Supporting Information

Organocatalytic asymmetric synthesis of 3-chlorooxindoles bearing adjacent quaternary – tertiary centers

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General

Full assignment of ^{1}H and ^{13}C chemical shifts is based on the 1D and 2D FT NMR spectra on a 400 MHz instrument. Solvent peaks ($CHCl_3$ δ=7.26/77.16) were used as chemical shift references. Chiral HPLC was performed using Chiralcel OD-H, Chiralpak AD-H and Lux 3u Amylose-2 columns. Precoated silica gel 60 F_{254} plates were used for TLC, whereas for column chromatography Merck silica gel was used. Commercial reagents were generally used as received. DCM and EtOAc were distilled from P_2O_5.

Synthesis of catalysts

Catalysts **5**,[1] **6**,[2] **7**,[3] **9**[4] and **10**[5] were prepared according to literature procedures. Catalyst **8**[6] was commercially available from Strem and used as received. Catalyst **4** was prepared analogously to catalyst **5**.

1-(2,6-diisopropylphenyl)-3-((1*S*)-((2*S*,4*S*,5*R*)-5-ethylquinuclidin-2-yl)(6-methoxyquinolin-4-yl)methyl)thiourea 4. 9-*epi*-9-Amino-9-deoxydihydroquinine (2 mmol, 650 mg) and 1,3-diisopropyl-2-isothiocyanatobenzene (2 mmol, 439 mg) were dissolved in THF (3 mL) and left stirring at ambient temperature until TLC showed full conversion. The mixture was concentrated and directly purified by silica gel column chromatography (DCM/MeOH 20/1 to 10/1) to yield 848 mg of product (78%) as white crystals. ^{1}H NMR (400 MHz, Chloroform-d) δ 8.67 (d, *J* = 4.6 Hz, 1H), 7.98 (d, *J* = 9.2 Hz, 1H), 7.88 (s, 1H), 7.42 – 7.33 (m, 3H), 7.28 – 7.20 (m, 2H), 7.07 (s, 1H), 6.54 (s, 1H), 5.81 (d, *J* = 10.7 Hz, 1H), 4.02 (s, 3H), 3.19 (p, *J* = 6.8 Hz, 1H), 3.09 (s, 1H), 2.97 (t, *J* = 11.5 Hz, 2H), 2.69 (s, 1H), 2.55 (ddd, *J* = 15.1, 11.8, 5.1 Hz, 1H), 2.14 – 2.04 (m, 1H), 1.65 – 1.51 (m, 2H), 1.50 – 1.40 (m, 1H), 1.30 (d, *J* = 6.8 Hz, 6H), 1.17 (d, *J* = 6.8 Hz, 6H), 1.13 – 1.08 (m, 2H), 1.04 (d, *J* = 6.7 Hz, 2H),

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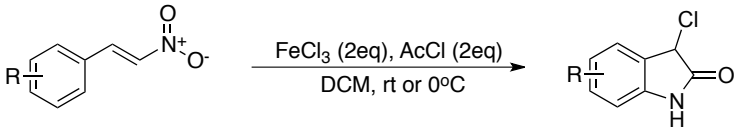
[1] Vakulya, B.; Varga, S.; Csámpai, A.; Soós, T. *Org. Lett*. **2005**, *7*, 1967–1969.
[2] Liu, T.-Y.; Long, J.; Li, B.-J.; Jiang, L.; Li, R.; Wu, Y.; Ding, L.-S.; Chen, Y.-C. *Org. Biomol. Chem*. **2006**, *4,* 2097–2099.
[3] Zhou, L.; Tan, C. K.; Jiang, X.; Chen, F.; Yeung, Y.-Y. *J. Am. Chem. Soc*. **2010**, *132*, 15474–15476.
[4] Lee, J. W.; Ryu, T. H.; Oh, S.; Bae, H. Y.; Jang, H. B.; Song, C. E. *Chem. Commun*. **2009**, 7224–7226.
[5] Bae, H. Y.; Some, S.; Lee, J. H.; Kim, J.-Y.; Song, M. J.; Lee, S.; Zhang, Y. J.; Song, C. E. *Adv. Synth. Catal*. **2011**, *353*, 3196–3202.
[6] McCooey, S. H.; Connon, S. J. *Angew. Chem. Int. Ed*. **2005**, *44*, 6367–6370.

0.95 – 0.86 (m, 1H), 0.72 (t, J = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 181.69, 157.87, 148.03, 147.42, 144.77, 131.52, 130.52, 129.95, 124.41, 124.14, 122.04, 118.71, 102.59, 61.56, 57.40, 55.90, 55.65, 41.15, 37.30, 28.77, 28.45, 27.43, 25.44, 25.29, 25.03, 24.79, 22.73, 22.35, 12.02. IR ν = 3168, 2959, 2866, 1622, 1509, 1473, 1361, 1263, 1227, 1031, 797 cm^{-1}; Mp =120 – 121^{o}C; HRMS (ESI): calcd for $[M+H]^+$ $(C_{33}H_{45}N_4OS)^+$ requires m/z 545.3309, found 545.3306.

Synthesis of starting materials

Nitroolefines *β*–nitrostyren **2a**, *(E)*-1-bromo-4-(2-nitrovinyl)benzene **2b**, (*E*)-1-(2-nitrovinyl)-4-(trifluoromethoxy)benzene **2c** and (*E*)-1-methoxy-4-(2-nitrovinyl)benzene **2k** were commercially available from Aldrich or Alfa Aesar and used as received. Nitroalkenes (*E*)-1-nitro-4-(2-nitrovinyl)benzene **2d**, (*E*)-2-(2-nitrovinyl)thiophene **2e**, (*E*)-2-(2-nitrovinyl)naphthalene **2f**, (*E*)-3-(2-nitrovinyl)pyridine **2g**, (*E*)-1-bromo-3-(2-nitrovinyl)benzene **2h**, (*E*)-1-methyl-3-(2-nitrovinyl)benzene **2i**, (*E*)-2-(2-nitrovinyl)furan **2j** and (*E*)-(2-nitrovinyl)cyclohexane **2l** were prepared according to literature procedures.[7] 3-chlorooxindols **1a**, **1b**, **1c** and **1e** were prepared as described by Guillaumel *et al* (Scheme 1)[8] and **1e** was prepared analogously.

Scheme 1. Synthesis of 3-chlorooxindoles.



R = H (**1a**), 4-Cl (**1b**), 5-Br (**1c**), 5-Me (**1d**), 6-Cl (**1e**)

5-bromo-3-chloroindolin-2-one (1e). (*E*)-1-bromo-3-(2-nitrovinyl)benzene (1.14 g, 5 mmol) was dissolved in DCM (25 mL) and AcCl (0.7 mL, 10 mmol) was added at

[7] (a) Cheng, P.; Chen, J.-J.; Huang, N.; Wang, R.-R.; Zheng, Y.-T.; Liang, Y.-Z. Synthesis and Anti-Human Immunodeficiency Virus Type 1 Activity of (E)-N-Phenylstyryl-N-alkylacetamide Derivatives. *Molecules* **2009**, *14*, 3176-3186. (b) Cheng, P., Jiang, Z.-Y., Wang, R.-R., Zhang, X.-M., Wang, Q., Zheng, Y.-T., Zhan, J., Chen, J.-J. *Bioorg. Med. Chem. Lett*. **2007**, *17*, 4476-4480. (c) Kuster, G. .; Steeghs, R. .; Scheeren, H. *Eur. J. Org. Chem*. **2001**, *2001*, 553–560. Rodríguez, J. M.; Dolors Pujol, M. *Tetrahedron Letters* **2011**, *52*, 2629–2632. (d)Trost, B. M.; Müller, C. *J. Am. Chem. Soc.* **2008**, *130*, 2438–2439.

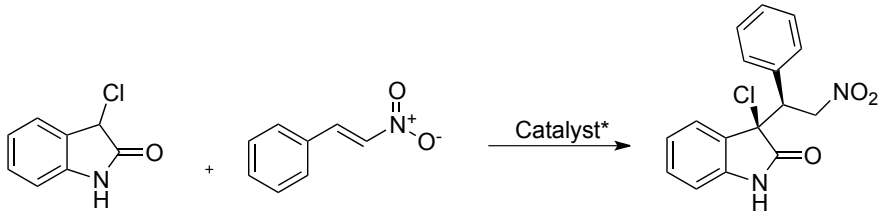
[8] Guillaumel, J., Demerseman, P., Clavel, J.-M., Royer, R. *J. Heterocyclic Chem.* **1980**, *17*, 1531.

once. Then $FeCl_3$ (1.6 g, 10 mmol) was added at 0 °C and stirring was maintained for 5 hours. Mixture was poured into 100 mL of aq 1N AcOH solution, extracted with DCM (2 x 50 mL) and dryed over $MgSO_4$. Reaction mixture was filtered, concentrated and purified by silica gel column chromatography using DCM as eluent to yield 318 mg (26%) of product as white solid. IR ν = 3142, 1744, 1683, 1619, 1473, 755 cm^{-1}. ^1H NMR (400 MHz, DMSO-d6) δ 10.90 (s, 1H), 7.58 – 7.51 (m, 1H), 7.48 (ddd, *J* = 8.3, 2.1, 0.7 Hz, 1H), 6.84 (d, *J* = 8.3 Hz, 1H), 5.59 (s, 1H). ^{13}C NMR (101 MHz, DMSO) δ 172.71, 141.71, 132.98, 128.87, 128.36, 113.71, 112.13, 51.61. HRMS (ESI): calcd for $[M+H]^+$ $(C_8H_5BrClNO)^+$ requires m/z 245.9316, found 245.9315.

Reaction optimization studies

Our initial studies were focused on the reaction of 3-chlorooxindole **1a** with *β*-nitrostyrene **2a** (Scheme 2) catalyzed by thiourea or squaramide catalyst (Scheme 2).

Scheme 2. Model reaction between 3-chloroxoindole and *β*-nitrostyrene.



1a **2a** **3a**

Preliminary screening of catalysts was conducted in chloroform at ambient temperature using 10 mol % of the appropriate catalyst (**4 – 10**, Figure 1). Although, catalyst **4** provided the product with 70% yield within 5 hours, both diastereo – and enantioselectivities remained moderate (Table 1, entry 1).

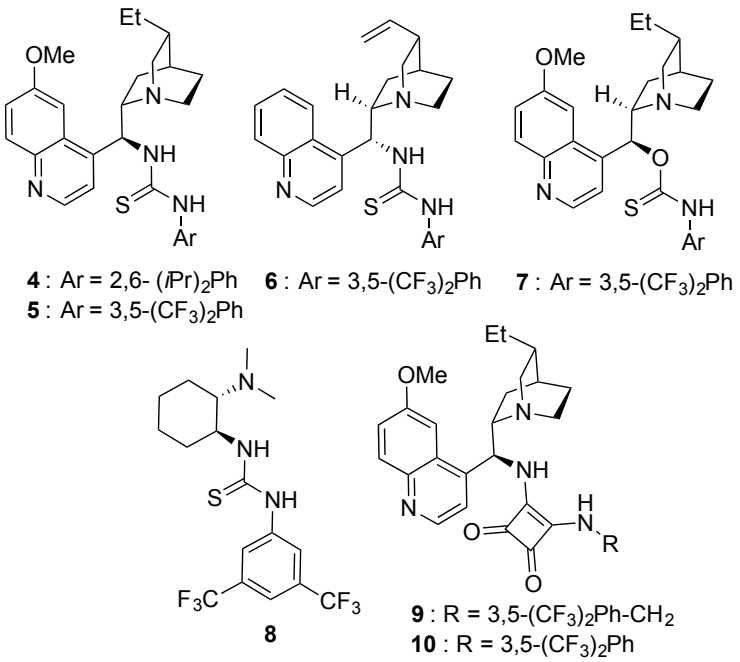


Figure 1. Catalysts used in the screening.

More traditional thiourea **5**, derived from dihydroquinine, yielded the product with superior stereocontrol (Table 1, entry 2). Slight modification in the catalyst structure (double bond) resulted in the formation of the product with higher lever of diastereoselectivity but with opposite and lower enantioselectivity (catalyst derived from cinchonidine) (Table 1, entry 3). When thiocarbamate **7** was used as catalyst, no product was isolated, confirming that activation of nitroolefin by two hydrogen bonds was necessary to provide sufficient level of activation. Takemoto's bifunctional chiral thiourea **8** enhanced enantiocontrol with good diastereoselectivity (Table 1, entry 5).

Table 1. Reaction optimization studies. [a]

Entry	Catalyst (mol %)	Solvent	Temp (^{o}C)	Time (h)	Yield (%)	dr[b]	ee (%)[c]
1	**4** (10 mol %)	$CHCl_3$	rt	5	70	3.5:1	24
2	**5** (10 mol %)	$CHCl_3$	rt	2	88	4:1	63
3	**6** (10 mol %)	$CHCl_3$	rt	8	70	4.5:1	-54
4	**7** (10 mol %)	$CHCl_3$	rt	24	*traces*	-	-
5	**8** (10 mol %)	$CHCl_3$	rt	5	79	4:1	-71
6	**9** (10 mol %)	$CHCl_3$	rt	1	92	3:1	93
7	**10** (10 mol %)	$CHCl_3$	rt	0.5	95	6:1	90
8	**10** (3 mol %)	$CHCl_3$	-20	72	44	13:1	90
9	**10** (5 mol %)	$CHCl_3$	4	15	95	10:1	91
10	**10** (5 mol %)	Toluene	4	16	76	9:1	84
11	**10** (5 mol %)	MTBE	4	16	95	8:1	79

[a] Reaction conditions: 0.10 mmol (1eq) of **1a**, 0.12 mmol (1.2eq) of **2a** and catalyst were dissolved in 0.5 mL of solvent and stirred at temperature indicated and monitoring the reaction progress by TLC analysis; [b] Determined by 1H NMR; [c] Determined by chiral HPLC analysis;

Chiral squaramides (**9** and **10**) are known to have higher catalytic activity in hydrogen bond activated reaction than their thiourea counterparts.[9] Squaramide functionality differs from ureas and thioureas in having more rigid structure, more flexible hydrogen bond angles, longer spacing between NH hydrogen's, duality in binding and significantly different pK_a of NH hydrogen's. Those factors all contribute to the increased reactivity associated with squaramide catalyzed reactions.

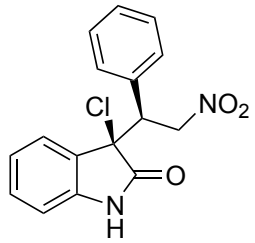
To our delight, the same tendency was observed when catalyst **9** was used as product **3a** was isolated with 92% yield and 93% *ee* just after 1 hour at room temperature (Table 1, entry 6). Due to moderate diastereoselectivity, however, it was envisioned that shortening the linker between NH and aryl group of the catalyst by one carbon could increase diastereocontrol, as a result of amplified steric influence closer to the reaction center. Indeed, under otherwise same reaction conditions catalyst **10** provided the product with twofold increase in diastereoselectivity (6:1) and with high *ee* (Table 1, entry 7). To further improve upon the diastereoselectivity, reaction temperature was lowered as well as catalyst loading reduced as squaramide **10** showed extremely high reactivity at ambient temperature. Although, by far the highest diastereoselectivity was observed at -20^{o}C (Table 1, entry 8), with no changes in enantioselectivity, the reaction rate was significantly decreased. This last tendency can partially be explained by the low solubility of 3-chlorooxindole **1a** in chloroform, that was further reduced by lowering the reaction temperature as well as decreased reactivity of the catalyst. As a middle ground, catalyst loading was increased to 5 mol % and reaction conduced at 4^{o}C. Under those conditions product was obtained with 95% yield, 91% *ee* and dr 10:1 (Table 1, entry 9). Switching solvent from chloroform to toluene or MTBE did not improve diastereo- or enantioselectivity (Table 1, entry 10 – 11).

General procedure for the synthesis of 3-chlorooxindoles 3

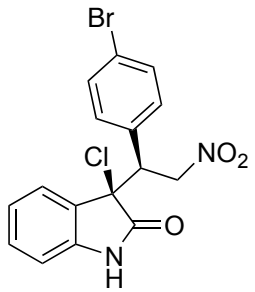
3-chlorooxindole **1a-e** (0.1 mmol, 1 eq), nitroolefine **2** (0.12 mmol, 1.2eq) and squaramide **10** (0.05 mmol, 3.2 mg, 5 mol %) were dissolved in chloroform (0.5 mL) precooled to 0^{o}C and stirred at 4^{o}C until TLC showed full conversion. Reaction

[9] Alemán, J.; Parra, A.; Jiang, H.; Jørgensen, K. A. *Chem. Eur. J.* **2011**, *17*, 6890–6899.

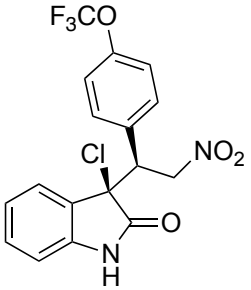
mixture was directly purified by silica gel column chromatography using DCM.



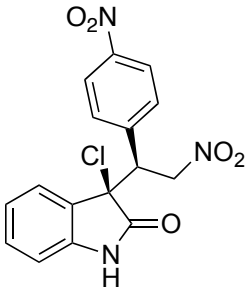
(*R*)-3-chloro-3-((*S*)-2-nitro-1-phenylethyl)indolin-2-one 3a. Synthesized according to the general procedure from 3-chloroindolin-2-one **1a** and *β*–nitrostyrene **2a.** Product was isolated in 95% yield (30 mg) as white solid with dr 10:1 by 1H NMR and *ee* 91% (Chiralcel OD-H, Hex/*i*PrOH 85/15, 1 mL/min, 230 nm; major (10.9 min) and minor (8.7 min). IR ν = 2254, 1731, 1620, 1559, 1473, 1377, 1326 cm^{-1}; ^{1}H NMR (400 MHz, Chloroform-d) δ 8.28 (s, 1H), 7.31 (td, *J* = 7.8, 1.2 Hz, 1H), 7.27 – 7.22 (m, 1H), 7.19 – 7.13 (m, 2H), 7.04 (td, *J* = 7.7, 1.0 Hz, 1H), 7.00 – 6.95 (m, 2H), 6.87 (d, *J* = 7.9 Hz, 1H), 6.81 (dt, *J* = 7.8, 0.7 Hz, 1H), 5.67 (dd, *J* = 13.4, 3.6 Hz, 1H), 5.14 (dd, *J* = 13.3, 11.3 Hz, 1H), 4.27 (dd, *J* = 11.2, 3.7 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.31, 139.98, 132.66, 131.17, 129.48, 129.17, 128.71, 128.64, 127.26, 126.02, 123.47, 110.96, 75.63, 66.23, 50.68. HRMS (ESI): calcd for $[M+H]^+$ $(C_{16}H_{14}ClN_2O_3)^+$ requires m/z 317.0687, found 317.0684.



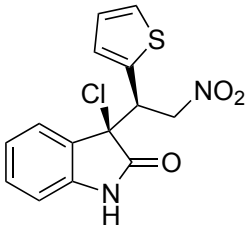
(*R*)-3-((*S*)-1-(4-bromophenyl)-2-nitroethyl)-3-chloroindolin-2-one 3b. Synthesized according to the general procedure from 3-chloroindolin-2-one **1a** and (*E*)-1-bromo-4-(2-nitrovinyl)benzene **2b.** Product was isolated in 96% yield (38 mg) as white solid with dr 11:1 by 1H NMR and *ee* 90% (Chiralcel OD-H, Hex/*i*PrOH 90/10, 1 mL/min, 230 nm; major (16.5 min) and minor (11.6 min). IR ν = 3248, 1732, 1619, 1556, 1473, 1377, 1328, 754 cm^{-1}; ^{1}H NMR (400 MHz, Chloroform-d) δ 8.21 (s, 1H), 7.35 – 7.29 (m, 3H), 7.08 (t, *J* = 7.6 Hz, 1H), 6.95 (d, *J* = 7.7 Hz, 1H), 6.87 – 6.80 (m, 3H), 5.64 (dd, *J* = 13.4, 3.6 Hz, 1H), 5.08 (dd, *J* = 13.4, 11.4 Hz, 1H), 4.27 (dd, *J* = 11.3, 3.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.91, 139.97, 131.89, 131.68, 131.38, 131.07, 126.85, 125.88, 123.65, 123.53, 111.16, 75.38, 65.84, 50.22. HRMS (ESI): calcd for $[M+H]^+$ $(C_{16}H_{13}BrClN_2O_3)^+$ requires m/z 394.9793, found 394.9784.



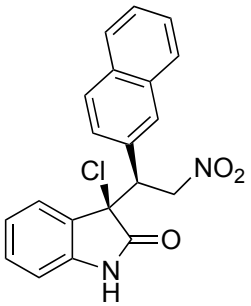
(*R*)-3-chloro-3-((*S*)-2-nitro-1-(4-(trifluoromethoxy)phenyl)ethyl)indolin-2-one 3c. Synthesized according to the general procedure from 3-chloroindolin-2-one **1a** and (*E*)-1-(2-nitrovinyl)-4-(trifluoromethoxy)benzene **2c.** Product was isolated in 90% yield (36 mg) as white solid with dr 7.7:1 by 1H NMR and *ee* 86% (Chiralcel OD-H, Hex/*i*PrOH 90/10, 1 mL/min, 230 nm; major (14.4 min) and minor (10.0 min). IR ν = 3259, 1734, 1620, 1558, 1511, 1474, 1272, 1217, 1167, 754 cm^{-1}; ^{1}H NMR (400 MHz, Chloroform-d) δ 8.18 (s, 1H), 7.33 (td, *J* = 7.8, 1.2 Hz, 1H), 7.07 (td, *J* = 7.7, 1.0 Hz, 1H), 7.03 (s, 4H), 6.90 (d, *J* = 7.6 Hz, 1H), 6.84 (d, *J* = 7.8 Hz, 1H), 5.67 (dd, *J* = 13.5, 3.7 Hz, 1H), 5.10 (dd, *J* = 13.5, 11.3 Hz, 1H), 4.32 (dd, *J* = 11.3, 3.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.93, 149.73 (q, *J* = 1.8 Hz), 139.93, 131.44, 131.31, 131.03, 126.86, 125.90, 123.66, 120.81, 120.40 (d, *J* = 258.0 Hz), 111.11, 75.42, 65.92, 50.03. HRMS (ESI): calcd for $[M+H]^+$ $(C_{17}H_{13}ClF_3N_2O_4)^+$ requires m/z 401.0510, found 401.0511.



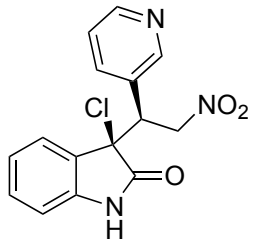
(*R*)-3-chloro-3-((*S*)-2-nitro-1-(4-nitrophenyl)ethyl)indolin-2-one 3d. Synthesized according to the general procedure from 3-chloroindolin-2-one **1a** and (*E*)-1-nitro-4-(2-nitrovinyl)benzene **2d.** Product was isolated in 91% yield (33 mg) as white solid with dr 6.7:1 by 1H NMR and *ee* 87% (Chiralcel OD-H, Hex/*i*PrOH 90/10, 1 mL/min, 230 nm; major (33.2 min) and minor (26.6 min). IR ν = 3387, 1735, 1619, 1558, 1524, 1473, 1377, 1350, 857, 756 cm^{-1}; ^{1}H NMR (400 MHz, Chloroform-d) δ 8.05 (d, *J* = 8.9 Hz, 2H), 7.35 (td, *J* = 7.8, 1.3 Hz, 1H), 7.19 (d, *J* = 8.8 Hz, 1H), 7.12 (td, *J* = 7.7, 1.0 Hz, 2H), 7.01 – 6.97 (m, 1H), 6.79 (dt, *J* = 8.0, 0.8 Hz, 1H), 5.70 (dd, *J* = 13.7, 3.5 Hz, 1H), 5.15 (dd, *J* = 13.7, 11.6 Hz, 1H), 4.45 (dd, *J* = 11.6, 3.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.49, 148.31, 140.06, 139.87, 131.71, 130.61, 126.41, 125.80, 123.88, 123.72, 111.32, 75.05, 65.52, 50.35. HRMS (ESI): calcd for $[M+H]^+$ $(C_{16}H_{13}ClN_3O_5)^+$ requires m/z 362.0538, found 362.0541.



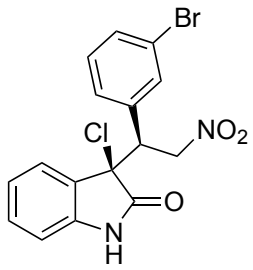
(*R*)-3-chloro-3-((*R*)-2-nitro-1-(thiophen-2-yl)ethyl)indolin-2-one 3e. Synthesized according to the general procedure from 3-chloroindolin-2-one **1a** and (*E*)-2-(2-nitrovinyl)thiophene **2e.** Product was isolated in 96% yield (31 mg) as yellow syrup with dr 10:1 by 1H NMR and *ee* 90% (Chiralpak AD-H, Hex/*i*PrOH 90/10, 1 mL/min, 230 nm; major (15.2 min) and minor (16.3 min). IR ν = 3092, 1727, 1619, 1556, 1473, 1423, 1371, 1338, 1237, 881, 852, 754, 708 cm^{-1}; ^{1}H NMR (400 MHz, Chloroform-d) δ 8.48 (s, 1H), 7.34 (td, *J* = 7.7, 1.2 Hz, 1H), 7.18 (ddd, *J* = 5.1, 1.3, 0.6 Hz, 1H), 7.07 (td, *J* = 7.7, 1.0 Hz, 1H), 6.94 (d, *J* = 7.6 Hz, 1H), 6.88 (d, *J* = 7.8 Hz, 1H), 6.84 (dd, *J* = 5.1, 3.6 Hz, 1H), 6.80 (dd, *J* = 3.7, 1.2 Hz, 1H), 5.70 (dd, *J* = 13.2, 3.4 Hz, 1H), 5.02 (dd, *J* = 13.2, 11.1 Hz, 1H), 4.62 (dd, *J* = 11.1, 3.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.17, 140.34, 134.54, 131.44, 129.47, 127.05, 126.90, 126.80, 125.95, 123.67, 111.11, 77.10, 65.70, 46.69. HRMS (ESI): calcd for $[M+H]^+$ $(C_{14}H_{12}ClN_2O_3S)^+$ requires m/z 323.0252, found 323.0247.



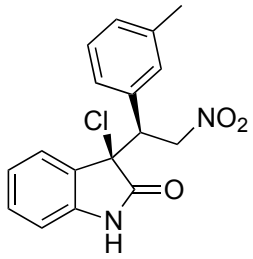
(*R*)-3-chloro-3-((*S*)-1-(naphthalen-2-yl)-2-nitroethyl)indolin-2-one 3f. Synthesized according to the general procedure from 3-chloroindolin-2-one **1a** and (*E*)-2-(2-nitrovinyl)naphthalene **2f.** Product was isolated in 95% yield (35 mg) as white solid with dr 10:1 by 1H NMR and *ee* 90% (Chiralcel OD-H, Hex/*i*PrOH 90/10, 1 mL/min, 230 nm; major (30.3 min) and minor (16.4 min). IR ν = 3260, 1730, 1619, 1556, 1472, 1377, 1327, 1232, 750 cm^{-1}; ^{1}H NMR (400 MHz, Chloroform-d) δ 8.15 (s, 1H), 7.77 – 7.72 (m, 1H), 7.65 – 7.59 (m, 2H), 7.48 – 7.38 (m, 3H), 7.28 (td, *J* = 7.8, 1.3 Hz, 1H), 7.06 – 6.99 (m, 2H), 6.94 – 6.90 (m, 1H), 6.74 (dt, *J* = 7.8, 0.8 Hz, 1H), 5.71 (dd, *J* = 13.3, 3.6 Hz, 1H), 5.23 (dd, *J* = 13.3, 11.3 Hz, 1H), 4.43 (dd, *J* = 11.2, 3.7 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.11, 140.01, 133.32, 132.92, 131.17, 130.11, 129.46, 128.35, 128.26, 127.68, 127.26, 126.90, 126.53, 126.31, 126.01, 123.47, 111.01, 75.74, 66.25, 50.81. HRMS (ESI): calcd for $[M+H]^+$ $(C_{20}H_{16}ClN_2O_3)^+$ requires m/z 367.0844, found 367.0843.



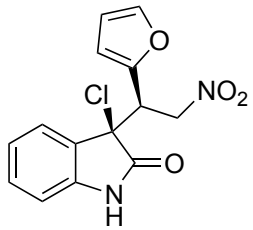
(*R*)-3-chloro-3-((*S*)-2-nitro-1-(pyridin-3-yl)ethyl)indolin-2-one 3g. Synthesized according to the general procedure from 3-chloroindolin-2-one **1a** and (*E*)-3-(2-nitrovinyl)pyridine **2g.** Product was isolated in 91% yield (29mg) as yellow syrup with dr 9.1:1 by 1H NMR and *ee* 90% (Chiralcel OD-H, Hex/*i*PrOH 85/15, 1 mL/min, 230 nm; major (18.8 min) and minor (16.0 min). IR ν = 3066, 1735, 1620, 1555, 1472, 1430, 1377, 1327, 1186, 755 cm^{-1}; ^{1}H NMR (400 MHz, Chloroform-d) δ 8.97 (s, 1H), 8.50 (dd, *J* = 4.9, 1.6 Hz, 1H), 8.24 (dd, *J* = 2.4, 0.8 Hz, 1H), 7.37 (dt, *J* = 8.0, 2.0 Hz, 1H), 7.32 (td, *J* = 7.8, 1.2 Hz, 1H), 7.16 (ddd, *J* = 8.0, 4.8, 0.9 Hz, 1H), 7.09 – 7.03 (m, 1H), 6.95 – 6.89 (m, 1H), 6.80 (dt, *J* = 8.0, 0.7 Hz, 1H), 5.69 (dd, *J* = 13.6, 3.6 Hz, 1H), 5.14 (dd, *J* = 13.6, 11.4 Hz, 1H), 4.34 (dd, *J* = 11.4, 3.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.70, 150.63, 150.12, 140.24, 136.74, 131.57, 129.03, 126.57, 125.77, 123.66, 123.54, 111.26, 74.91, 65.83, 48.51. HRMS (ESI): calcd for $[M+H]^+$ $(C_{15}H_{13}ClN_3O_3)^+$ requires m/z 318.0640, found 318.0644.



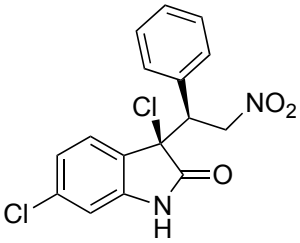
(*R*)-3-((*S*)-1-(3-bromophenyl)-2-nitroethyl)-3-chloroindolin-2-one 3h. Synthesized according to the general procedure from 3-chloroindolin-2-one **1a** and (*E*)-1-bromo-3-(2-nitrovinyl)benzene **2h.** Product was isolated in 96% yield (38 mg) as white solid with dr 11:1 by 1H NMR and *ee* 90% (Chiralcel OD-H, Hex/*i*PrOH 90/10, 1 mL/min, 230 nm; major (16.2 min) and minor (11.4 min). IR ν = 3164, 1727, 1621, 1560, 1474, 1373, 754 cm^{-1}; ^{1}H NMR (400 MHz, Chloroform-d) δ 8.22 (s, 1H), 7.34 (ddd, *J* = 7.9, 2.0, 1.0 Hz, 1H), 7.27 (td, *J* = 7.8, 1.2 Hz, 1H), 7.05 (t, *J* = 1.9 Hz, 1H), 7.03 – 6.95 (m, 2H), 6.87 (dt, *J* = 7.9, 1.3 Hz, 1H), 6.80 (dd, *J* = 13.4, 7.7 Hz, 2H), 5.59 (dd, *J* = 13.6, 3.6 Hz, 1H), 5.01 (dd, *J* = 13.6, 11.2 Hz, 1H), 4.17 (dd, *J* = 11.2, 3.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.98, 139.92, 135.03, 132.49, 132.40, 131.44, 130.16, 128.15, 126.84, 125.93, 123.64, 122.57, 111.14, 75.29, 65.89, 50.25. HRMS (ESI): calcd for $[M-HCl+H]^+$ $(C_{16}H_{12}BrN_2O_3)^+$ requires m/z 359.0026, found 359.0021.



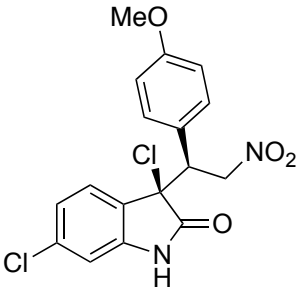
(*R*)-3-chloro-3-((*S*)-2-nitro-1-(m-tolyl)ethyl)indolin-2-one 3i. Synthesized according to the general procedure from 3-chloroindolin-2-one **1a** and (*E*)-1-methyl-3-(2-nitrovinyl)benzene **2i.** Product was isolated in 91% yield (30 mg) as white solid with dr 11:1 by 1H NMR and *ee* 91% (Chiralpak AD-H, Hex/*i*PrOH 95/5, 1 mL/min, 230 nm; major (18.5 min) and minor (21.0 min). IR ν = 3093, 130, 1620, 1556, 1473, 1375, 1331, 1236, 1187, 907, 754 cm^{-1}; ^{1}H NMR (400 MHz, Chloroform-d) δ 8.18 (s, 1H), 7.30 (td, *J* = 7.8, 1.2 Hz, 1H), 7.07 – 7.00 (m, 3H), 6.91 – 6.86 (m, 1H), 6.81 (dt, *J* = 7.9, 0.7 Hz, 1H), 6.78 – 6.74 (m, 2H), 5.65 (dd, *J* = 13.3, 3.6 Hz, 1H), 5.12 (dd, *J* = 13.3, 11.2 Hz, 1H), 4.23 (dd, *J* = 11.2, 3.6 Hz, 1H), 2.17 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.25, 140.00, 138.29, 132.55, 131.09, 130.29, 129.89, 128.43, 127.39, 126.38, 126.07, 123.38, 110.84, 75.70, 66.25, 50.66, 21.44. HRMS (ESI): calcd for $[M+H]^+$ $(C_{17}H_{16}ClN_2O_3)^+$ requires m/z 331.0844, found 331.0846.



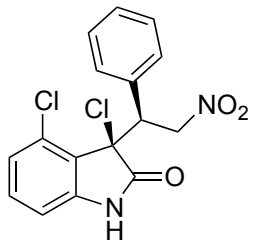
(*R*)-3-chloro-3-((*R*)-1-(furan-2-yl)-2-nitroethyl)indolin-2-one 3j. Synthesized according to the general procedure from 3-chloroindolin-2-one **1a** and (*E*)-2-(2-nitrovinyl)furan **2j.** Product was isolated in 95% yield (29 mg) as yellow syrup with dr 5.6:1 by 1H NMR and *ee* 88% (Chiralpak AD-H, Hex/*i*PrOH 95/5, 1 mL/min, 230 nm; major (33.3 min) and minor (50.4 min). IR ν = 3257, 1732, 1620, 1557, 1473, 1376, 1330, 744 cm^{-1}; ^{1}H NMR (400 MHz, Chloroform-d) δ 8.81 (s, 1H), 7.30 (td, *J* = 7.8, 1.2 Hz, 1H), 7.28 – 7.23 (m, 1H), 7.04 (td, *J* = 7.7, 1.0 Hz, 1H), 6.92 – 6.88 (m, 1H), 6.81 (dt, *J* = 7.7, 2.9 Hz, 1H), 6.25 (ddd, *J* = 18.8, 3.4, 1.3 Hz, 2H), 5.64 (dd, *J* = 13.6, 3.5 Hz, 1H), 5.15 (dd, *J* = 13.5, 10.9 Hz, 1H), 4.44 (dd, *J* = 10.9, 3.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.65, 146.94, 143.20, 139.68, 131.15, 127.55, 125.71, 123.62, 111.03, 110.92, 110.88, 73.88, 65.08, 44.49. HRMS (ESI): calcd for $[M+H]^+$ $(C_{14}H_{12}ClN_2O_4)^+$ requires m/z 307.0480, found 307.0480.



(*R*)-3,6-dichloro-3-((*S*)-2-nitro-1-phenylethyl)indolin-2-one 3k. Synthesized according to the general procedure from 3,6-dichloroindolin-2-one **1b** and *β*–nitrostyrene **2a.** Product was isolated in 97% yield (34 mg) as white solid with dr 5:1 by 1H NMR and *ee* 90% (Lux 3u Amylose-2, Hex/*i*PrOH 90/10, 1 mL/min, 230 nm; major (16.8 min) and minor (14.4 min). IR ν = 3153, 1732, 1618, 1558, 1486, 1454, 1376, 1325, 701 cm^{-1}; ^{1}H NMR (400 MHz, Chloroform-d) δ 8.65 (s, 1H), 7.32 – 7.27 (m, 1H), 7.25 – 7.18 (m, 2H), 7.07 – 7.01 (m, 2H), 6.99 (dd, *J* = 8.2, 1.8 Hz, 1H), 6.88 (d, *J* = 1.9 Hz, 1H), 6.65 (d, *J* = 8.2 Hz, 1H), 5.67 (dd, *J* = 13.5, 3.7 Hz, 1H), 5.11 (dd, *J* = 13.4, 11.1 Hz, 1H), 4.22 (dd, *J* = 11.0, 3.7 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.53, 140.89, 136.95, 132.43, 129.39, 128.72, 127.02, 125.64, 123.46, 111.58, 75.29, 65.57, 50.20. HRMS (ESI): calcd for $[M+H]^+$ $(C_{16}H_{13}Cl_2N_2O_3)^+$ requires m/z 351.0298, found 351.0299.

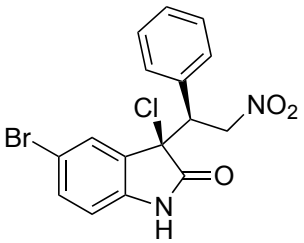


(*R*)-3,6-dichloro-3-((*S*)-1-(4-methoxyphenyl)-2-nitroethyl)indolin-2-one 3l. Synthesized according to the general procedure from 3,6-dichloroindolin-2-one **1b** and (*E*)-1-methoxy-4-(2-nitrovinyl)benzene **2k.** Product was isolated in 99% yield (38 mg) as white solid with dr 6.3:1 by 1H NMR and *ee* 90% (Chiralpak AD-H, Hex/*i*PrOH 90/10, 1 mL/min, 230 nm; major (21.2 min) and minor (23.0 min). IR ν = 3256, 1737, 1614, 1556, 1513, 1254, 1182 cm^{-1}; ^{1}H NMR (400 MHz, Chloroform-d) δ 8.33 (s, 1H), 7.01 (dd, *J* = 8.2, 1.9 Hz, 1H), 6.96 – 6.91 (m, 2H), 6.86 (d, *J* = 1.8 Hz, 1H), 6.76 – 6.71 (m, 3H), 5.63 (dd, *J* = 13.2, 3.7 Hz, 1H), 5.06 (dd, *J* = 13.2, 11.2 Hz, 1H), 4.18 (dd, *J* = 11.2, 3.8 Hz, 1H), 3.75 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.40, 160.14, 141.02, 136.99, 130.64, 127.13, 125.84, 124.19, 123.54, 114.18, 111.60, 75.57, 65.71, 55.34, 49.74. HRMS (ESI): calcd for $[M-HCl+H]^+$ $(C_{17}H_{14}ClN_2O_4)^+$ requires m/z 345.0637, found 345.0635.

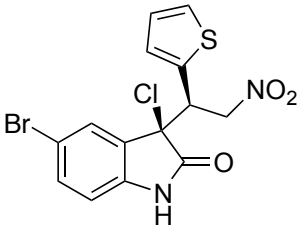


(*R*)-3,4-dichloro-3-((*S*)-2-nitro-1-phenylethyl)indolin-2-one 3m. Synthesized according to the general procedure from 3,4-dichloroindolin-2-one **1c** and *β*–nitrostyrene **2a.** Product

was isolated in 99% yield (35 mg) as white solid with dr 8.3:1 by 1H NMR and *ee* 76% (Chiralpak AD-H, Hex/*i*PrOH 95/5, 1 mL/min, 230 nm; major (24.0 min) and minor (21.0 min). IR ν = 3187, 1748, 1618, 1587, 1558, 1448, 1376, 1175, 785, 735, 700 cm^{-1}; ^1H NMR (400 MHz, Chloroform-d) δ 8.44 (s, 1H), 7.30 – 7.03 (m, 5H), 6.98 – 6.89 (m, 2H), 6.65 (dd, *J* = 7.8, 1.0 Hz, 1H), 5.50 (dd, *J* = 13.5, 3.2 Hz, 1H), 5.37 (dd, *J* = 13.4, 11.6 Hz, 1H), 4.55 (dd, *J* = 11.6, 3.3 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.65, 142.06, 132.18, 132.15, 131.79, 129.08, 128.98, 128.54, 125.04, 124.08, 109.47, 77.68, 66.85, 52.16. HRMS (ESI): calcd for $[M+H]^+$ $(C_{16}H_{13}Cl_2N_2O_3)^+$ requires m/z 351.0298, found 351.0297.

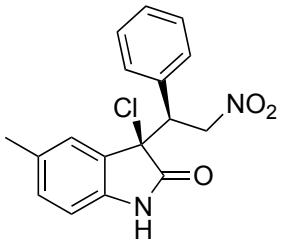


(*R*)-5-bromo-3-chloro-3-((*S*)-2-nitro-1-phenylethyl)indolin-2-one 3n. Synthesized according to the general procedure from 5-bromo-3-chloroindolin-2-one **1d** and *β*–nitrostyrene **2a** with the exception that reaction was conducted at room temperature**.** Product was isolated in 99% yield (39 mg) as white solid with dr 9.1:1 by 1H NMR and *ee* 92% (Chiralcel OD-H, Hex/*i*PrOH 90/10, 1 mL/min, 230 nm; major (13.9 min) and minor (11.3 min). IR ν = 3100, 1728, 1618, 1556, 1473, 1372, 1179, 699 cm^{-1}; ^1H NMR (400 MHz, Chloroform-d) δ 8.41 (s, 1H), 7.43 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.33 – 7.28 (m, 1H), 7.27 – 7.19 (m, 2H), 7.07 – 6.99 (m, 2H), 6.80 (d, *J* = 1.9 Hz, 1H), 6.73 (d, *J* = 8.3 Hz, 1H), 5.65 (dd, *J* = 13.5, 3.7 Hz, 1H), 5.12 (dd, *J* = 13.4, 11.0 Hz, 1H), 4.22 (dd, *J* = 11.0, 3.7 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.89, 138.70, 133.89, 132.25, 129.40, 129.36, 129.24, 129.14, 128.70, 115.81, 112.26, 75.13, 65.62, 50.20. HRMS (ESI): calcd for $[M-HCl+H]^+$ $(C_{16}H_{12}BrN_2O_3)^+$ requires m/z 359.0026, found 359.0029.

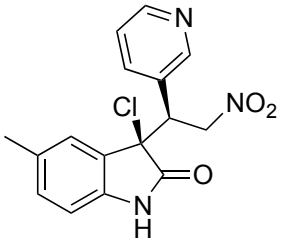


(*R*)-5-bromo-3-chloro-3-((*R*)-2-nitro-1-(thiophen-2-yl)ethyl)indolin-2-one 3o. Synthesized according to the general procedure from 5-bromo-3-chloroindolin-2-one **1d** and (*E*)-2-(2-nitrovinyl)thiophene **2e** with the exception that reaction was conducted at room temperature**.** Product was isolated in 97% yield (39 mg) as yellow syrup with dr 7.1:1 by 1H NMR and *ee* 87% (Chiralpak AD-H, Hex/*i*PrOH/EtOH 90/4/6, 1 mL/min, 230 nm; major (16.4 min) and minor (13.7 min).

IR ν = 3249, 1733, 1618, 1557, 1474, 1435, 1376, 1179, 706 cm^{-1}; ^1H NMR (400 MHz, Chloroform-d) δ 8.53 (s, 1H), 7.47 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.24 (ddd, *J* = 5.1, 1.3, 0.6 Hz, 1H), 6.92 (d, *J* = 2.0 Hz, 1H), 6.90 (dd, *J* = 5.1, 3.6 Hz, 1H), 6.85 (ddd, *J* = 3.6, 1.2, 0.4 Hz, 1H), 6.78 (dd, *J* = 8.3, 0.4 Hz, 1H), 5.67 (dd, *J* = 13.3, 3.4 Hz, 1H), 5.00 (dd, *J* = 13.3, 10.9 Hz, 1H), 4.57 (dd, *J* = 10.9, 3.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.86, 139.15, 134.27, 134.18, 129.62, 129.17, 129.05, 127.07, 126.96, 116.13, 112.52, 76.75, 65.27, 46.34. HRMS (ESI): calcd for $[M+H]^+$ $(C_{14}H_{11}BrClN_2O_3S)^+$ requires m/z 400.9357, found 400.9352.



(*R*)-3-chloro-5-methyl-3-((*S*)-2-nitro-1-phenylethyl)indolin-2-one 3p. Synthesized according to the general procedure from 3-chloro-5-methylindolin-2-one **1e** and *β*–nitrostyrene **2a.** Product was isolated in 94% yield (31 mg) as white solid with dr 10:1 by 1H NMR and *ee* 92% (Chiralcel OD-H, Hex/*i*PrOH 90/10 1 mL/min, 230 nm; major (10.6 min) and minor (8.6 min). IR ν = 3246, 1730, 1625, 1556, 1493, 1377, 1211, 908, 733, 699 cm^{-1}; ^1H NMR (400 MHz, Chloroform-d) δ 8.22 (s, 1H), 7.29 – 7.22 (m, 1H), 7.19 – 7.13 (m, 2H), 7.10 (ddd, *J* = 7.9, 1.8, 0.8 Hz, 1H), 7.00 – 6.95 (m, 2H), 6.70 (d, *J* = 8.0 Hz, 1H), 6.66 (s, 1H), 5.65 (dd, *J* = 13.3, 3.6 Hz, 1H), 5.14 (dd, *J* = 13.3, 11.3 Hz, 1H), 4.26 (dd, *J* = 11.3, 3.6 Hz, 1H), 2.29 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.31, 137.53, 133.17, 132.72, 131.56, 129.51, 129.11, 128.57, 127.21, 126.59, 110.67, 75.67, 66.44, 50.76, 21.27. HRMS (ESI): calcd for $[M+H]^+$ $(C_{17}H_{16}ClN_2O_3)^+$ requires m/z 331.0844, found 331.0843.

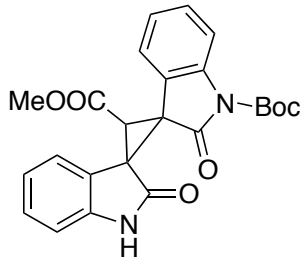


(*R*)-3-chloro-5-methyl-3-((*S*)-2-nitro-1-(pyridin-3-yl)ethyl)indolin-2-one 3r. Synthesized according to the general procedure from 3-chloro-5-methylindolin-2-one **1e** and (*E*)-1-nitro-4-(2-nitrovinyl)benzene **2d.** Product was isolated in 90% yield (30 mg) as yellow syrup with dr 8.3:1 by 1H NMR and *ee* 91% (Chiralcel OD-H, Hex/*i*PrOH 90/10, 1 mL/min, 230 nm; major (21.9 min) and minor (18.3 min). IR ν = 2922, 1733, 1626, 1555, 1492, 1430, 1377, 1211, 909, 732 cm^{-1}; ^1H NMR (400 MHz, Chloroform-d) δ 8.84 (s, 1H), 8.50 (dd, *J* = 4.9, 1.6 Hz, 1H), 8.23 (dd, *J* = 2.3, 0.8 Hz, 1H), 7.37 (dt, *J* = 8.0, 2.0 Hz, 1H),

7.16 (ddd, *J* = 8.0, 4.8, 0.8 Hz, 1H), 7.12 (ddd, *J* = 8.0, 1.8, 0.8 Hz, 1H), 6.76 – 6.74 (m, 1H), 6.70 (d, *J* = 8.0 Hz, 1H), 5.66 (dd, *J* = 13.6, 3.6 Hz, 1H), 5.14 (dd, *J* = 13.6, 11.5 Hz, 1H), 4.33 (dd, *J* = 11.5, 3.6 Hz, 1H), 2.31 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.70, 150.49, 149.97, 137.75, 136.95, 133.49, 132.03, 129.12, 126.49, 126.25, 123.53, 111.04, 74.97, 66.02, 48.62, 21.28. HRMS (ESI): calcd for $[M+H]^+$ $(C_{16}H_{15}ClN_3O_3)^+$ requires m/z 332.0796, found 332.0799.

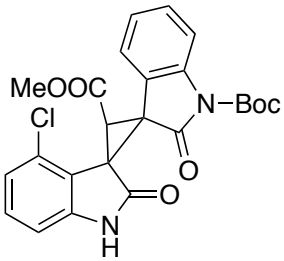
General procedure for the synthesis of spiro-bisoxindoles 12

3-chlorooxindole **1** (0.1 mmol, 1eq), tert-butyl (*E*)-3-(2-methoxy-2-oxoethylidene)-2-oxoindoline-1-carboxylate **11** (0.12 mmol, 1 eq), sodium hydrogen carbonate (8.4 mg, 0.10 mmol, 1 eq) and squaramide **10** were dissolved in chloroform (0.5 mL) and stirred at ambient temperature until TLC showed full conversion. Mixture was directly purified by silica gel column chromatography using a mixture of heptane – EtOAc as eluent.



1-(tert-butyl)-3'-methyl-2,2''-dioxodispiro[indoline-3,1'-cyclopropane-2',3''-indoline]-1,3'-dicarboxylate 12a. Synthesized according to the general procedure from 3-chloroindolin-2-one **1a** and (*E*)-3-(2-methoxy-2-oxoethylidene)-2-oxoindoline-1-carboxylate **11.** Product was isolated in 99% yield (43 mg) as white solid with dr 1.4:1 by 1H NMR and *ee* 96/96% respectively (Chiralcel OD-H, Hex/*i*PrOH 95/5, 1 mL/min, 230 nm; for major isomer: major (20.9 min) and minor (24.9 min) and for minor isomer: major (17.7 min) and minor (11.9 min). IR ν = 3308, 1786, 1734, 1620, 1467, 1151, 751 cm^{-1}; NMR for the mixture of isomers (normalized to minor isomer): ^{1}H NMR (400 MHz, Chloroform-d) δ 8.49 (s, 1H), 8.46 (s, 1.2H), 7.87 (ddd, *J* = 8.0, 2.9, 1.3 Hz, 2.4H), 7.75 – 7.71 (m, 2.4H), 7.31 (tt, *J* = 8.0, 1.6 Hz, 2.4H), 7.25 – 7.20 (m, 2.4H), 7.15 (tdd, *J* = 7.8, 3.1, 1.1 Hz, 2.4H), 7.03 (tt, *J* = 7.8, 1.1 Hz, 2.4H), 6.87 – 6.80 (m, 2.4H), 3.93 (s, 1H), 3.87 (s, 1.4H), 3.82 (s, 3.8H), 3.81 (s, 2.7H), 1.58 (s, 9H), 1.57 (s, 11H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.69, 171.01, 168.79, 167.71, 164.79, 164.70, 148.50, 148.39, 141.52, 141.43, 140.31, 140.13, 129.05, 128.95, 128.92, 128.83, 128.29, 127.79, 125.56, 125.01, 123.67, 123.43, 123.38, 122.27, 122.15, 121.92, 120.88, 119.68, 114.34, 114.03, 109.64, 109.53, 84.79, 84.73, 52.71, 52.62, 47.09,

46.37, 46.07, 45.76, 36.86, 36.64, 28.07. HRMS (ESI): calcd for $[M+Na]^+$ $(C_{24}H_{22}N_2O_6Na)^+$ requires m/z 457.1370, found 457.1370.

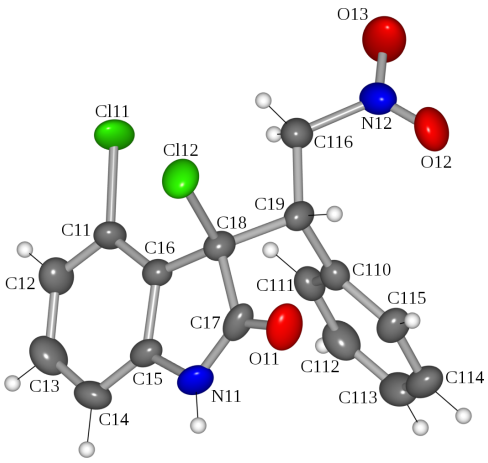


1-(tert-butyl)-3'-methyl-4''-chloro-2,2''-dioxodispiro[indoline-3,1'-cyclopropane-2',3''-indoline]-1,3'-dicarboxylate 12b. Synthesized according to the general procedure from 3,4-dichloroindolin-2-one **2c** and (*E*)-3-(2-methoxy-2-oxoethylidene)-2-oxoindoline-1-carboxylate **11.** Product was isolated in 96% yield (45 mg) as white solid with dr 14:1 by 1H NMR and *ee* 95% for the major isomer (Chiralcel OD-H, Hex/*i*PrOH 95/5, 1 mL/min, 230 nm; major (16.6 min) and minor (18.0 min). IR ν = 3303, 1789, 1740, 1615, 1150 cm^{-1}; For the main isomer: ^{1}H NMR (400 MHz, Chloroform-d) δ 7.77 – 7.73 (m, 1H), 7.65 – 7.48 (m, 2H), 7.33 (tt, *J* = 8.0, 1.3 Hz, 1H), 7.17 – 7.08 (m, 2H), 6.99 (ddd, *J* = 8.3, 2.2, 1.0 Hz, 1H), 6.68 (dd, *J* = 7.7, 1.0 Hz, 1H), 5.02 (s, 1H), 3.85 (s, 3H), 1.56 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.99, 168.53, 164.27, 148.58, 143.42, 140.55, 133.95, 129.82, 129.36, 127.74, 124.96, 123.32, 118.97, 118.93, 114.05, 108.27, 84.88, 52.82, 49.73, 47.40, 34.34, 28.16. HRMS (ESI): calcd for $[M+Na]^+$ $(C_{24}H_{21}ClN_2O_6Na)^+$ requires m/z 491.0980, found 491.0980.

x-ray analysis of 3-chlorooxindole 3m

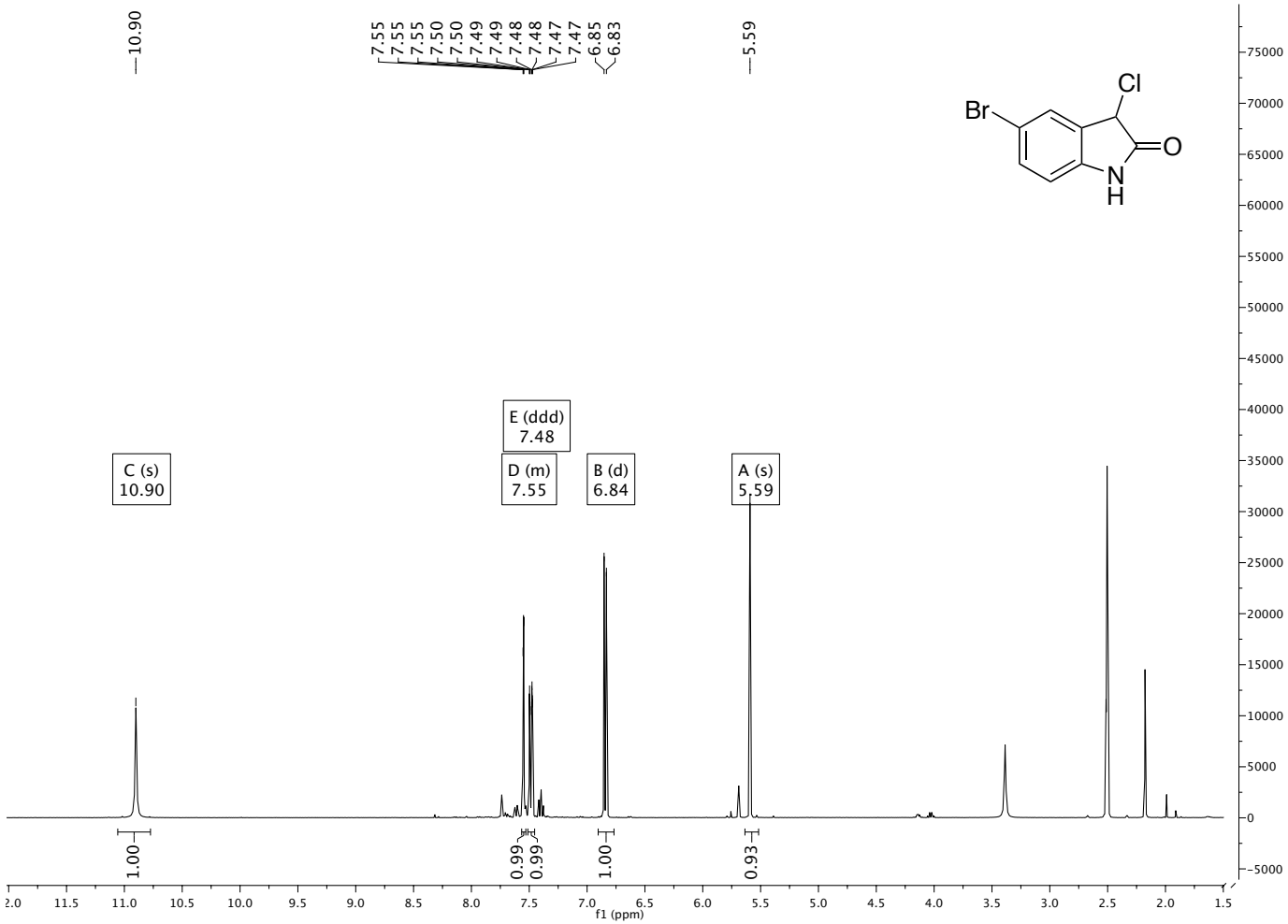
Single crystals of oxindole **3m** were grown by solvent diffusion of hexane into a solution of the compound in CH_2Cl_2 at 4°C (volume ratio hexane/CH_2Cl_2 ≈ 2 : 1). Diffraction data was collected on a Bruker SMART X2S at 200 K. The crystallographic data were deposited with the Cambridge Crystallographic Data Centre (CCDC 891526) and are included in the supporting information.

Crystal data:

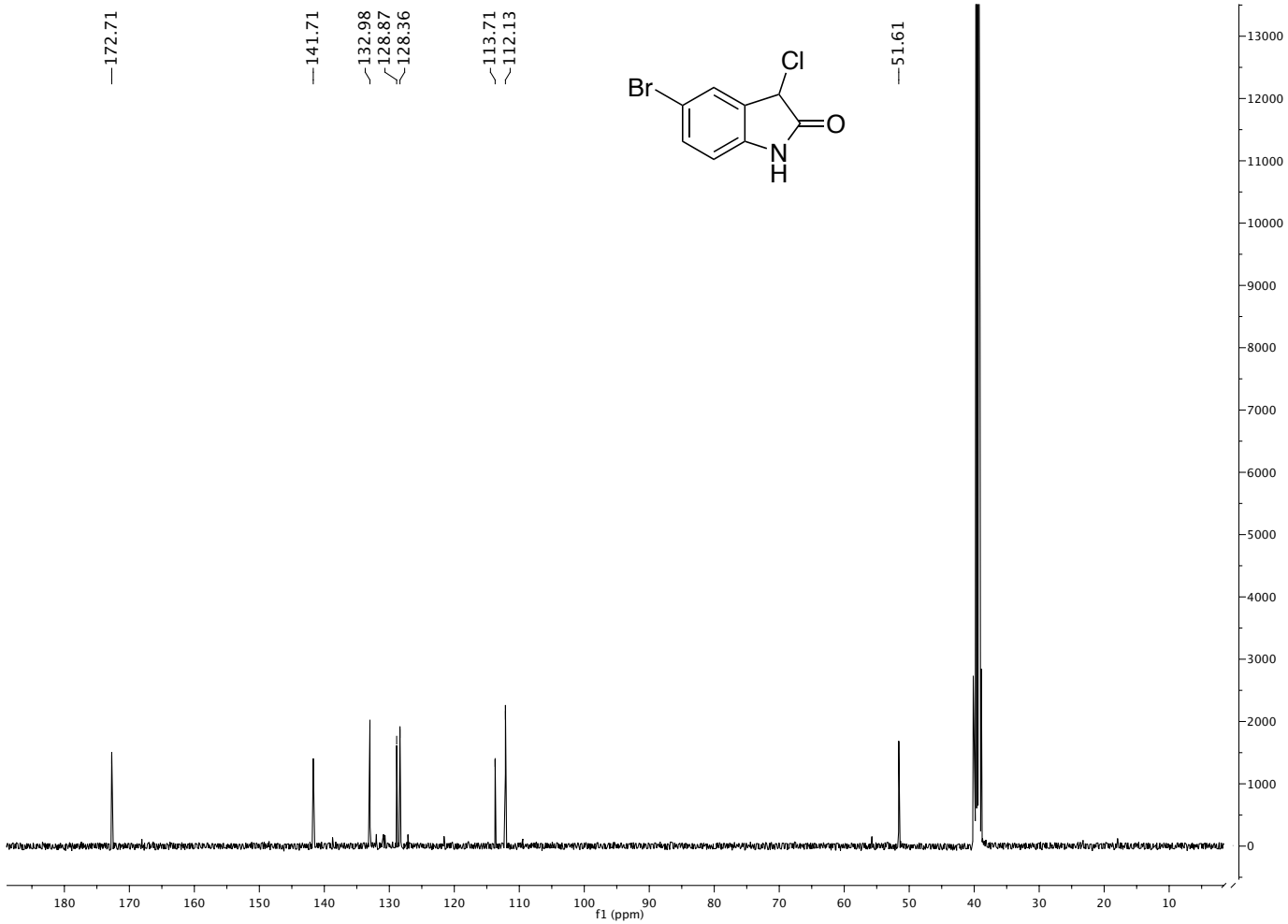


$C_{16}H_{12}Cl_2N_2O_3$, M = 351.18, monoclinic, a = 8.2024(6), b =13.1986(9), c = 22.0399(16) Å, β = 90.798(3)°, V = 2385.8(3) Å^3, T = 200 K, space group $P2_1$ (no. 4), Z = 6, Z' = 3, reflections measured 15411, unique 8239 (R_{int} = 0.0364), Flack parameter x = -0.02(4), final $R1$ = 0.0457 and $wR2$ = 0.0901 for all data.

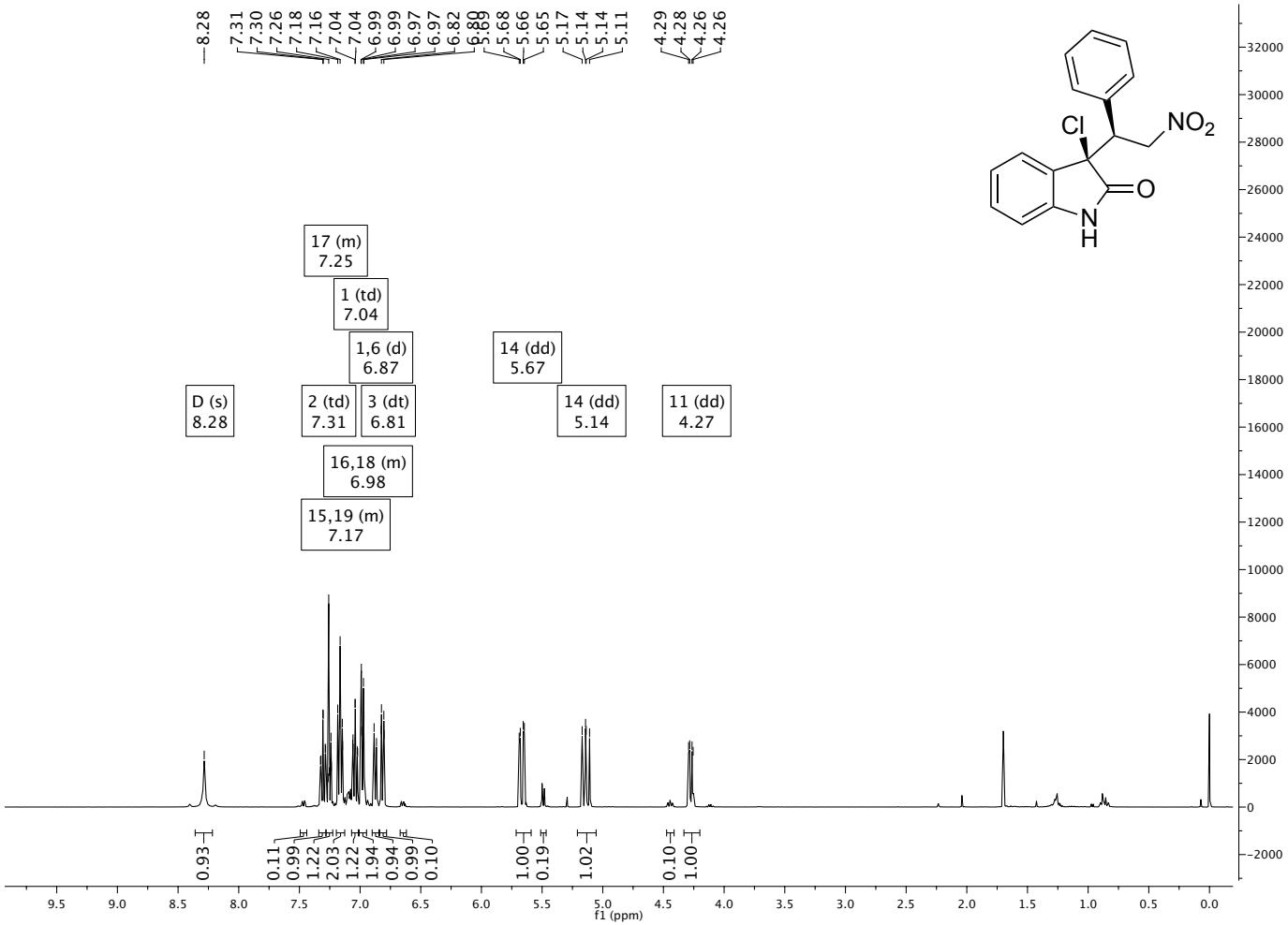
Oxindole 1e (^{1}H NMR) in DMSO-d_6



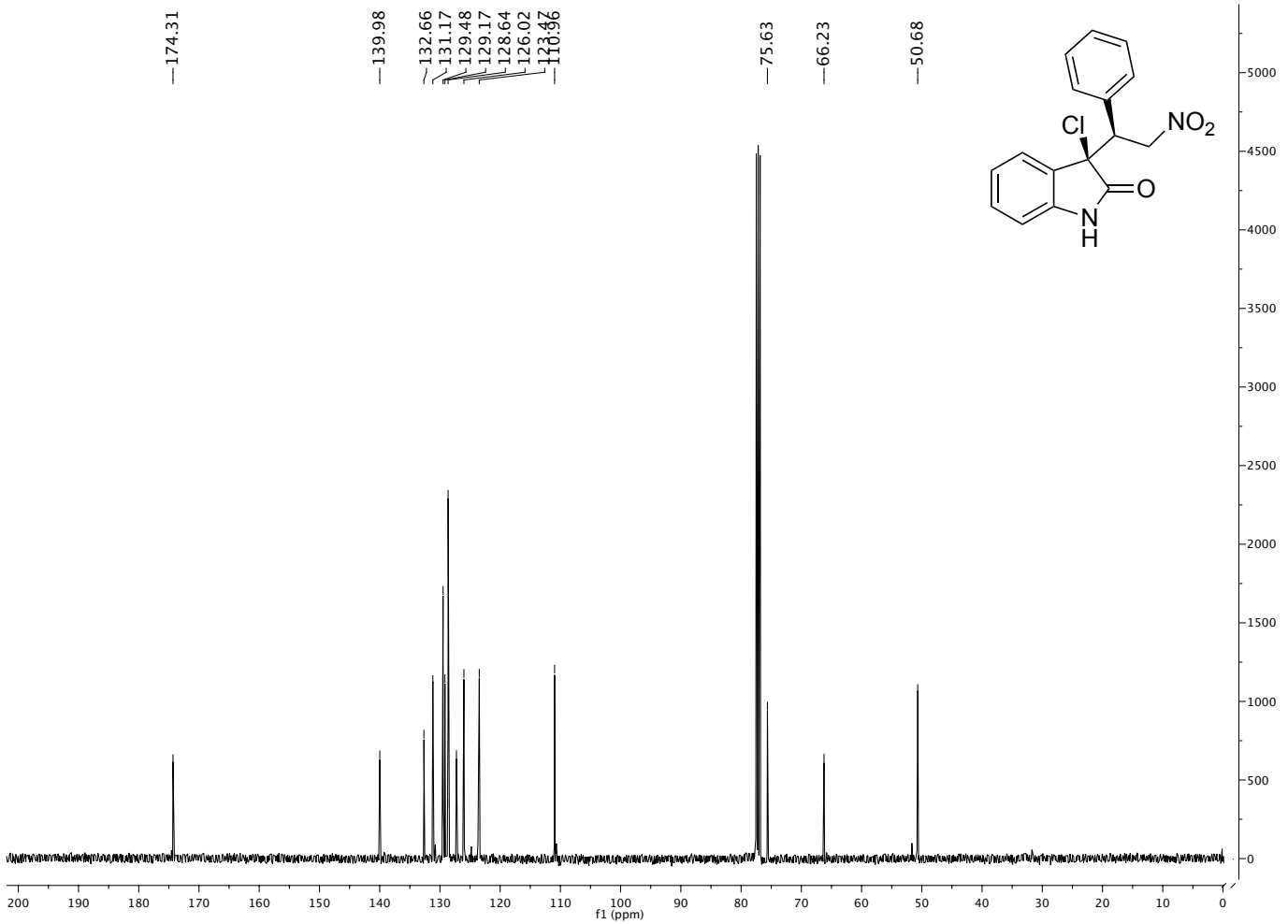
Oxindole 1e (^{13}C NMR) in DMSO-d_6



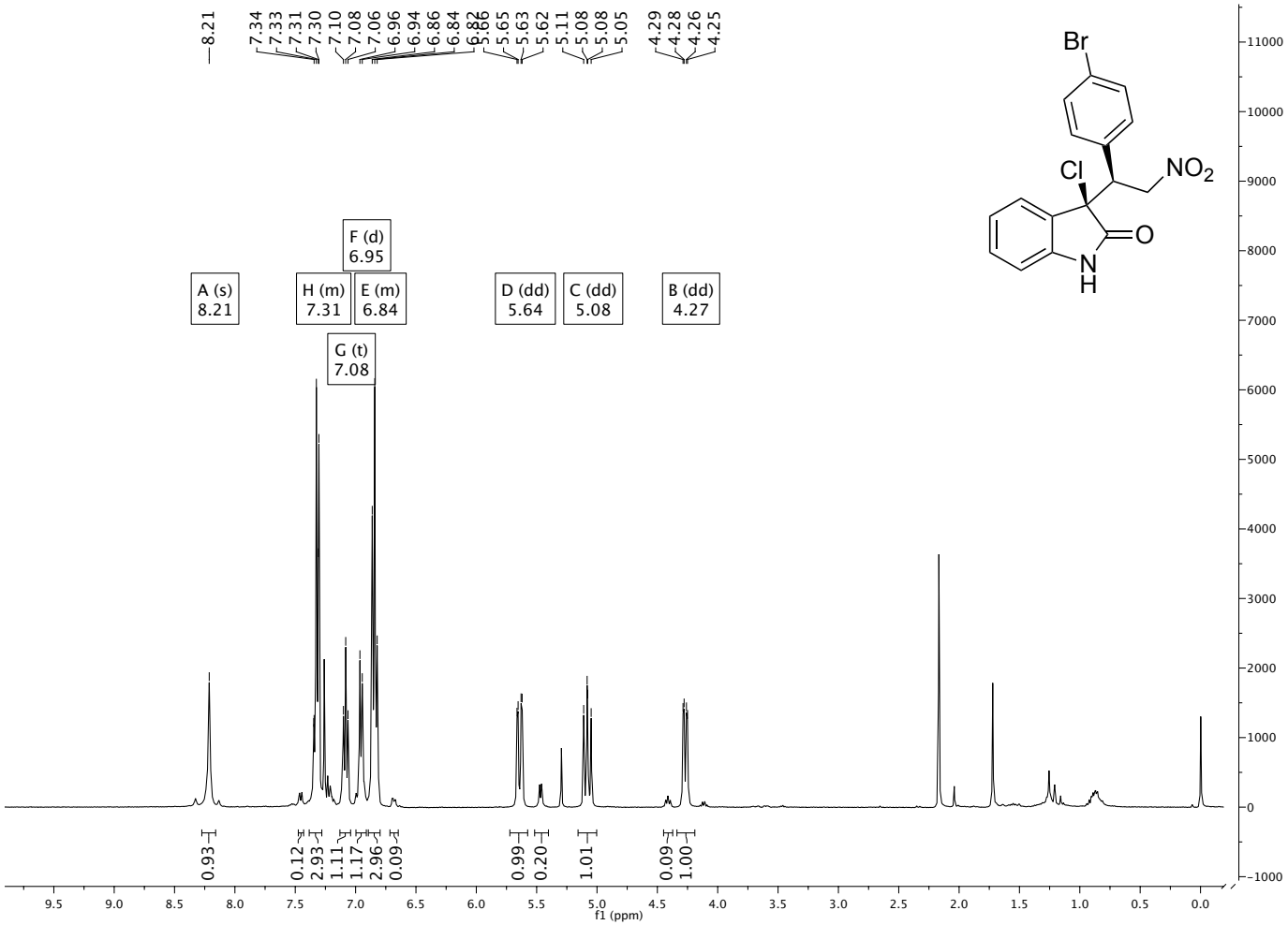
3a (^{1}H NMR) in $CDCl_3$



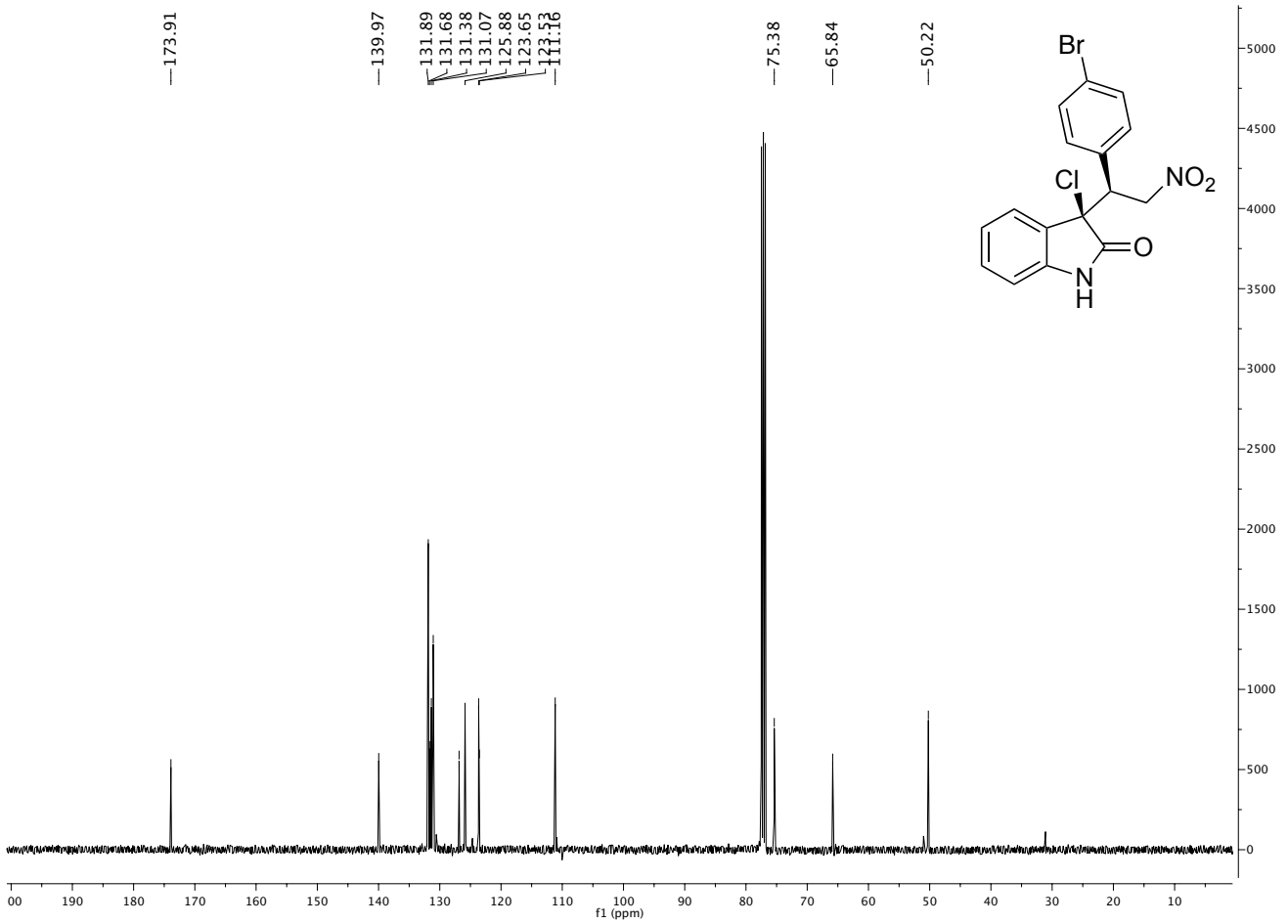
3a (^{13}C NMR) in $CDCl_3$



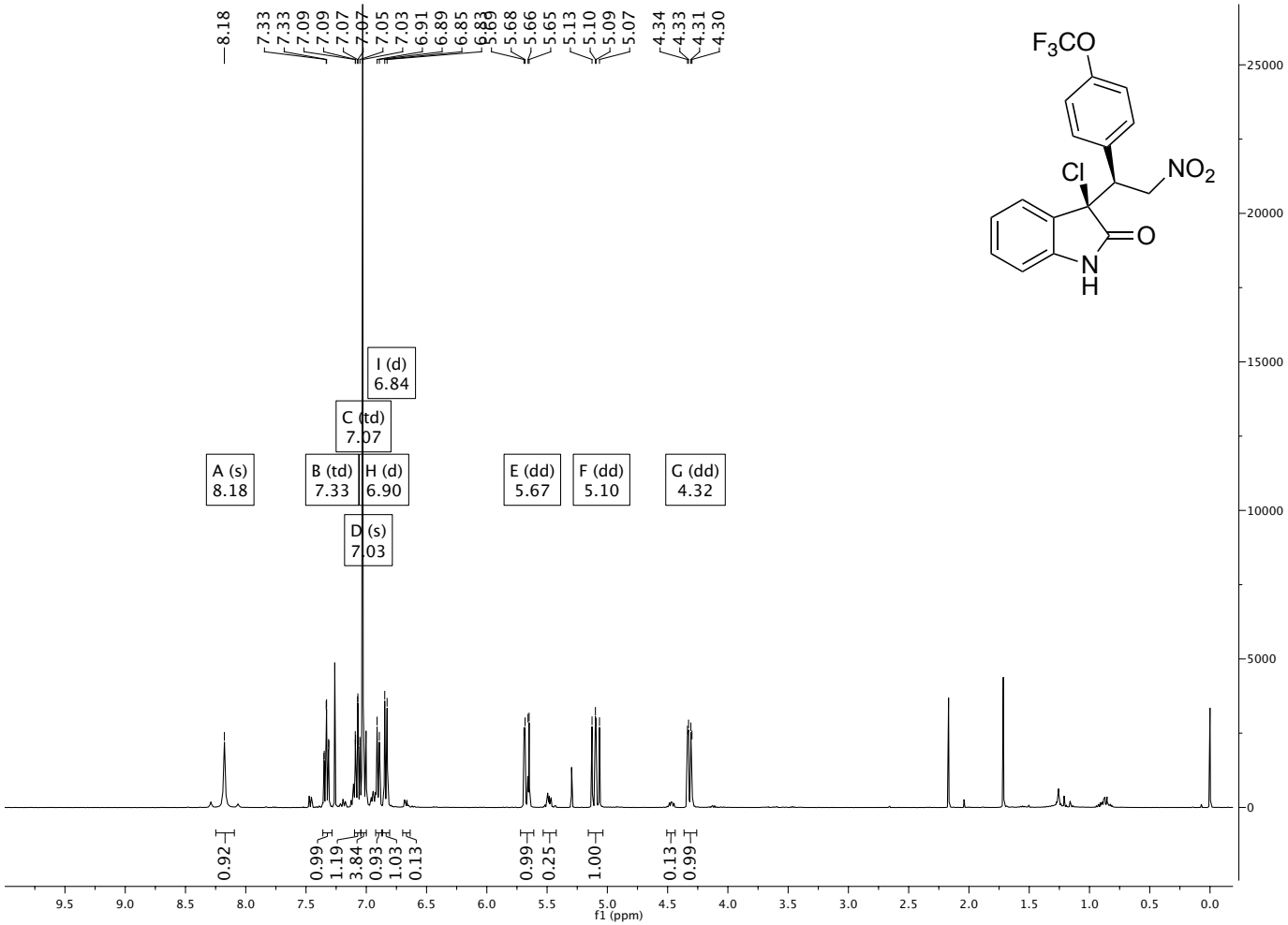
3b (^{1}H NMR) in $CDCl_3$



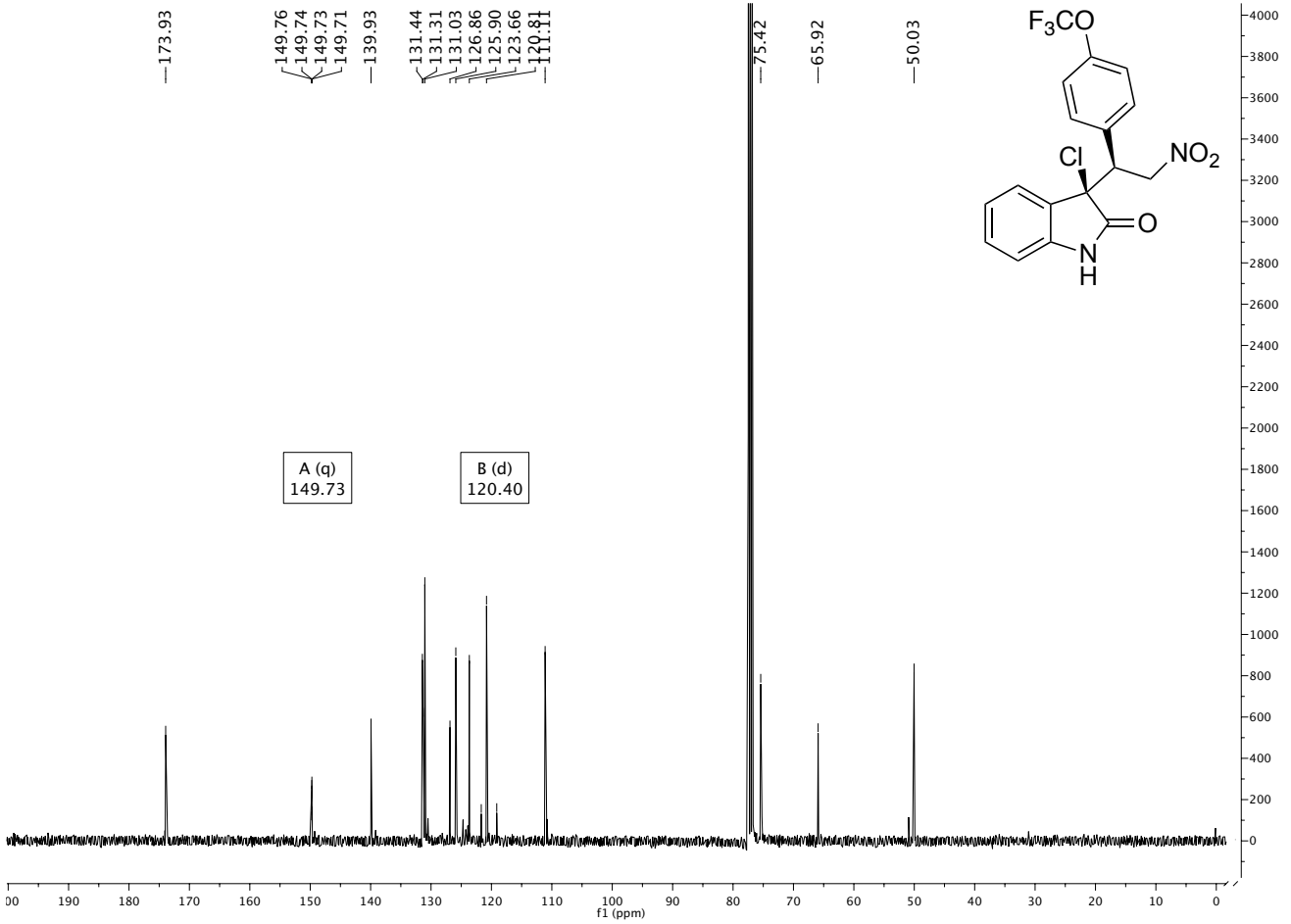
3b (^{13}C NMR) in $CDCl_3$



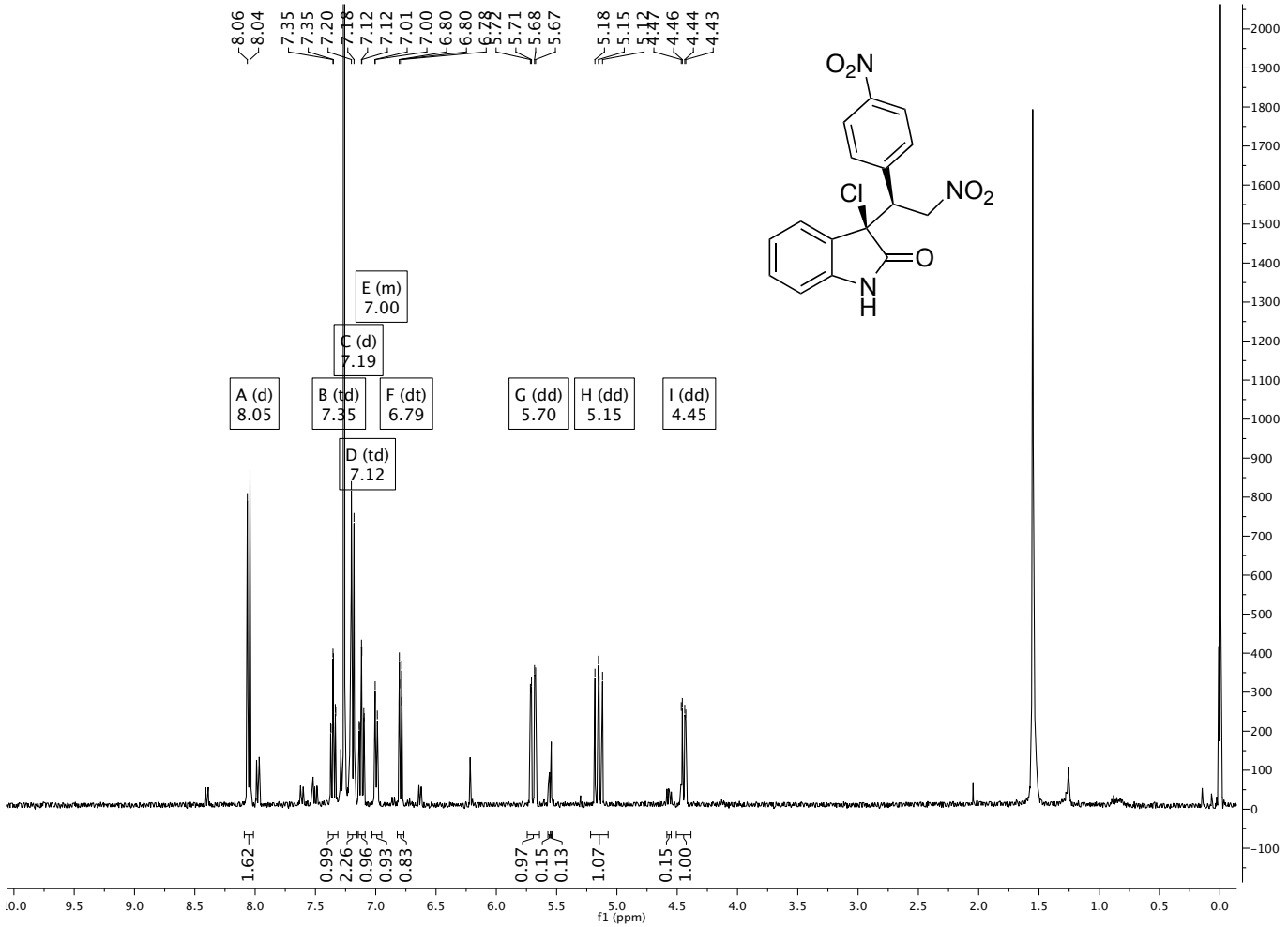
3c (^{1}H NMR) in $CDCl_3$



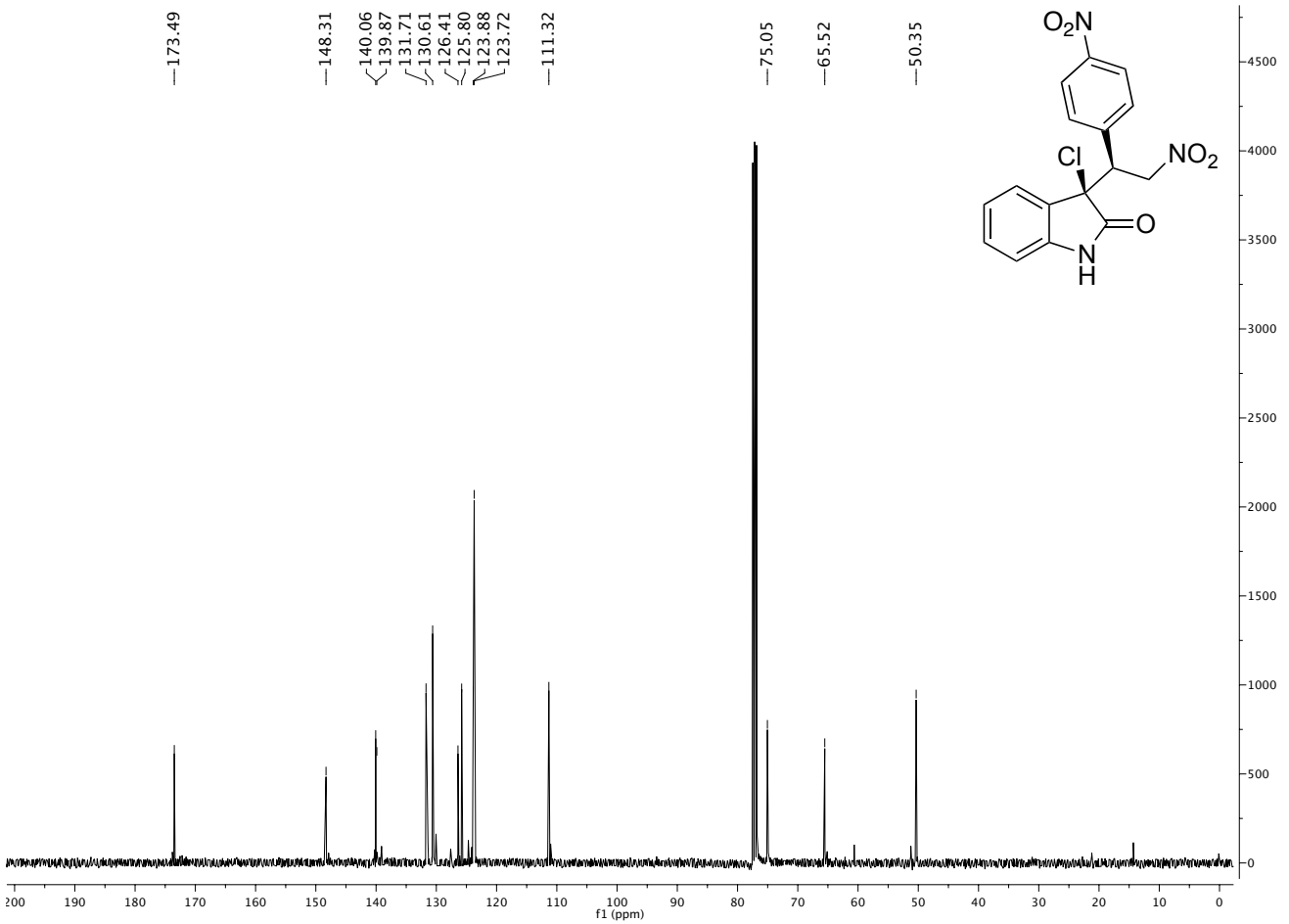
3c (^{13}C NMR) in $CDCl_3$



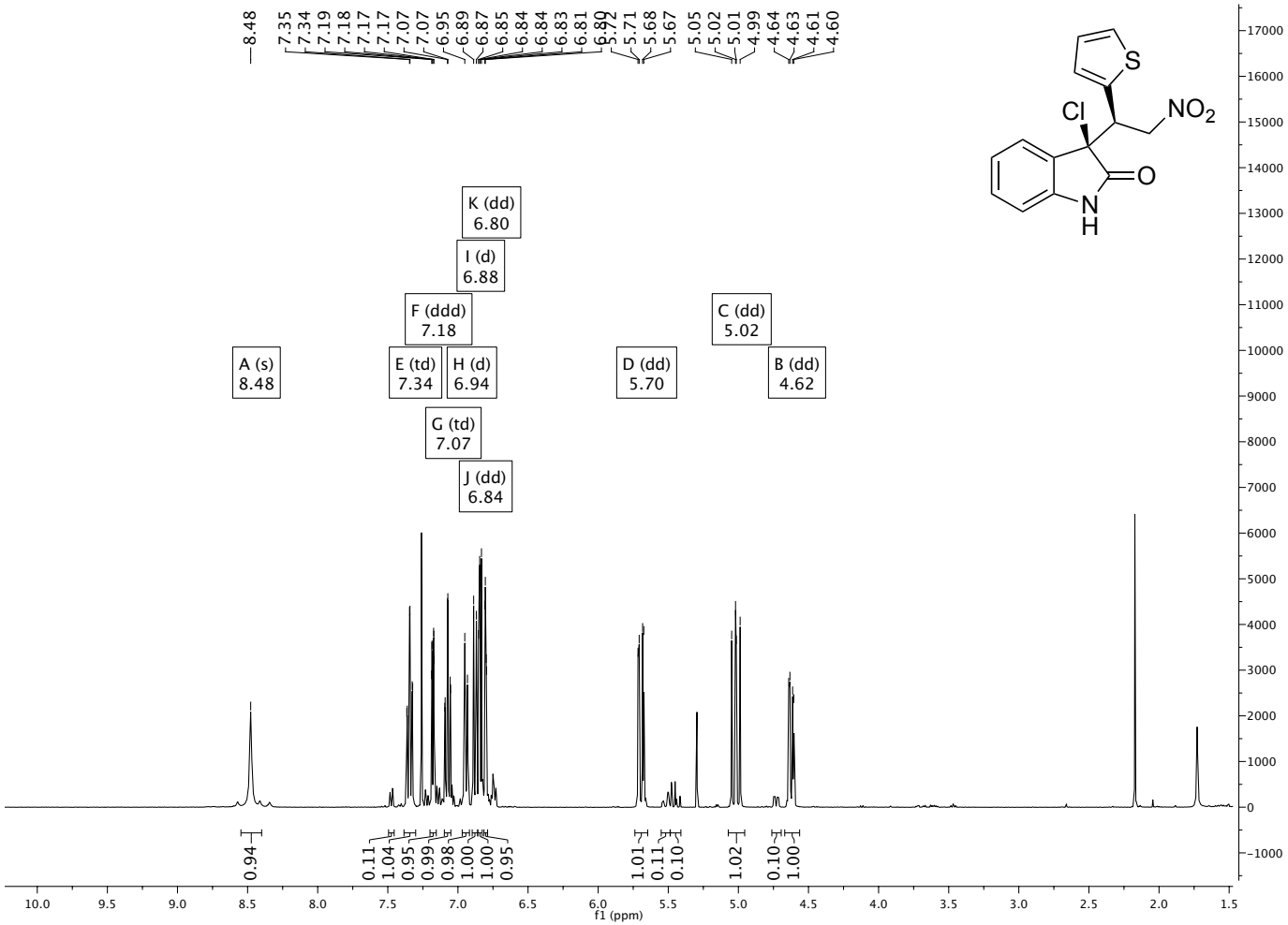
3d (^{1}H NMR) in $CDCl_3$



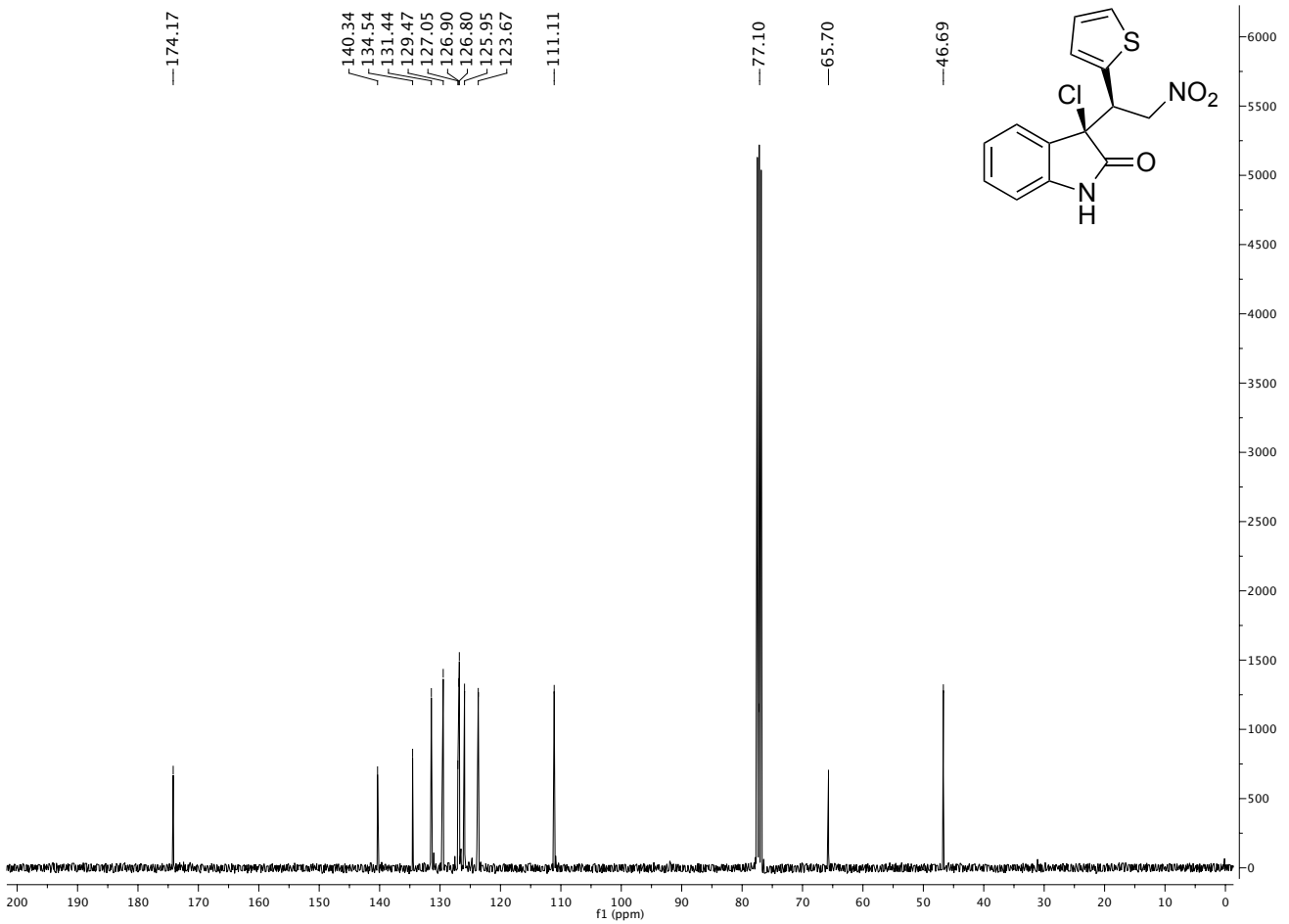
3d (^{13}C NMR) in $CDCl_3$



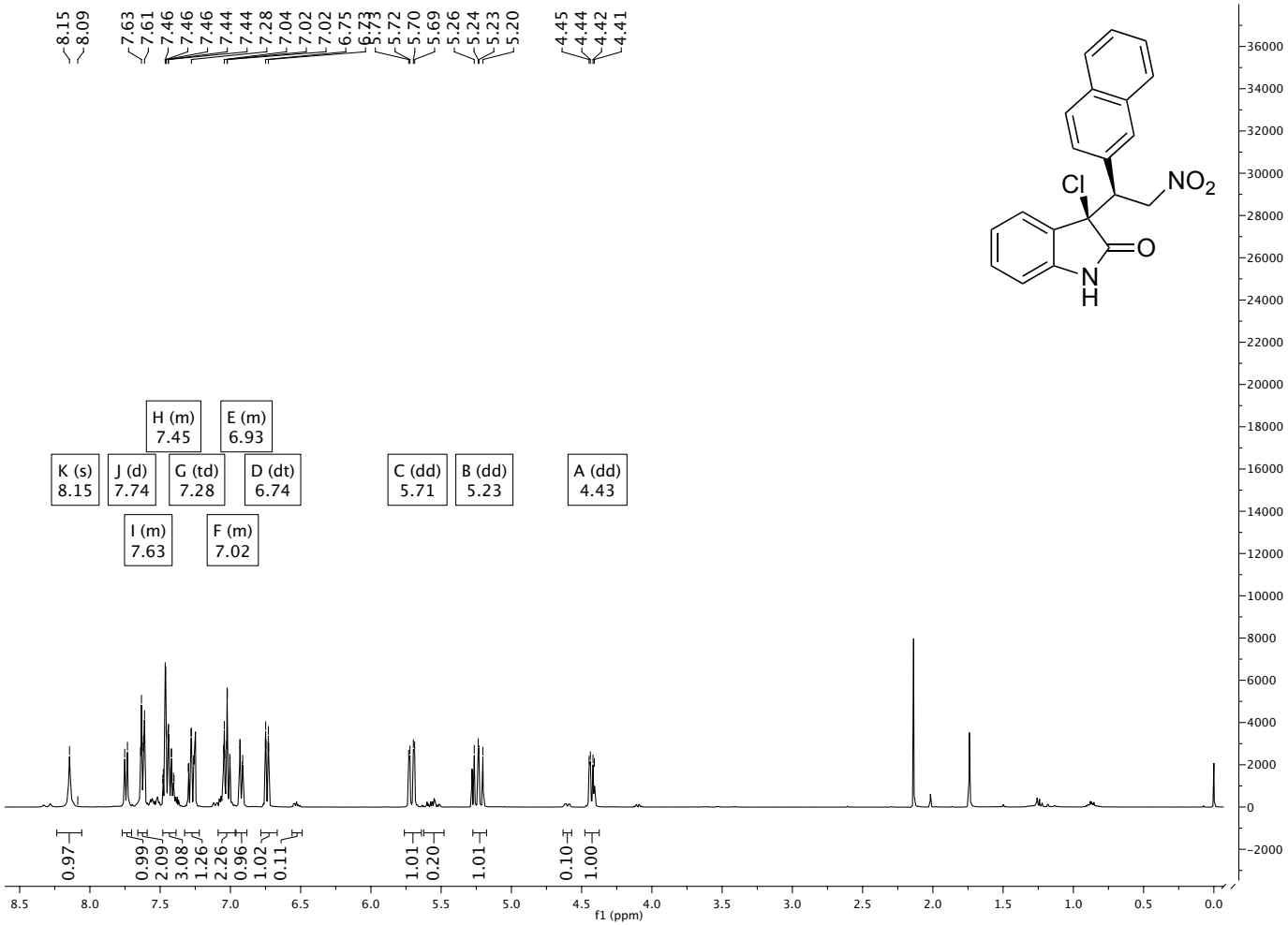
3e (^{1}H NMR) in $CDCl_3$



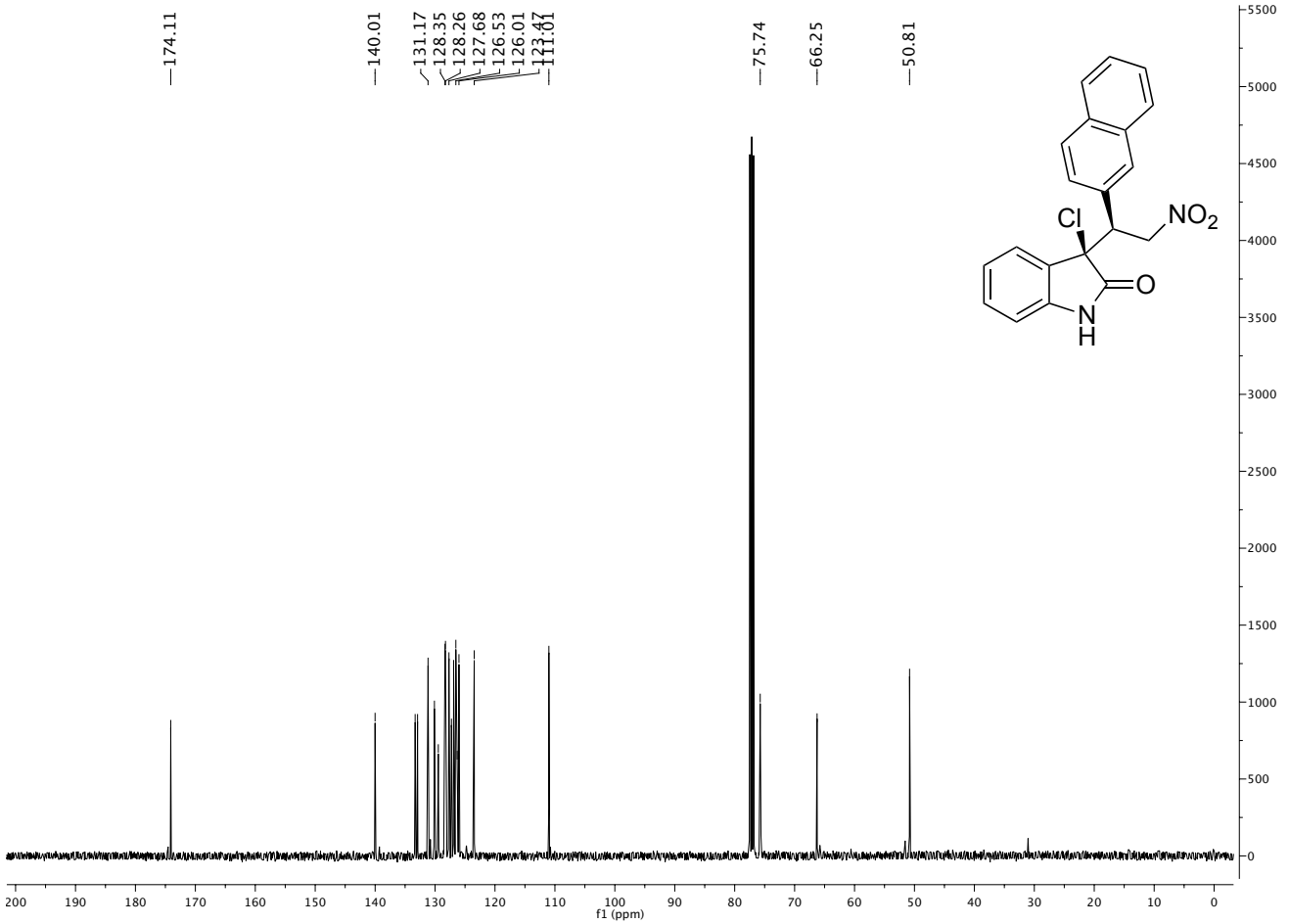
3e (^{13}C NMR) in $CDCl_3$



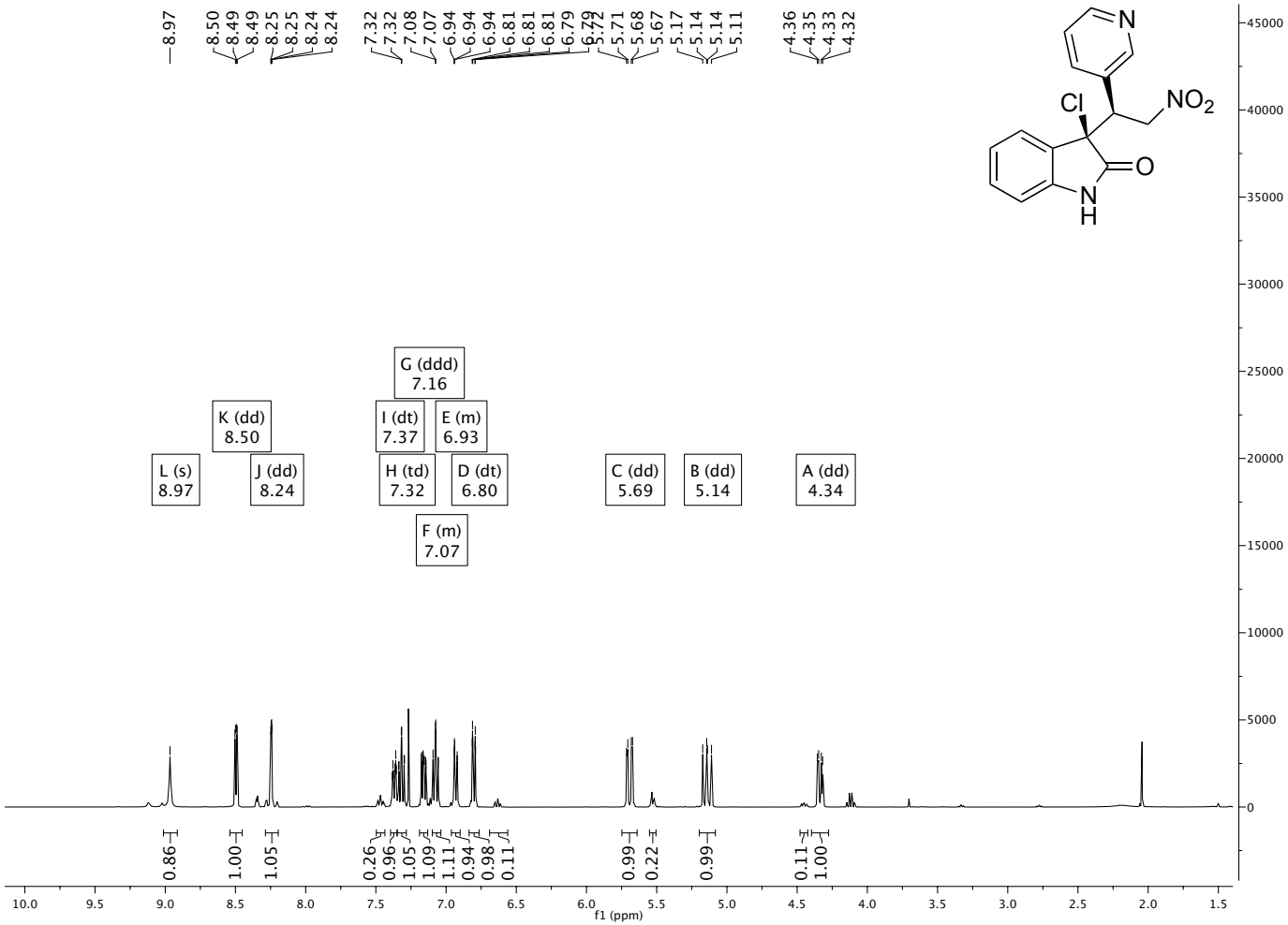
3f (^{1}H NMR) in $CDCl_3$



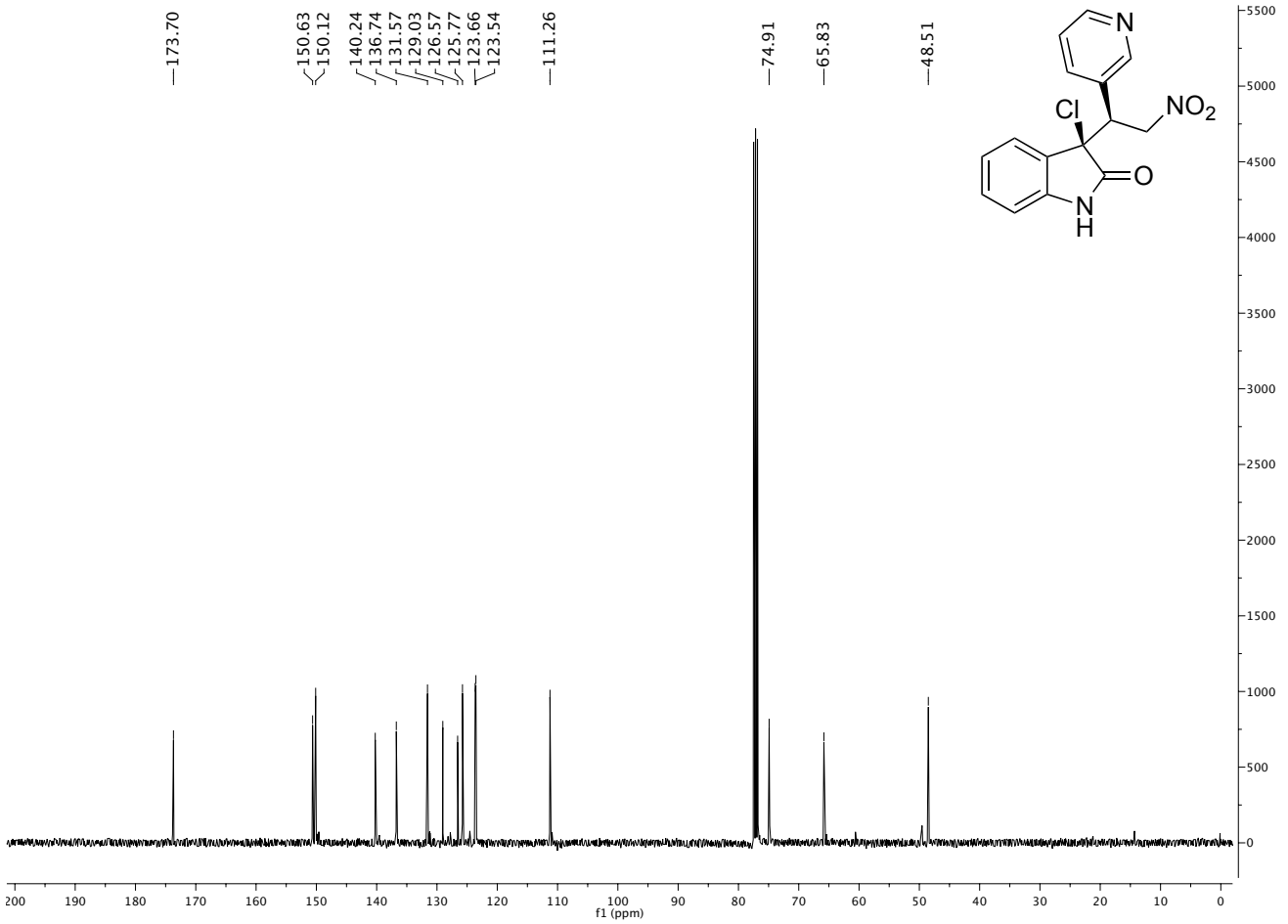
3f (^{13}C NMR) in $CDCl_3$



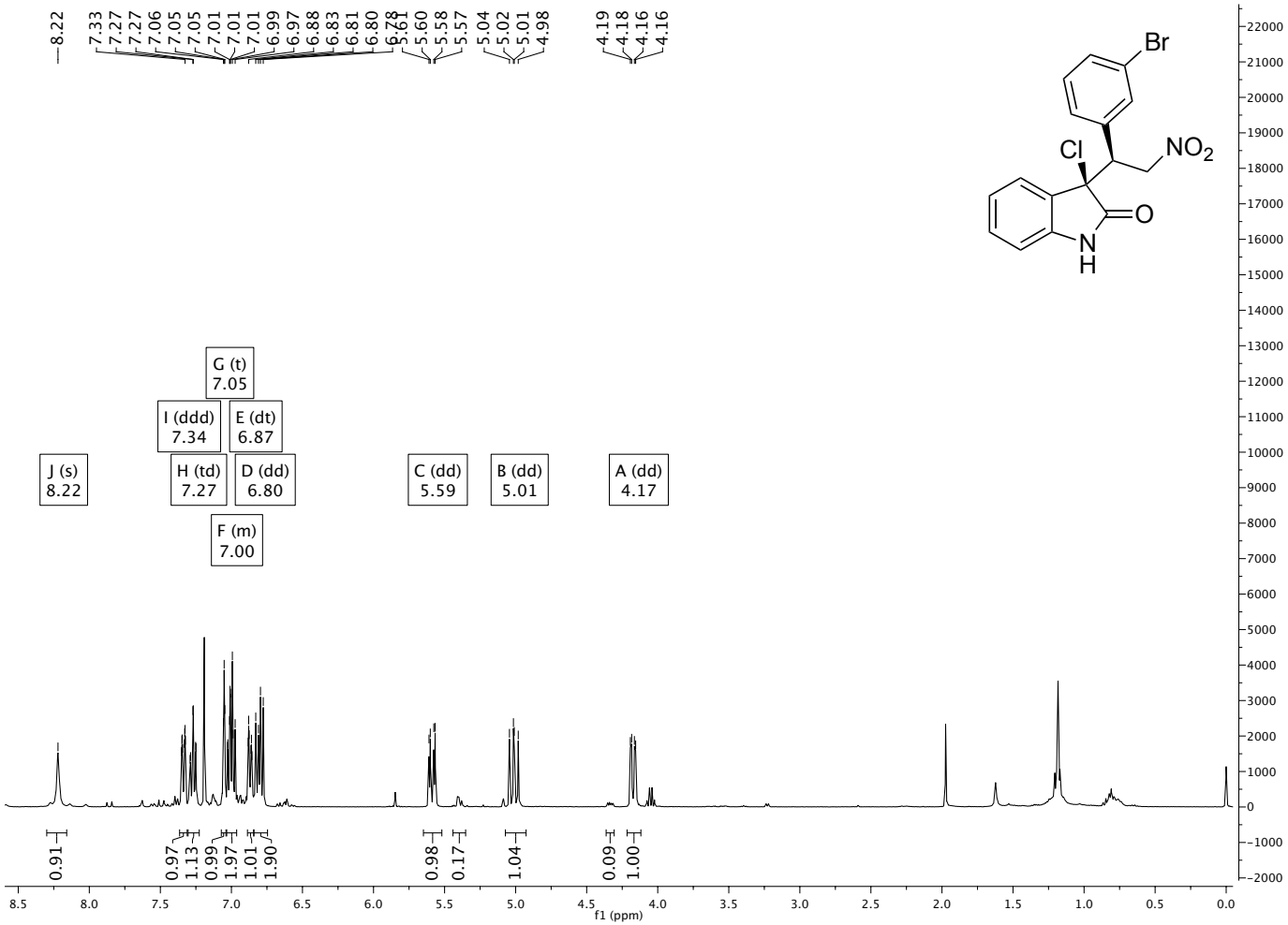
3g (^{1}H NMR) in $CDCl_3$



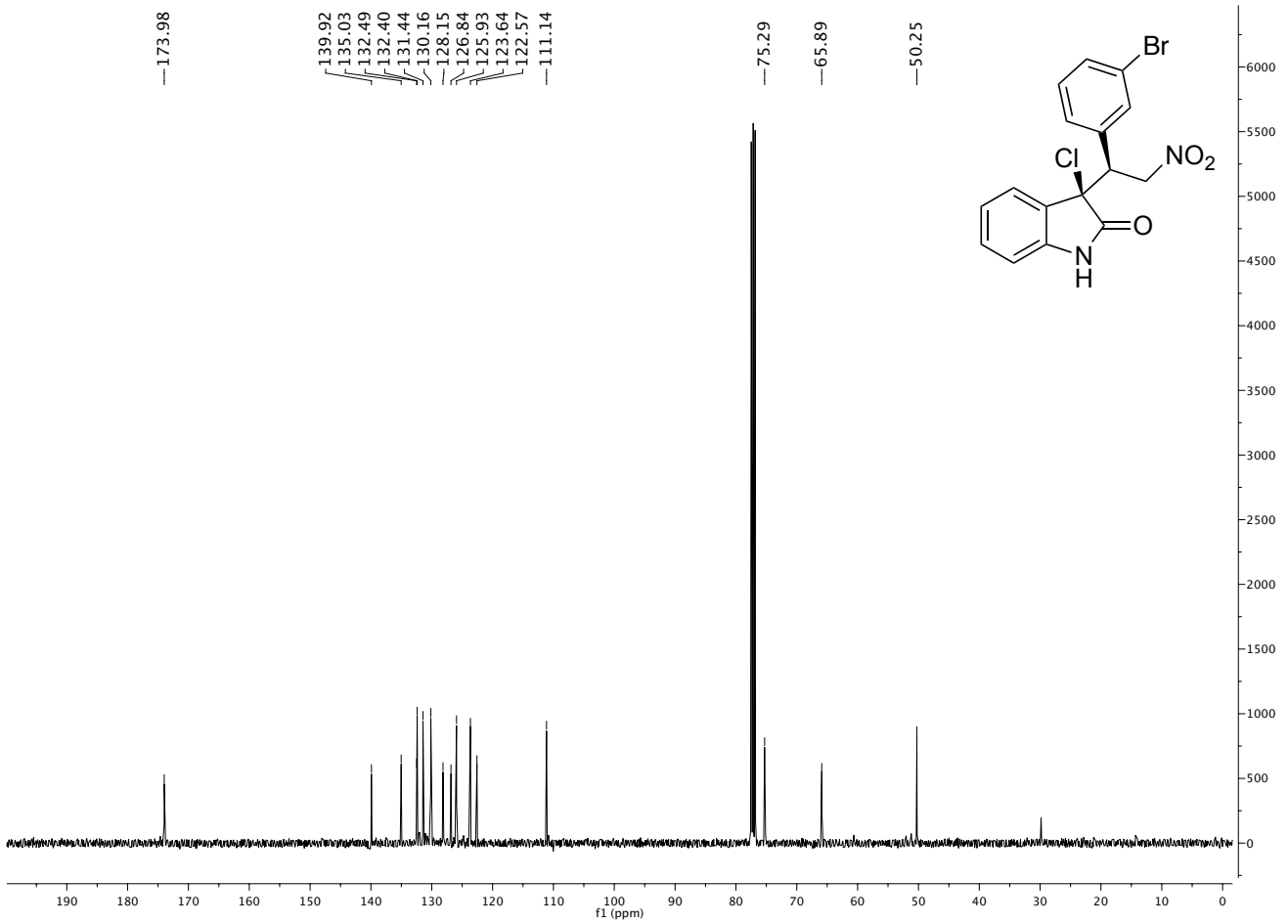
3g (^{13}C NMR) in $CDCl_3$



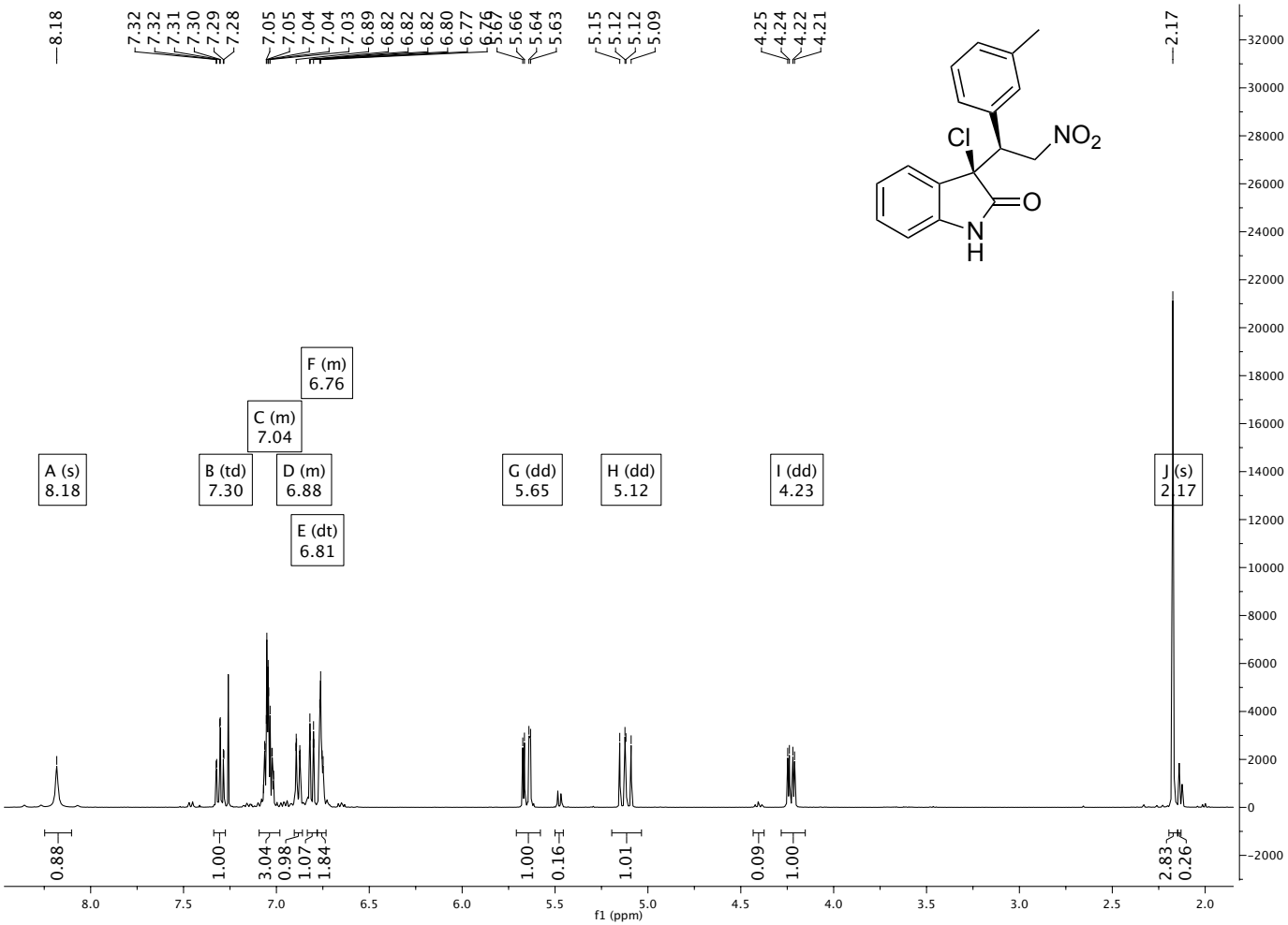
3h (^{1}H NMR) in $CDCl_3$



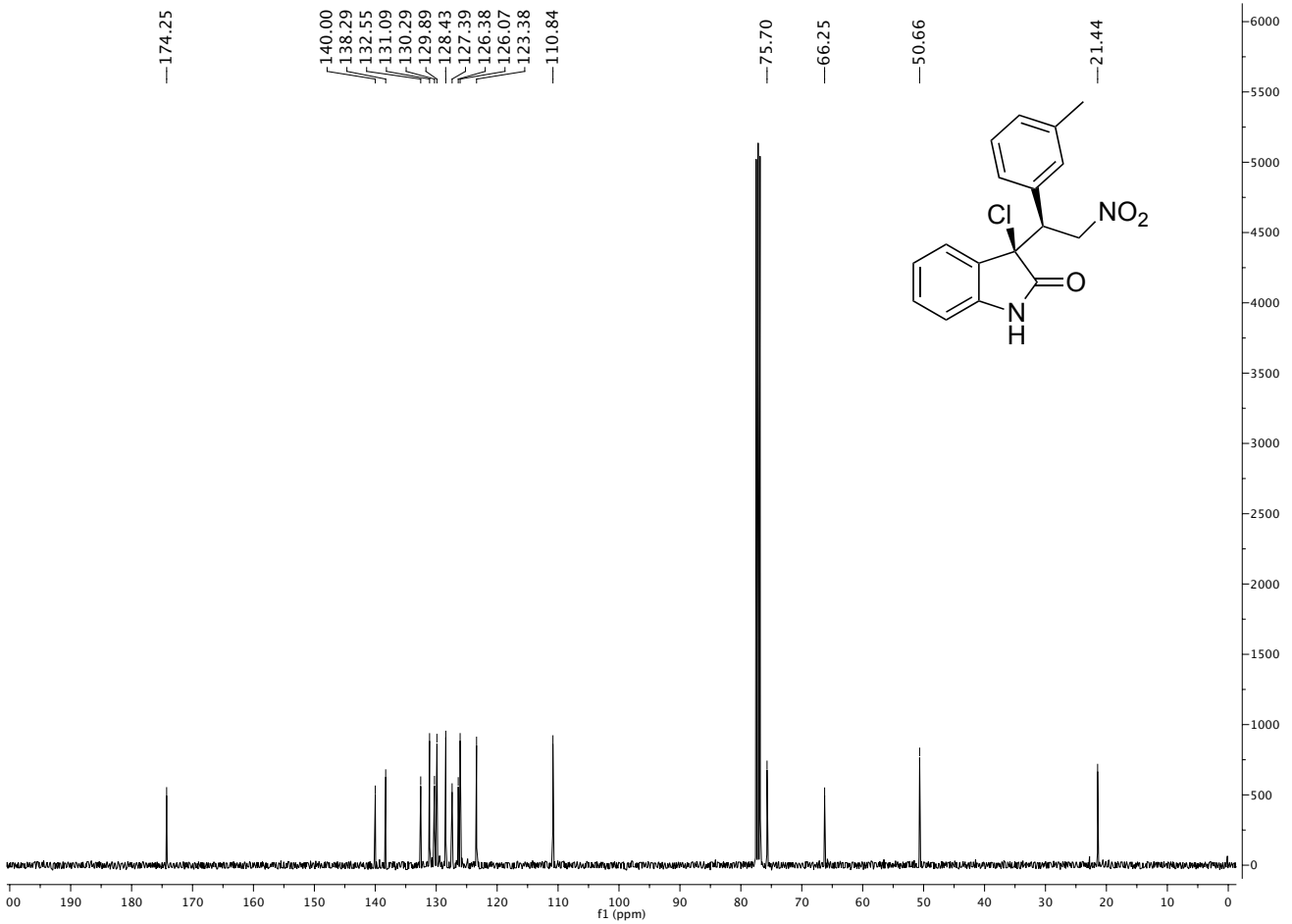
3h (^{13}C NMR) in $CDCl_3$



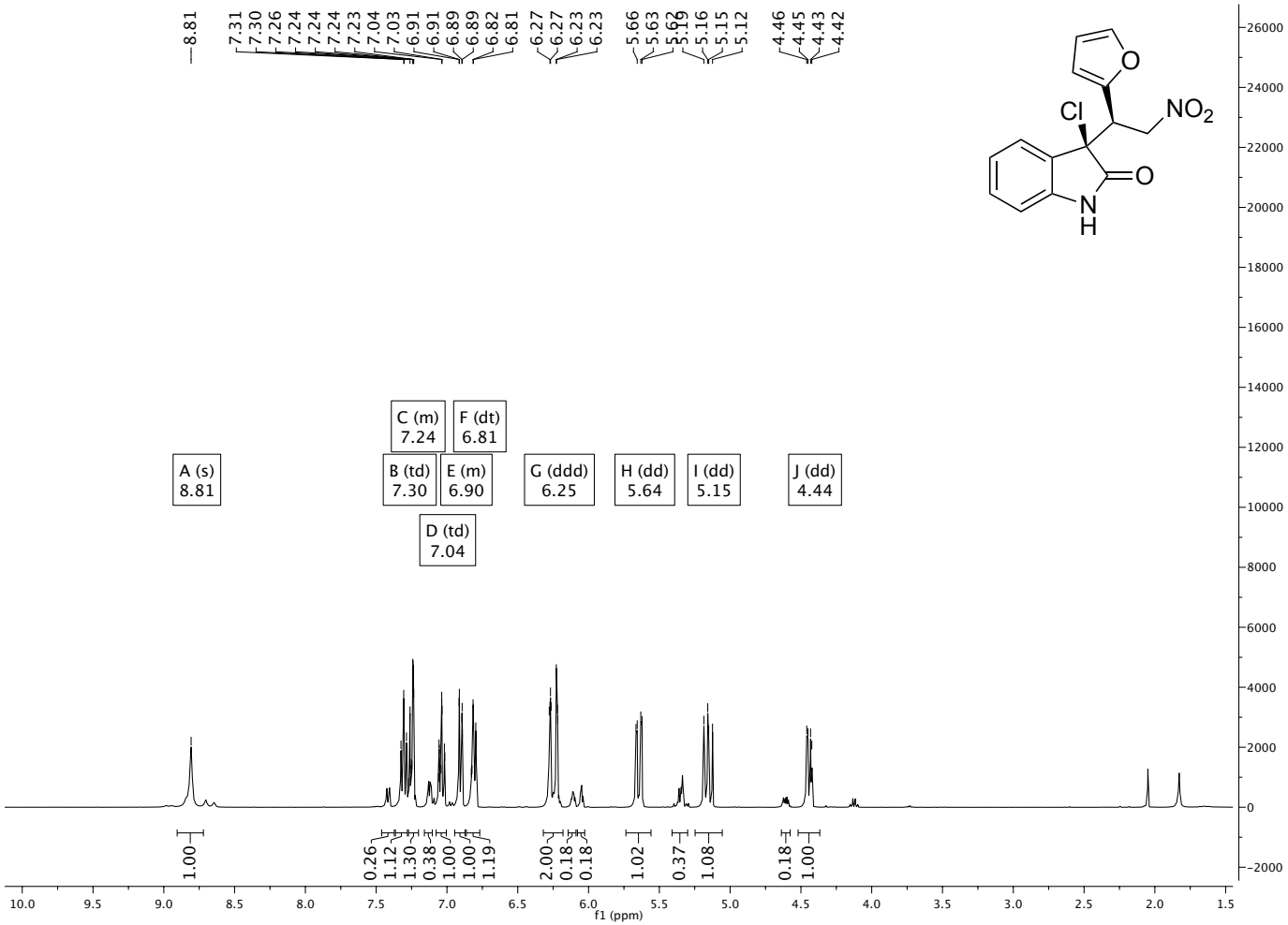
3i (^{1}H NMR) in $CDCl_3$



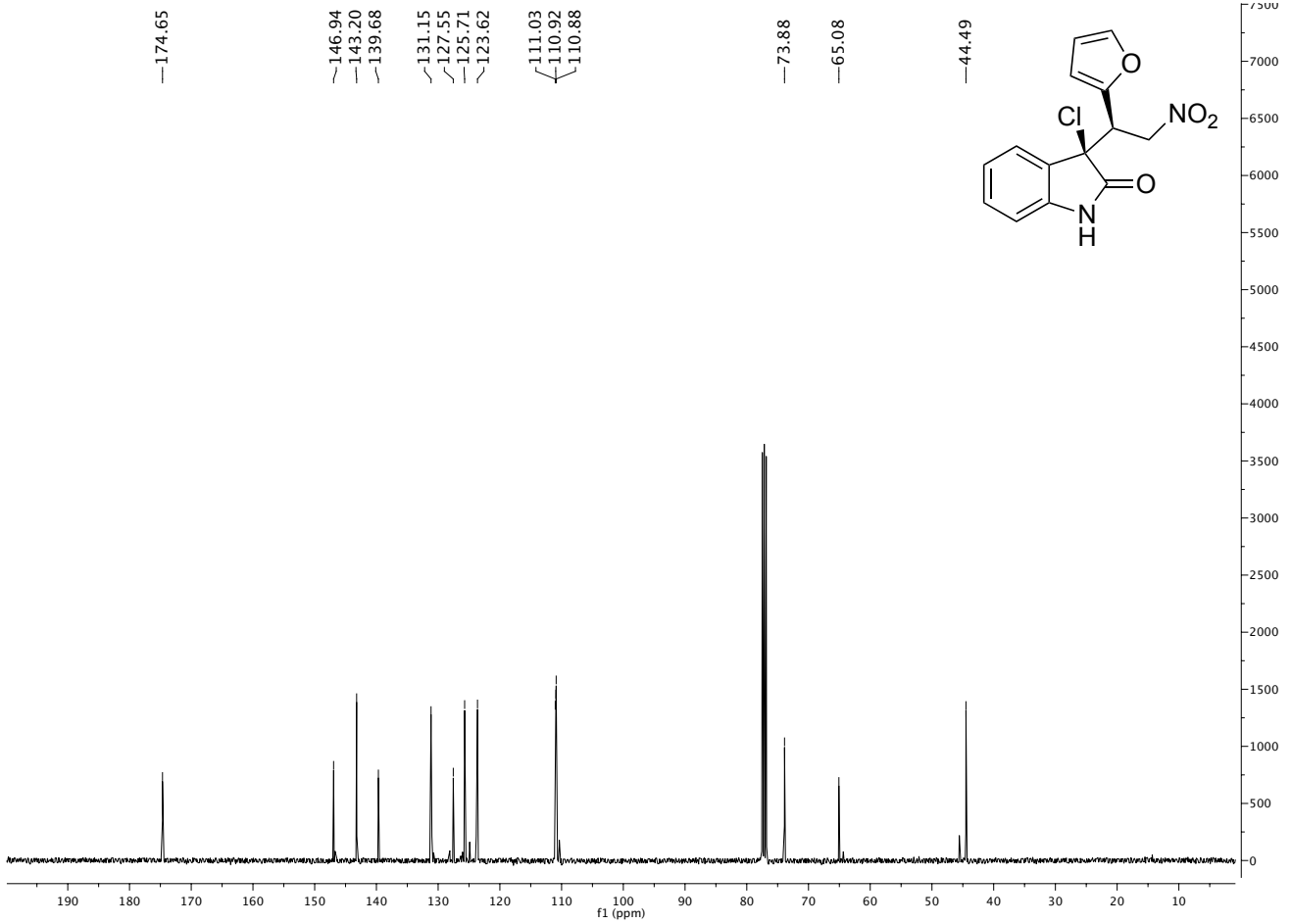
3i (^{13}C NMR) in $CDCl_3$



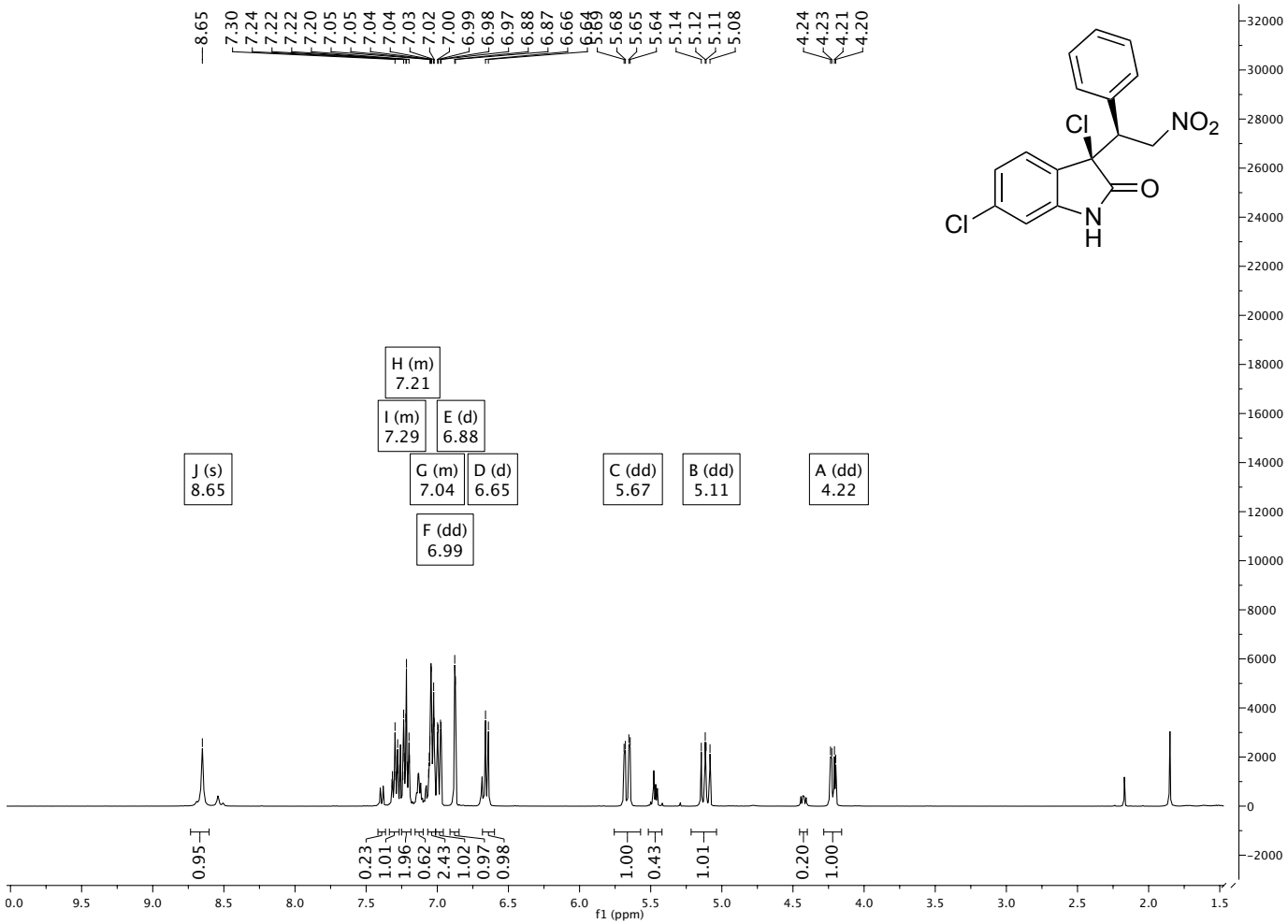
3j (^{1}H NMR) in $CDCl_3$



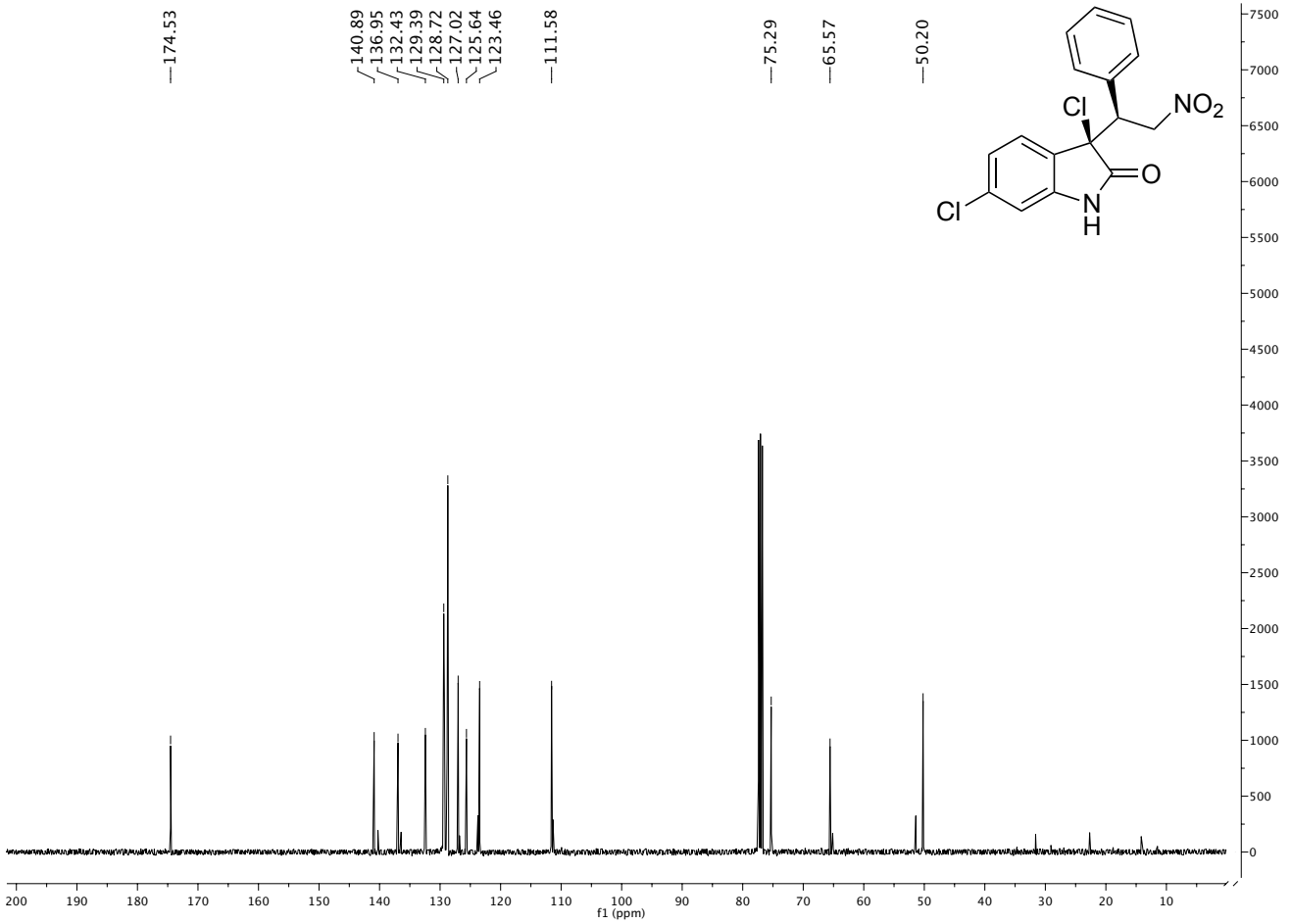
3j (^{13}C NMR) in $CDCl_3$



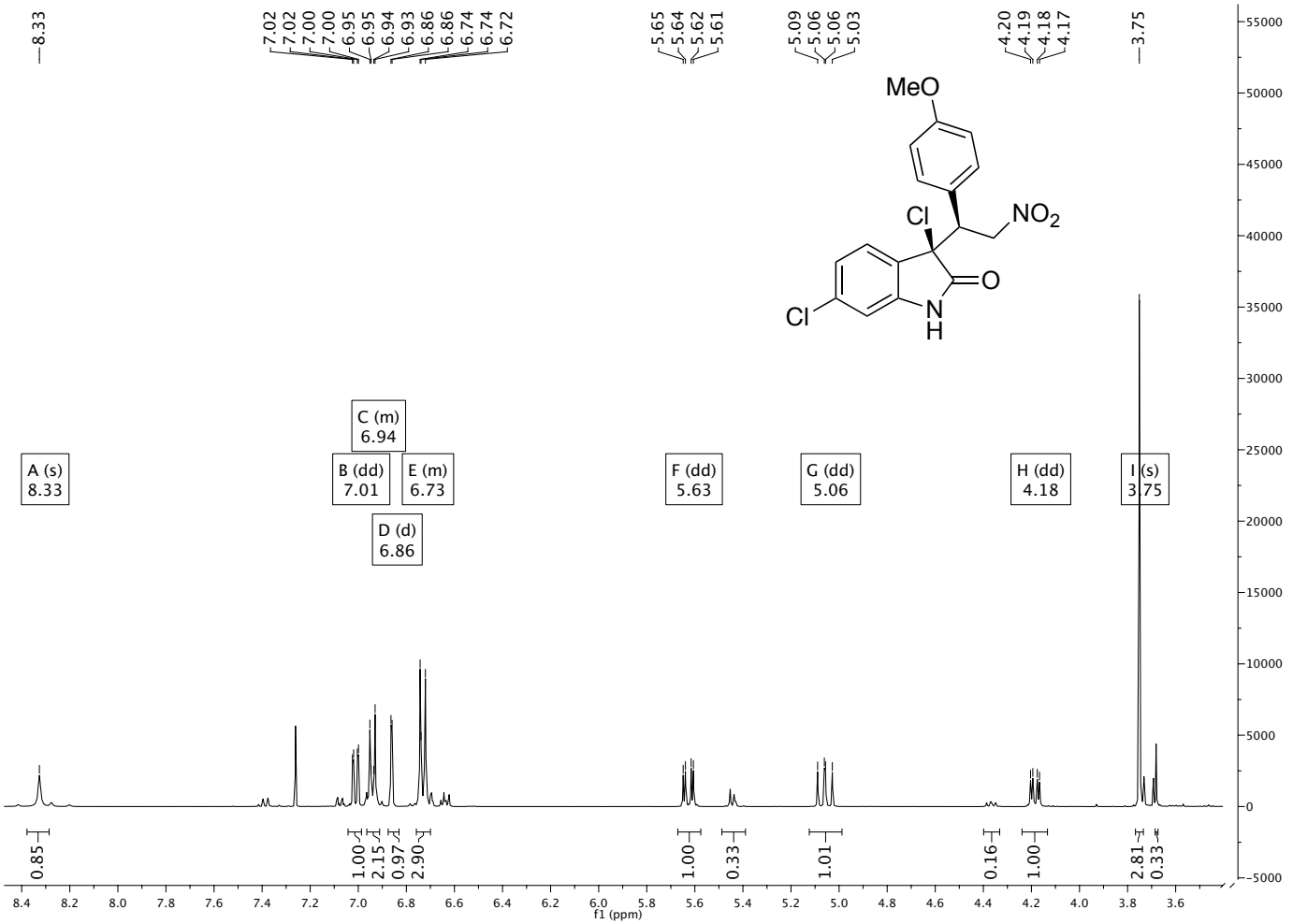
3k (^{1}H NMR) in $CDCl_3$



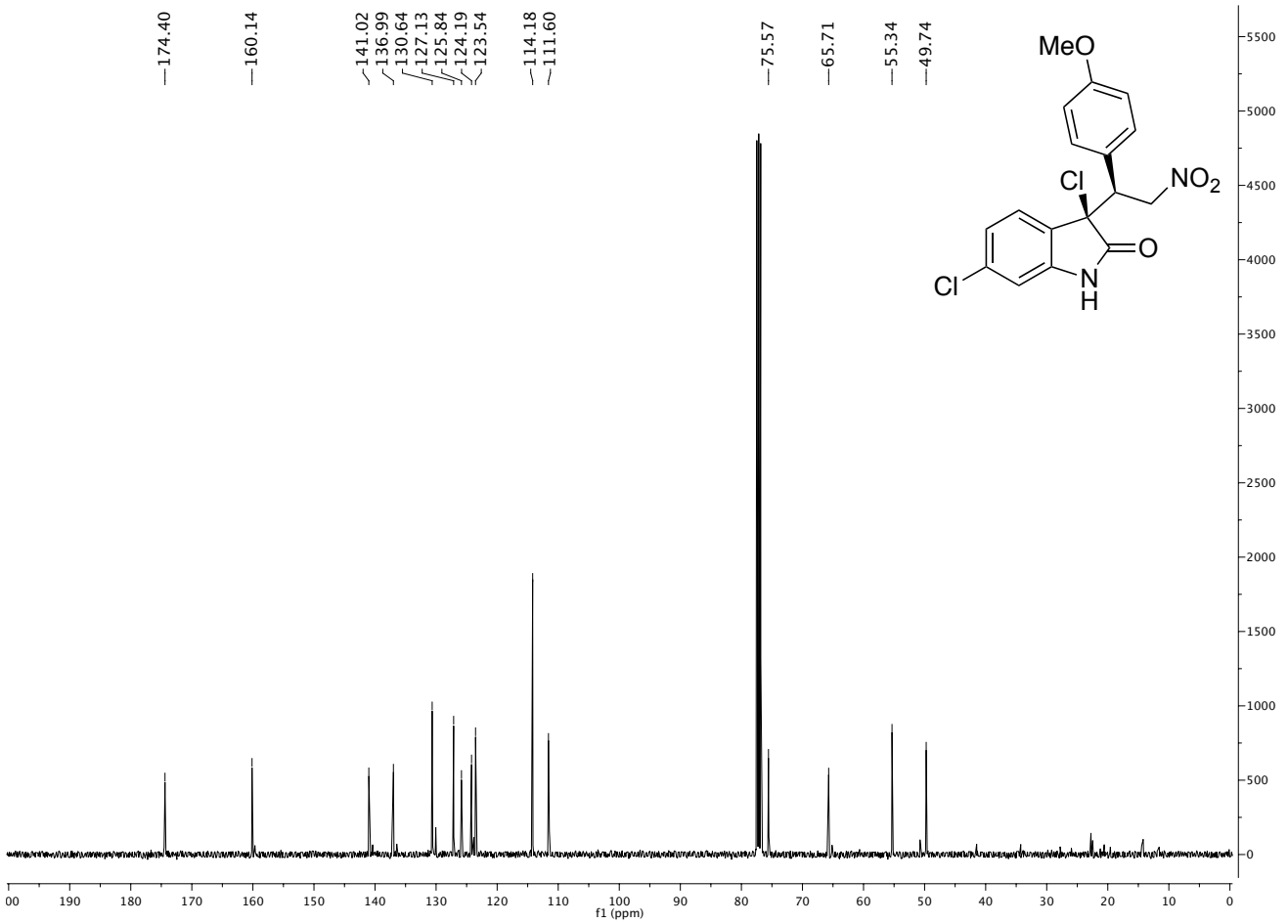
3k (^{13}C NMR) in $CDCl_3$



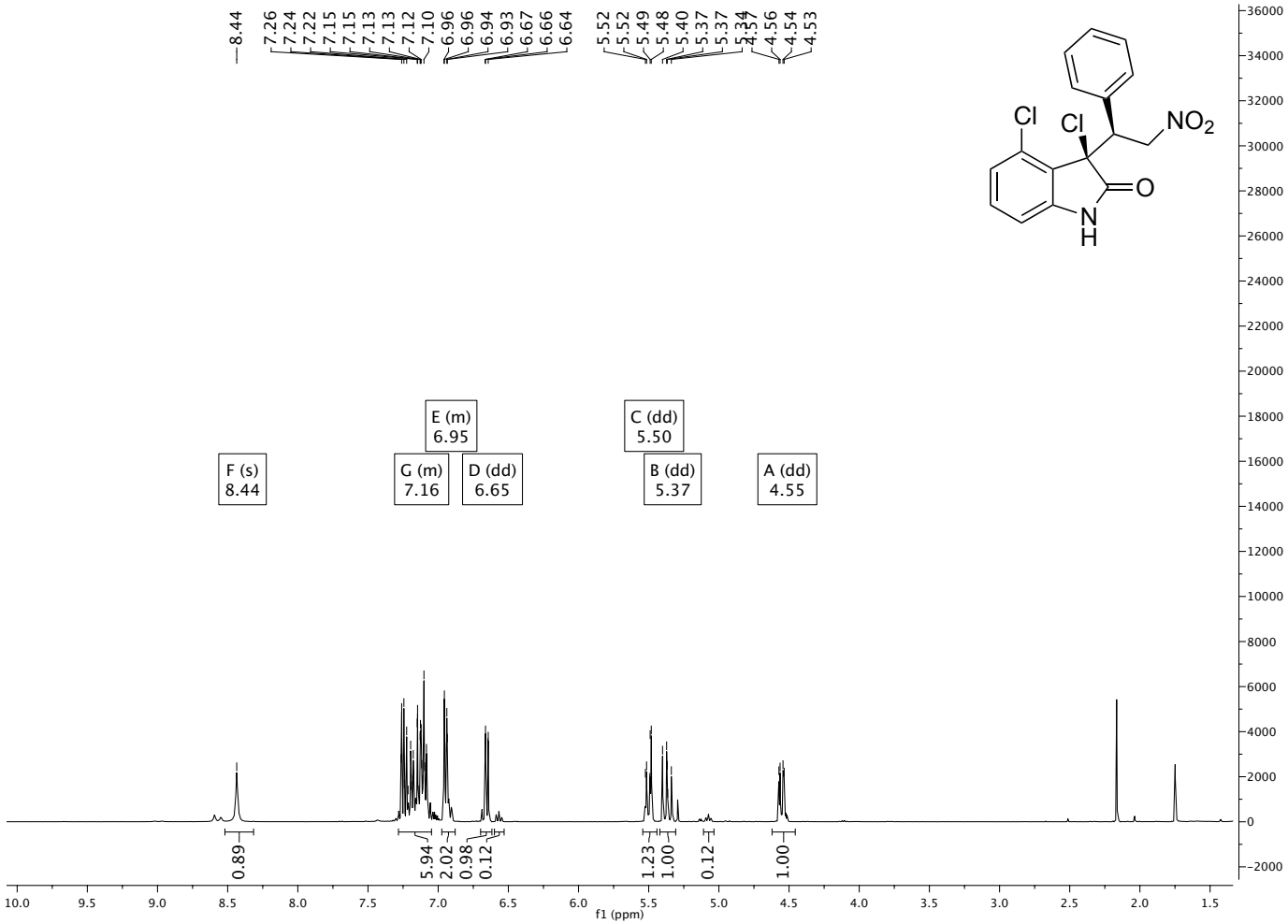
3l (^{1}H NMR) in $CDCl_3$



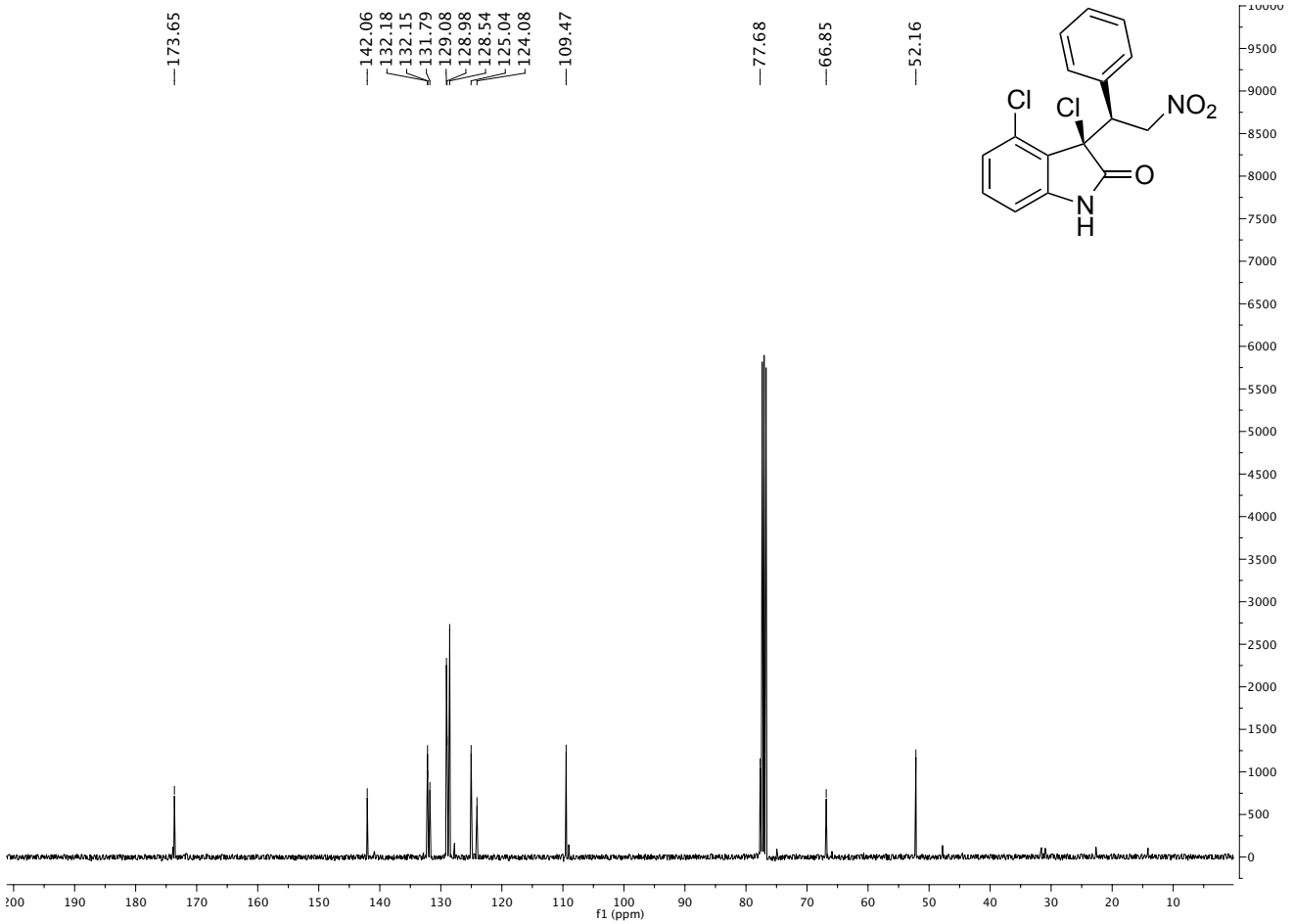
3l (^{13}C NMR) in $CDCl_3$



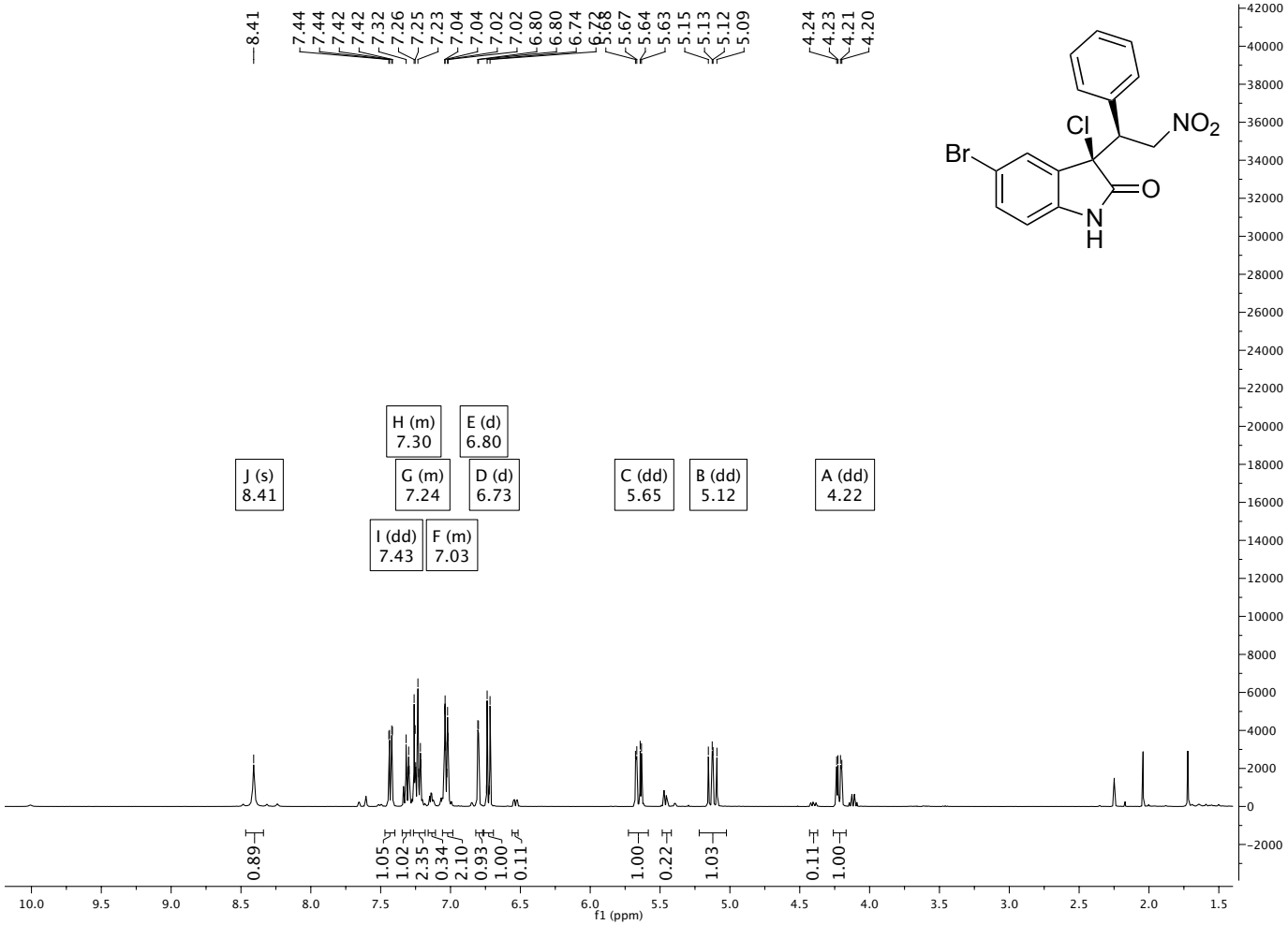
3m (^{1}H NMR) in $CDCl_3$



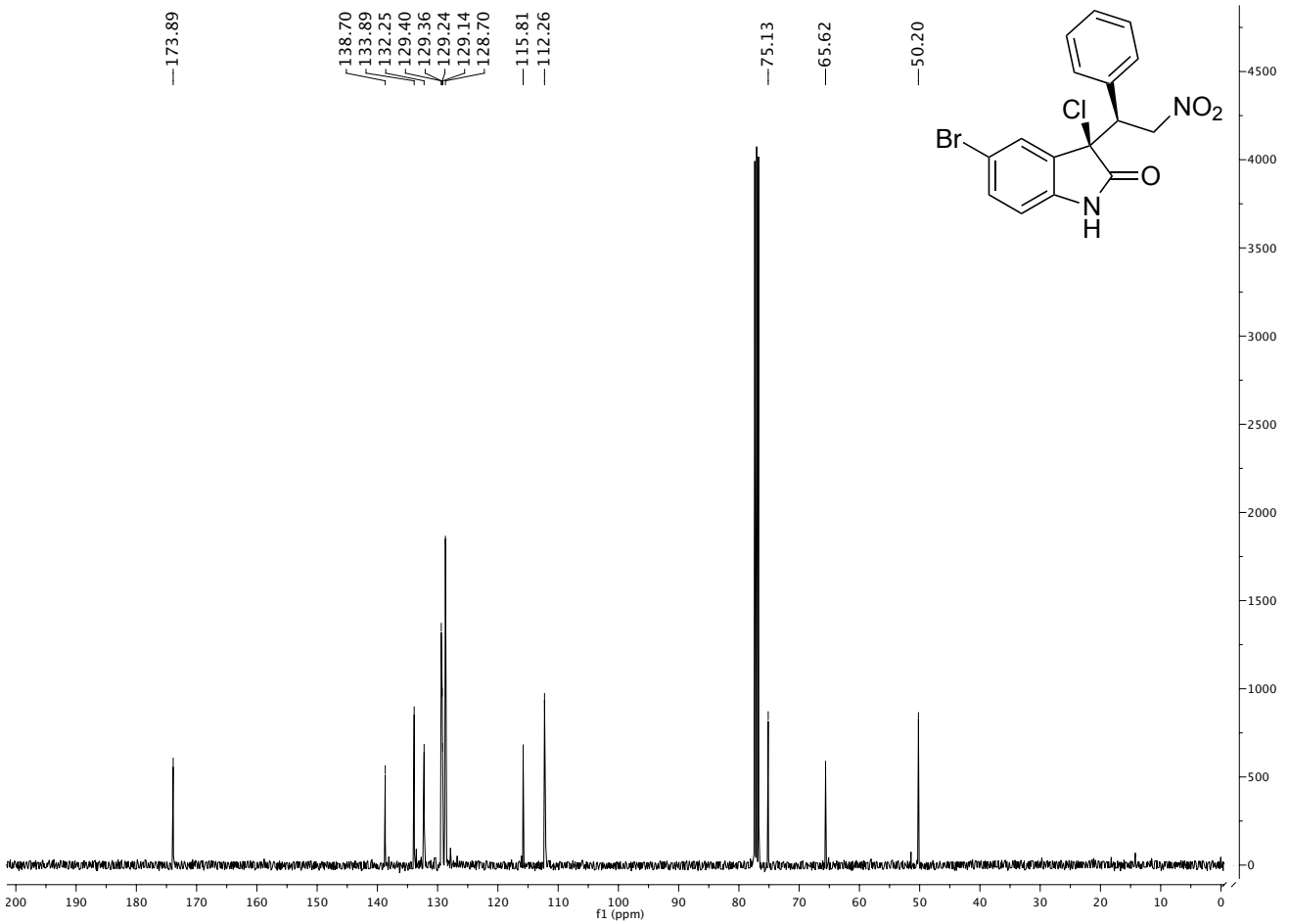
3m (^{13}C NMR) in $CDCl_3$



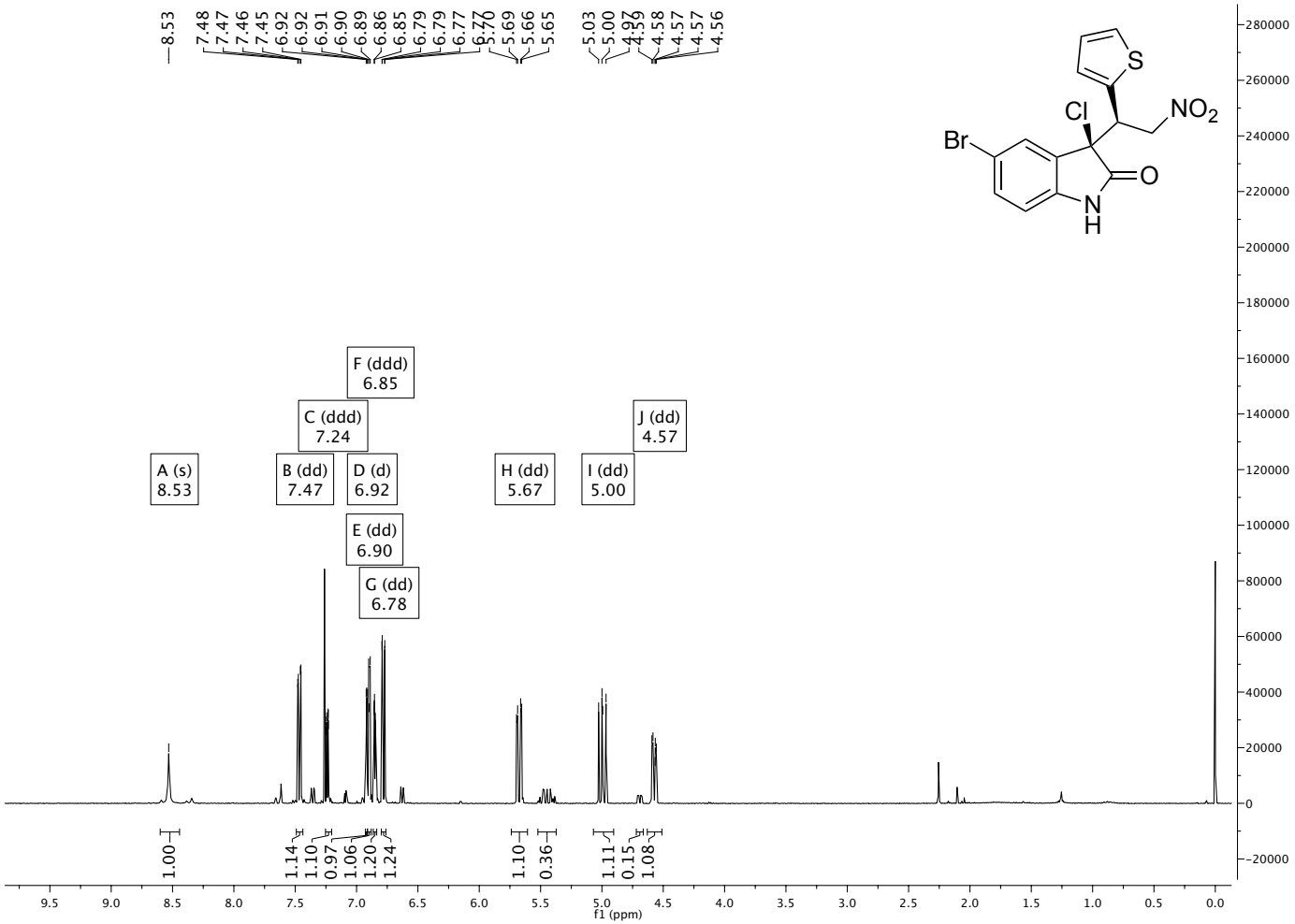
3n (^{1}H NMR) in $CDCl_3$



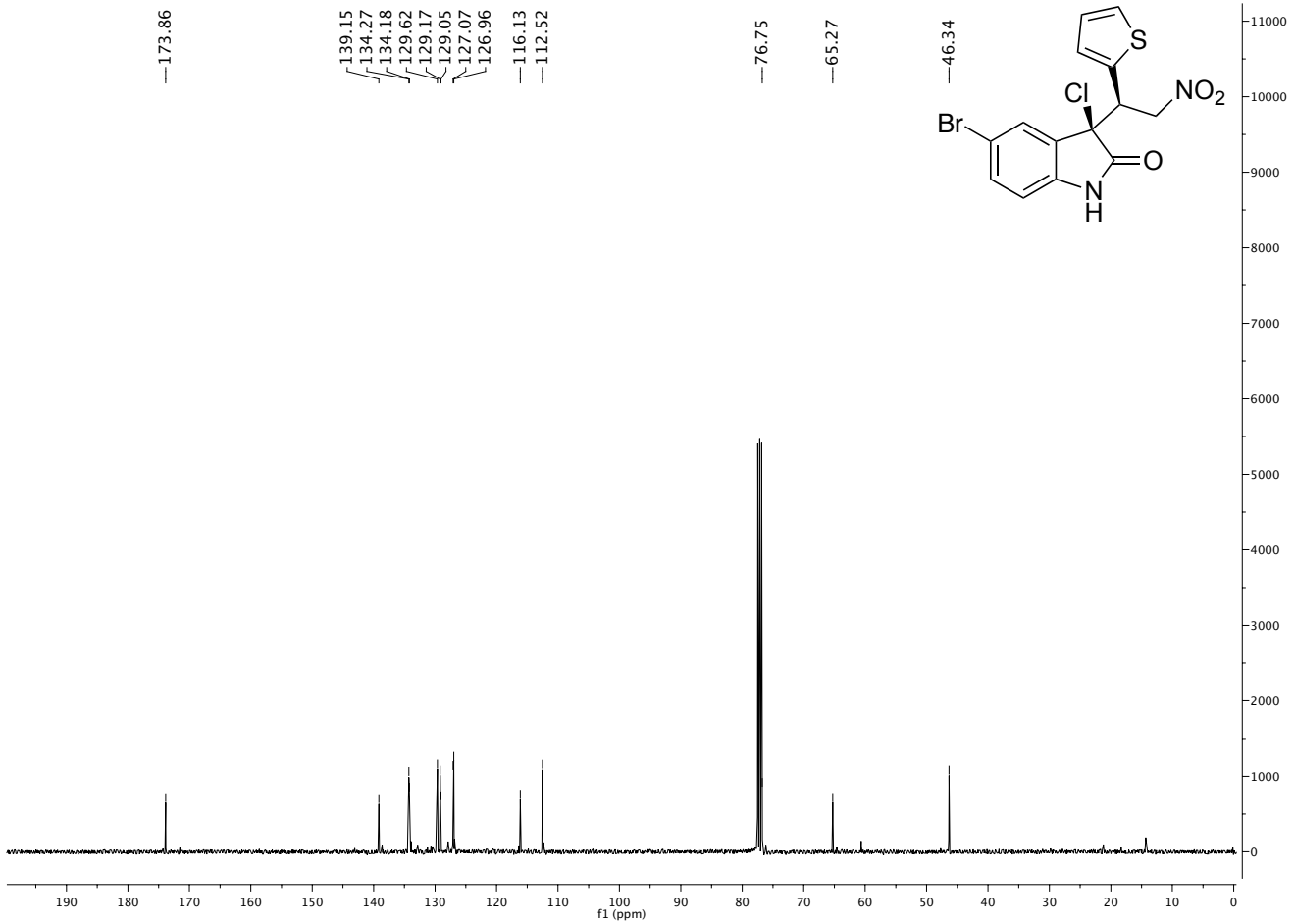
3n (^{13}C NMR) in $CDCl_3$



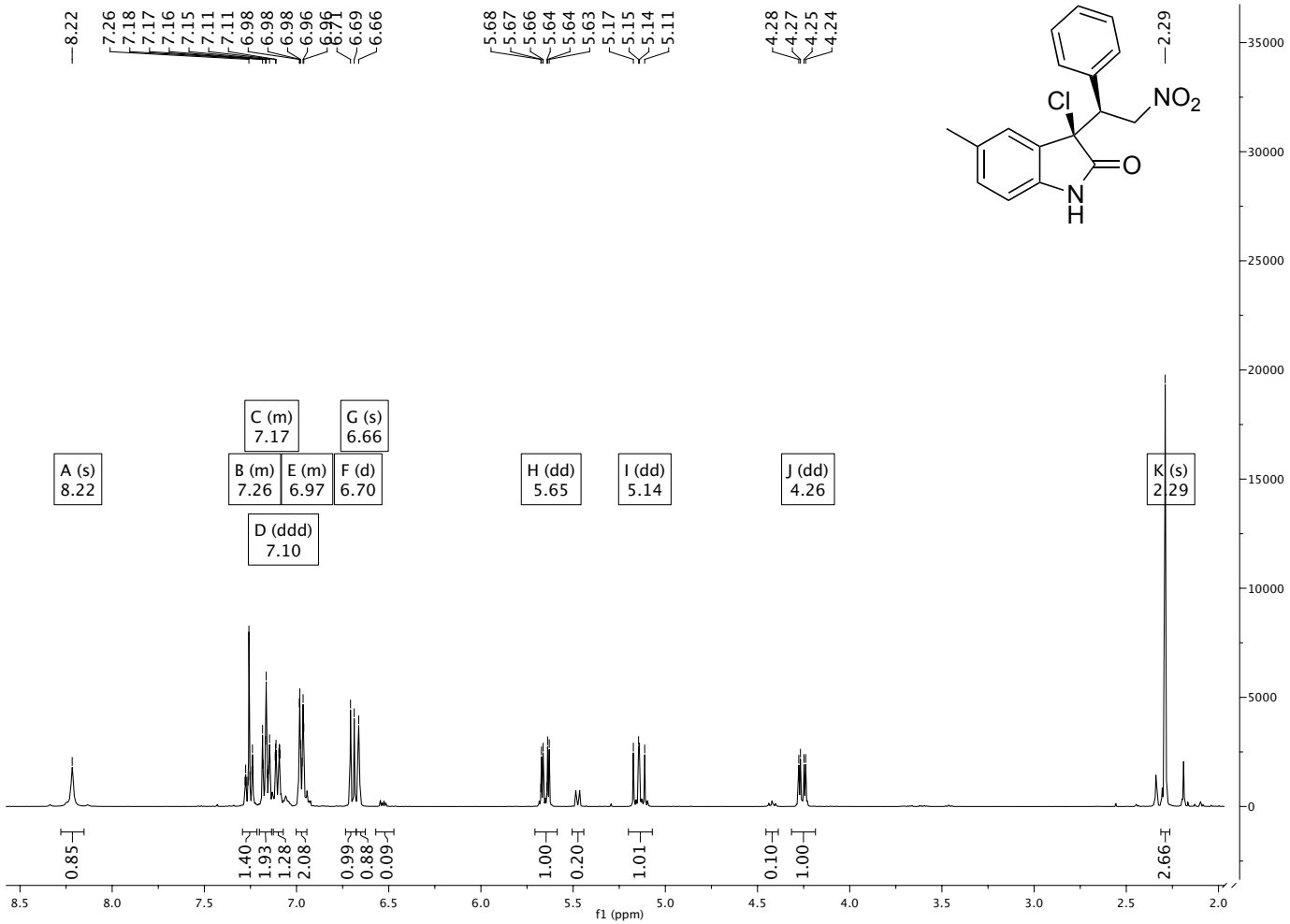
3o (^{1}H NMR) in $CDCl_3$



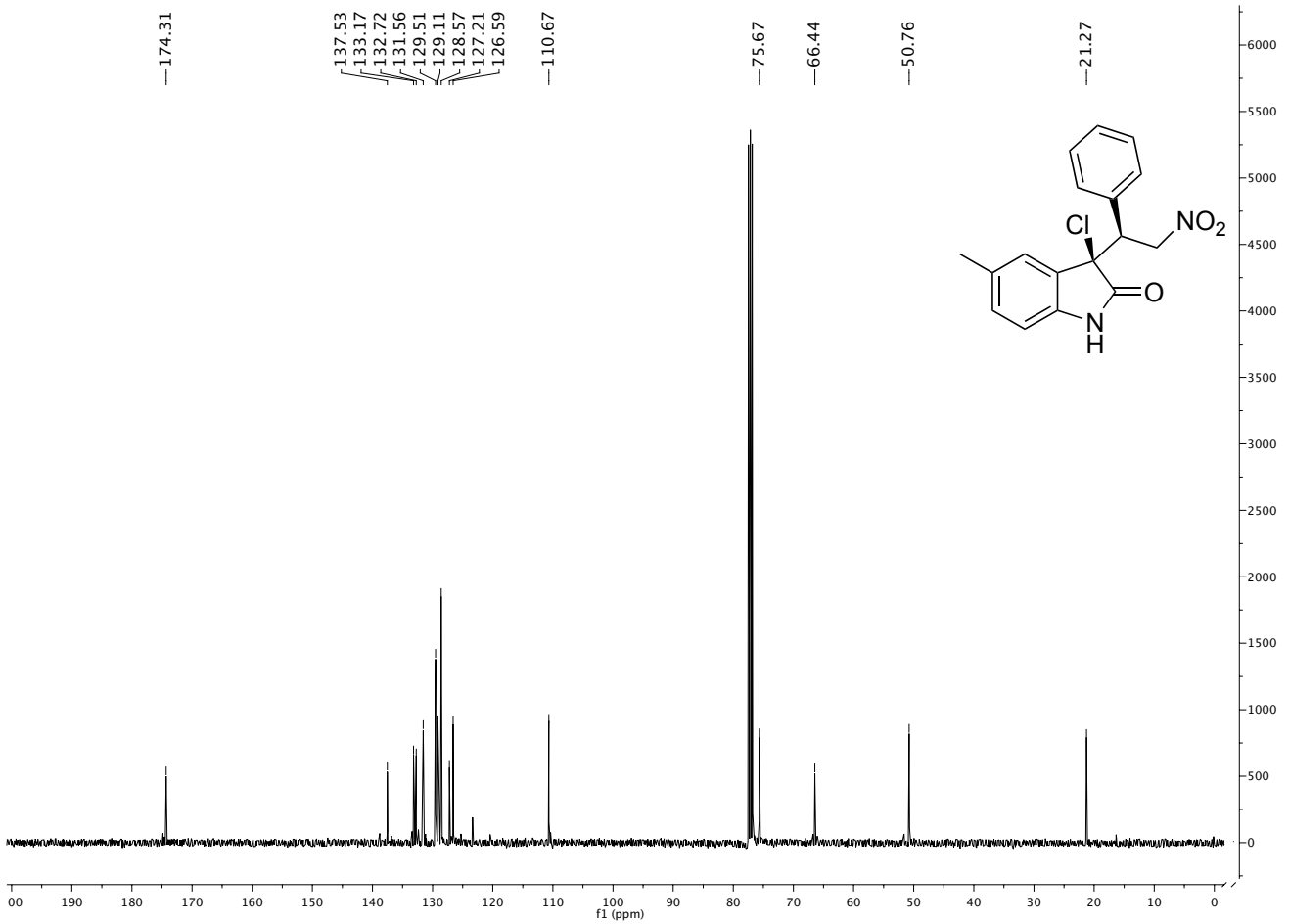
3o (^{13}C NMR) in $CDCl_3$



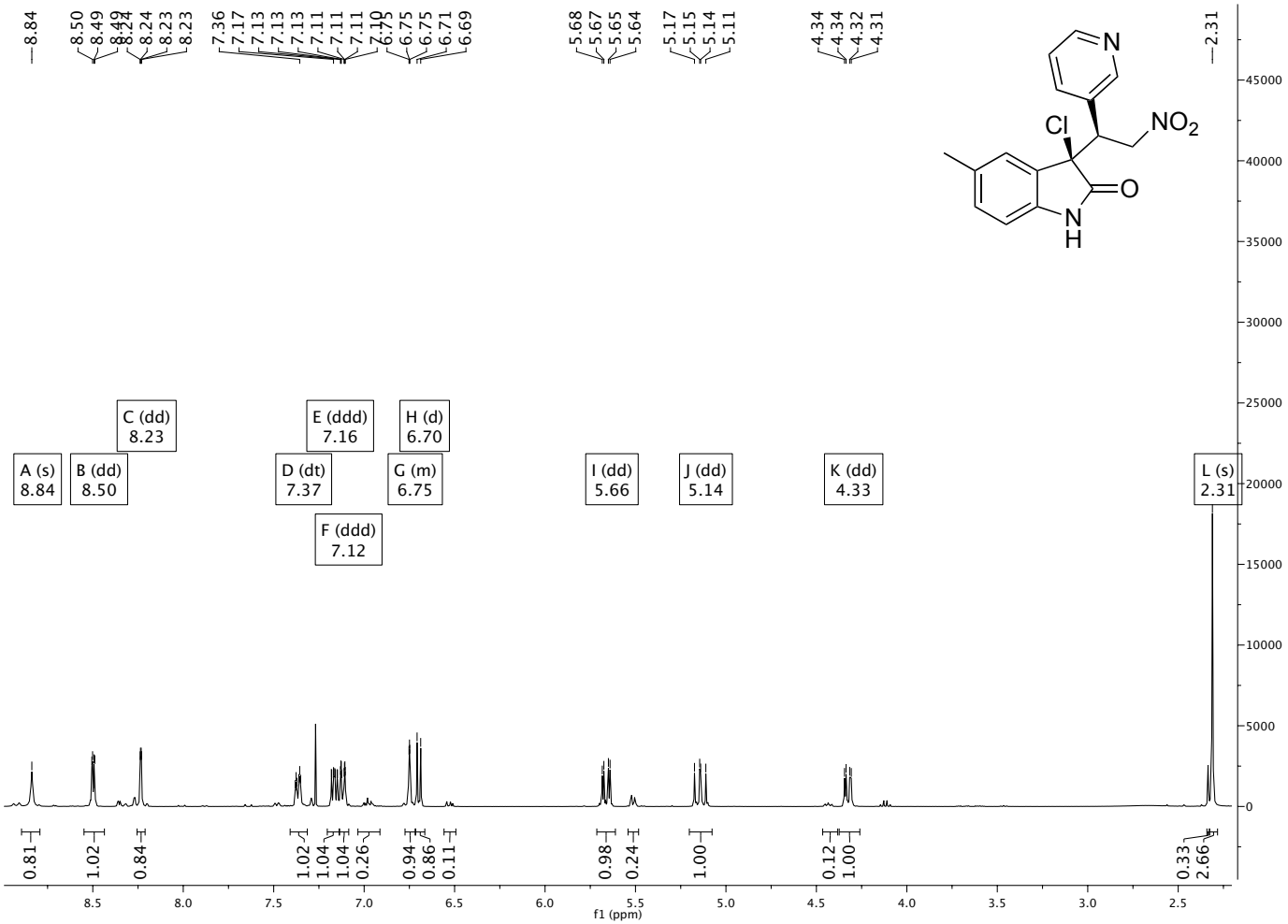
3p (^{1}H NMR) in $CDCl_3$



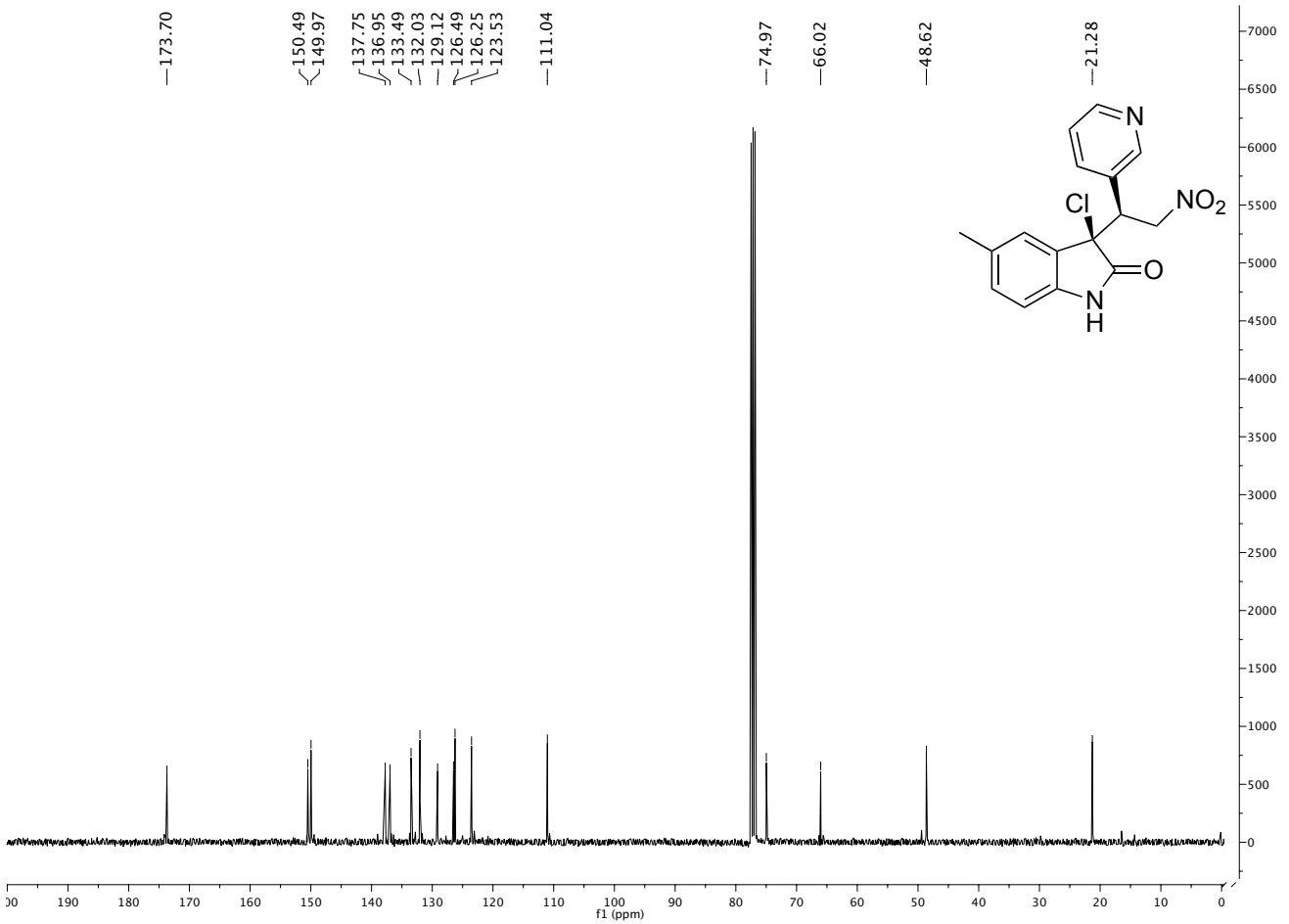
3p (^{13}C NMR) in $CDCl_3$



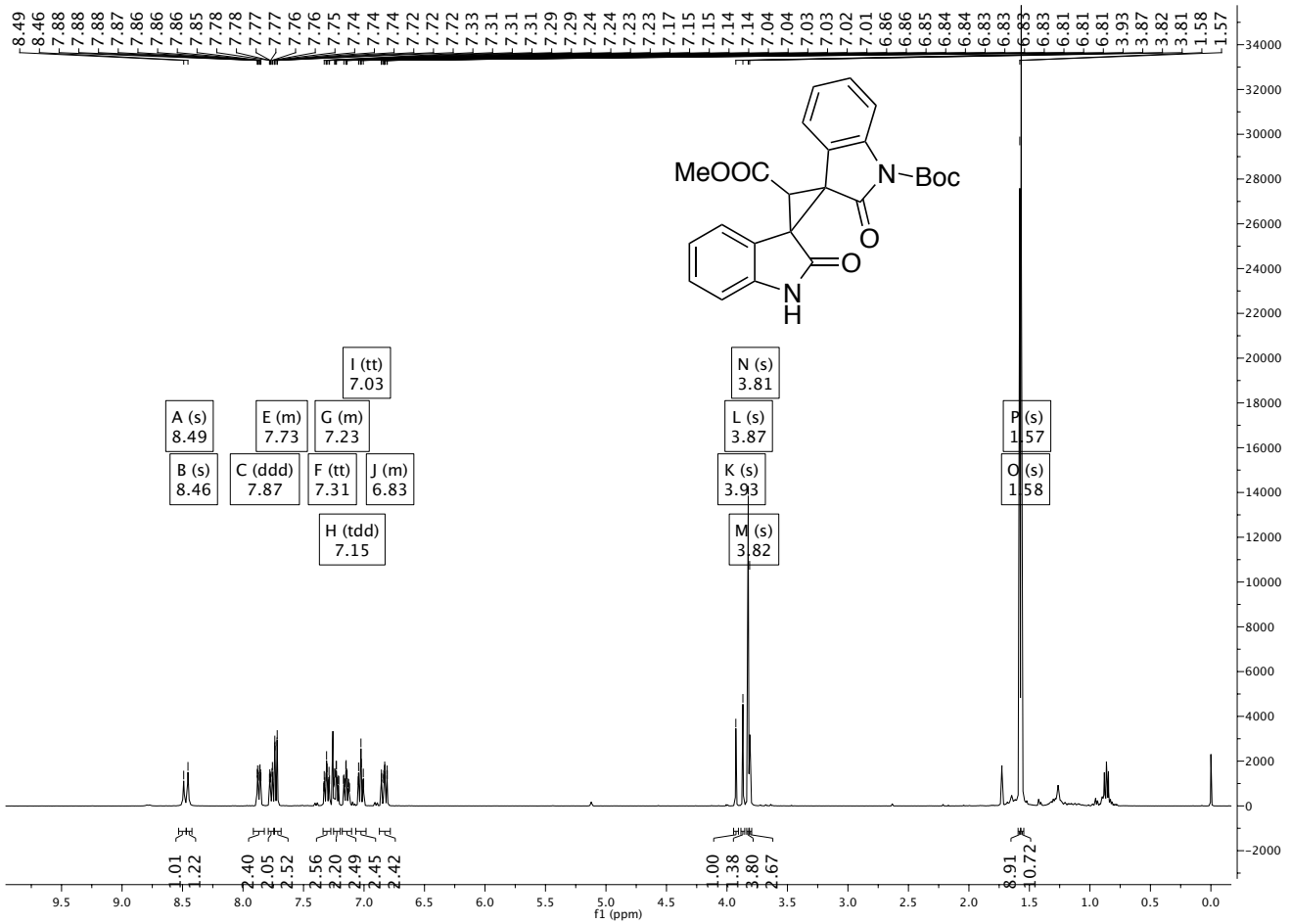
3r (^{1}H NMR) in $CDCl_3$



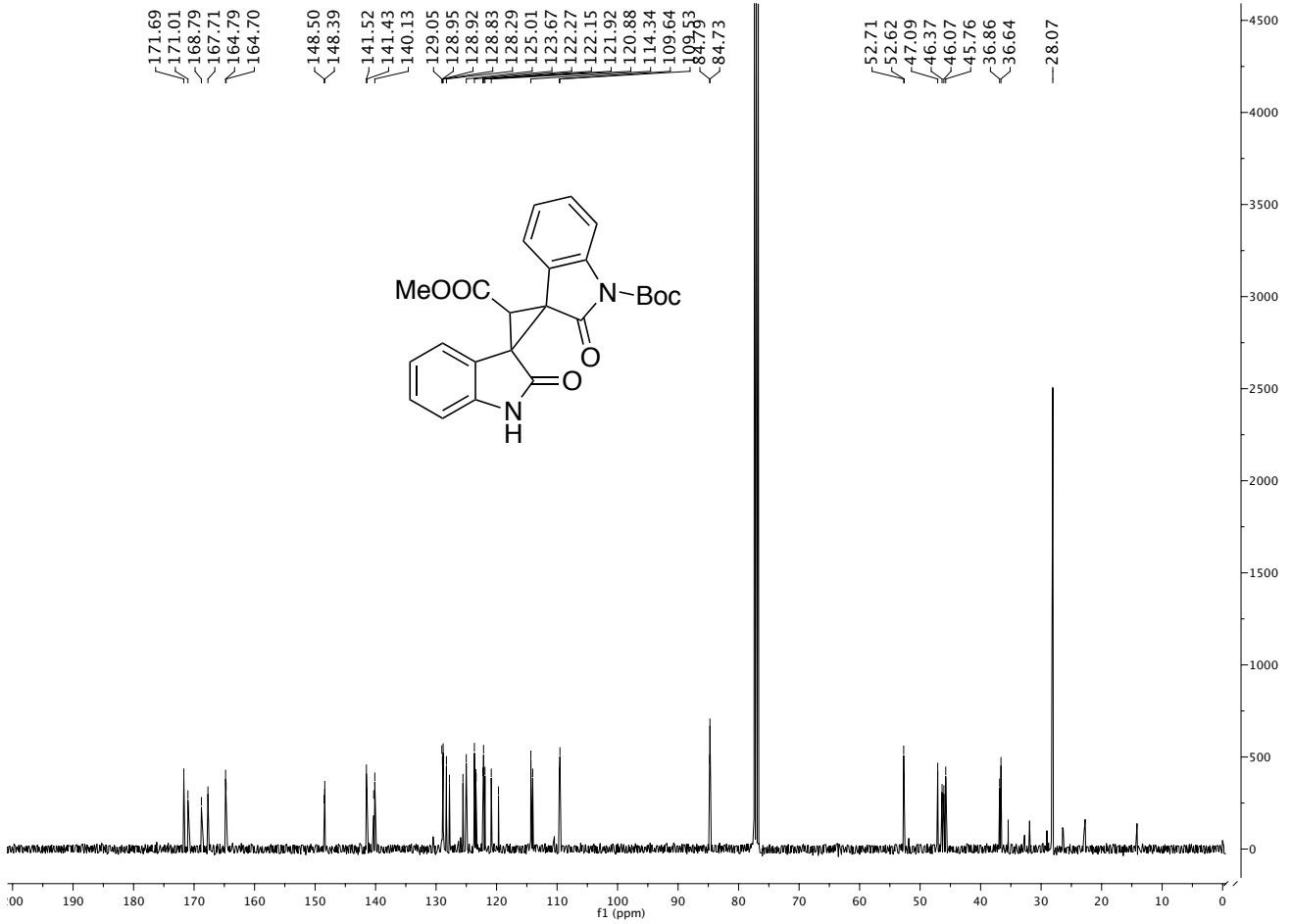
3r (^{13}C NMR) in $CDCl_3$



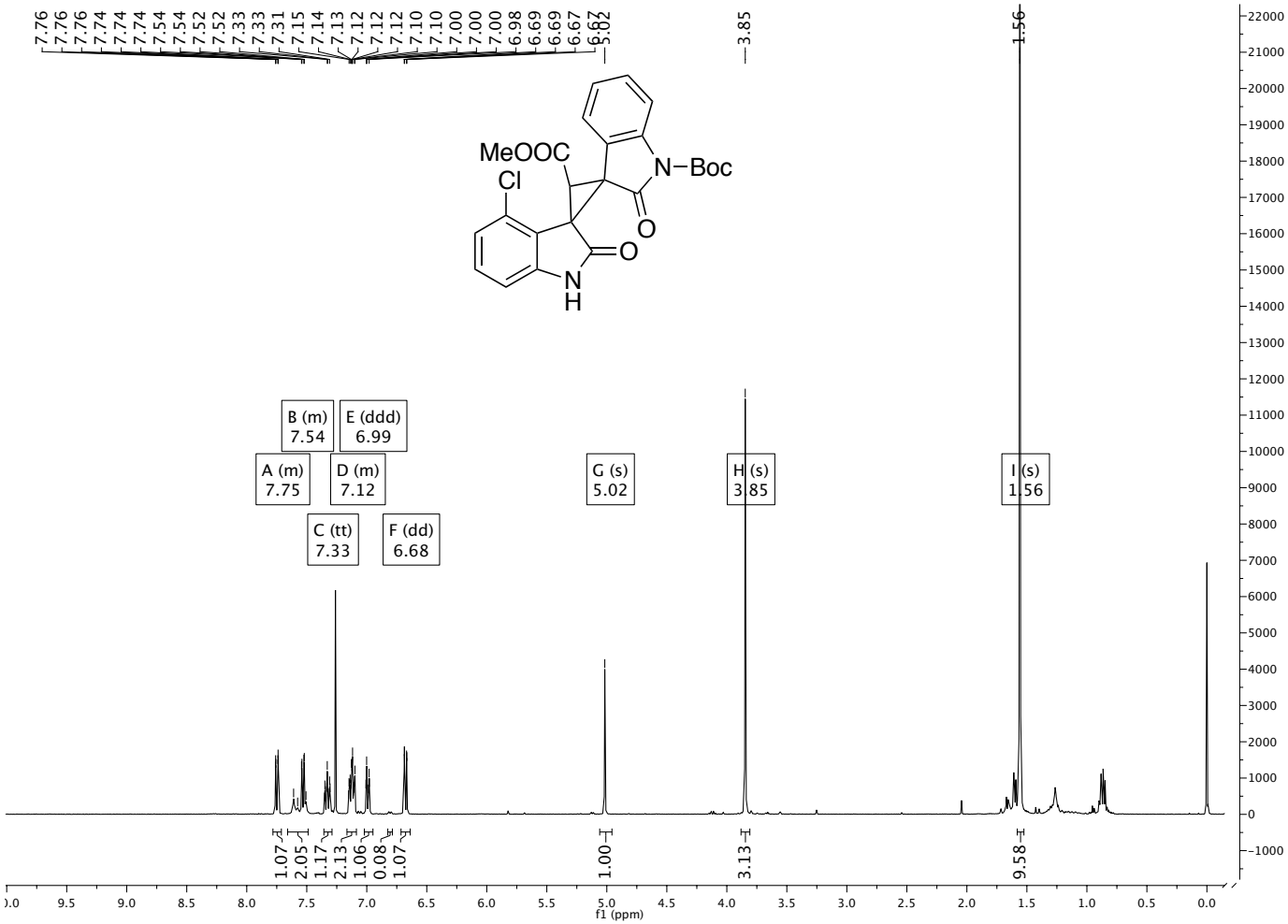
12a (^{1}H NMR) in $CDCl_3$



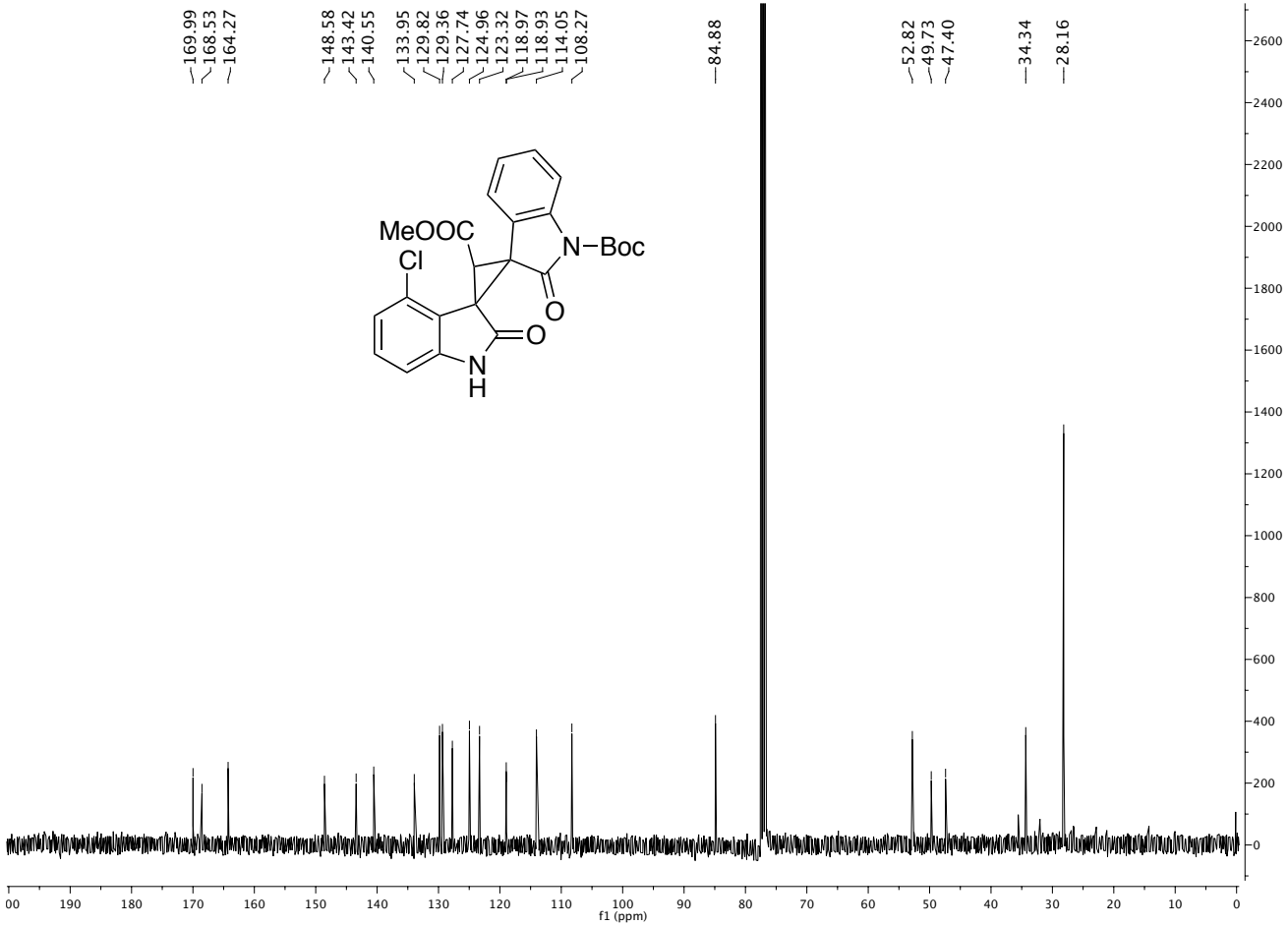
12a (^{13}C NMR) in $CDCl_3$



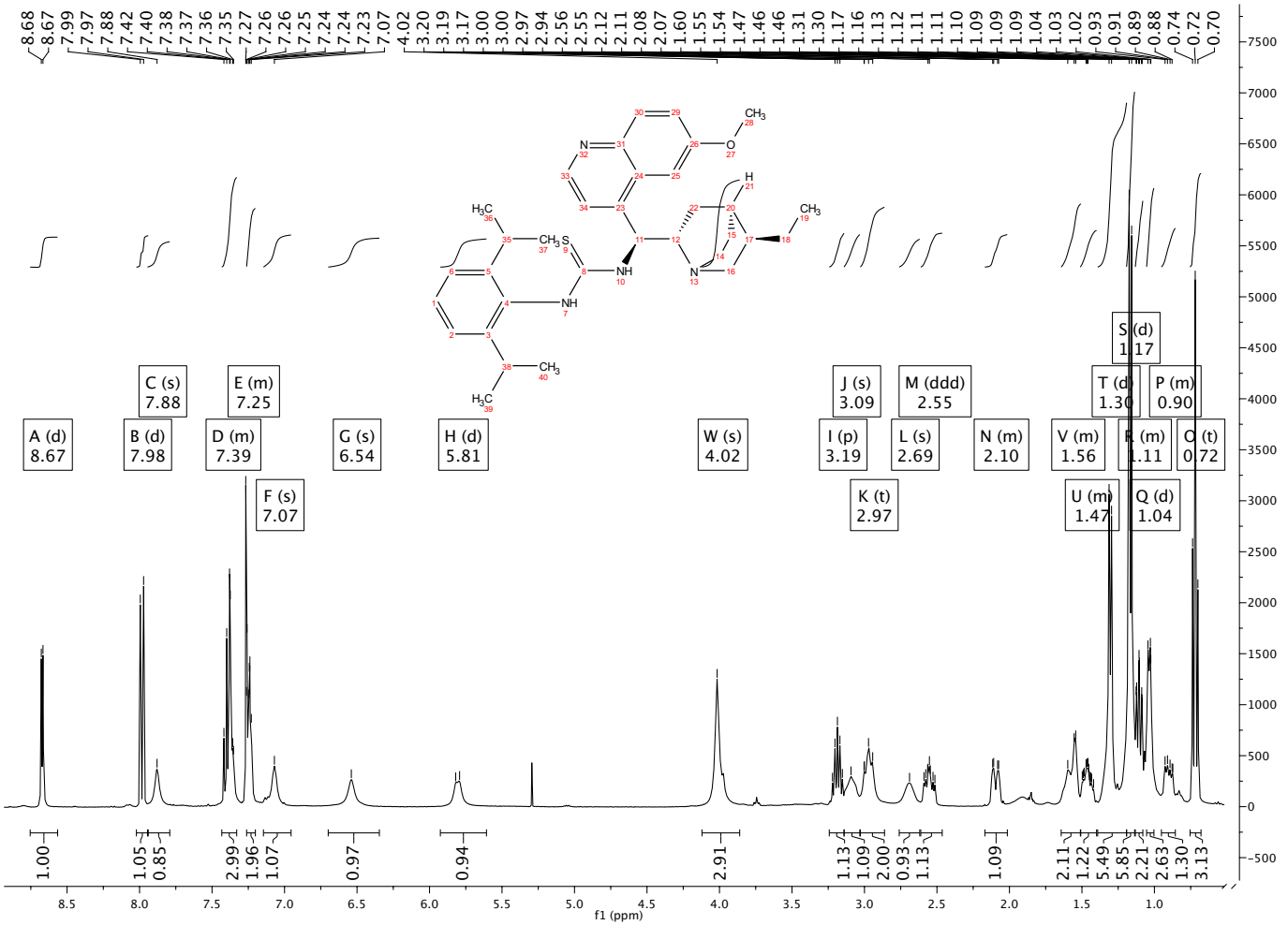
12b (^{1}H NMR) in $CDCl_3$



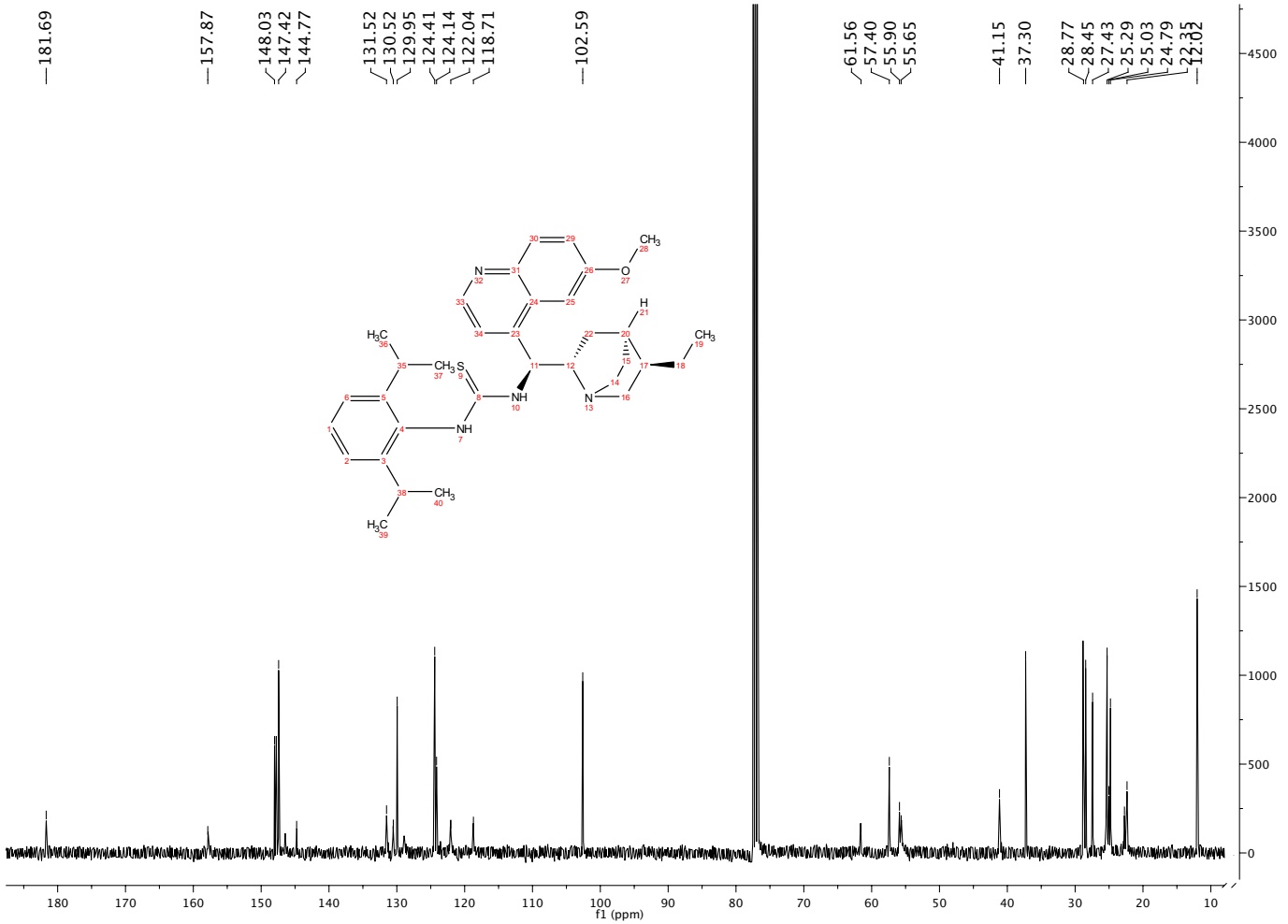
12b (^{13}C NMR) in $CDCl_3$



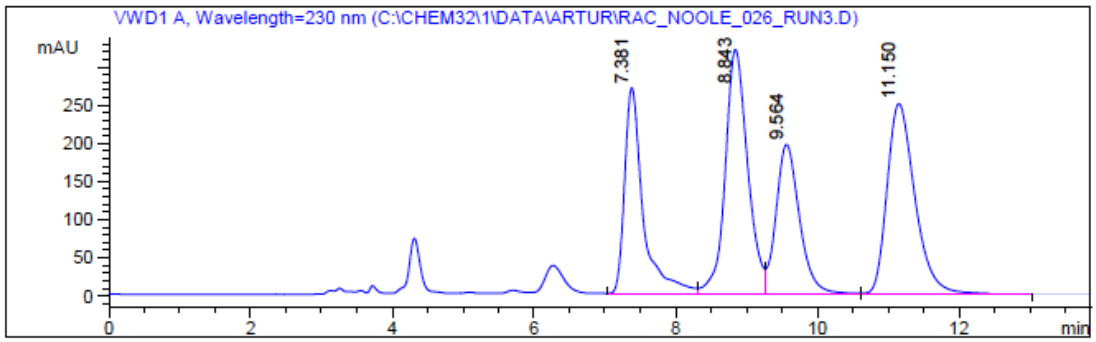
Catalyst 4 (^{1}H NMR) in $CDCl_3$



Catalyst 4 (^{13}C NMR) in $CDCl_3$



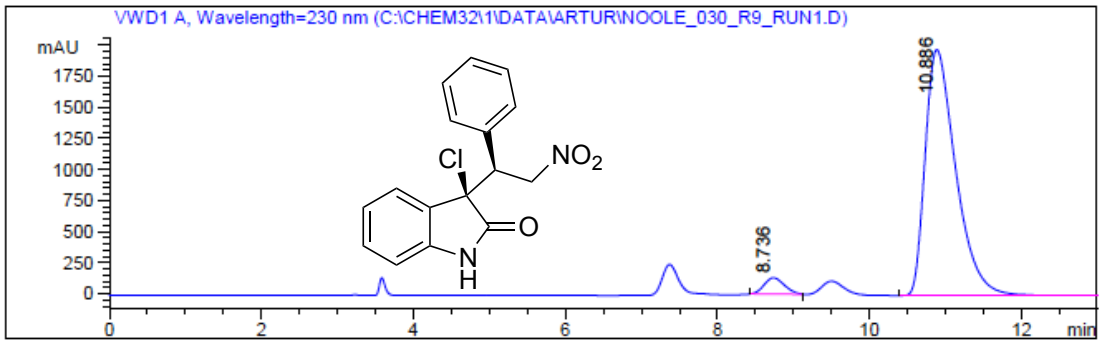
rac 3a



Signaal 1 VWD1 A, Wavelength=230 nm

Piigi nr	RT [min]	Tüüp	Laius [min]	Pindala	Pindala %	Nimi
1	7.381	VV	0.270	4956.261	21.200	
2	8.843	VV	0.333	7064.780	30.219	
3	9.564	VV	0.349	4522.460	19.344	
4	11.150	VB	0.418	6835.042	29.236	

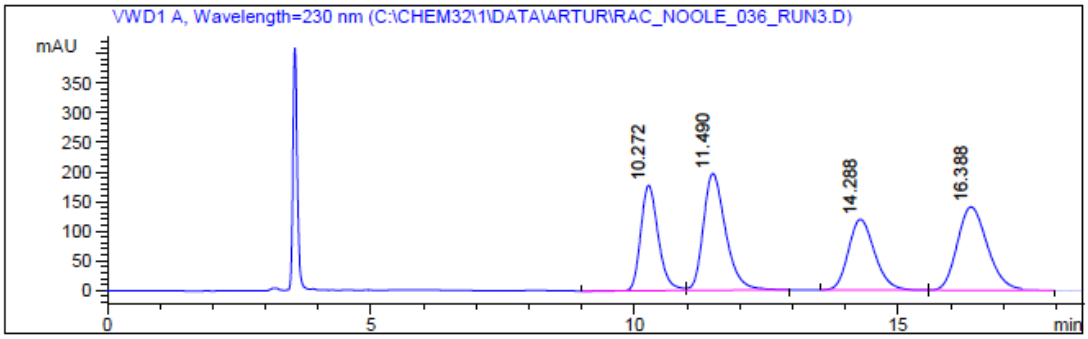
3a



Signaal 1 VWD1 A, Wavelength=230 nm

Piigi nr	RT [min]	Tüüp	Laius [min]	Pindala	Pindala %	Nimi
1	8.736	MM	0.308	2420.828	4.195	
2	10.886	VBA	0.427	5.529e4	95.805	

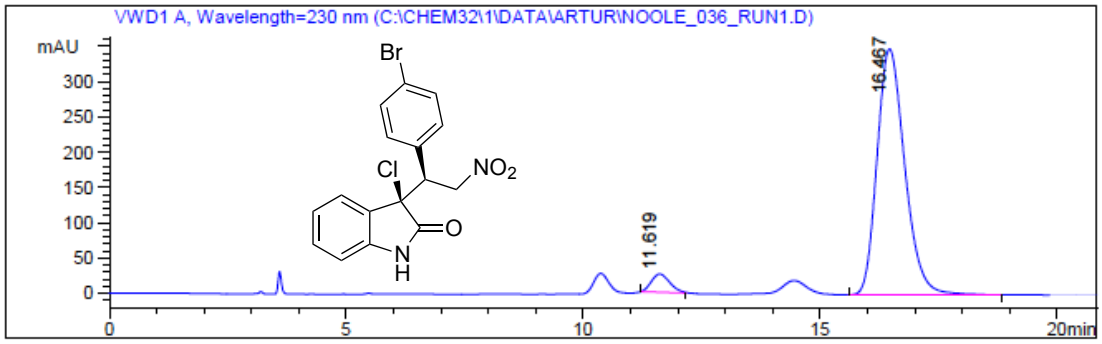
rac 3b



Signaal 1 VWD1 A, Wavelength=230 nm

Piigi nr	RT [min]	Tüüp	Laius [min]	Pindala	Pindala %	Nimi
1	10.272	VV	0.356	4104.594	20.903	
2	11.490	VB	0.449	5792.785	29.500	
3	14.288	BB	0.536	4128.727	21.026	
4	16.388	BB	0.620	5610.212	28.571	

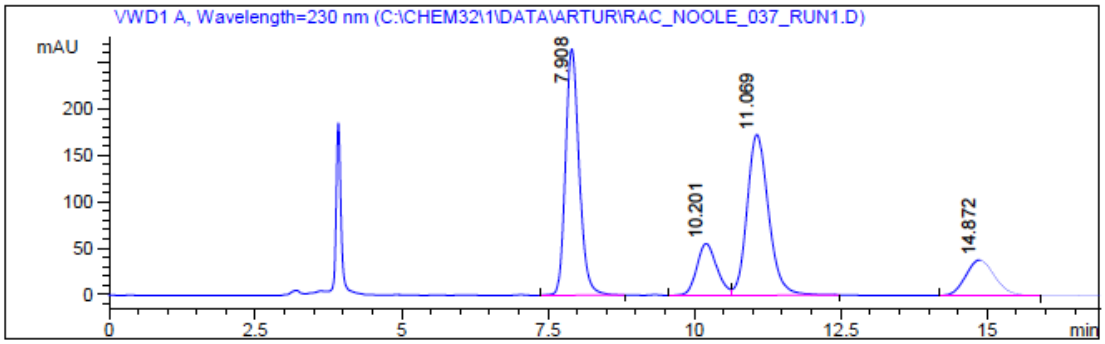
3b



Signaal 1 VWD1 A, Wavelength=230 nm

Piigi nr	RT [min]	Tüüp	Laius [min]	Pindala	Pindala %	Nimi
1	11.619	MM	0.452	699.612	4.706	
2	16.467	BB	0.627	1.417e4	95.294	

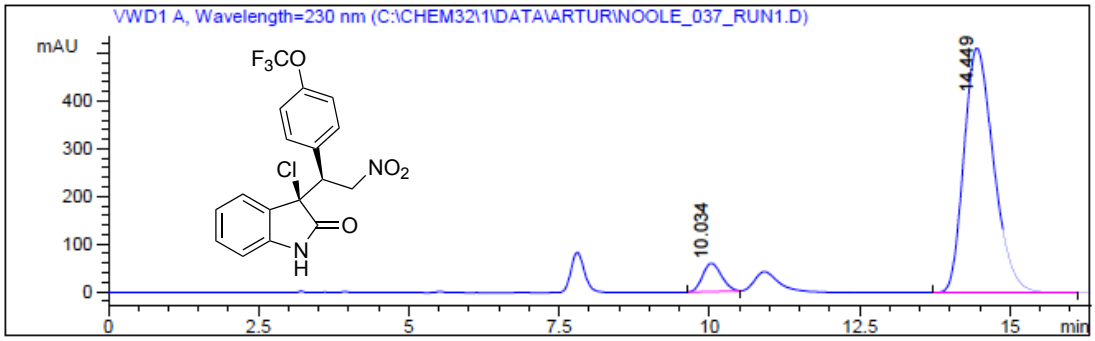
rac 3c



Signaal 1 VWD1 A, Wavelength=230 nm

Piigi nr	RT [min]	Tüüp	Laius [min]	Pindala	Pindala %	Nimi
1	7.908	BB	0.252	4332.939	37.964	
2	10.201	VV	0.366	1327.523	11.631	
3	11.069	VB	0.395	4428.158	38.798	
4	14.872	BB	0.539	1324.761	11.607	

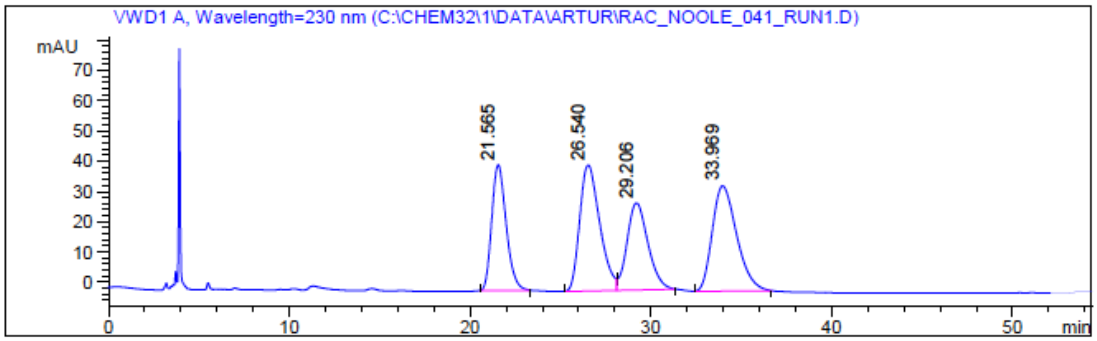
3c



Signaal 1 VWD1 A, Wavelength=230 nm

Piigi nr	RT [min]	Tüüp	Laius [min]	Pindala	Pindala %	Nimi
1	10.034	MM	0.360	1276.479	6.738	
2	14.449	BB	0.533	1.767e4	93.262	

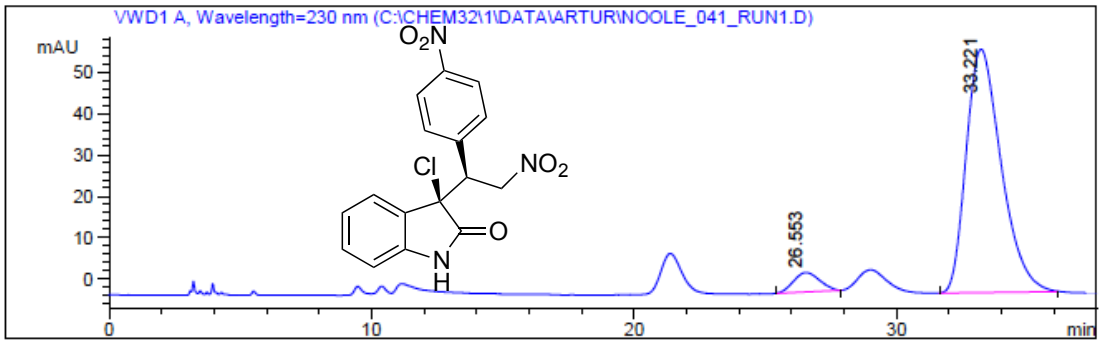
rac 3d



Signaal 1 VWD1 A, Wavelength=230 nm

Piigi nr	RT [min]	Tüüp	Laius [min]	Pindala	Pindala %	Nimi
1	21.565	BB	0.836	2310.304	20.803	
2	26.540	BV	1.156	3206.901	28.877	
3	29.206	VB	1.222	2317.211	20.866	
4	33.969	BB	1.418	3271.026	29.454	

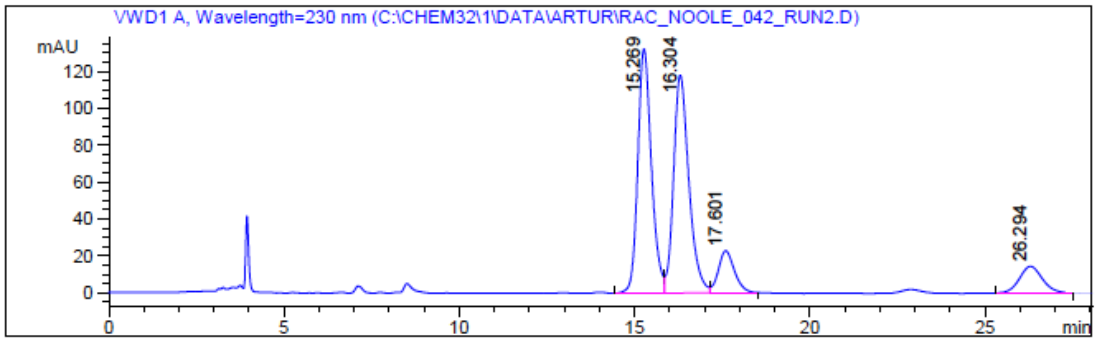
3d



Signaal 1 VWD1 A, Wavelength=230 nm

Piigi nr	RT [min]	Tüüp	Laius [min]	Pindala	Pindala %	Nimi
1	26.553	MM	1.159	323.939	5.599	
2	33.221	BB	1.380	5461.681	94.401	

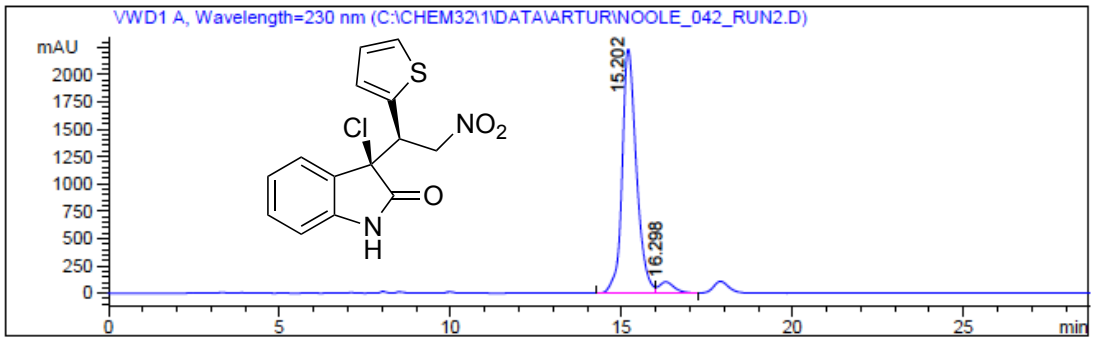
rac 3e



Signaal 1 VWD1 A, Wavelength=230 nm

Piigi nr	RT [min]	Tüüp	Laius [min]	Pindala	Pindala %	Nimi
1	15.269	VV	0.410	3578.121	41.746	
2	16.304	VV	0.459	3587.480	41.855	
3	17.601	VB	0.485	731.439	8.534	
4	26.294	BB	0.709	674.108	7.865	

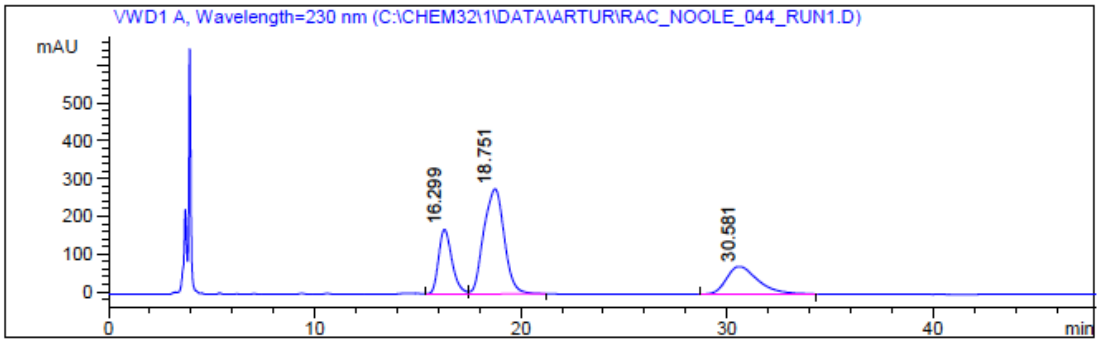
3e



Signaal 1 VWD1 A, Wavelength=230 nm

Piigi nr	RT [min]	Tüüp	Laius [min]	Pindala	Pindala %	Nimi
1	15.202	VV	0.437	6.492e4	95.205	
2	16.298	VV	0.466	3269.923	4.795	

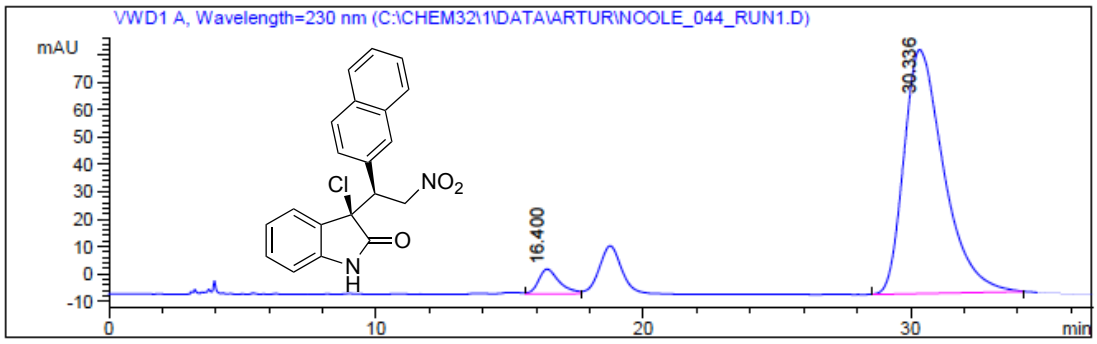
rac 3f



Signaal 1 VWD1 A, Wavelength=230 nm

Piigi nr	RT [min]	Tüüp	Laius [min]	Pindala	Pindala %	Nimi
1	16.299	VV	0.697	7787.199	22.383	
2	18.751	VB	1.133	1.920e4	55.199	
3	30.581	BB	1.570	7799.409	22.418	

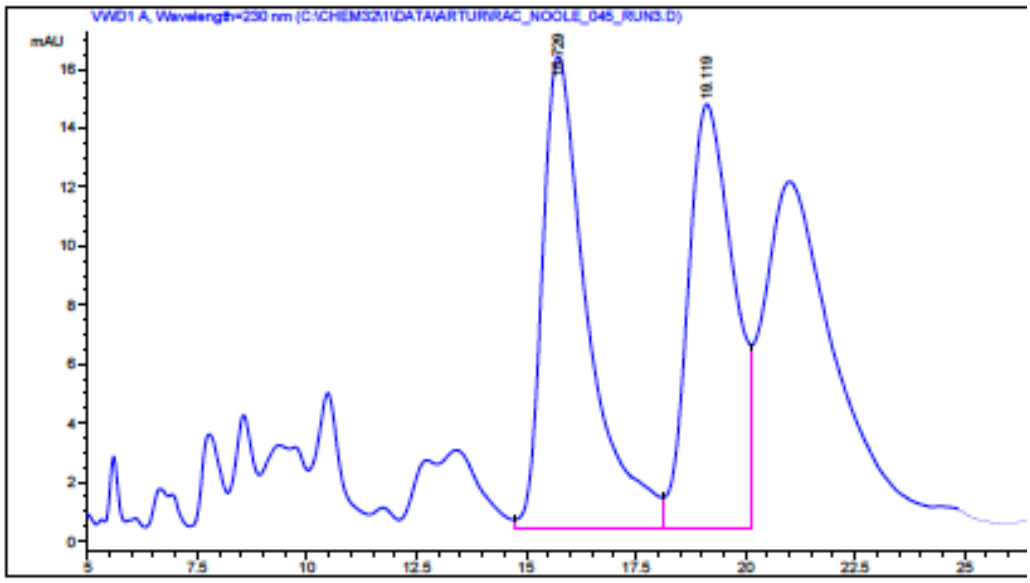
3f



Signaal 1 VWD1 A, Wavelength=230 nm

Piigi nr	RT [min]	Tüüp	Laius [min]	Pindala	Pindala %	Nimi
1	16.400	BV	0.805	485.724	4.987	
2	30.336	BB	1.532	9254.379	95.013	

rac 3g

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------------------------------------------------------------------------
                        Area Percent Report
------------------------------------------------------------------------

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      5.0000
Sample Amount         :     10.00000  [ng/ul]    (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=230 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  15.729 VV    1.0322 1137.13855   15.95989 262.0697
   2  19.119 VV    1.0410 1032.39624   14.33727 237.9303
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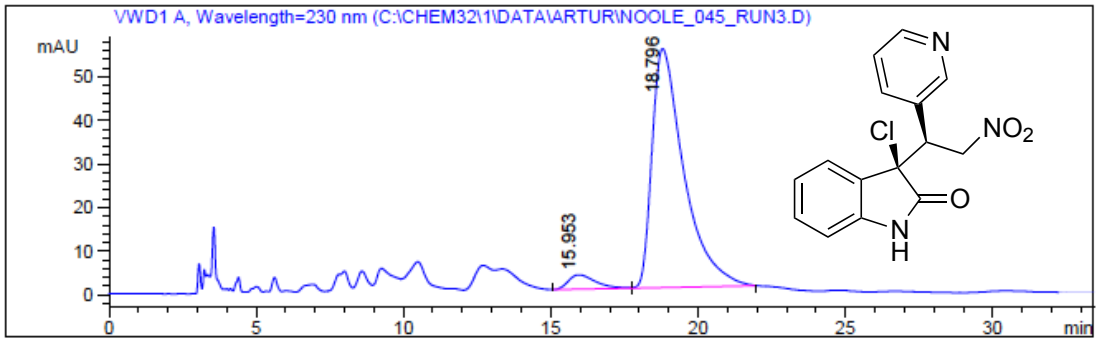
3g

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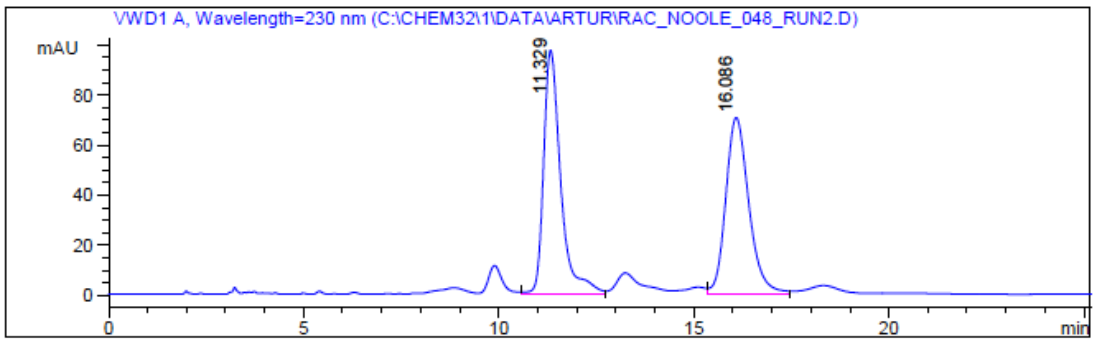
  Signaal      1 VWD1 A, Wavelength=230 nm
|Piigi|    RT      |  Tüüp  | Laius   |Pindala |Pindala |      Nimi      |
| nr  |   [min]    |        | [min]   |        |   %    |                |
|-----|------------|--------|---------|--------|--------|----------------|
|1    |15.953      |VV      |0.902    |213.620 |4.916   |                |
|2    |18.796      |VB      |1.107    |4131.890|95.084  |                |
------------------------------------------------------------------------
```

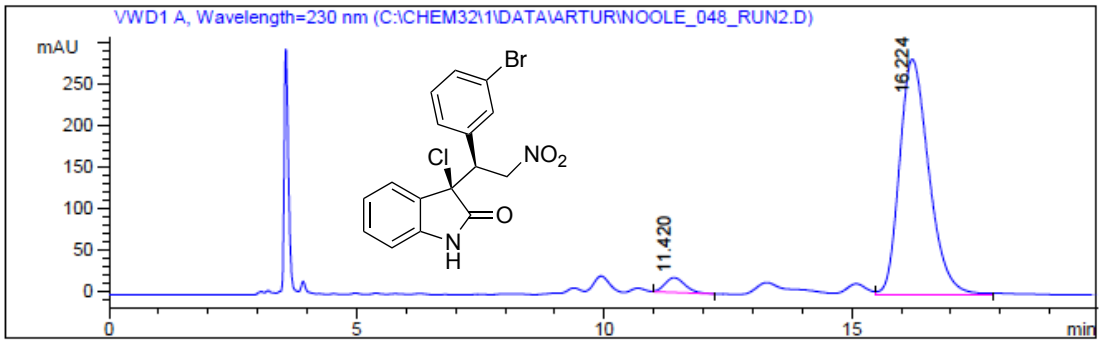
rac 3h



Signaal 1 VWD1 A, Wavelength=230 nm

Piigi nr	RT [min]	Tüüp	Laius [min]	Pindala	Pindala %	Nimi
1	11.329	VV	0.460	2975.082	50.748	
2	16.086	VB	0.630	2887.331	49.252	

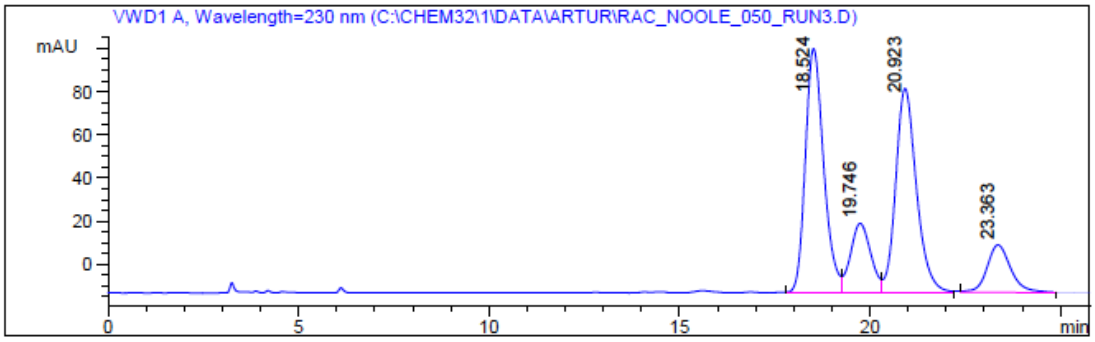
3h



Signaal 1 VWD1 A, Wavelength=230 nm

Piigi nr	RT [min]	Tüüp	Laius [min]	Pindala	Pindala %	Nimi
1	11.420	MM	0.466	495.320	4.079	
2	16.224	VB	0.636	1.165e4	95.921	

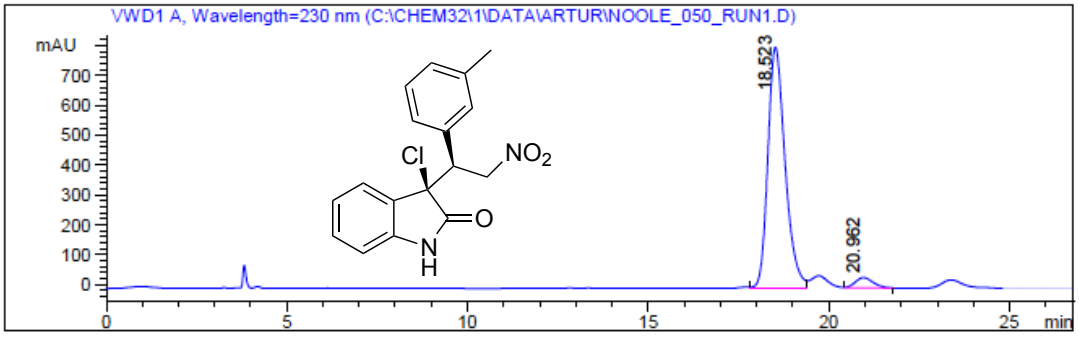
rac 3i



Signaal 1 VWD1 A, Wavelength=230 nm

Piigi nr	RT [min]	Tüüp	Laius [min]	Pindala	Pindala %	Nimi
1	18.524	BV	0.513	3776.388	39.695	
2	19.746	VV	0.568	1188.948	12.497	
3	20.923	VB	0.577	3585.893	37.693	
4	23.363	BB	0.657	962.310	10.115	

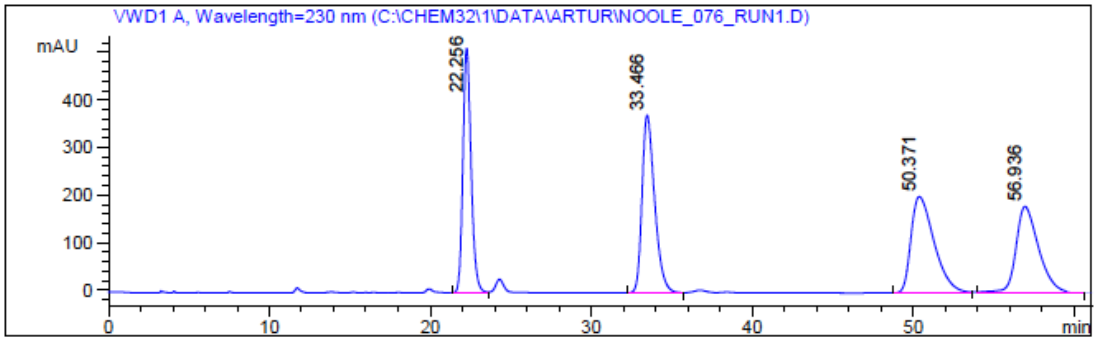
3i



Signaal 1 VWD1 A, Wavelength=230 nm

Piigi nr	RT [min]	Tüüp	Laius [min]	Pindala	Pindala %	Nimi
1	18.523	VV	0.507	2.687e4	95.880	
2	20.962	MM	0.567	1154.795	4.120	

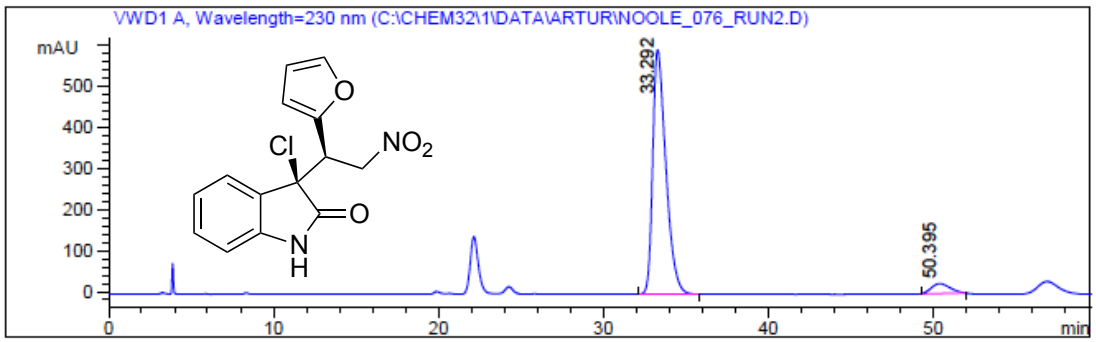
rac 3j



Signaal 1 VWD1 A, Wavelength=230 nm

Piigi nr	RT [min]	Tüüp	Laius [min]	Pindala	Pindala %	Nimi
1	22.256	BV	0.539	1.815e4	23.578	
2	33.466	BB	0.834	2.040e4	26.508	
3	50.371	BB	1.564	2.035e4	26.445	
4	56.936	BB	1.481	1.806e4	23.469	

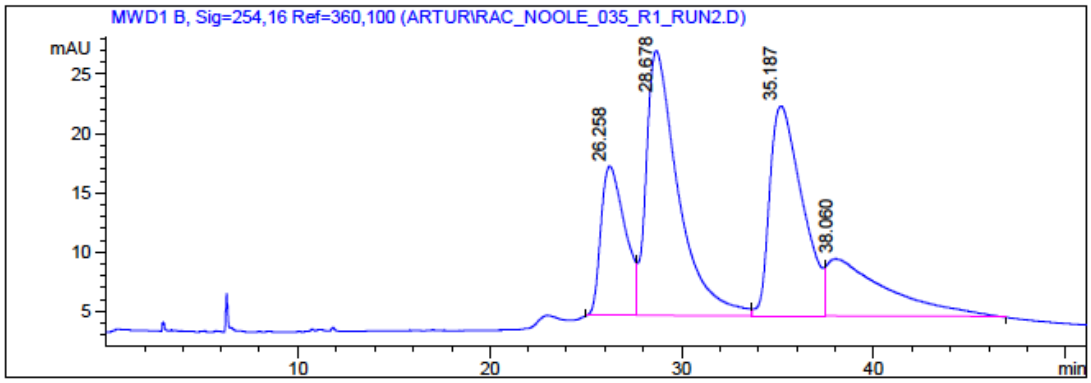
3j



Signaal 1 VWD1 A, Wavelength=230 nm

Piigi nr	RT [min]	Tüüp	Laius [min]	Pindala	Pindala %	Nimi
1	33.292	BB	0.841	3.299e4	94.566	
2	50.395	MM	1.309	1895.936	5.434	

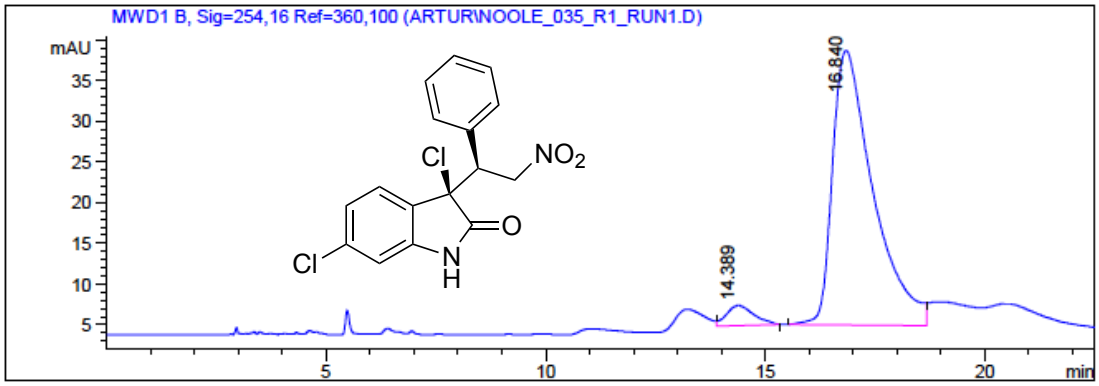
rac 3k



Signaal 1 MWD1 B, Sig=254,16 Ref=360,100

Piigi nr	RT [min]	Tüüp	Laius [min]	Pindala	Pindala %	Nimi
1	26.258	MF	1.453	1094.388	15.957	
2	28.678	MF	1.950	2607.111	38.015	
3	35.187	MF	1.989	2106.812	30.720	
4	38.060	FM	3.642	1049.831	15.308	

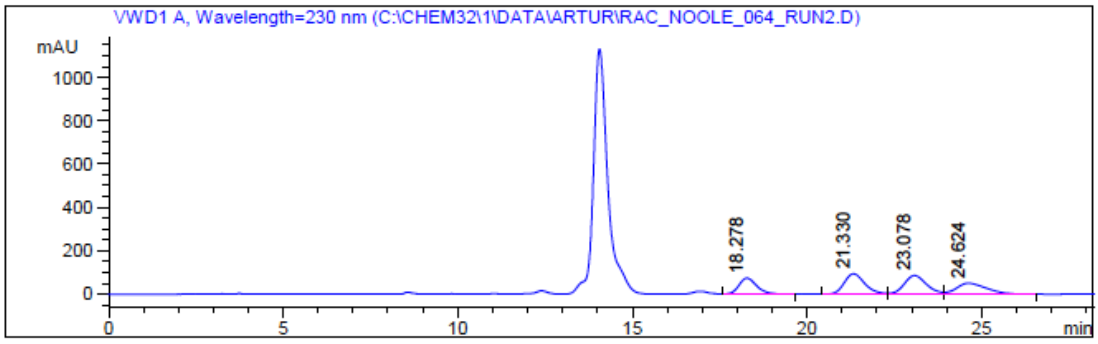
3k



Signaal 1 MWD1 B, Sig=254,16 Ref=360,100

Piigi nr	RT [min]	Tüüp	Laius [min]	Pindala	Pindala %	Nimi
1	14.389	FM	0.726	106.760	4.688	
2	16.840	MF	1.073	2170.496	95.312	

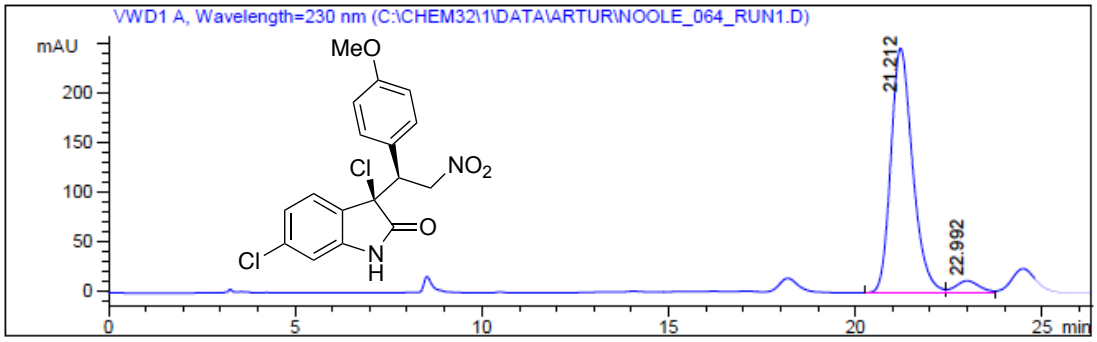
rac 3l



Signaal 1 VWD1 A, Wavelength=230 nm

Piigi nr	RT [min]	Tüüp	Laius [min]	Pindala	Pindala %	Nimi
1	18.278	VB	0.549	2694.115	19.788	
2	21.330	BV	0.635	3927.852	28.850	
3	23.078	VV	0.686	3889.834	28.570	
4	24.624	VB	0.909	3103.149	22.792	

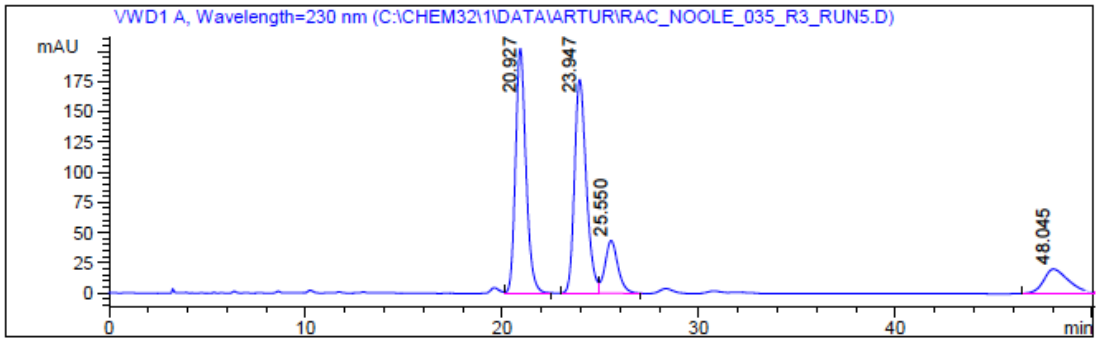
3l



Signaal 1 VWD1 A, Wavelength=230 nm

Piigi nr	RT [min]	Tüüp	Laius [min]	Pindala	Pindala %	Nimi
1	21.212	BV	0.620	1.004e4	94.833	
2	22.992	VV	0.686	547.059	5.167	

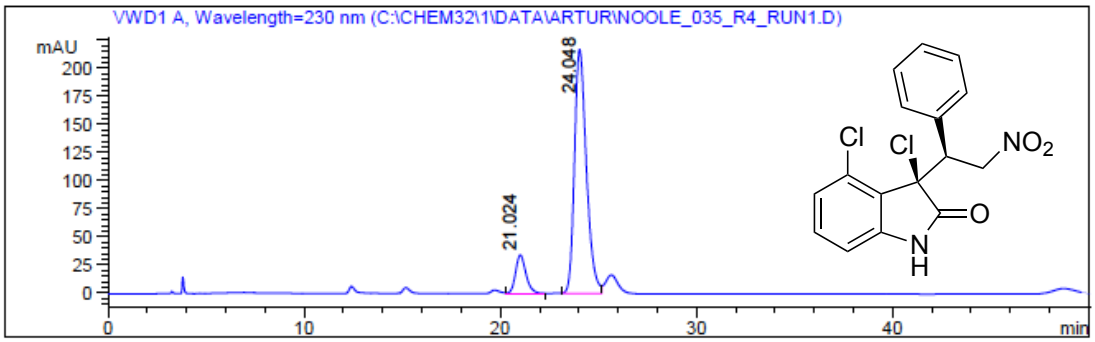
rac 3m



Signaal 1 VWD1 A, Wavelength=230 nm

Piigi nr	RT [min]	Tüüp	Laius [min]	Pindala	Pindala %	Nimi
1	20.927	VB	0.564	7473.975	39.894	
2	23.947	BV	0.641	7411.341	39.559	
3	25.550	VB	0.689	2003.663	10.695	
4	48.045	BBA	1.285	1845.740	9.852	

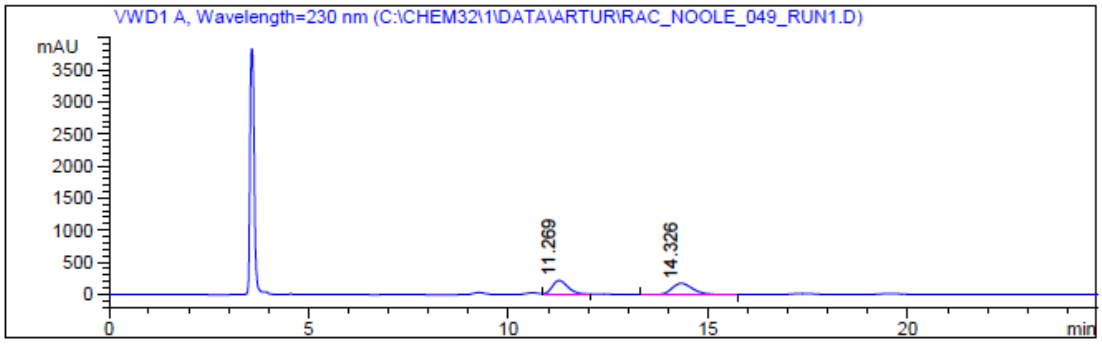
3m



Signaal 1 VWD1 A, Wavelength=230 nm

Piigi nr	RT [min]	Tüüp	Laius [min]	Pindala	Pindala %	Nimi
1	21.024	VB	0.566	1265.532	12.129	
2	24.048	BV	0.644	9168.277	87.871	

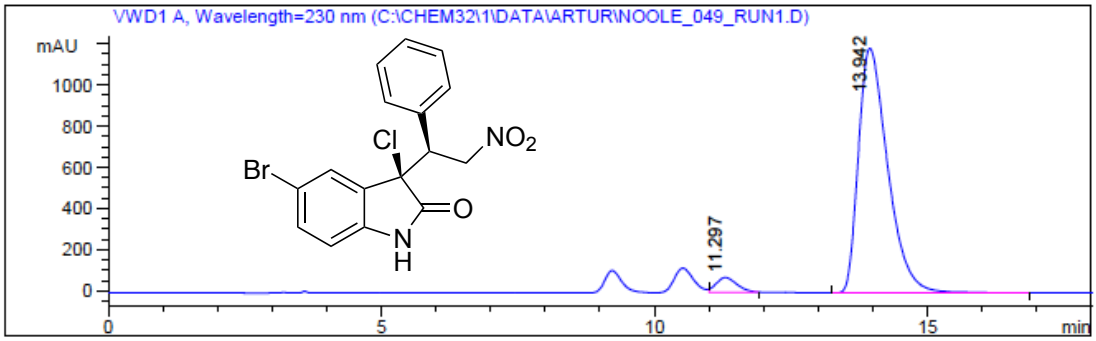
rac 3n



Signaal 1 VWD1 A, Wavelength=230 nm

Piigi nr	RT [min]	Tüüp	Laius [min]	Pindala	Pindala %	Nimi
1	11.269	VV	0.438	6398.707	49.964	
2	14.326	VB	0.562	6408.038	50.036	

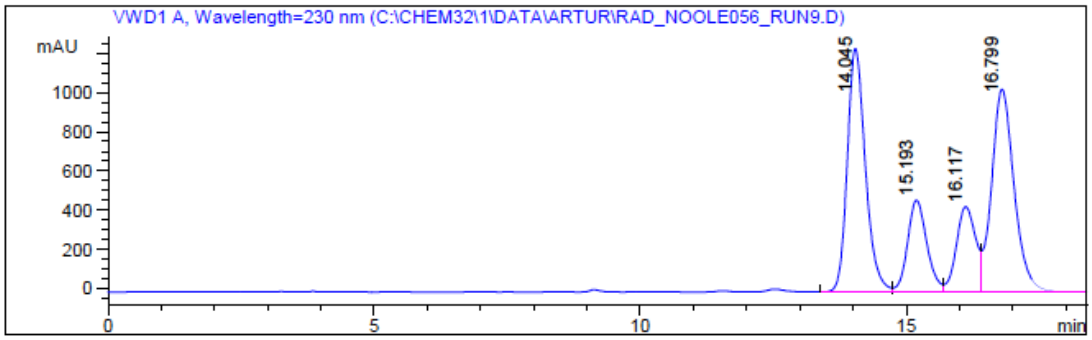
3n



Signaal 1 VWD1 A, Wavelength=230 nm

Piigi nr	RT [min]	Tüüp	Laius [min]	Pindala	Pindala %	Nimi
1	11.297	FM	0.442	1905.535	4.120	
2	13.942	VB	0.572	4.435e4	95.880	

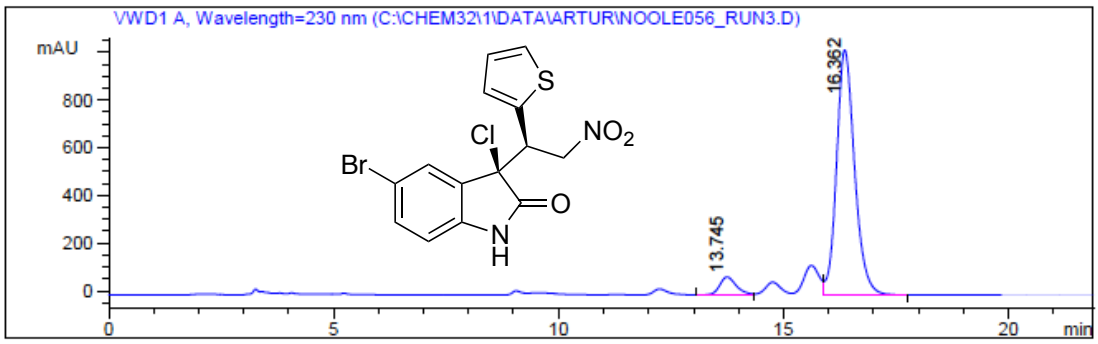
rac 3o



Signaal 1 VWD1 A, Wavelength=230 nm

Piigi nr	RT [min]	Tüüp	Laius [min]	Pindala	Pindala %	Nimi
1	14.045	BV	0.362	2.942e4	35.550	
2	15.193	VV	0.385	1.186e4	14.336	
3	16.117	VV	0.387	1.101e4	13.305	
4	16.799	VBA	0.446	3.046e4	36.809	

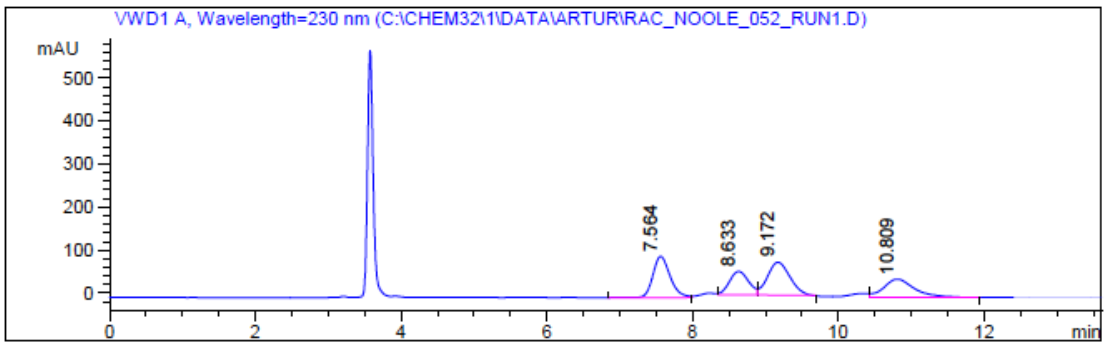
3o



Signaal 1 VWD1 A, Wavelength=230 nm

Piigi nr	RT [min]	Tüüp	Laius [min]	Pindala	Pindala %	Nimi
1	13.745	VV	0.393	1975.905	6.456	
2	16.362	VB	0.425	2.863e4	93.544	

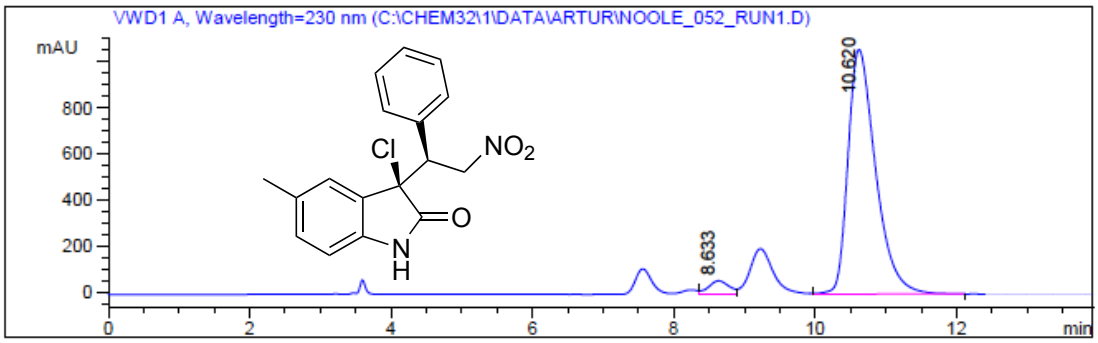
rac 3p



Signaal 1 VWD1 A, Wavelength=230 nm

Piigi nr	RT [min]	Tüüp	Laius [min]	Pindala	Pindala %	Nimi
1	7.564	BV	0.254	1580.974	28.955	
2	8.633	MF	0.305	994.484	18.214	
3	9.172	FM	0.355	1626.193	29.783	
4	10.809	VB	0.440	1258.437	23.048	

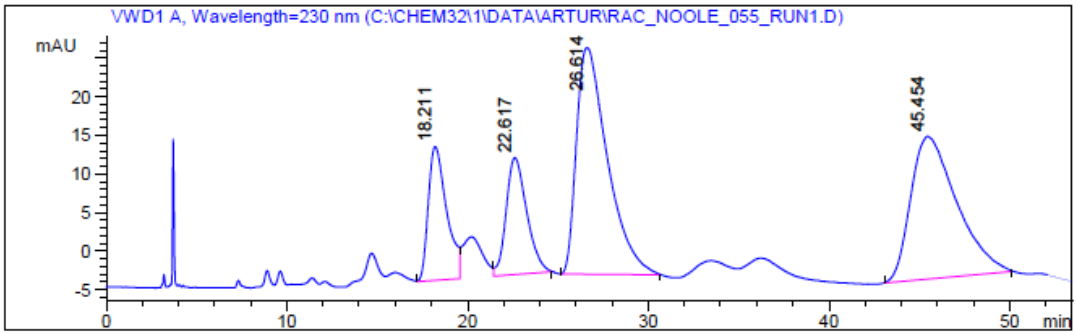
3p



Signaal 1 VWD1 A, Wavelength=230 nm

Piigi nr	RT [min]	Tüüp	Laius [min]	Pindala	Pindala %	Nimi
1	8.633	VV	0.306	1188.079	3.949	
2	10.620	VB	0.414	2.890e4	96.051	

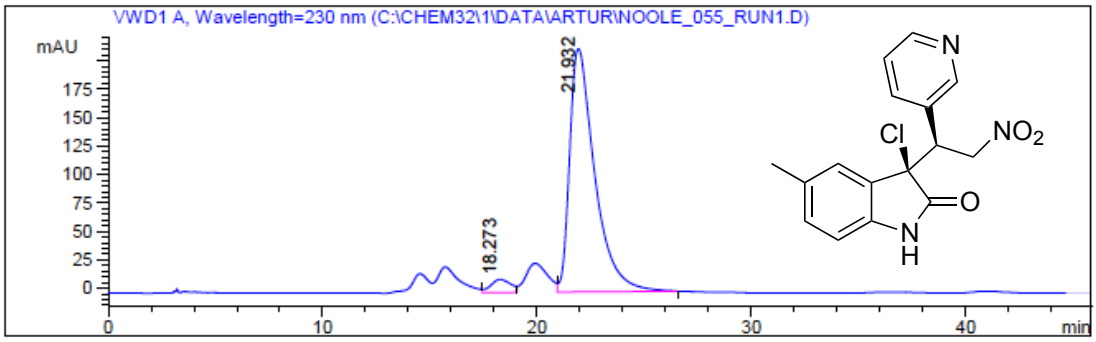
rac 3r



Signaal 1 VWD1 A, Wavelength=230 nm

Piigi nr	RT [min]	Tüüp	Laius [min]	Pindala	Pindala %	Nimi
1	18.211	BV	1.050	1224.820	13.317	
2	22.617	VB	1.162	1198.934	13.036	
3	26.614	BB	1.659	3506.743	38.128	
4	45.454	BB	2.154	3266.812	35.519	

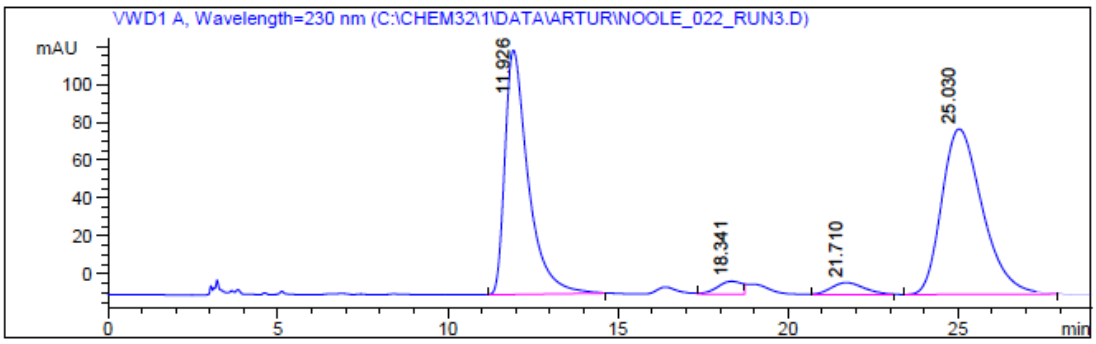
3r



Signaal 1 VWD1 A, Wavelength=230 nm

Piigi nr	RT [min]	Tüüp	Laius [min]	Pindala	Pindala %	Nimi
1	18.273	VV	0.966	743.870	4.097	
2	21.932	VB	1.186	1.741e4	95.903	

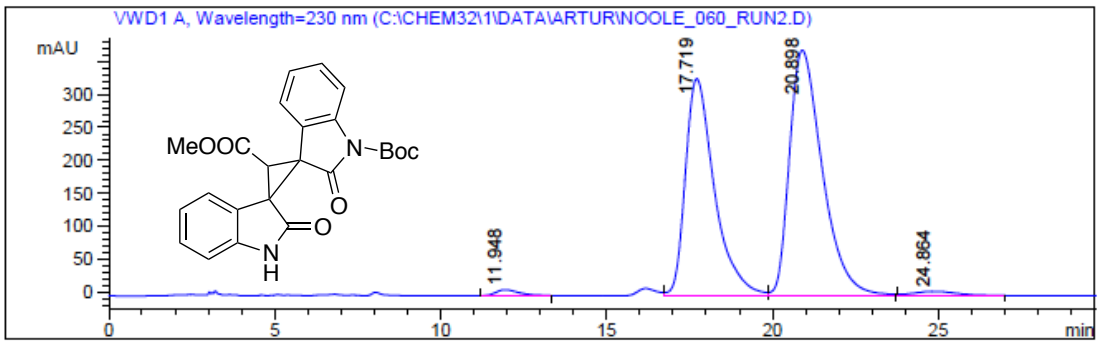
***ent*-12a**



Signaal 1 VWD1 A, Wavelength=230 nm

Piigi nr	RT [min]	Tüüp	Laius [min]	Pindala	Pindala %	Nimi
1	11.926	BB	0.709	6154.739	43.383	
2	18.341	MF	0.832	338.693	2.387	
3	21.710	MM	1.138	429.360	3.026	
4	25.030	VB	1.258	7264.125	51.203	

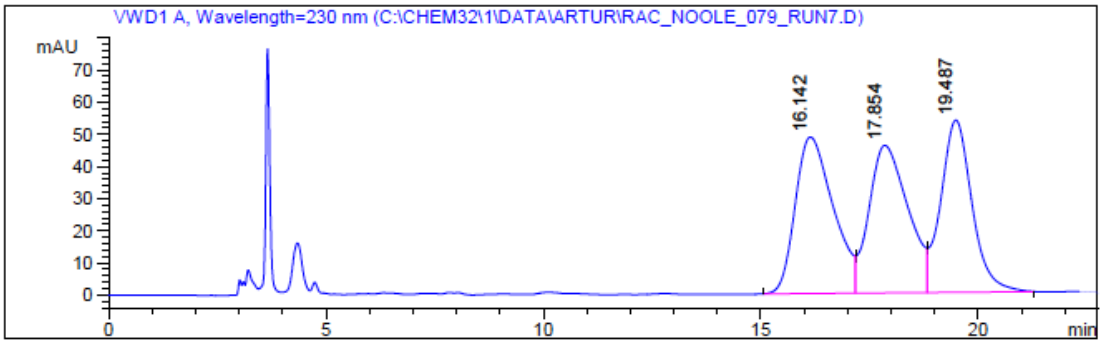
12a



Signaal 1 VWD1 A, Wavelength=230 nm

Piigi nr	RT [min]	Tüüp	Laius [min]	Pindala	Pindala %	Nimi
1	11.948	BB	0.719	430.246	0.917	
2	17.719	VV	0.924	2.014e4	42.941	
3	20.898	VB	1.056	2.574e4	54.886	
4	24.864	BB	1.234	589.110	1.256	

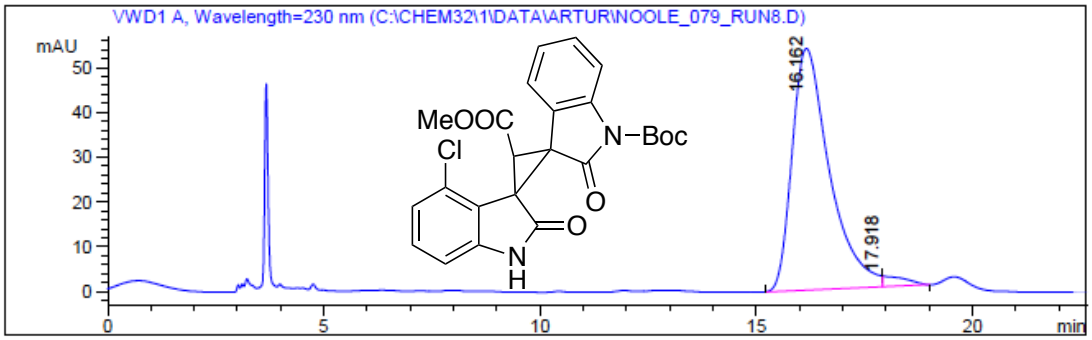
rac 12b



Signaal 1 VWD1 A, Wavelength=230 nm

Piigi nr	RT [min]	Tüüp	Laius [min]	Pindala	Pindala %	Nimi
1	16.142	BV	0.922	2958.678	34.720	
2	17.854	VV	0.939	2873.118	33.716	
3	19.487	VB	0.758	2689.834	31.565	

12b



Signaal 1 VWD1 A, Wavelength=230 nm

Piigi nr	RT [min]	Tüüp	Laius [min]	Pindala	Pindala %	Nimi
1	16.162	MF	1.003	3243.150	97.473	
2	17.918	FM	0.584	84.071	2.527	