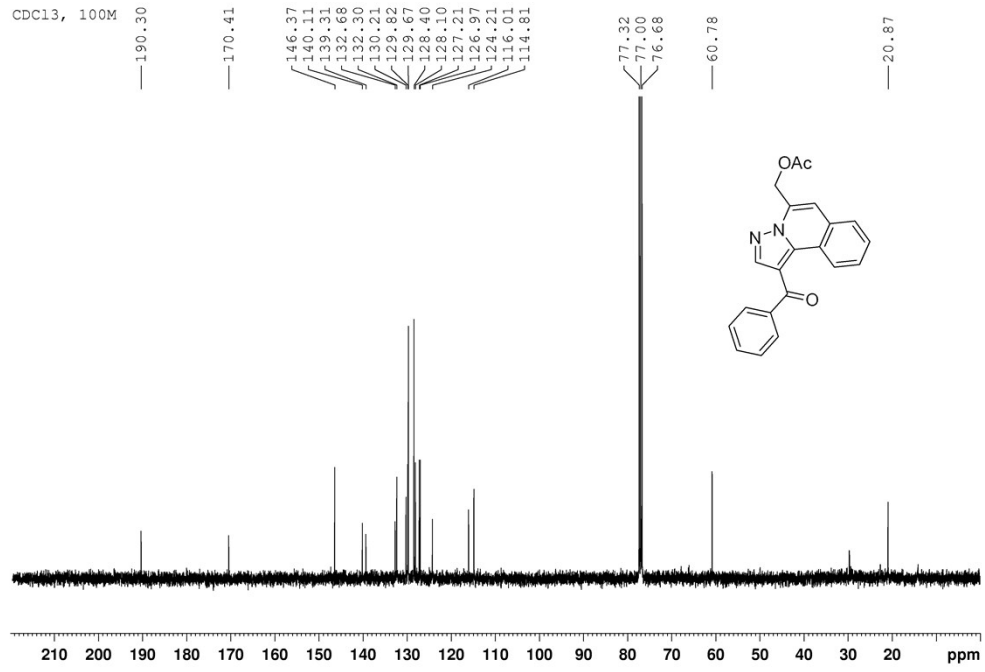
Phenyl(5-(thiophen-3-yl)pyrazolo[5,1-a]isoquinolin-1-yl)methanone (**2g**)



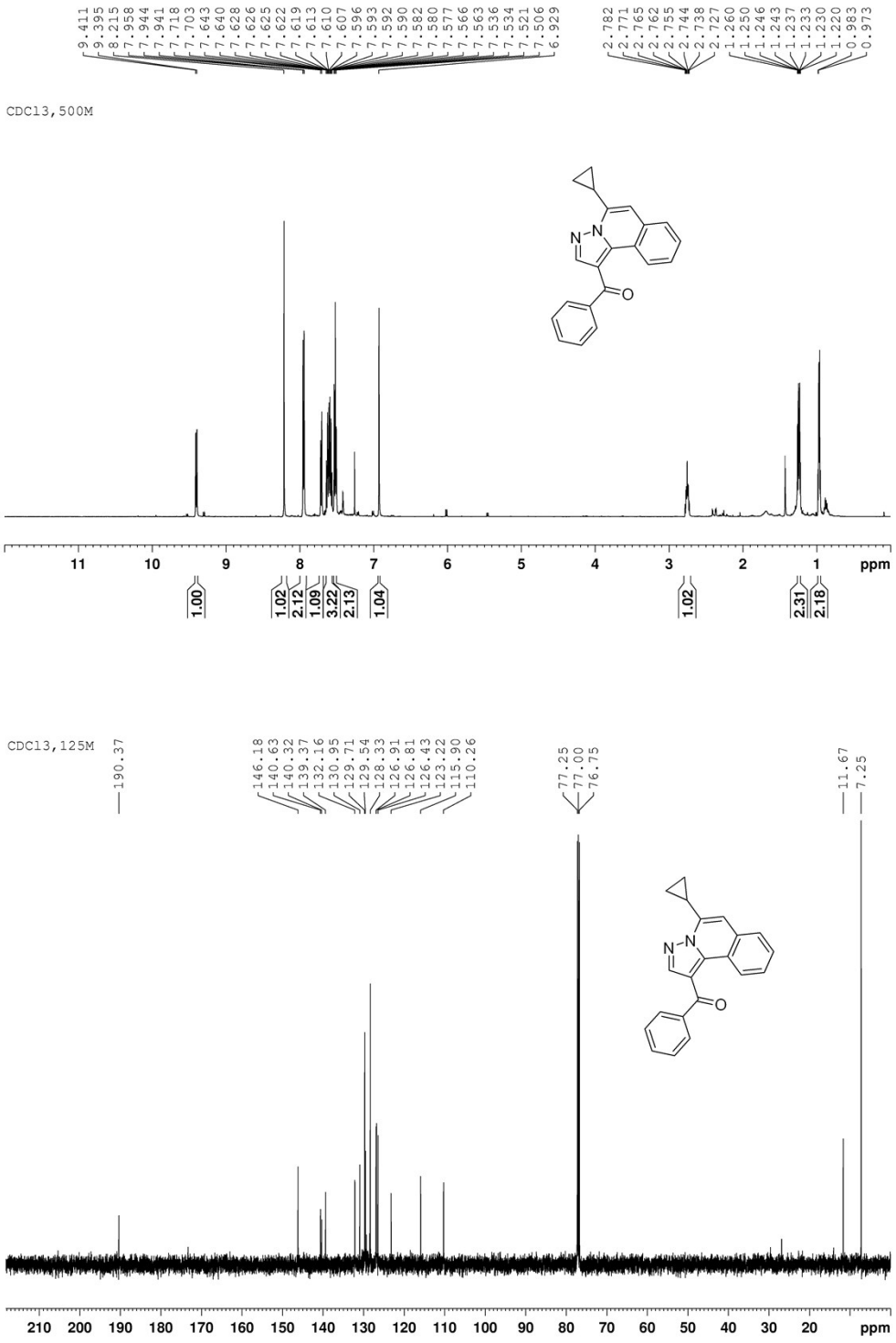


(1-Benzoylpyrazolo[5,1-a]isoquinolin-5-yl)methyl acetate (**2i**)

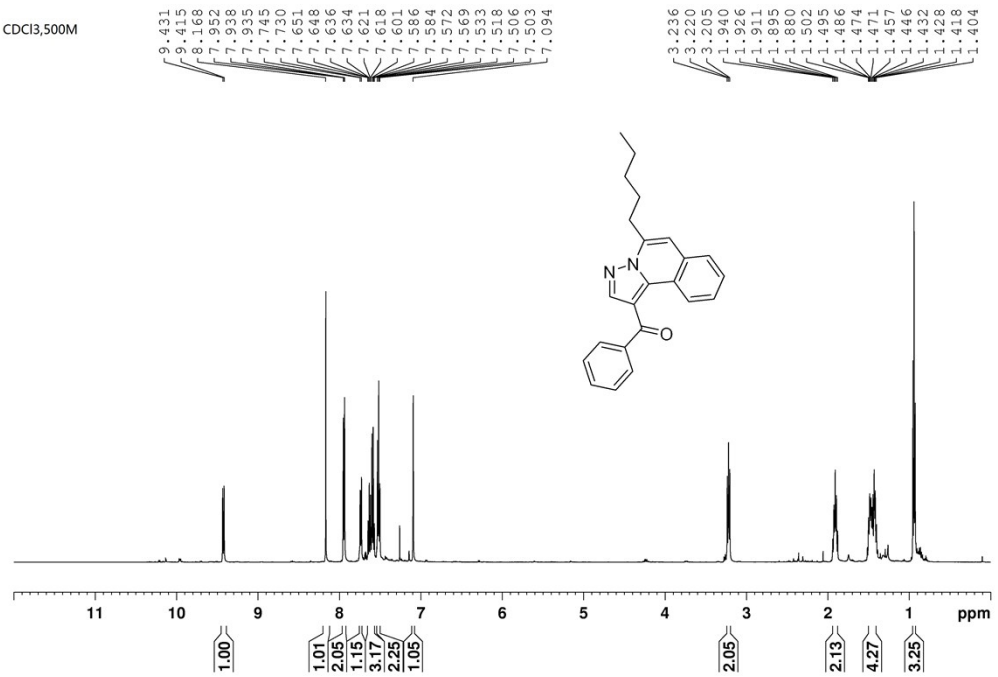


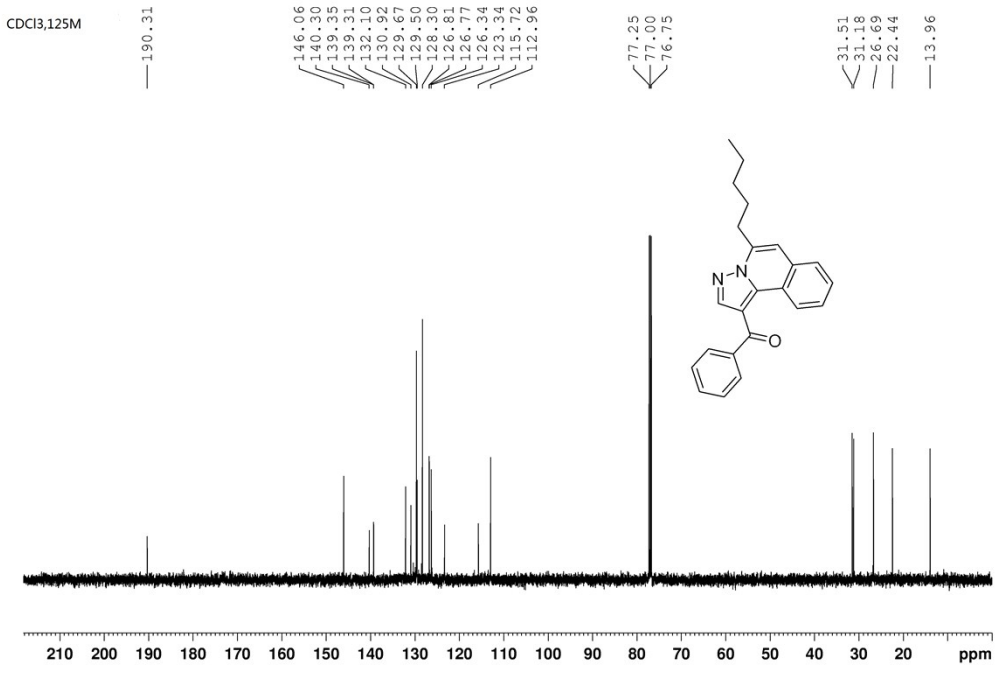


(5-Cyclopropylpyrazolo[5,1-a]isoquinolin-1-yl)(phenyl)methanone (**2j**)

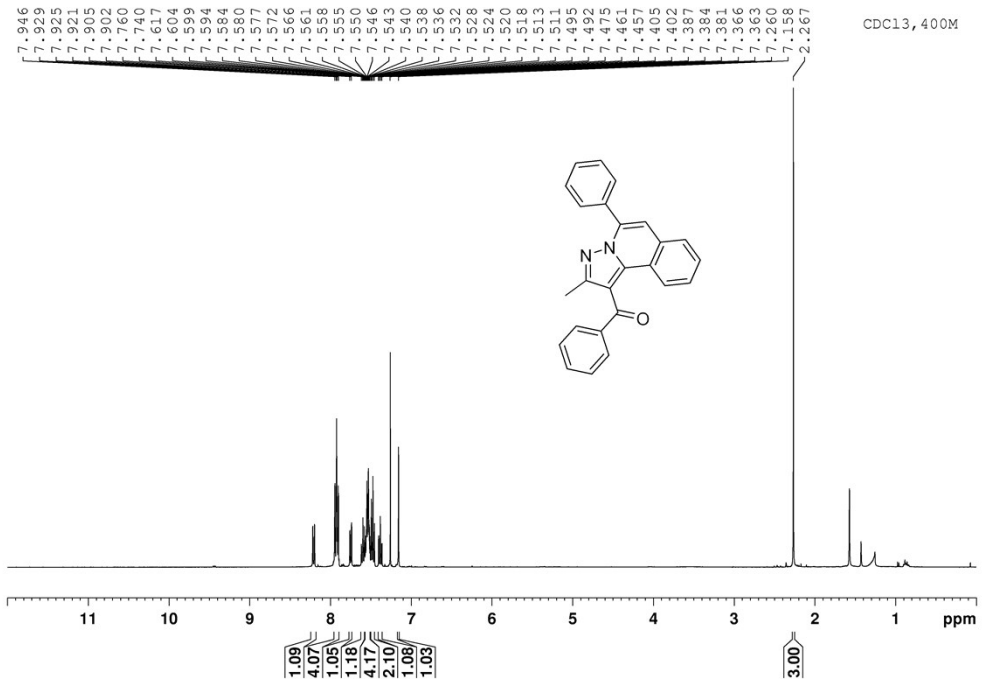


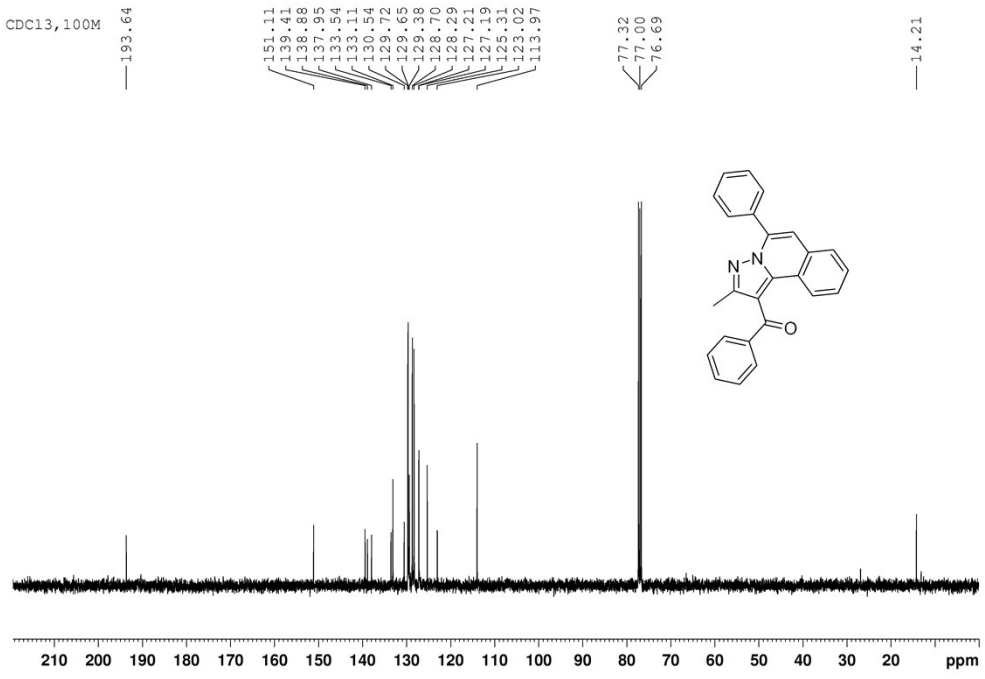
(5-Pentylpyrazolo[5,1-a]isoquinolin-1-yl)(phenyl)methanone (**2k**)



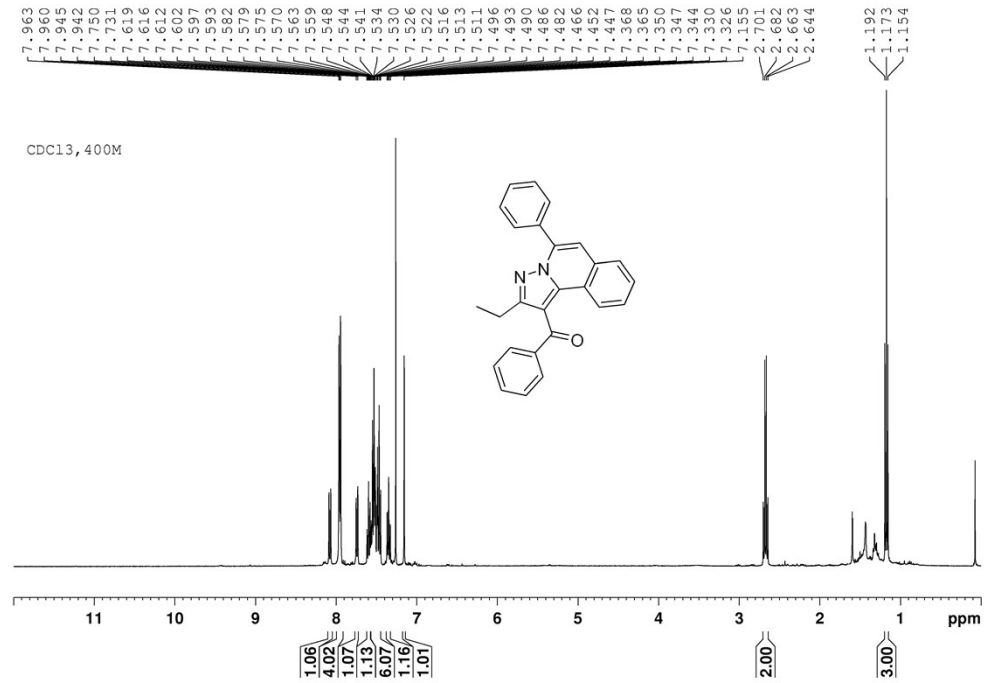


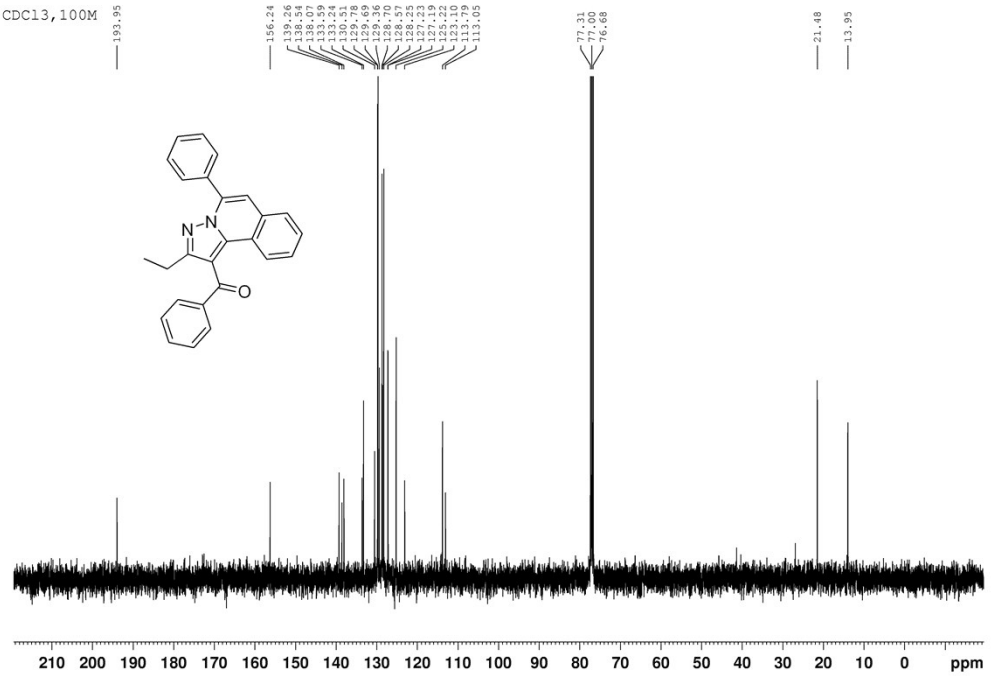
(2-Methyl-5-phenylpyrazolo[5,1-a]isoquinolin-1-yl)(phenyl)methanone (**2l**)



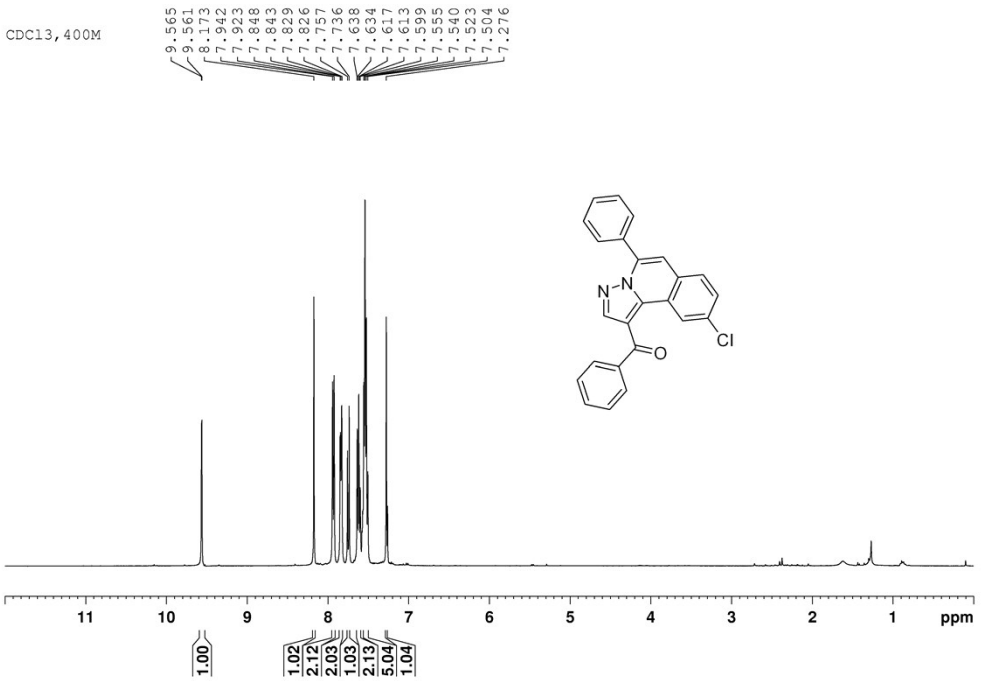


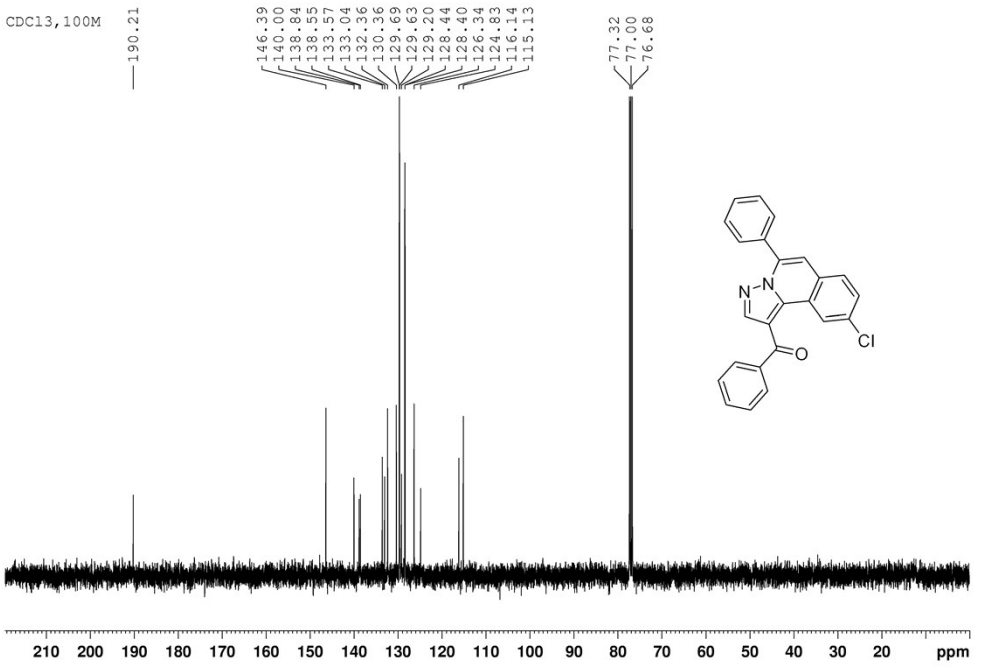
(2-Ethyl-5-phenylpyrazolo[5,1-a]isoquinolin-1-yl)(phenyl)methanone (**2m**)



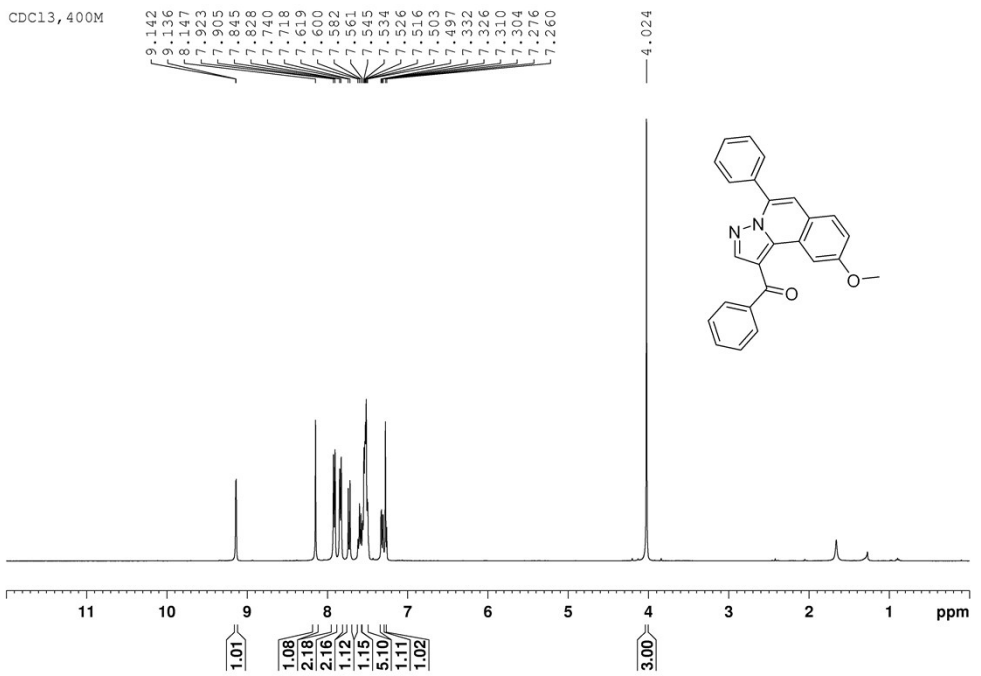


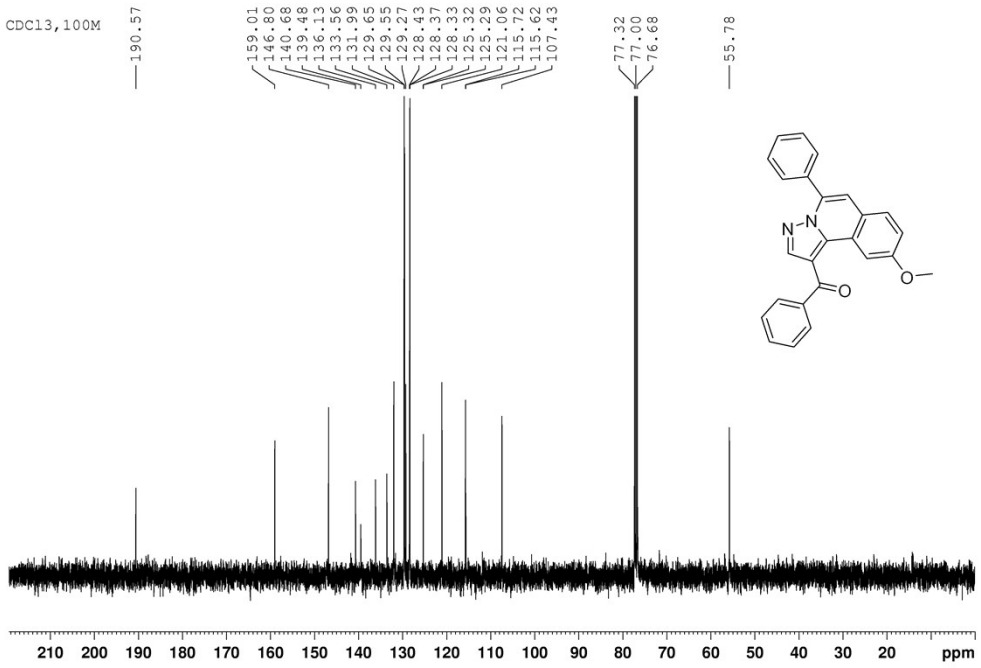
(9-Chloro-5-phenylpyrazolo[5,1-a]isoquinolin-1-yl)(phenyl)methanone (**2n**)



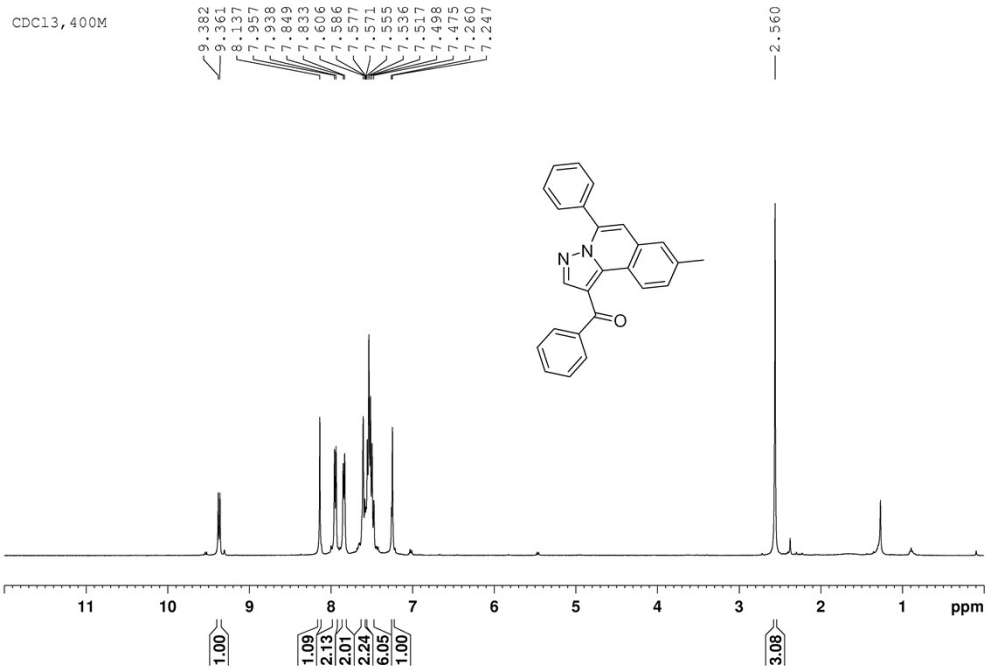


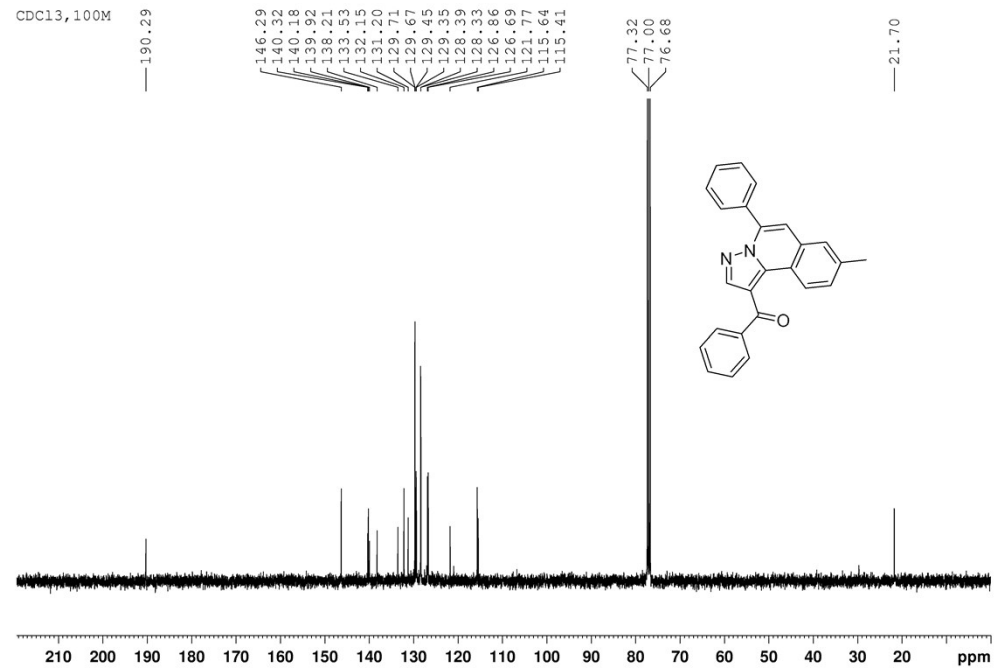
(9-Methoxy-5-phenylpyrazolo[5,1-a]isoquinolin-1-yl)(phenyl)methanone (**2o**)



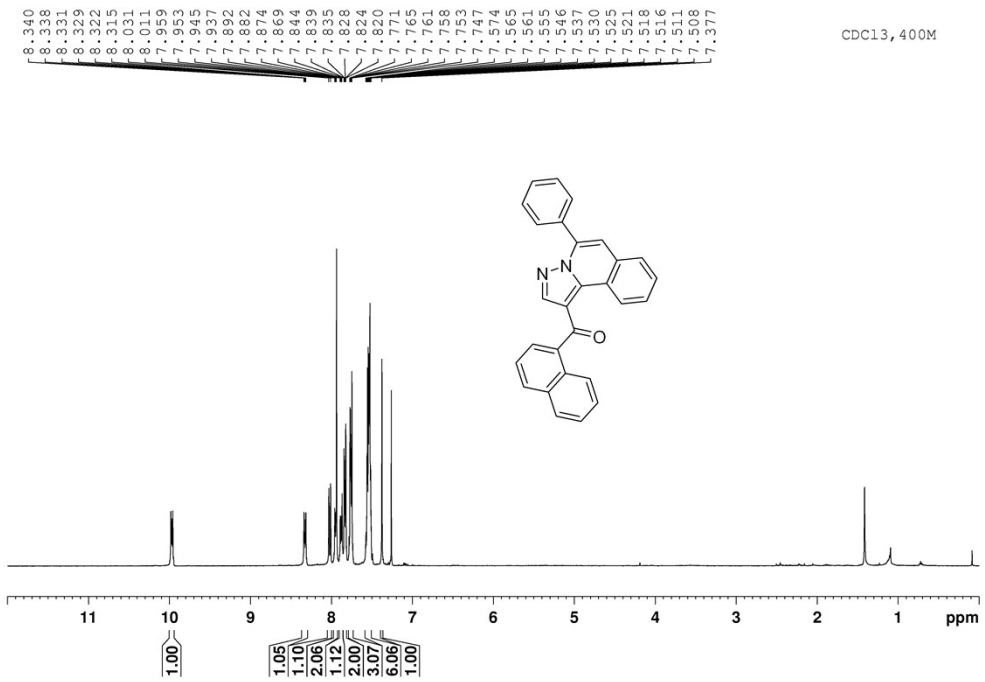


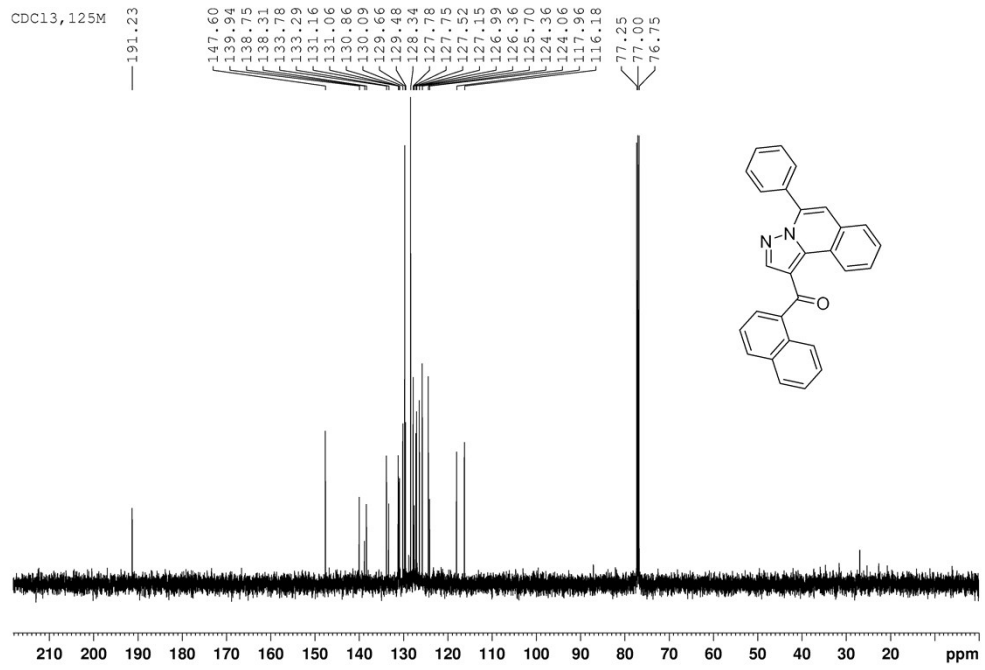
(8-Methyl-5-phenylpyrazolo[5,1-a]isoquinolin-1-yl)(phenyl)methanone (**2p**)



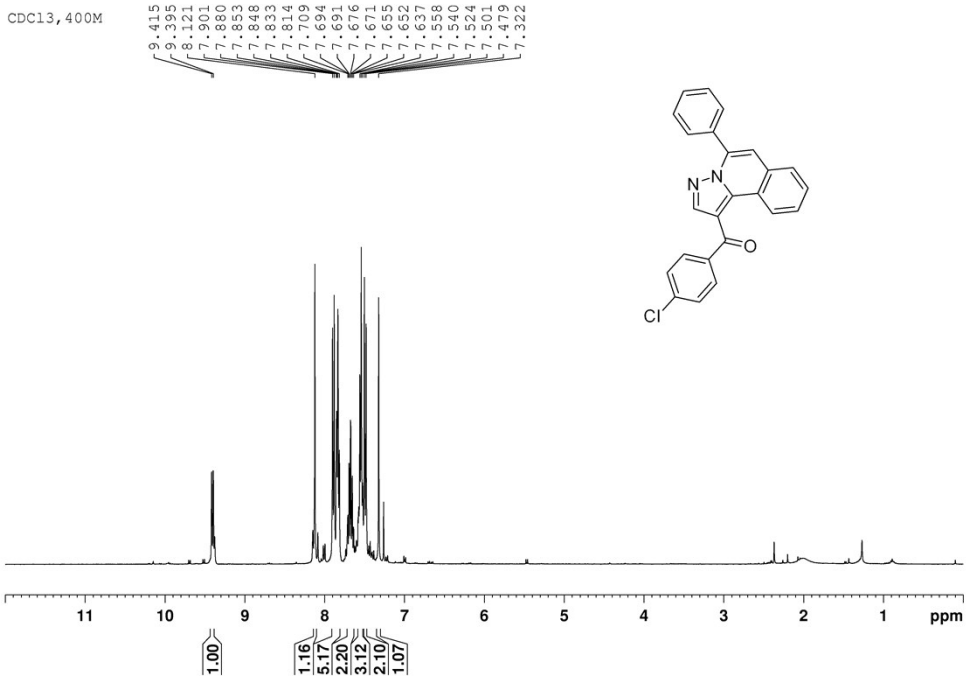


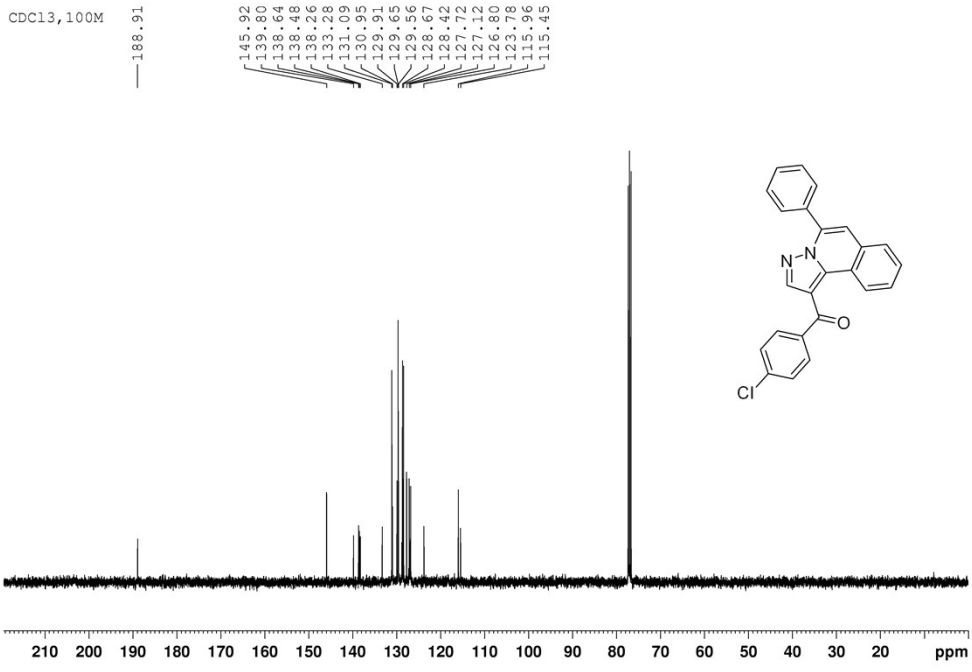
Naphthalen-1-yl(5-phenylpyrazolo[5,1-a]isoquinolin-1-yl)methanone (**2q**)



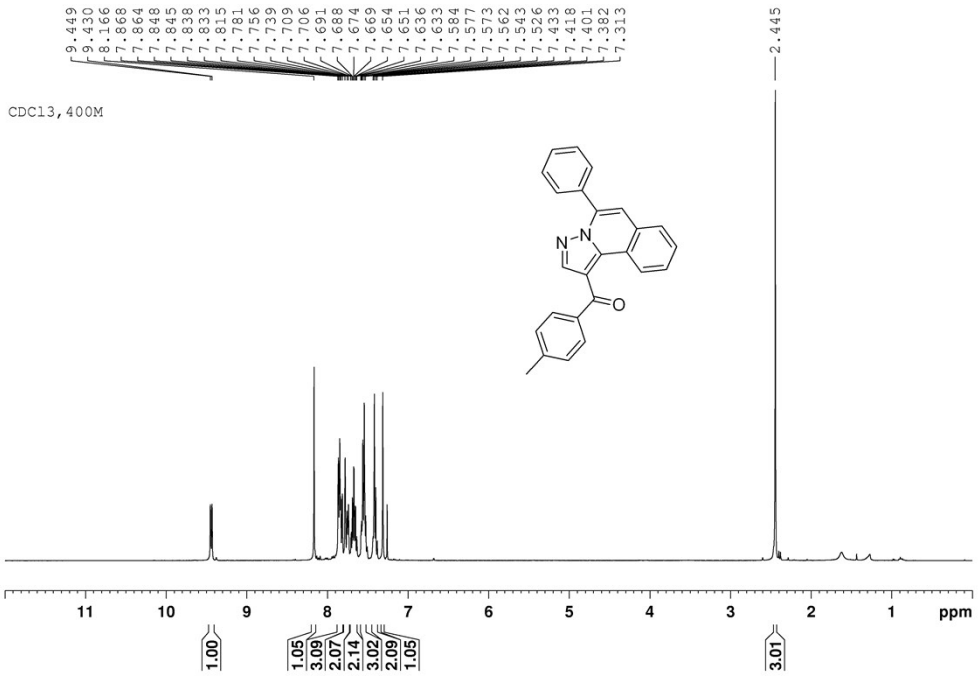


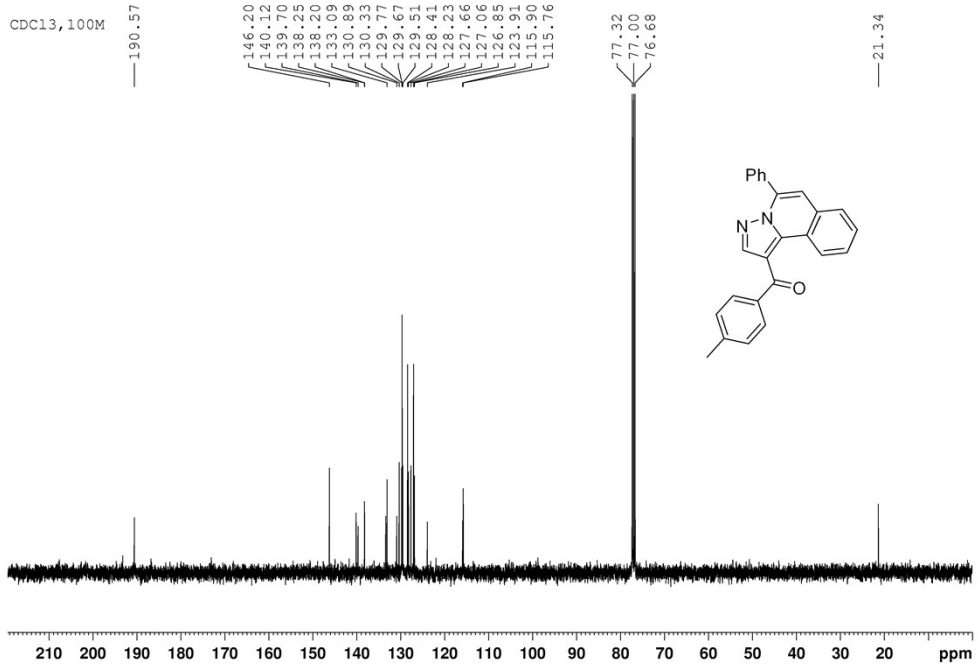
(4-Chlorophenyl)(5-phenylpyrazolo[5,1-a]isoquinolin-1-yl)methanone (**2r**)



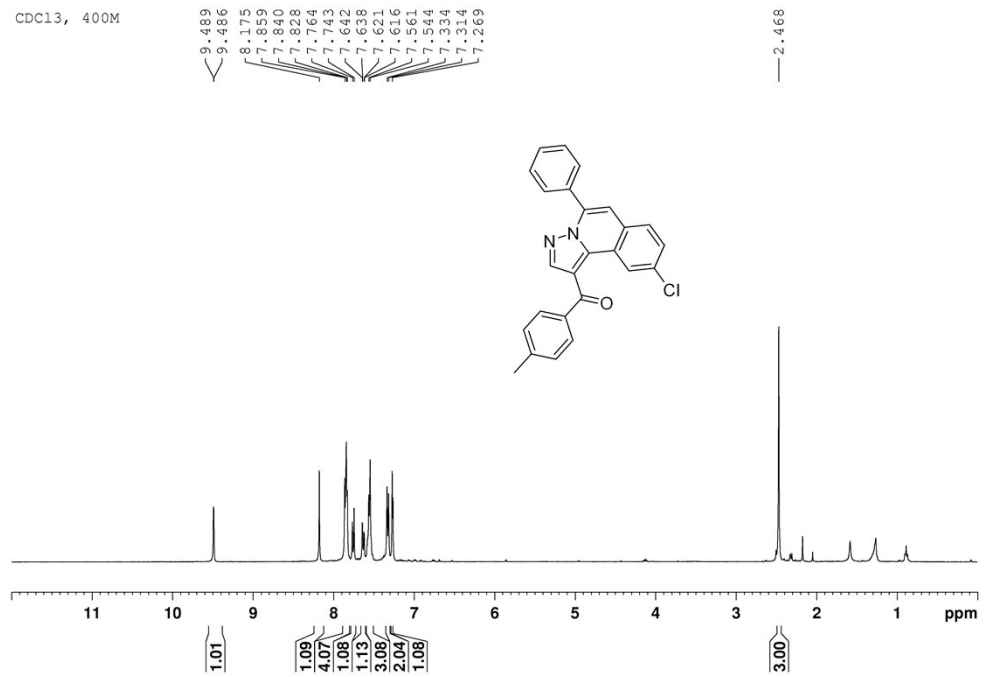


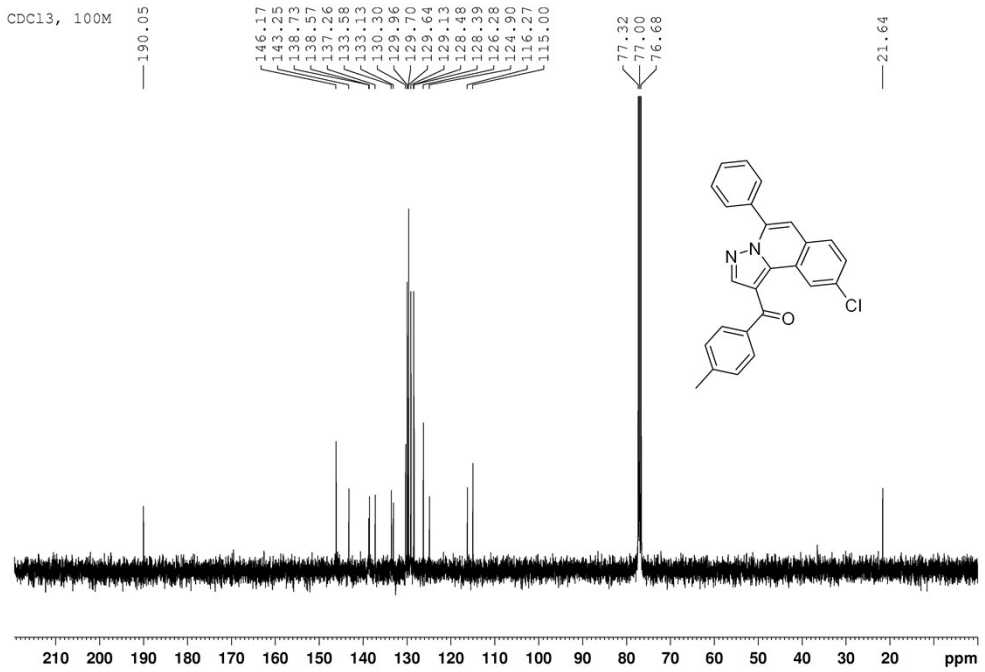
(5-Phenylpyrazolo[5,1-a]isoquinolin-1-yl)(p-tolyl)methanone (**2s**)



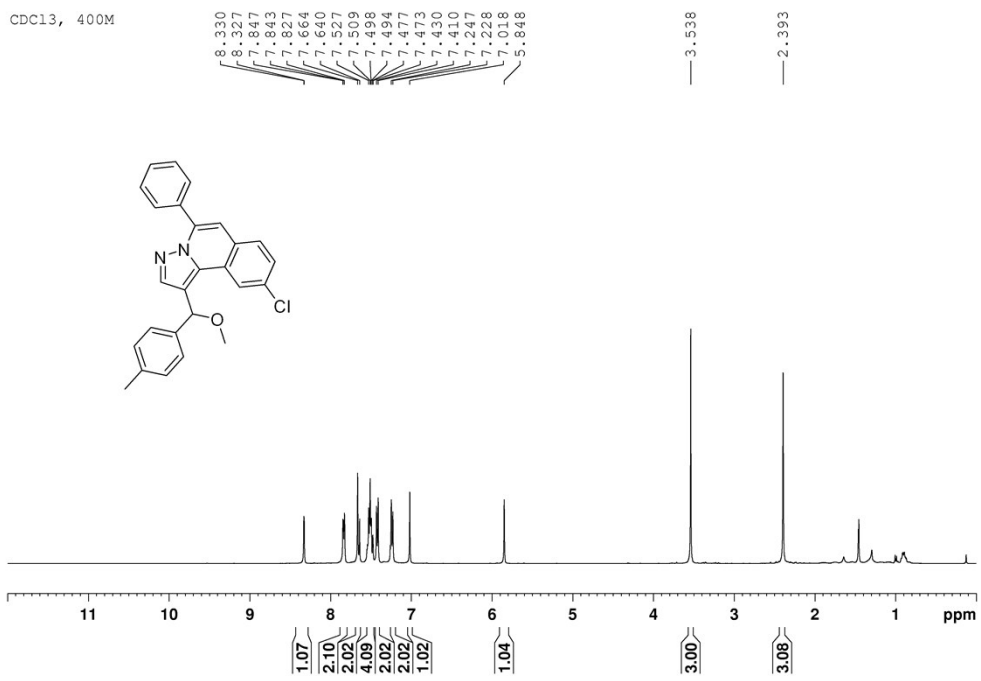


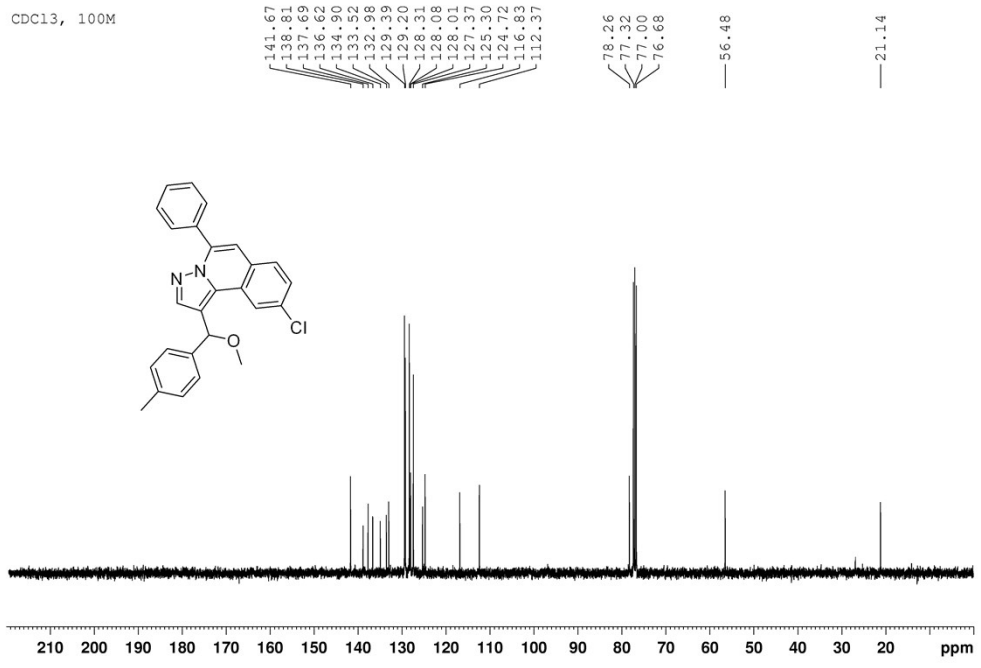
(9-Chloro-5-phenylpyrazolo[5,1-a]isoquinolin-1-yl)(p-tolyl)methanone (**2v**)





9-Chloro-1-(methoxy(p-tolyl)methyl)-5-phenylpyrazolo[5,1-a]isoquinoline (**4v**)





3-phenylisoquinoline (**12a**)