SUPPORTING INFORMATION

Chiral 2-Aminobenzimidazoles in deep eutectic mixtures: recyclable organocatalysts for the enantioselective Michael addition of 1,3-dicarbonyl compounds to β-nitroalkenes

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Total No. of Pages: 41 (Pages S1-S41).

Total No. of Figures: 17 (Figures S1-S17).

Total No. of Schemes: 6 (Schemes S1-S6).

Total No. of Tables: 2 (Table S1-S2).

References: 6 (Ref S1-S6).

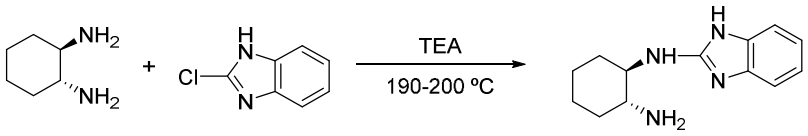
INDEX

1. General

Unless otherwise noted, all commercial reagents and solvents were used without further purification. Reactions under argon atmosphere were carried out in oven-dried glassware sealed with a rubber septum using anhydrous solvents. Melting points were determined with a hot plate apparatus and are uncorrected. ^{1}HNMR (300 or 400 MHz) and ^{13}CNMR (75 or 101 MHz) spectra were obtained on a Bruker AC-300 or AC-400, using $CDCl_3$ as solvent and TMS (0.003%) as reference, unless otherwise stated. Chemical shifts (δ) are reported in ppm values relative to TMS and coupling constants (*J*) in Hz. Low-resolution mass spectra (MS) were recorded in the electron impact mode (EI, 70 eV, He as carrier phase) using an Agilent 5973 Network Mass Selective Detector spectrometer, being the samples introduced through a GC chromatograph Agilent 6890N equipped with a HP-5MS column [(5%-phenyl)-methylpolysiloxane; length 30 m; ID 0.25 mm; film 0.25 mm]. IR spectra were obtained using a JASCO FT/IR 4100 spectrophotometer equipped with an ATR component; wavenumbers are given in cm^{-1}. Analytical TLC was performed on Merck aluminium sheets with silica gel 60 F254. Analytical TLC was visualized with UV light at 254 nm Silica gel 60 (0.04-0.06 mm) was employed for flash chromatography whereas P/UV254 silica gel with CaSO4 (28-32%) supported on glass plates was employed for preparative TLC. Chiral HPLC analyses were performed on an Agilent 1100 Series (Quat Pump G1311A, DAD G1315B detector and automatic injector) equipped with chiral columns using mixtures of hexane/isopropanol as mobile phase, at 25 ºC.

2. Synthesis and spectroscopic data of chiral organocatalysts

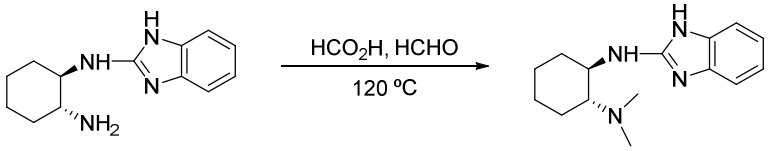
*(1R,2R)-N^1-(1H-benzo[d]imidazol-2-yl)cyclohexane-1,2-diamine (**4**)*



Scheme S1. Synthesis of chiral organocatalyst **4**.

A mixture of 2-chloro-1*H*-benzo[*d*]imidazole (233 mg, 1.53 mmol, 1 equiv), (1*R*,2*R*)-cyclohexane-1,2-diamine (698 mg, 6.12 mmol, 4 equiv), and TEA (213 μL, 1.53 mmol, 1 equiv) was heated at 190-200 ºC during 16 h in a sealed pressure tube. Then, the reaction mixture was allowed to reach ~50 °C, and water (20 mL) was added. The obtained mixture was quickly extracted with CH_2Cl_2 (3 × 20 mL) before the temperature of the reaction reached rt in order to avoid solubility problems. The collected organic phases were dried over $MgSO_4$. After filtration, the organic solvents were evaporated under reduced pressure to give a crude mixture, which was purified by precipitation in CH_2Cl_2 to obtain **7a** (229 mg, 65%) as a pale yellow solid: mp 235-240 °C (CH_2Cl_2); IR 2929, 2855, 1700, 1644, 1606, 1580, 1468, 1270, 1116, 1030; δ_H (300 MHz, CD_3OD) 1.19-1.49 (m, 4H, 2×CH_2), 1.74-1.77 (m, 2H, CH_2), 1.98-2.11 (m, 2H, CH_2), 2.50-2.58 (m, 1H, CH, C*H*NH_2), 3.34-3.40 (m, 1H, C*H*NH), 6.93-6.97 (m, 2H, ArH), 7.15-7.18 (m, 2H, ArH); *m/z* 230 [M^+, 10%], 160 (24), 134 (100), 133 (59), 97 (28).

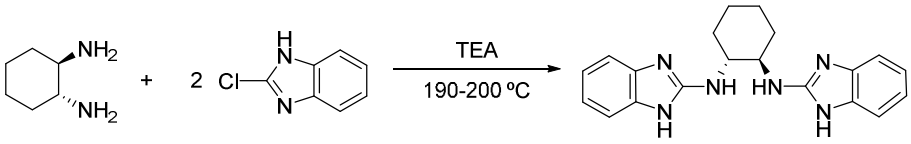
*(1R,2R)-N^1-(1H-benzo[d]imidazol-2-yl)-N^2,N^2-dimethylcyclohexane-1,2-diamine (**1**)*



Scheme S2. Synthesis of chiral organocatalyst **1**.

A mixture of **4** (168 mg, 0.73 mmol, 1 equiv), 80% HCO_2H (3.5 mL), and a 36% aqueous solution of HCHO (127 μL, 1.61 mmol, 2.2 equiv) was stirred at 120 °C for 16 h. Then, the solvent was removed under reduced pressure. Saturated $NaHCO_3$ solution (15 mL) and 10% NaOH solution (until pH 8) were added in this order, and the resulting mixture was extracted with CH_2Cl_2 (3×15 mL). The organic phases were dried over $MgSO_4$. After filtration, the organic solvent was evaporated under reduced pressure to give a crude mixture, which was purified by precipitation in CH_3CN to afford pure **1** (87 mg, 46%) as a white solid; mp 248-250 °C (CH_3CN); IR 2923, 2856, 2818, 2775, 1700, 1633, 1576, 1499, 1461, 1375, 1265, 1064; δ_H (300 MHz, $CDCl_3$) 1.09-1.42 (m, 4H, 2×CH_2), 1.65-1.70 (m, 1H, CH), 1.82-1.87 (m, 2H, CH_2), 2.22 (s, 6H, CH_3), 2.33 (td, *J* = 10.9, 3.2 Hz, 1H, C*H*CNMe_2), 2.65-2.69 (m, 1H, CH), 3.44 (td, *J* = 10.4, 4.0 Hz, 1H, C*H*NH), 5.46 (br. s, 1H, NH), 6.91-6.96 (m, 2H, ArH), 7.14-7.20 (m, 2H, ArH); *m/z* 258 [M^+, 1.5%], 133 (30), 125 (100), 84 (20).

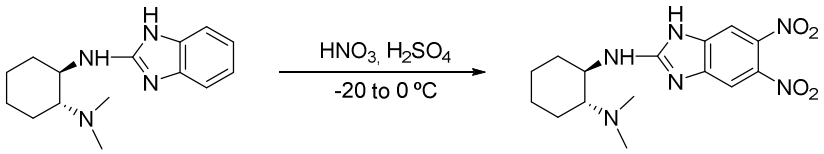
*(1R,2R)-N^1,N^2-bis(1H-benzo[d]imidazol-2-yl)cyclohexane-1,2-diamine (**2**)*



Scheme S3. Synthesis of chiral organocatalyst **2**.

2-chloro-1*H*-benzo[*d*]imidazole (2.064 g, 13.56 mmol) was added to (1*R*,2*R*)-cyclohexane-1,2-diamine (773.9 mg, 6.78 mmol) and the resulting mixture was stirred at 195-200 ºC for 20 h. After this time, the reaction mixture was allowed to reach 50 ºC and water (40 mL) was added. Then, the reaction was basified until pH 8 with a saturated aqueous solution of $NaHCO_3$ and the obtained mixture was extracted with CH_2Cl_2 (5×50 mL). The combined organic phases were dried over $MgSO_4$. After filtration, the organic solvent was evaporated under reduced pressure to give the corresponding crude product which was purified by flash chromatography (EtOAc/MeOH) to give pure **2** as a white solid (1.87 g, 40% yield); mp 193-196 ºC (Et_2O); IR 2944, 2916, 2847, 1630, 1603, 1580, 1461,1410, 1259, 1112, 1047; δ_H (300 MHz, CD_3OD,) 1.35-1.47 (m, 4H, 2×CH_2), 1.76 (br. s, 2H, CH_2), 2.18-2.23 (m, 2H, CH_2), 3.71-3.74 (m, 2H, 2×C*H*NH), 6.9-6.95 (m, 4H, ArH), 7.11-7.15 (m, 4H, ArH); *m/z* 346 [M^+, 33%], 214 (64), 213 (100), 212 (36), 184 (16), 173 (19), 172 (15), 170 (10), 160 (14), 159 (21), 158 (11), 146 (11), 145 (16), 134 (32), 133 (37), 132 (16).

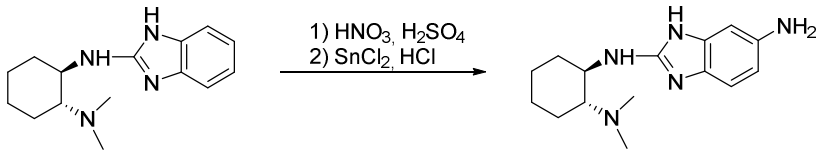
*(1R,2R)-N^1-(5,6-dinitro-1H-benzo[d]imidazol-2-yl)-N^2,N^2-dimethylcyclohexane-1,2-diamine (**5**)*



Scheme S4. Synthesis of chiral organocatalyst **5**.

Catalyst **1** (50 mg, 0,2 mmol, 1 equiv.) was dissolved in concentrated H_2SO_4 (0,2 mL, 98%) and stirred vigorously during 5 minutes; after this time concentrated HNO_3 (0,4 mL, 65%) was carefully added to the mixture at -20 ºC. Then, the reaction was stirred at room temperature during 16 hours. After this period, the mixture was treated with cold water and basified until pH 8 with a 25% aqueous solution of NH_3. Finally, the aqueous phase was extracted with AcOEt (3×20 mL). The collected organic phases were dried over anhydrous $MgSO_4$. After filtration, the organic solvent was removed under reduced pressure to give catalyst **5** without further purification as a red solid (74% yield, 52 mg, 0,15 mmol) ; mp 110-115 ºC (CH_2Cl_2, decompose); δ_H (300 MHz, $CDCl_3$) 1.19-1.49 (m, 4H, 2×CH_2), 1.63-1.98 (m, 4H, 2×CH_2), 2.37 (s, 6H, 2×Me), 2.51 (m, 1H, C*H*NMe_2), 3.66 (bs, 1H, C*H*NH),7.49 (s, 2H, ArH); δ_C (75 MHz, $CDCl_3$) 21.7, 24.4, 24.6, 33.2, 39.8, 53.8, 67.8, 108.3, 136.8, 142.0, 161.8; *m/z* 348 [M^+, <1%] 128 (10), 126 (11), 125 (100), 124 (25), 84 (64), 71 (24), 58 (20), 44 (10); HRMS calcd. for $C_{13}H_{13}N_5O_4$ [M^+-$NHMe_2$] 303.0968, found 303.0964.

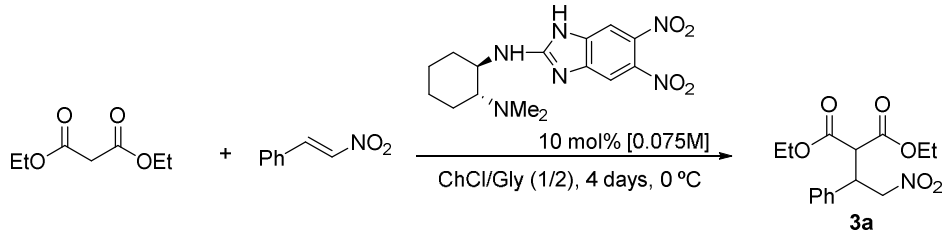
*N^2-((1R,2R)-2-(dimethylamino)cyclohexyl)-1H-benzo[d]imidazole-2,6-diamine (**6**)*



Scheme S5. Synthesis of chiral organocatalyst **6**.

Catalyst **1** (50 mg, 0,2 mmol, 1 equiv.) was dissolved in concentrated H_2SO_4 (0,2 mL, 98%) and stirred vigorously for 5 minutes; after this time, concentrated HNO_3 (0,4 mL, 65%) was added to the mixture carefully at -20 °C. The reaction was then stirred at 0 °C for 5 minutes. After this period, the mixture was treated with cold water (15 mL) and basified until pH 8 with 25% aqueous solution of NH_3 (25%). The aqueous phase was extracted with AcOEt (3×20 mL) and the collected organic phases were dried over anhydrous $MgSO_4$. After filtration, the organic solvent was evaporated under reduced pressure to give a yellow oil. The yellow solid (71% yield, 43 mg, 0,14 mmol 1 equiv) was introduced in a round bottom flask with $SnCl_2$ (95 mg, 0,5 mmol, 3,5 equiv.) and then a concentrated HCl solution (40 µL, 12 M) was added. The resulting mixture was stirred for 4 hours. After this time, the reaction was quenched with cold water (mL)and the solution was basified until pH=8 with NaOH (6M). The aqueous phase was extracted with AcOEt (3×20 mL) and the collected organic phases were dried over anhydrous $MgSO_4$. After filtration, the solvent was evaporated under reduced pressure to give catalyst **6** as a white solid (yield, mg, mmol); δ_H (300 MHz, $CDCl_3$) 1.27-0.93 (m, 4H, 2×CH_2), 1.62-1.38 (m, 1H, CH), 1.84-1.62 (m, 2H, CH_2), 2.17 (s, 6H, 2×Me), 2.41-2.20 (m, 1H, CH), 2.69-2.48 (m, *J* = 10.4 Hz, 1H, $CHNMe_2$), 3.48 (td, *J* = 10.5, 3.9 Hz, 1H, C*H*CNH), 5.60 (br. s, 1H, NH), 6.37 (dd, *J* = 8.2, 2.1 Hz, 1H, ArH), 6.54 (d, *J* = 1.9 Hz, 1H, ArH), 7.00 (d, *J* = 8.2 Hz, 1H, ArH); δ_C (75 MHz, $CDCl_3$) 21.3, 24.3, 25.1, 29.6, 33.2, 39.7, 53.6, 66.9, 99.6, 108.8, 112.5, 131.7, 138.8, 140.2, 155.3; *m/z* 274 (M^++1, 4%), 273 (M^+, 19), 228 (32), 227 (10), 215 (11), 201 (13), 189 (11), 188 (18), 173 (11), 149 (28), 148 (62), 147(15), 126 (21), 125 (100),124 (34), 97 (12), 84 (23), 71 (20), 70 (13), 58 (13), 57 (11), 44 (30), 43 (48), 42 (11), 41 (11); HRMS calcd. for $C_{15}H_{23}N_5$ (M^+): 273.1953; found: 273.1936.

3. Experimental Procedure for the Conjugate Addition of Diethyl Malonate to β-Nitrostyrene Catalyzed by 5. Synthesis of 3a and recycling experiment



Scheme S6. Model reaction for the synthesis of the compound **3a**.

Catalyst **5** (5.22 mg, 0.015 mmol, 10 mol%) and β-nitrostyrene (22.4 mg, 0.15 mmol) were dissolved in a mixture of ChCl/Gly (1/2 molar ratio, 0.2 mL) and kept under stirring for 10 minutes at rt. Then, the mixture was cooled-down to 0 ºC and

diethyl malonate (50 μL, 0.30 mmol) was added. The reaction was vigorously stirred during 4 days at 0 ºC. After this period, water (3 mL) was added to the mixture and the reaction product was extracted with EtOAc (3×5 mL). The collected organic phases were dried over anhydrous $MgSO_4$ and, after filtration, the solvent was evaporated under reduced pressure to give crude **3a**. Purification by flash column chromatography on silica gel (hexane/EtOAc: 4/1) afforded pure **3a** (38.2 mg, 83% yield). δ_H (300 MHz, $CDCl_3$) 1.04, 1.26 (2t, J = 7.1, 6H), 3.82 (d, J = 9.4 Hz, 1H), 4.00 (q, J = 7.1 Hz, 2H), 4.18-4.28 (m, 3H), 4.86 (dd, J = 13.1, 9.0 Hz, 1H), 4.93 (dd, J = 13.1, 5.2 Hz, 1H), 7.22-7.37 (m, 5H); m/z 263,[M^+ - NO_2, 25%], 189 (100), 171 (44), 161 (43), 115 (54), 104 (26), 103 (28), 102 (26), 91 (29), 76 (37). The enantiomeric excess of **3a** was determined by chiral HPLC analysis (Chiralpack AD, hexane/*i*PrOH: 90/10, 1 mL/min).

Recycling experiment

A mixture of catalyst **5** (5.22 mg, 0.015 mmol) and β-nitrostyrene (22.4 mg, 0.15 mmol) in ChCl/Gly (1/2 molar ratio, 0.2 mL) was stirred for 10 minutes at rt. Then, the mixture was cooled-down to 0 ºC and diethyl malonate (50 μL, 0.30 mmol) was added. The reaction was vigorously stirred for 4 days at 0 ºC. After this period, the corresponding organic solvent was added (3 mL) and the mixture was stirred for 10 minutes at rt. The stirring was stopped to allow phase separation and the upper organic layer was removed. This extractive procedure was repeated two more times and the combined organic extracts were washed with water (3×5 mL), dried ($MgSO_4$), filtered, and evaporated under reduced pressure to afford the reaction product The residual volatile organic solvent present in the DES/catalyst phase was removed under vacuum evaporation. Then, the next reaction cycle was performed with the obtained DES/**5** mixture, adding fresh β-nitroestyrene and diethyl malonate. This reaction mixture was subjected again to the above-described procedure and further reaction cycles were repeated using the recycled deep eutectic solvent phase. In order to check if any of the organocatalyst was extracted together with the obtained products, the aqueous layer coming for the organic layer washings, was basified until pH 10 and extracted with 3 portions of EtOAc (5 mL). The organic layer was dried ($MgSO_4$), filtered, and evaporated under reduced pressure to give the above spectra in which the presence of organocatalyst is indicated by a green arrow.

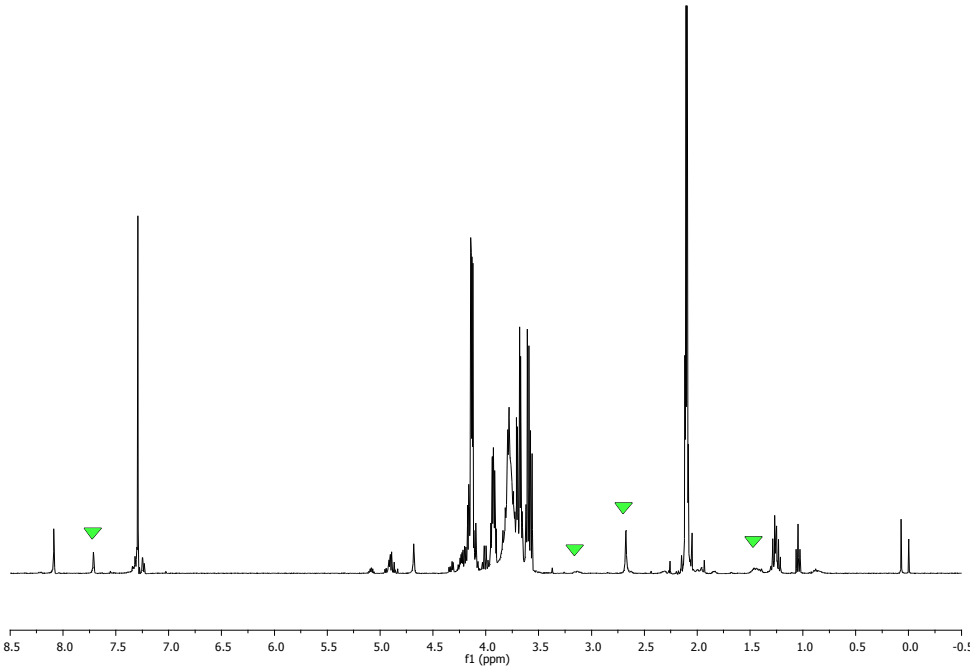
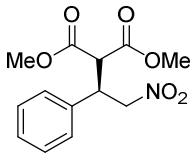


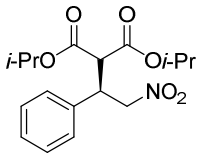
Figure S1. ^{1}H-NMR experiment (300 MHz, $CDCl_3$) of the organic waste extracted from the aqueous washing of DES.

4. Physical and spectroscopic data for compounds 3



*Dimethyl (R)-2-(2-nitro-1-phenylethyl)malonate (**3b**).*[3]

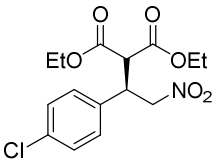
Yield 88%, white solid; mp 58-61 ºC; δ_H (400 MHz, $CDCl_3$) 3.57, 3.78 (2s, 6H, 2×CH_3), 3.88 [d, J = 9.1 Hz, 1H, $CH(CO_2Me)_2$], 4.26 (td, J = 9.0, 5.2 Hz, 1H, C*H*CH_2), 4.89 (dd, J = 13.2, 8.9 Hz, 1H, CH*H*NO_2), 4.95 (dd, J = 13.2, 5.2 Hz, 1H, C*H*HNO_2), 7.20-7.37 (m, 5H, ArH); *m/z* 281 [M^+, <1%], 176 (12), 175 (100), 171 (26), 116 (10), 115 (38), 104 (19), 103 (11), 91 (10).



*(R)-Diisopropyl 2-(2-nitro-1-phenylethyl)malonate (**3c**).*[3]

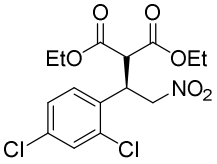
Yield 63%, white solid; mp 53-55 ºC; δ_H (300 MHz, $CDCl_3$) 1.01, 1.07 (2d, J = 6.3 Hz, 6H, 2×CH_3), 1.25 (d, J = 6.2 Hz, 6H, 2×CH_3), 3.76 [d, J = 9.6 Hz, 1H, C*H*$(CO_2i\text{-Pr})_2$], 4.21 (td, J = 9.4, 4.8 Hz, 1H, C*H*CH_2), 4.79-4.87 [m, 2H, C*H*$(CH_3)_2$, C*H*HNO_2], 4.92

(dd, J = 12.9, 4.8 Hz, 1H, CH*H*NO_2), 5.09 [sept, J = 6.3 Hz, 1H, C*H*$(CH_3)_2$], 7.23-7.34 (m, 5H, ArH); *m/z* 338 [M^+ +1, <1%], 291 (10), 218 (29), 207 (100), 205 (39), 203(43), 171 (26), 163 (63), 161 (98), 145 (30), 131 (29), 117 (24), 105 (28), 104 (25), 103 (32), 77 (27).



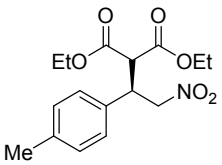
*(R)-Diethyl 2-[1-(4-chlorophenyl)-2-nitroethyl]malonate (**3d**).*[4]

Yield 84%, colourless oil; δ_H (300 MHz, $CDCl_3$) 1.08, 1.26 (2t, J = 7.1, 6H, 2×CH_3), 3.78 [d, J = 9.3 Hz, 1H, C*H*$(CO_2Et)_2$], 4.03 (q, J = 7.1 Hz, 2H, C*H*$_2CH_3$), 4.17-4.29 (m, 3H, C*H*CH_2, C*H*$_2CH_3$), 4.83 (dd, J = 13.2, 9.2 Hz, 1H, C*H*HNO_2), 4.91 (dd, J = 13.2, 4.9 Hz, 1H, CH*H*NO_2), 7.18-7.21, 7.27-7.32 (2m, 4H, 4×ArH); m/z 343 [M^+, <1%], 297 (16), 281 (13), 252 (11), 235 (10), 225 (28), 197 (14), 195 (36), 179 (18), 167 (12), 165 (21), 151 (11), 150 (11), 149 (10), 144 (10), 140 (13), 139 (15), 138 (34), 136 (11), 116 (14), 115 (32), 103 (14), 102 (12), 77 (12).



*(R)-Diethyl 2-[1-(2,4-dichlorophenyl]-2-nitroethyl)malonate (**3e**).*[1]

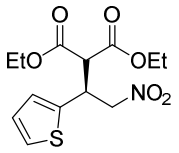
Yield 86%, colourless oil; δ_H (300 MHz, $CDCl_3$) 1.15, 1.25 (2t, J = 7.1, 6H, 2×CH_3), 4.04 [d, J = 8.7 Hz, 1H, C*H*$(CO_2Et)_2$], 4.10 (q, J = 7.1 Hz, 2H, C*H*$_2CH_3$), 4.15-4.27 (m, 2H, C*H*$_2CH_3$), 4.69 (td, J = 8.6, 4.3 Hz, 1H, C*H*CH_2), 4.92 (dd, J = 13.6, 4.3 Hz, 1H, C*H*HNO_2), 5.09 (dd, J = 13.6, 8.6 Hz, 1H, CH*H*NO_2), 7.21-7.23 (m, 2H, 2×ArH), 7.43-7.44 (m, 1H, ArH); *m/z* 377 [M^+, <1%], 344 (38), 343 (20), 342 (94), 333 (12), 331 (18), 286 (11), 285 (16), 281 (14), 273 (13), 272 (10), 271 (18), 261 (14), 259 (62), 258 (14), 257 (100), 253 (28), 244 (12), 242 (17), 241 (44), 239 (60), 234 (16), 231 (42), 229 (59), 217 (12), 215 (13), 213 (20), 209 (20), 201 (24), 199 (16), 186 (11), 185 (20), 184 (12), 183 (29), 174 (32), 173 (26), 172 (54) 171 (17), 161 (12), 159 (17), 151 (14), 150 (18), 149 (27), 137 (19), 136 (15), 135 (13), 115 (43), 102 (13), 101 (12).



*(R)-Diethyl 2-(2-nitro-1-p-tolylethyl)malonate (**3f**).*[3]

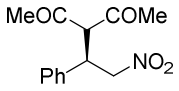
Yield 87%, colourless oil; δ_H (300 MHz, $CDCl_3$) 1.07 (t, J = 7.1, 3H, C*H*$_3CH_2$), 1.26 (t, J = 7.1, 3H, C*H*$_3CH_2$), 2.30 (s, 3H, CH_3Ar), 3.80 [d, J = 9.4 Hz, 1H, C*H*$(CO_2Et)_2$], 4.02 (q, J = 7.1 Hz, 2H, C*H*$_2CH_3$), 4.15-4.28 (m, 3H, C*H*CH_2, C*H*$_2CH_3$), 4.83 (dd, J = 13.0, 9.0 Hz, 1H, C*H*HNO_2), 4.90 (dd, J = 13.0, 5.1 Hz, 1H, CH*H*NO_2), 7.11 (s, 4H, ArH); *m/z* 323 [M^+, <1%], 277 (11), 232 (12), 215 (11), 204 (17), 203 (100), 185 (36), 175

(39), 159 (18), 145 (15), 131 (11), 130 (12), 129 (21), 118 (28), 117 (28), 116 (13), 115 (26), 91 (16).



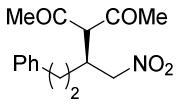
*(S)-Diethyl 2-[2-nitro-1-(thiophen-2-yl)ethyl]malonate (**3g**).*[4]

Yield 85%, yellow oil; δ_H (300 MHz, $CDCl_3$) 1.16, 1.27 (2t, J = 7.1, 6H, 2×CH_3), 3.87 [d, J = 8.1 Hz, 1H, C*H*(CO_2Et)$_2$], 4.12 (q, J = 7.1 Hz, 2H, C$H_2$$CH_3$), 4.17-4.28 (m, 2H, C$H_2$$CH_3$), 4.56 (td, J = 8.0, 5.6 Hz, 1H, C*H*CH_2), 4.89 (dd, J = 11.5, 6.1Hz, 1H, C*H*HNO_2), 4.95 (dd, J = 11.5, 3.7 Hz, 1H, C*H*HNO_2), 6.93 (dd, J = 5.0, 3.6 Hz, 1H, ArH), 6.96 (dd, J = 3.5, 0.9 Hz, 1H, ArH), 7.23 (dd, J = 5.0, 1.3 Hz, 1H, ArH); *m/z* 315 [M^+, <1%], 269 (11), 268 (20), 196 (12), 195 (100), 177 (23), 167 (41), 137 (10), 110 (30), 109 (11).



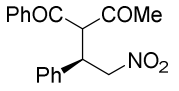
*(R)-3-(2-Nitro-1-phenylethyl)pentane-2,4-dione (**3h**).*[3]

Yield 88%, white solid; mp 124-126 ºC; δ_H (300 MHz, $CDCl_3$) 1.93, 2.28 (2s, 6H, 2×CH_3), 4.20-4.28 (m, 1H, C*H*CH_2), 4.38 [d, J = 10.8 Hz, 1H, C*H*($COMe$)$_2$], 4.17-4.28 (m, 2H, C$H_2$$CH_3$), 4.61 (dd, J = 12.5, 5.0 Hz, 1H, C*H*HNO_2), 4.66 (dd, J = 12.5, 7.5 Hz, 1H, CH*H*NO_2), 7.17-7.22 (m, 2H, ArH), 7.29-7.37 (m, 3H, ArH); *m/z* 203 [M^+ -NO_2 , 3%], 162 (11), 161 (80), 160 (27), 159 (100), 158 (14), 147 (12), 145 (28), 143 (21), 131 (18), 129 (11), 128 (17), 117 (22), 115 (32), 204 (18), 103 (22), 78 (10) , 77 (18).



*(S)-3-(1-Nitro-4-phenylbutan-2-yl)pentane-2,4-dione (**3i**).*[1]

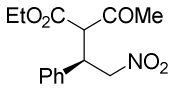
Yield 46%,white solid; mp 40-42 ºC; δ_H (400 MHz, $CDCl_3$) 1.56-1.65, 1.71-1.84 (2m, 2H, $PhCH_2$CH_2), 2.15, 2.22 (2s, 6H, 2×CH_3), 2.56-2.63, 2.78-2.87 (2m, 3H, C*H*CH_2, PhCH_2), 3.98 [d, J = 8.4 Hz, 1H, C*H*($COMe$)$_2$], 4.54 (dd, J =S15 12.6, 5.1 Hz, 1H, CH*H*NO_2), 4.59 (dd, J = 12.6, 4.6 Hz, 1H, C*H*HNO_2), 7.14 (d, J = 6.9 Hz, 1H, ArH), 7.20-7.23 (m, 1H, ArH), 7.26-7.32 (m, 2H, ArH); *m/z* 263 [M^+, >1%], 216 (16), 169 (17), 143 (10), 131 (23), 130 (31), 129 (32), 125 (10), 105 (15), 104 (22), 91 (100), 84 (13), 83 (11), 65 (15).



*2-[(R)-2-Nitro-1-phenylethyl]-1-phenylbutane-1,3-dione (**3j**).*[5]

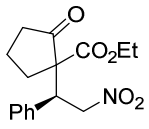
Yield 96%, white solid, mp 132-134 ºC; δ_H (400 MHz, $CDCl_3$) (1.02:1 mixture of diastereomers) 1.93 (s, 3H, CH_3), 4.49-4.57 (m, 1H, CHPh), 4.63-4.76 (m, 2H,

C$H_2$$NO_2$), 5.17 (d, *J* = 9.9 Hz, 1H, C*H*CO), 7.25-7.35 (m, 5H, ArH), 7.46-7.50 (m, 2H, ArH), 7.51- 7.54 (m, 1H, ArH), 7.81 (m, 2H, ArH); *m/z* 265 [M^+ -NO_2, 2%], 223 (24), 221 (15), 207 (30), 117 (10), 105 (100), 103 (10), 77 (34).



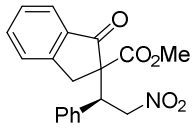
*(3R)-Ethyl 2-acetyl-4-nitro-3-phenylbutanoate (**3k**).*[3]

Yield 85%, colourless oil; δ_H (300 MHz, $CDCl_3$) 0.99 (t, *J* = 7.1 Hz, 2.4H, C$H_3$$CH_2$), 1.28 (t, *J* = 7.1 Hz, 3H, C$H_3$$CH_2$), 2.05 (s, 2.6H, C$H_3$CO), 2.30 (s, 3H, C$H_3$CO), 3.96 (q, *J* = 7.1 Hz, 2H, C$H_2$$CH_3$), 4.02 (d, *J* = 9.7 Hz, 0.85H, C*H*CO), 4.11 (d, *J* = 9.9 Hz, 1H, C*H*CO) 4.17-4.26 (m, 3.5H, C$H_2$$CH_3$, C*H*$CH_2$, C*H*$CH_2$), 4.71-4.78 (m, 2H, C$H_2$$NO_2$), 4.81 (dd, *J* = 12.9, 8.6 Hz, 0.85H, C*H*HNO_2), 4.85 (dd, *J* = 12.9, 5.1 Hz, 0.85H, CH*H*NO_2), 7.19-7.34 (m, 9.25H, ArH); *m/z* 233 [M^+-NO_2, 2%], 192 (11), 191 (90), 190 (29), 189 (100), 161 (24), (159 (70), 146 (11), 145 (95), 144 (27), 131 (37), 118 (10), 117 (31), 116 (16), 115 (51), 105 (15), 104 (30), 103 (29), 91 (34), 78 (11), 77 (22), 51 (10).



*Ethyl 1-[(S)-2-nitro-1-phenylethyl]-2-oxocyclopentanecarboxylate (**3l**).*[6]

Yield 66%, colourless oil; δ_H (400 MHz, $CDCl_3$) 1.27 (t, *J* = 7.2 Hz, 3.5H, CH_3), 1.75-2.07 (m, 4.5H, $CH_2CH_2CH_2C$=O), 2.26-2.47 (m, 2.4H, CH_2C=O), 4.08 (dd, *J* = 10.8, 4.0 Hz, 1H, C*H*Ph), 4.15-4.28 (m, 2.5H, C*H*Ph, C$H_2$$CH_3$), 4.83 (dd, *J* = 13.5, 3.4 Hz, 0.16H, C*H*HNO_2), 5.01 (dd, *J* = 13.6, 10.8 Hz, 1H, C*H*HNO_2), 5.18 (dd, *J* = 13.6, 4.0 Hz, 1H, CH*H*NO_2), 5.29 (dd, *J* = 13.5, 11.1 Hz, 0.15H, CH*H*NO_2), 7.18-7.33 (m, 5.8H, ArH); 259 [M^+-NO_2, 1%], 230 (25), 229 (42), 213 (22), 211 (30), 207 (43), 202 (25), 201 (18), 185 (55), 184 (59), 183 (58), 182 (18), 171 (22), 170 (21), 169 (20), 167 (21), 159 (12), 158 (53), 157 (53), 156 (17), 155 (55), 154 (13), 143 (75), 142 (31), 141 (55), 131 (14), 130 (28), 129 (100), 128 (70), 127 (33), 115 (79), 105 (23), 104 (79), 103 (47), 102 (12), 91 (66), 78 (31), 77 (40), 55 (36).



*Ethyl 1-[(S)-2-nitro-1-phenylethyl]-2-oxocyclopentanecarboxylate (**3m**).*[4]

Yield 52%, yellow oil; δ_H (400 MHz, $CDCl_3$) 3.18 (d, *J* = 17.7 Hz, 2H×CH_2), 3.22 (d, *J* = 17.7 Hz, 1H×CH_2C), 3.49 (d, *J* = 17.4 Hz, 2H×CH_2C), 3.64 (d, *J* = 17.4, 1H×CH_2C), 3.70 (s, 6H, CH_3), 3.74 (s, 3H, CH_3), 4.22 (dd, *J* = 11.0, 3.4 Hz, 1H, CHPh), 4.48 (dd, *J* = 11.3, 3.4 Hz, 2H, CHPh), 5.07 (dd, *J* = 13.4, 3.5 Hz, 2H, CH*H*NO_2), 5.17-5.23 (m, 3H, 1×CH*H*NO_2, 2×C*H*HNO_2), 5.43 (dd, *J* = 13.6, 3.5 Hz, 1H, C*H*HNO_2), 7.11-7.15 (m, 9H, ArH), 7.18-7.26 (m, 6H, ArH), 7.32-7.39 (m, 5H, ArH), 7.47-7,49 (m, 1H, ArH) 7.49-7.52 (m, 2H, ArH), 7.53 7.60 (m, 1H, ArH), 7.67 (d, *J* = 7.7 Hz, 1H, ArH), 7.76 (d, *J* = 7.7 Hz, 2H, ArH); *m/z* 293 [M^+-NO_2, >1%], 261 (16), 233 (38), 232 (23),

231 (20), 215 (28), 207 (11), 105 (17), 203 (16), 202 (15), 191 (14), 190 (28), 189 (100), 161 (16), 158 (11), 157 (72), 131 (10), 130 (20), 104 (32), 103 (18), 102 (14), 101 (11), 91 (23), 89 (11), 77 (19).

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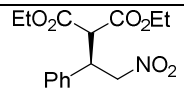
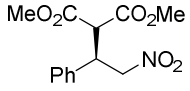
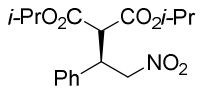
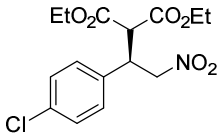
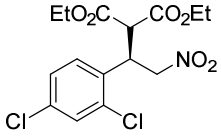
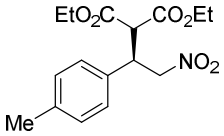
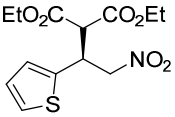
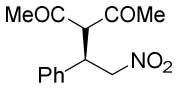
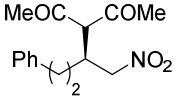
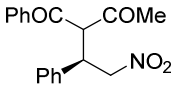
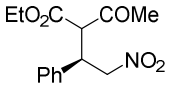
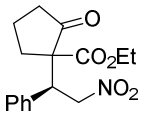
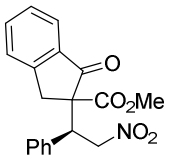
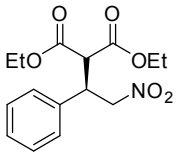
5. Table S1. HPLC conditions and retention times for compounds 3

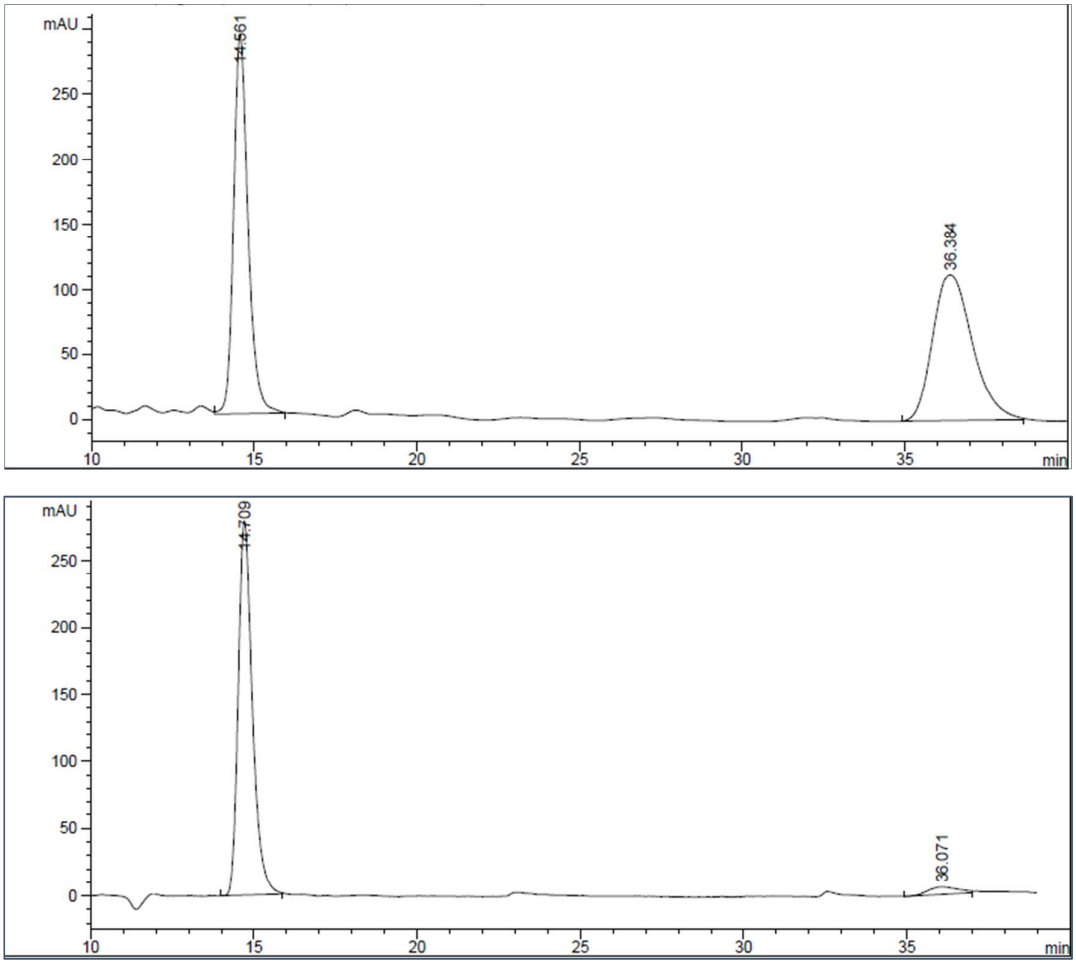
	Structure	Column λ (nm)	Eluent (Hx/ *i*-PrOH) flow rate (mL/min)	t_R (min)
3a		Chiralpak AD 230 nm	90/10 1 mL/min	**14.7** (major enantiomer) 36.1
3b		Chiralpak AD 210 nm	90/10 1 mL/min	**15.9** (major enantiomer) 23.0
3c		Chiralpak AD 230 nm	95/5 1 mL/min	**16.0** (major enantiomer) 34.6
3d		Chiralpak AD 240 nm	65/35 1 mL/min	**7.3**(major enantiomer) 16.2
3e		Chiralpak AD 240 nm	65/35 1 mL/min	**5.0** (major enantiomer) 22.3
3f		Chiralpak AD 240 nm	90/10 1 mL/min	**12.5** (major enantiomer) 28.9
3g		Chiralpak AD 254	90/10 1 mL/min	**11.9** (major enantiomer) 21.9
3h		Chiralpak AD-H 230 nm	95/5 1 mL/min	18.6 **26.3** (major enantiomer)
3i		Chiralpak OD-H 210 nm	90/10 1 mL/min	18.4 **19.6** (major enantiomer)

	Structure	Column λ (nm)	Eluent (Hx/ *i*-PrOH) flow rate (mL/min)	t_R (min) (minor diastereisomer)	t_R (min) (major diastereisomer)
3j		Chiralpak AD-H 210	90/10 Hx/EtOH 1 mL/min	14.1 **15.7** (major enantiomer)	18.8 **24.9** (major enantiomer)
3k		Chiralpak AD-H 210	95/5 0.8 mL/min	**24.9** (major enantiomer) 44.2	16.7 **26.3** (major enantiomer)
3l		Chiralpak OD-H 210	90/10 0.5 mL/min	26.7 35.2	22.6 **32.4** (major enantiomer)
3m		Chiralpak OD-H 254 nm	80/20 0.5 mL/min	24.2 **98.7** (major enantiomer)	27.1 **56.8** (major enantiomer

6. HPLC spectra for compounds 3

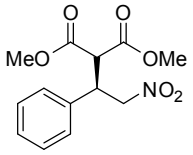


3a

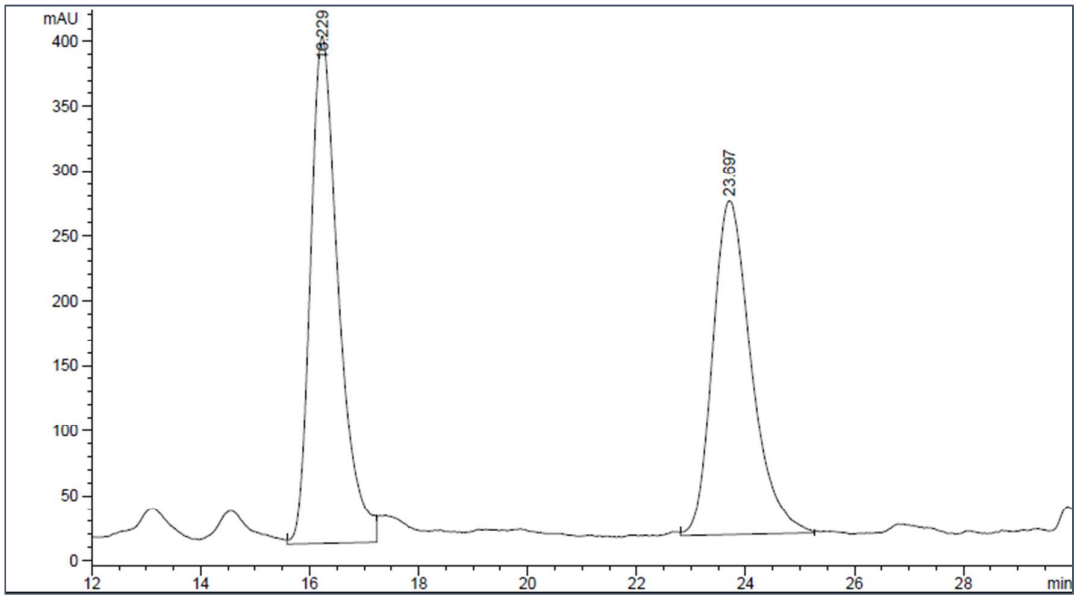


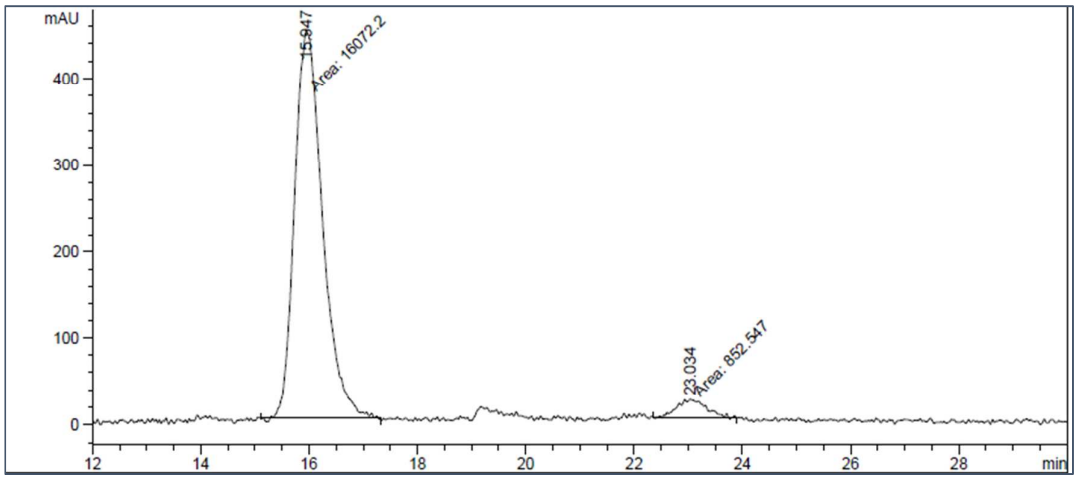
Peak	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.709	PB	0.4589	839.32041	279.06995	95.8665
2	36.071	PV	0.7579	361.88739	5.66028	4.1335

Figure S2. HPLC Chromatogram of compound **3a**.



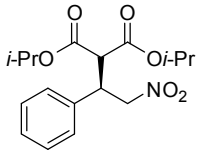
3b



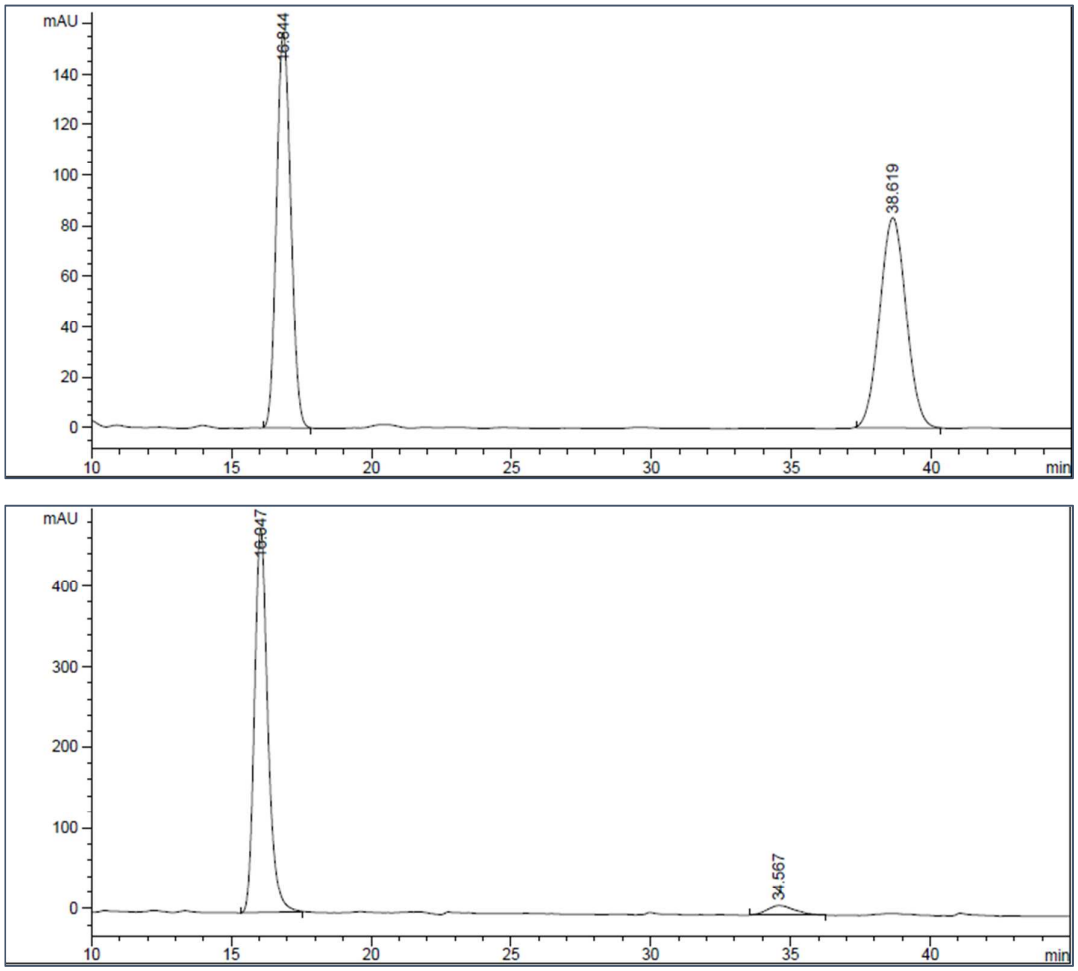


Peak	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.947	MM	0.5981	1.60722e4	447.89230	94.9627
2	23.034	MM	0.6629	852.54669	21.43616	5.0373

Figure S3. HPLC Chromatogram of compound **3b**.

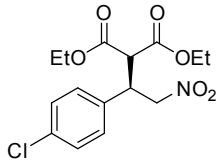


3c

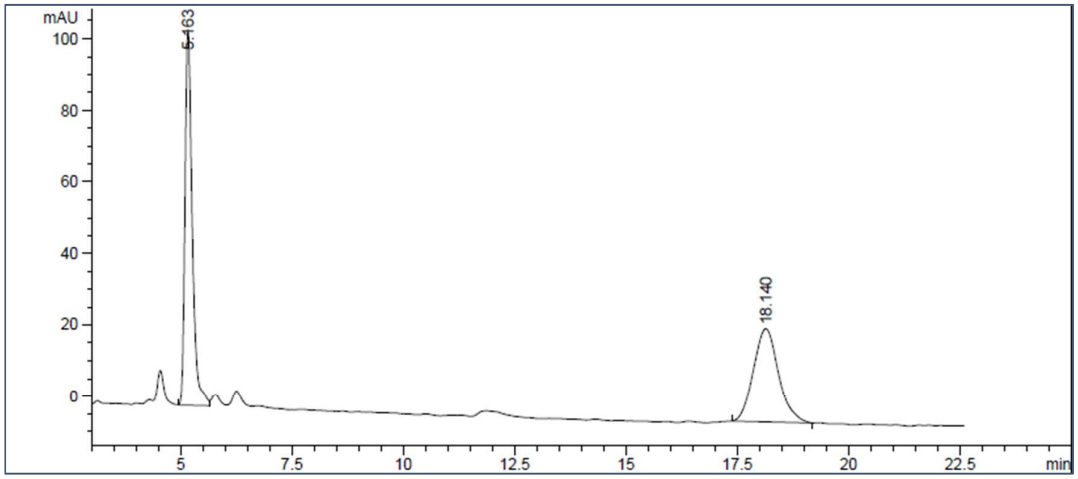


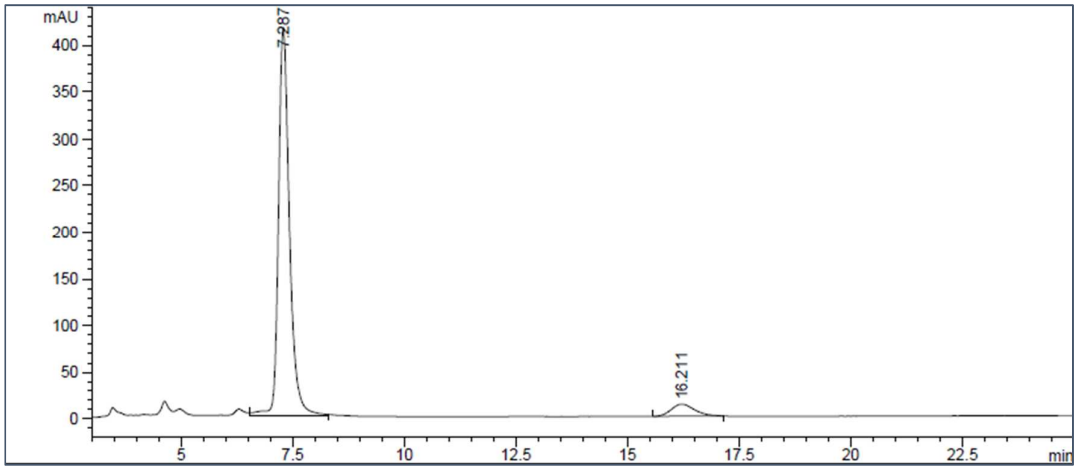
Peak	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.047	PB	0.5002	1,57662e4	47.622.092	95.2158
2	34.567	BB	0.8157	79.218.866	11.47162	4.7842

Figure S4. HPLC Chromatogram of compound **3c**.



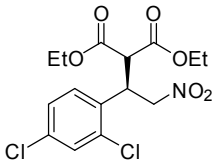
3d



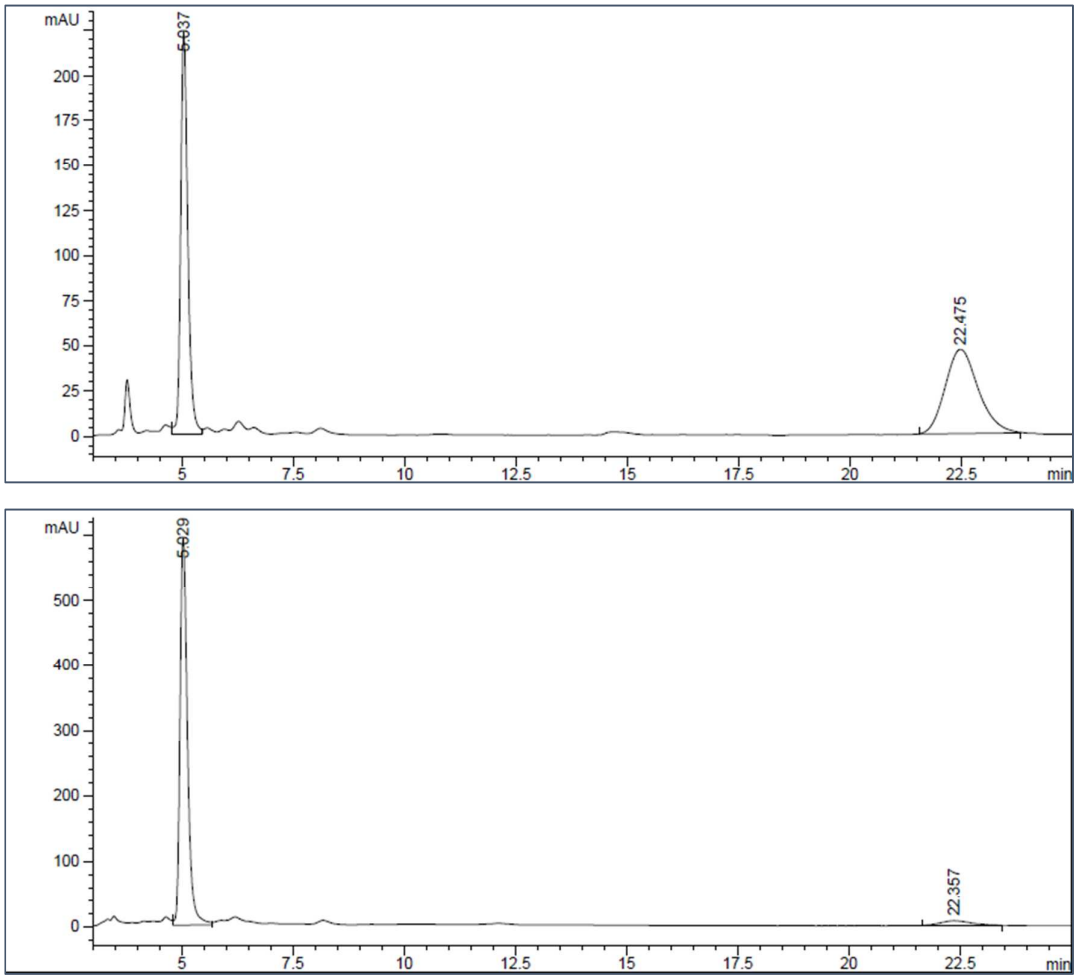


Peak	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.287	VB	0.2568	7081.58887	415.60367	93.6980
2	16.211	BB	0.5550	476.29910	12.83195	6.3020

Figure S5. HPLC Chromatogram of compound **3d**.

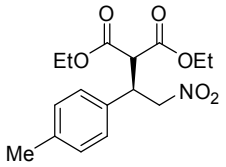


3e

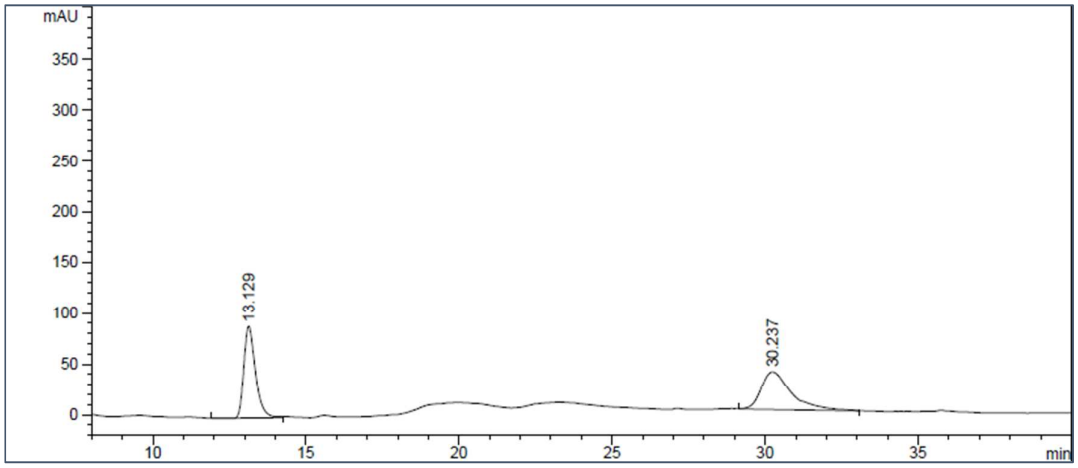


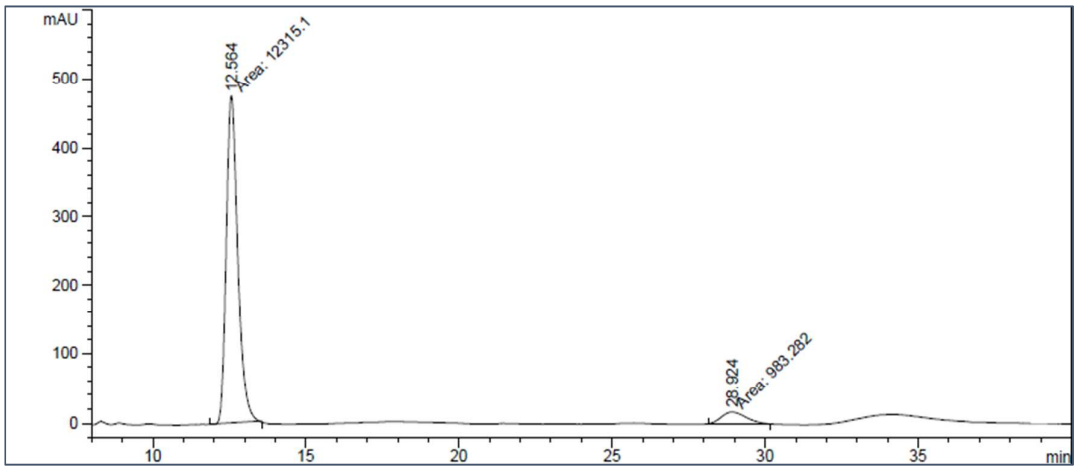
Peak	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.029	VB	0.1778	691.480176	594.10474	95.3253
2	22.357	BB	0.587	3.3909958	7.05258	4.6747

Figure S6. HPLC Chromatogram of compound **3e**.



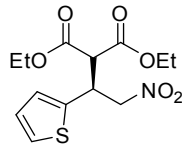
3f



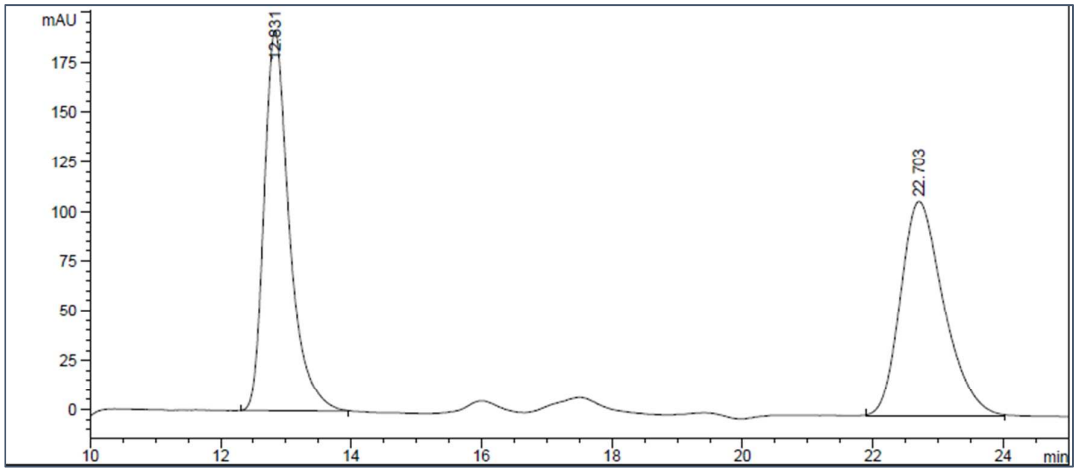


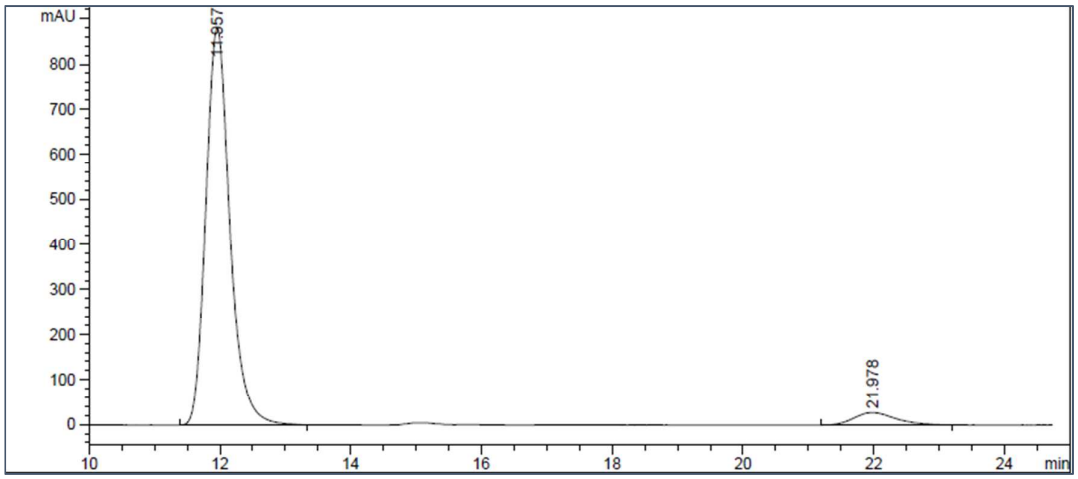
Peak	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.564	MM	0.4319	1.2315e4	475.18307	92.6060
2	28.924	MM	0.9618	983.28223	17.03.871	7.940

Figure S7. HPLC Chromatogram of compound **3f**.



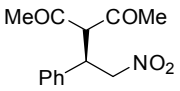
3g



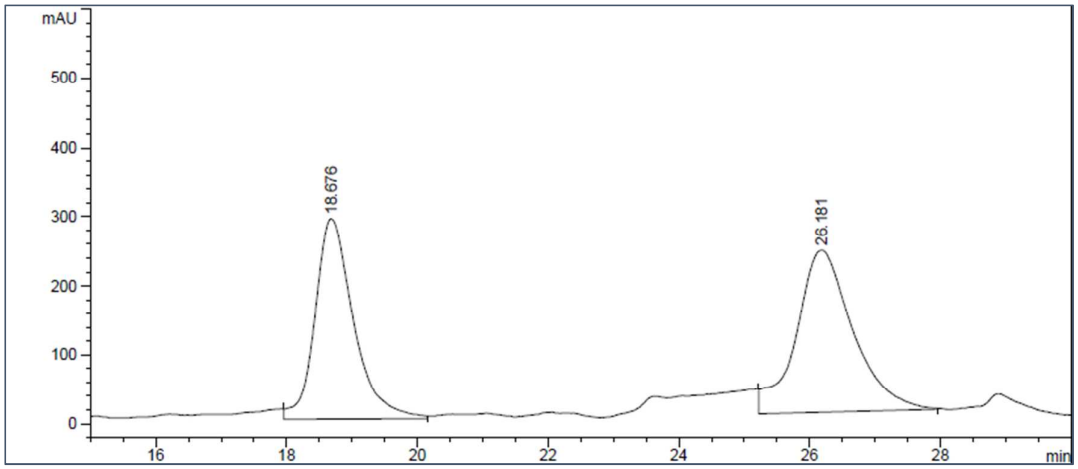


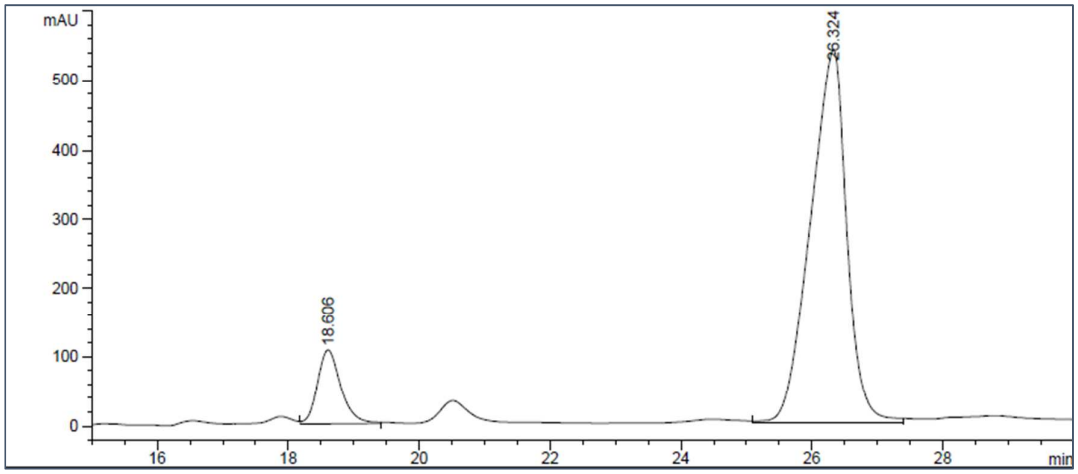
Peak	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.957	BB	0.3902	225117e4	880.62976	94.7830
2	21.978	BB	0.5909	1239.08386	27.64383	5.2170

Figure S8. HPLC Chromatogram of compound **3g**.



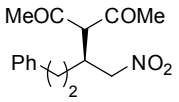
3h



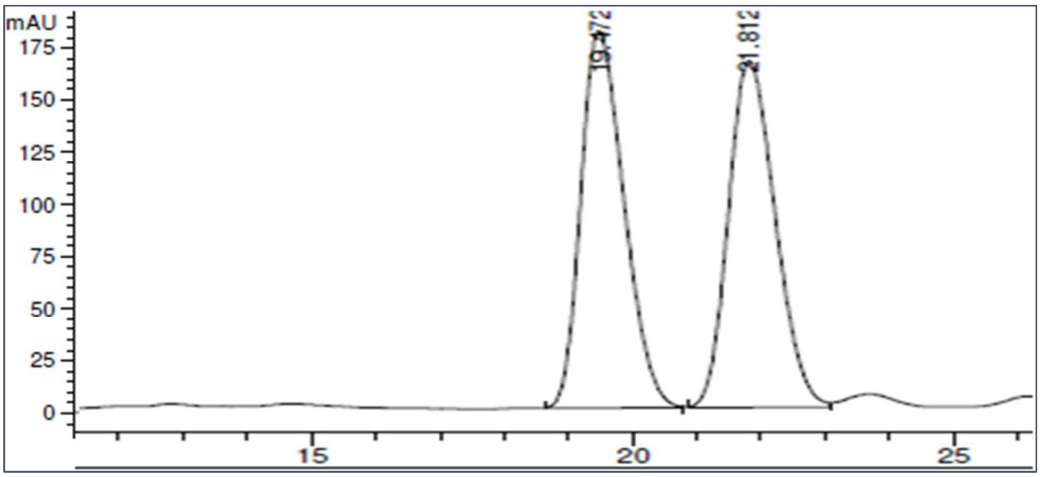


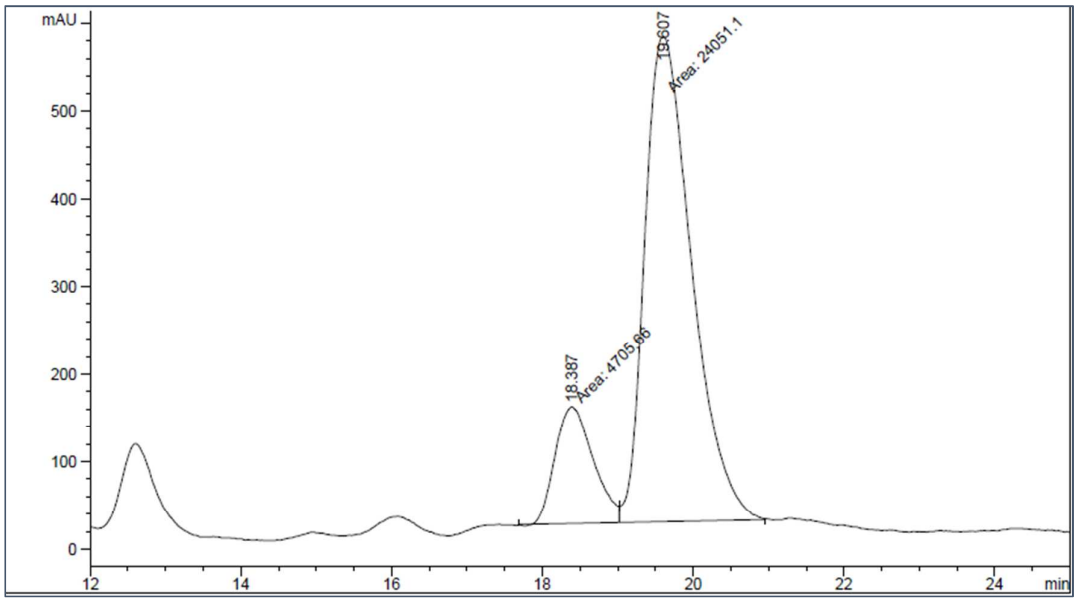
Peak	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.606	VB	0.3778	2656.85840	106.94601	11.3136
2	26.324	VB	0.5740	2.0827e4	539.95721	88.6864

Figure S9. HPLC Chromatogram of compound **3h**.



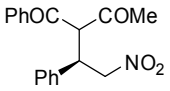
3i



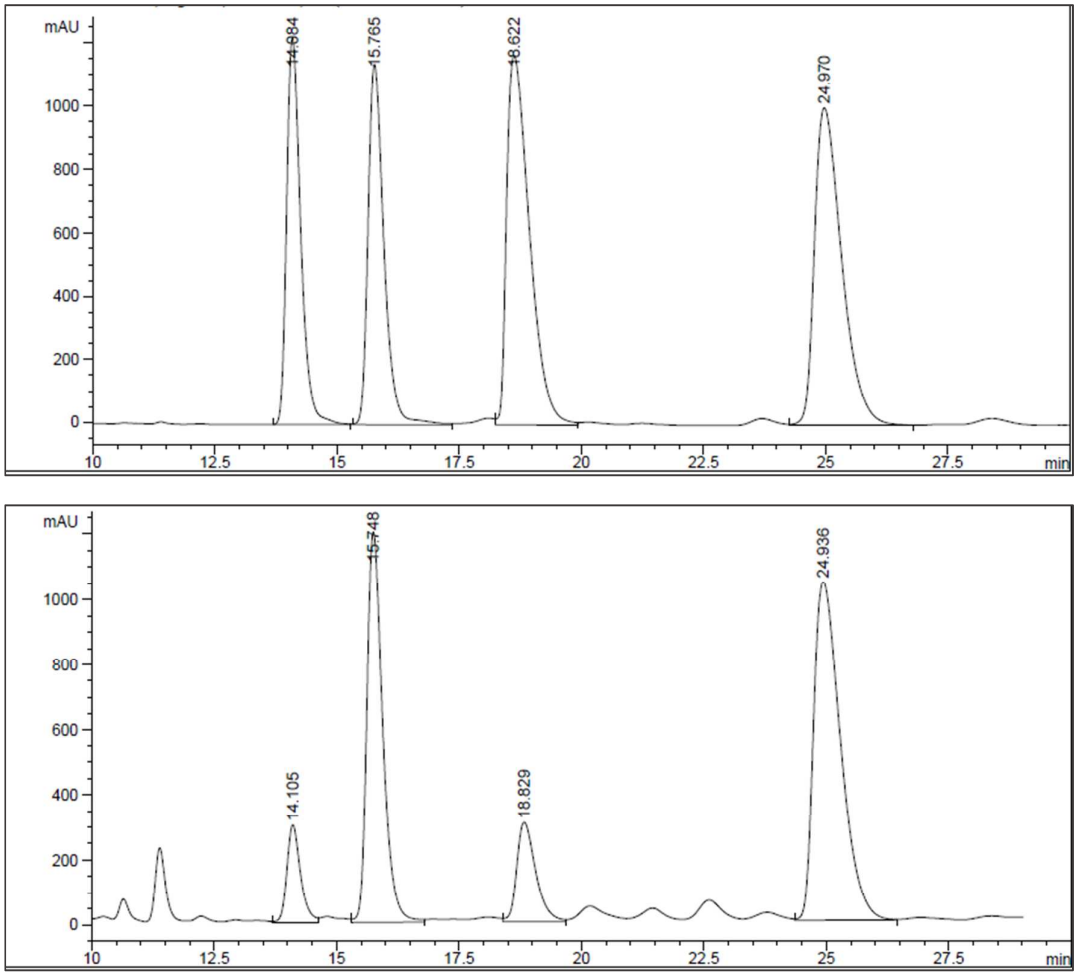


Peak	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.387	MF	0.5912	4784.45654	134.88641	16.7178
2	19.607	FM	0.7195	2.38344e4	552.10687	83.2822

Figure S10. HPLC Chromatogram of compound **3i**.

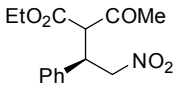


3j

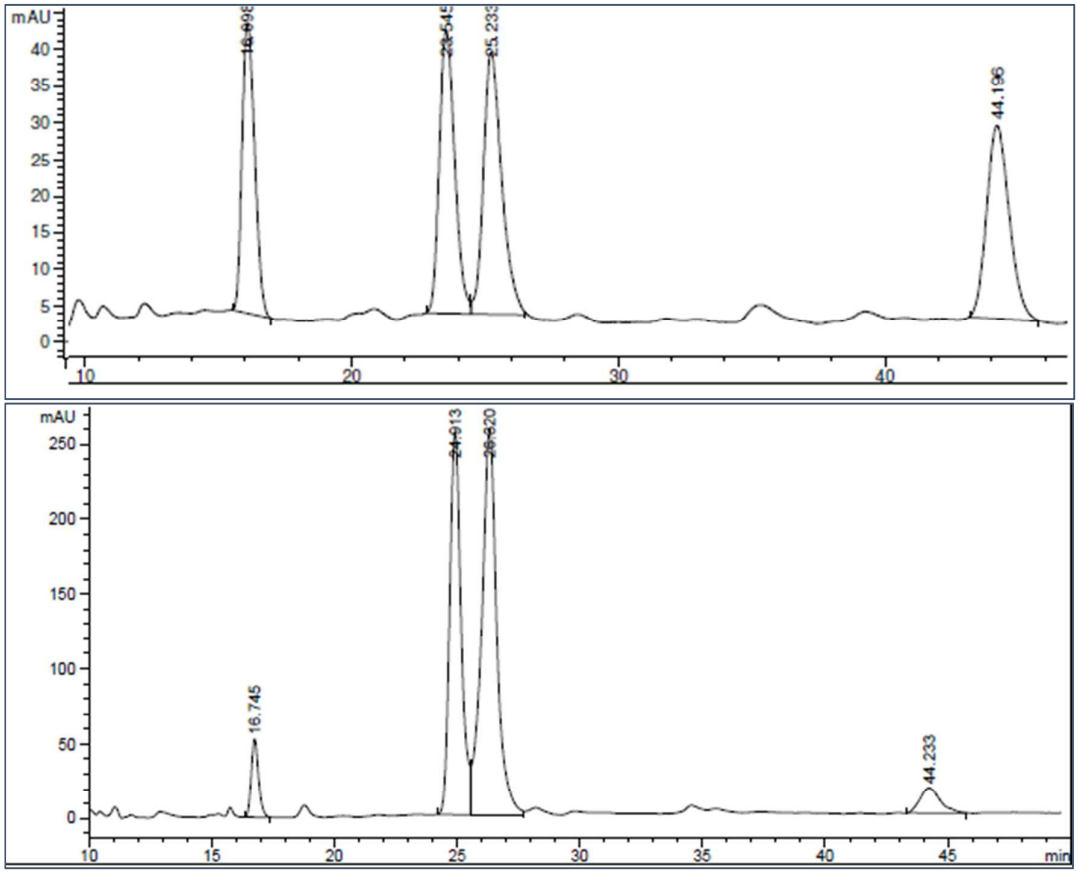


Peak	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.105	VV	0.2957	5923.27930	300.7926	7.3036
2	15.748	VB	0.3430	2.70370e04	1199.55566	33.3377
3	18.829	VV	0.4167	8287.24902	305.27301	10.2185
4	24.936	VV	0.5944	3.98528e04	1041.56799	49.1402

Figure S11. HPLC Chromatogram of compound **3j**.

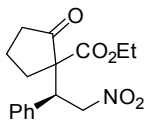


3k

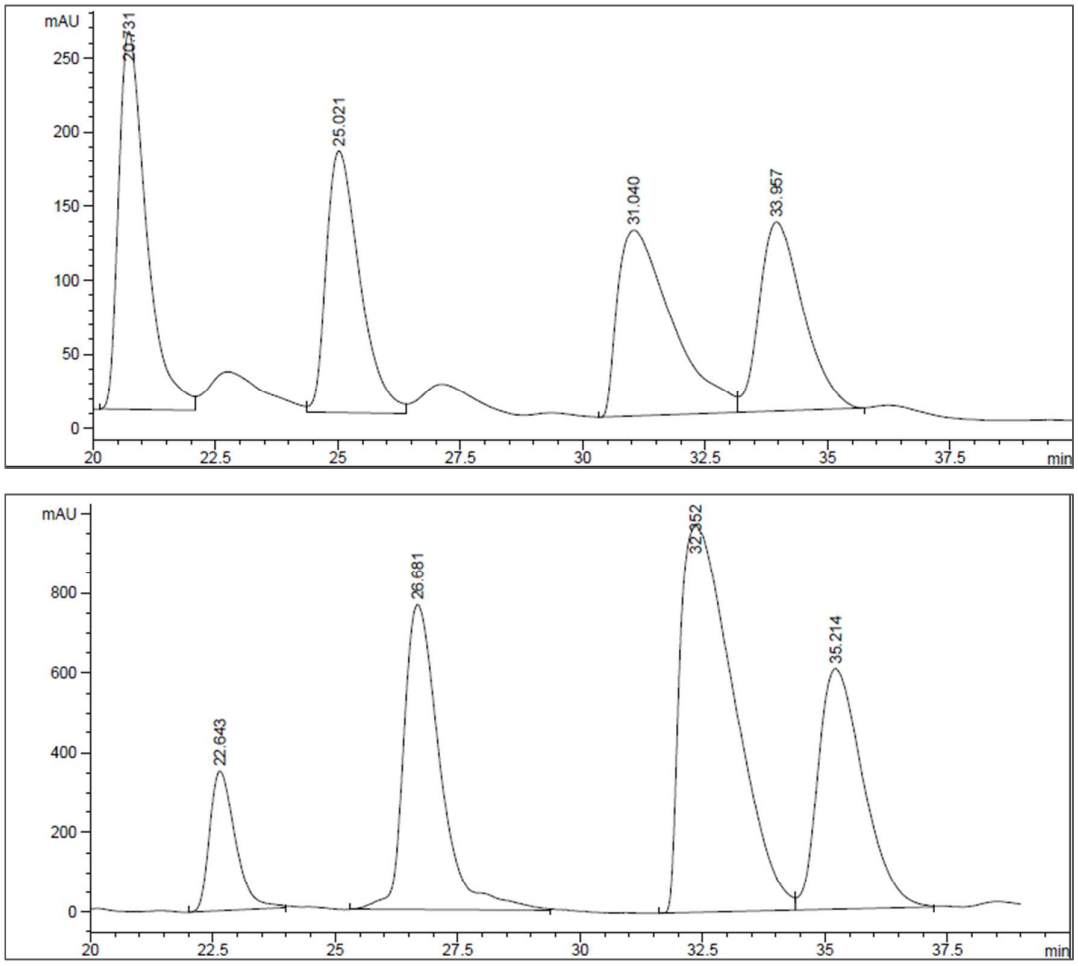


Peak	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.745	BB	0.3177	1092.67188	52.74049	5.0934
2	24.913	BV	0.4957	8252.22949	256.27417	38.4668
3	26.320	VB	0.6199	1.11159e4	258.38541	51.8156
4	44.233	PB	0.6845	992.03082	17.26221	4.6242

Figure S12. HPLC Chromatogram of compound **3k**.

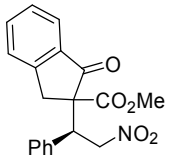


3l

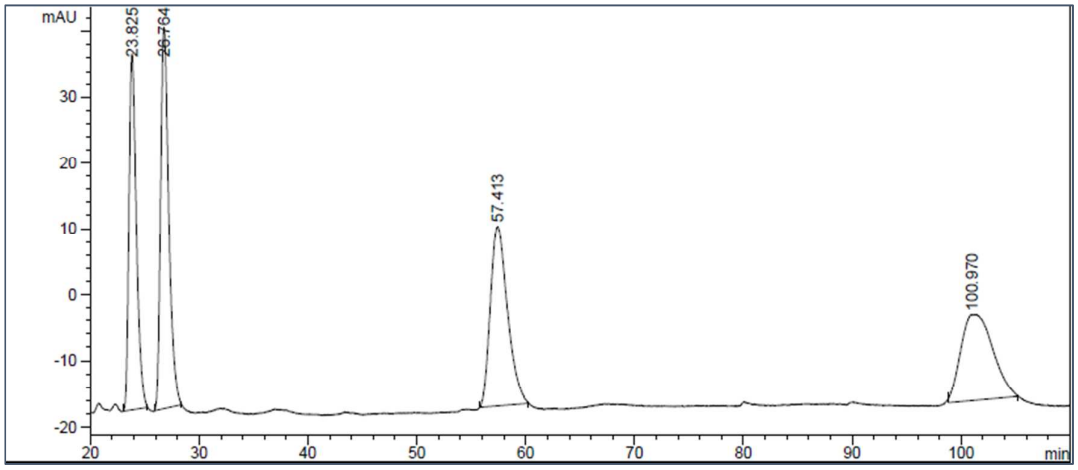


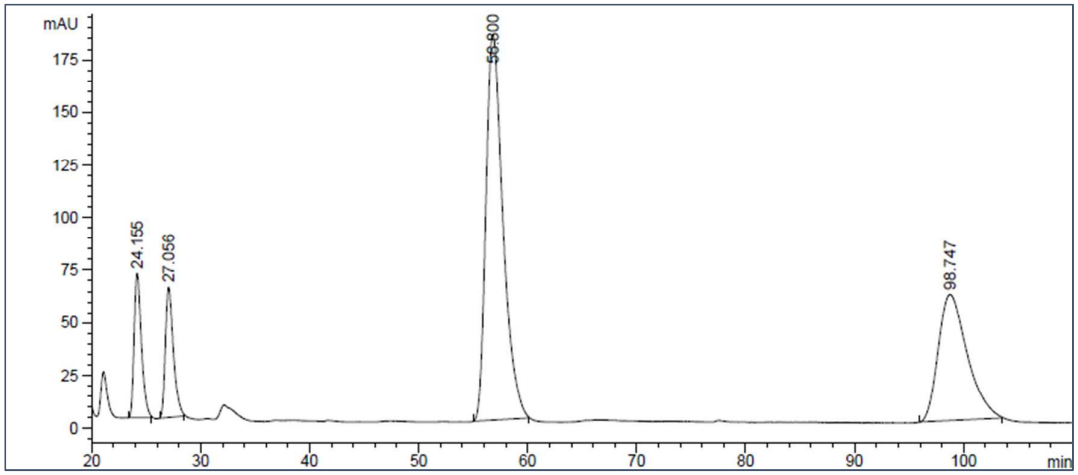
Peak	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.643	VB	0.5431	1.28660e4	351.41293	7.7837
2	26.681	PB	0.7549	3.95442e4	765.24133	23.9235
3	32.352	PV	1.0109	7.40441e4	974.03198	44.7952
4	35.214	VB	0.9057	3.88404e4	604.42853	23.4977

Figure S13. HPLC Chromatogram of compound **3l**.



3m

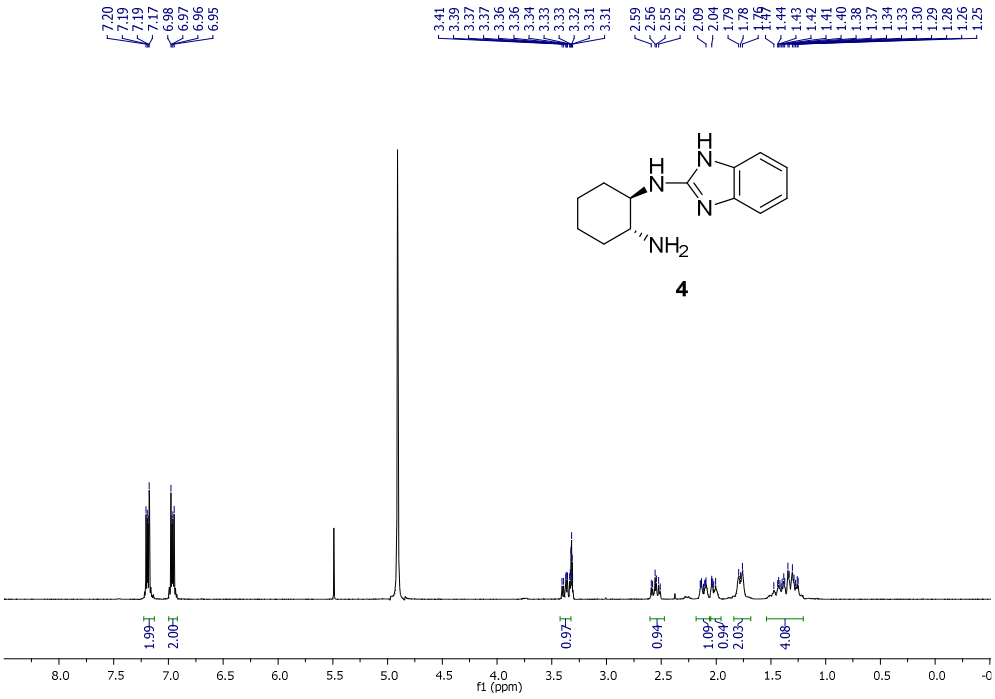


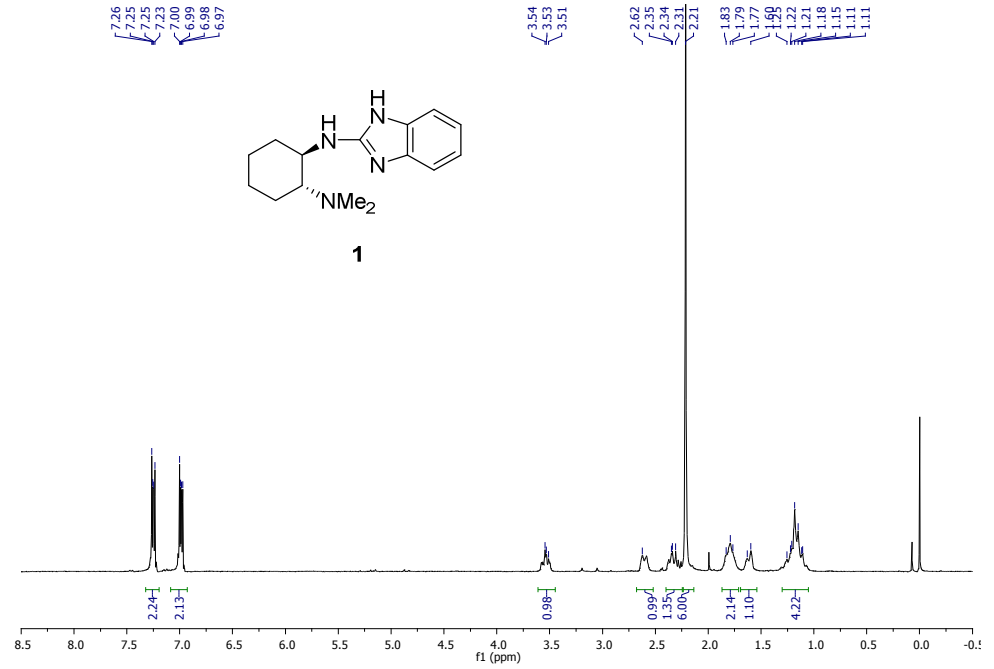


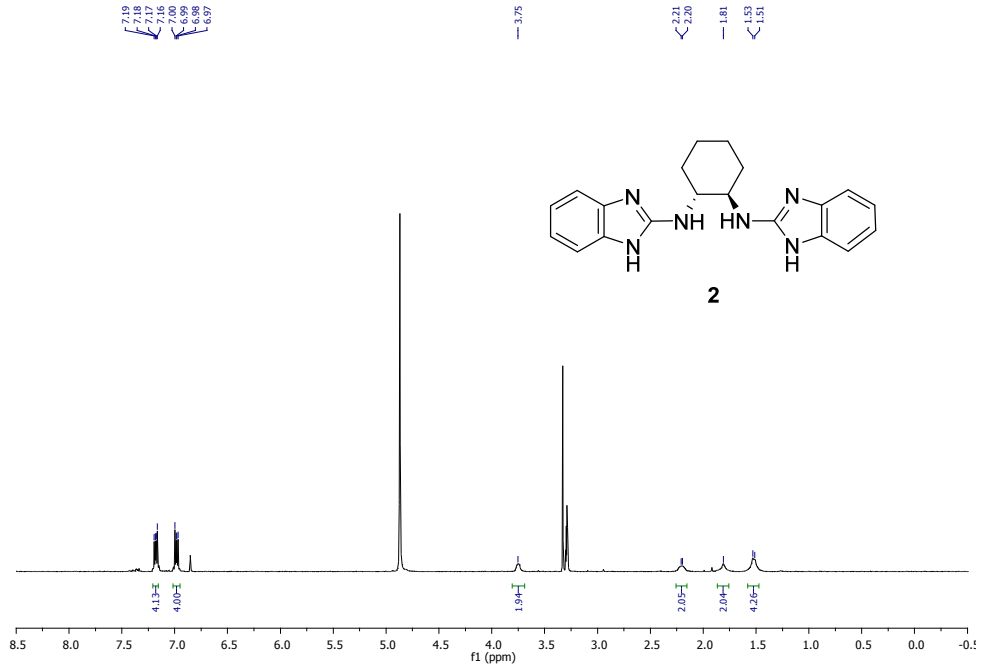
Peak	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.155	BB	0.6759	3202.46655	68.69846	8.5688
2	27.056	BB	0.7103	3165.27588	62.13305	8.4693
3	56.800	BB	1.4554	1.99380e4	183.52771	53.3483
4	98.747	BB	2.1555	1.10676e4	60.12577	29.6136

Figure S14. HPLC Chromatogram of compound **3m**.

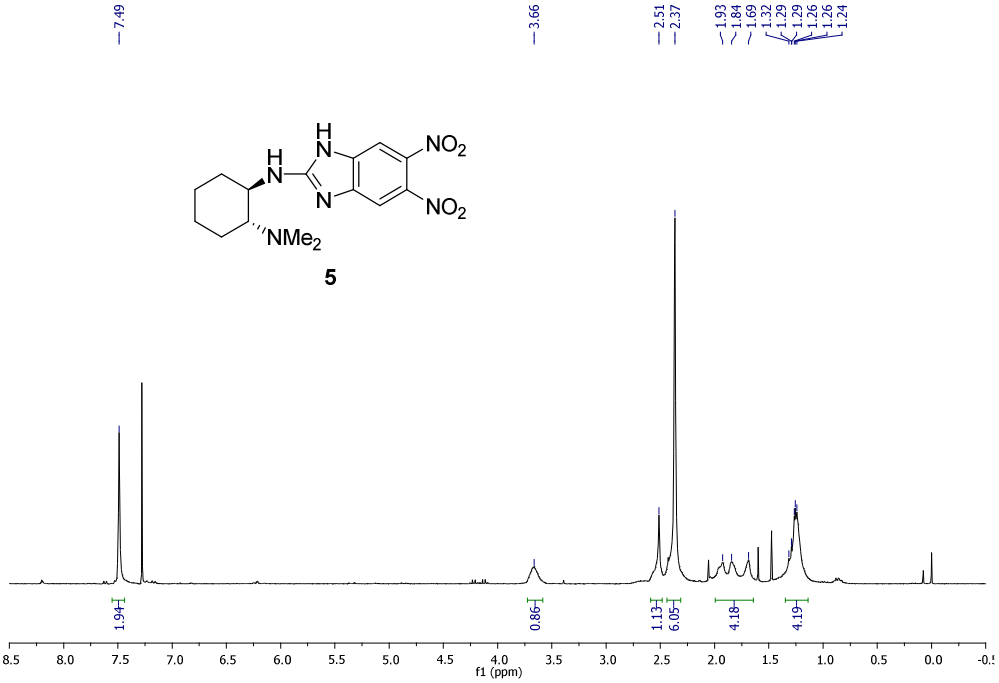
7. NMR spectra for compounds 1-6



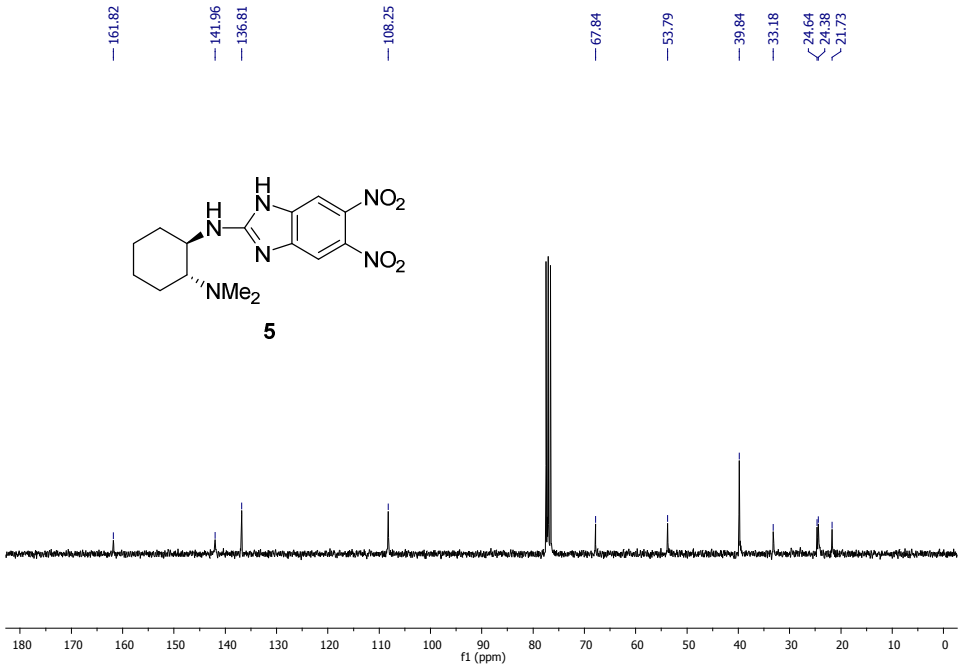



7.19
7.18
7.17
7.16
7.00
6.99
6.98
6.97
3.75
2.21
2.20
1.81
1.53
1.51
NH
HN
N
H
4.13
4.00
1.94
2.05
2.04
4.26
f1 (ppm)

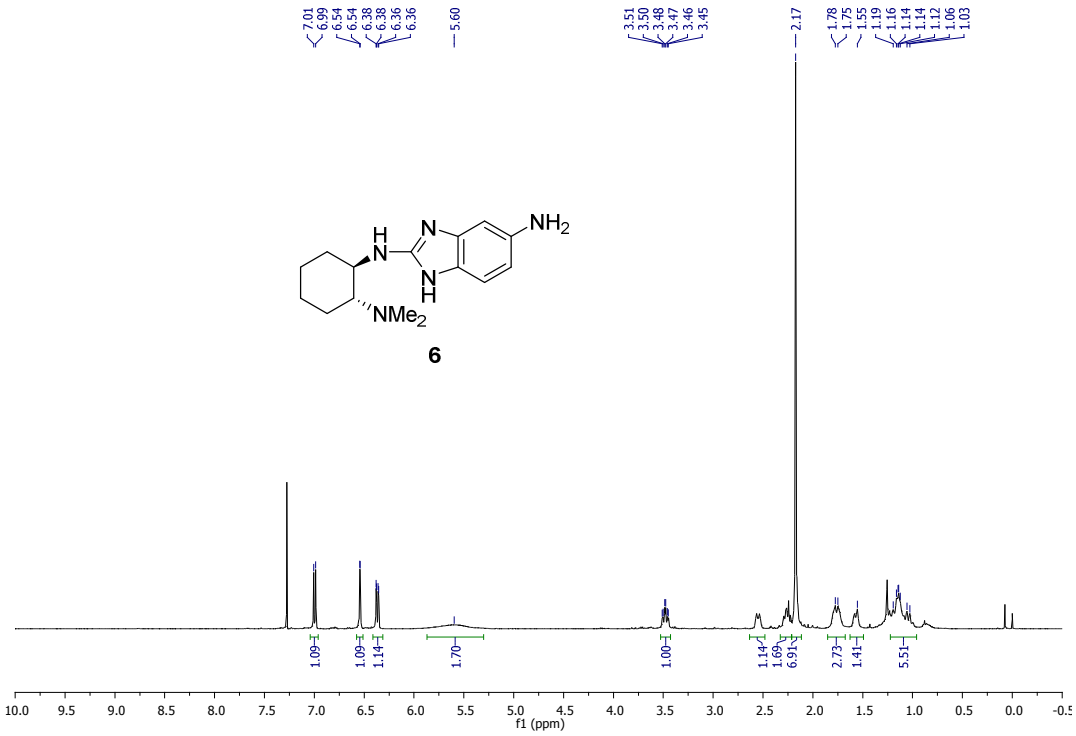
2


7.49
3.66
2.51
2.37
1.93
1.84
1.69
1.32
1.29
1.29
1.26
1.26
1.24
NO2
NO2
NMe2
1.94
0.86
1.13
6.05
4.18
4.19
f1 (ppm)

5


161.82
141.96
136.81
108.25
67.84
53.79
39.84
33.18
24.64
24.38
21.73
NO2
NO2
NMe2
f1 (ppm)

5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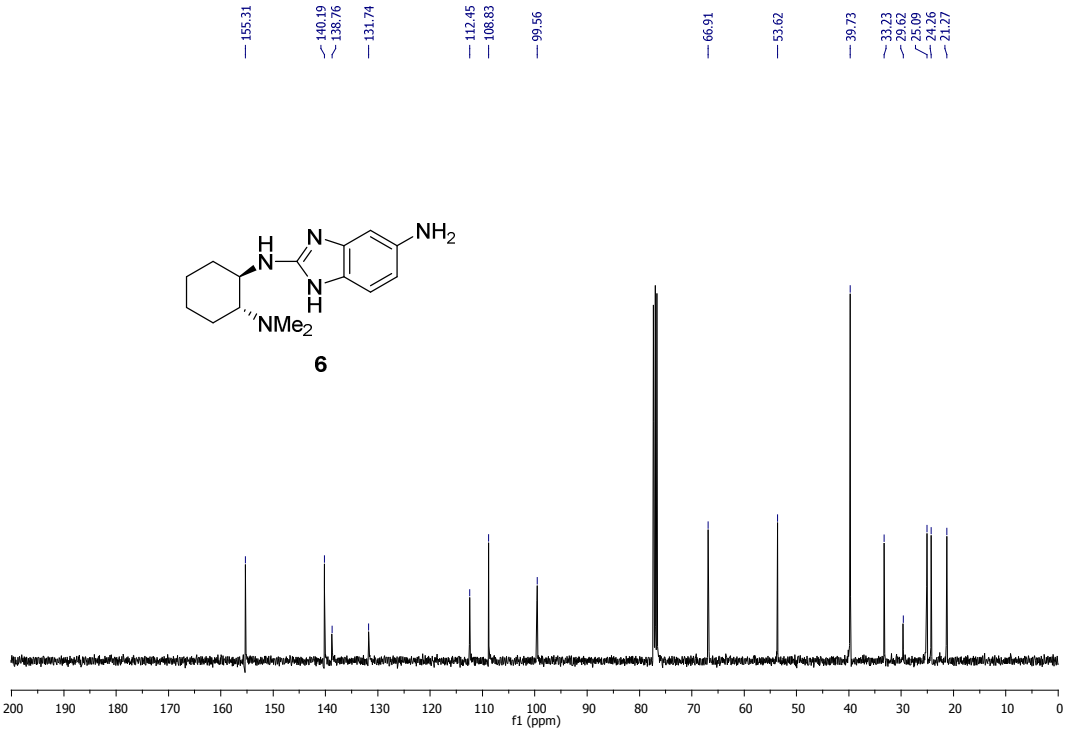
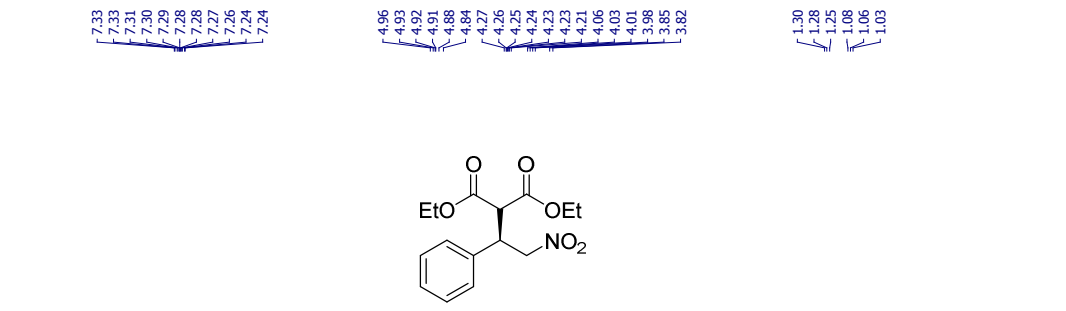
6.99
6.54
6.54
6.38
6.38
6.36
6.36
5.60
3.51
3.50
3.48
3.47
3.46
3.45
2.17
1.78
1.75
1.55
1.19
1.16
1.14
1.14
1.12
1.06
1.03
NH2
NMe2
1.09
1.09
1.14
1.70
1.00
1.14
1.69
6.91
2.73
1.41
5.51
f1 (ppm)

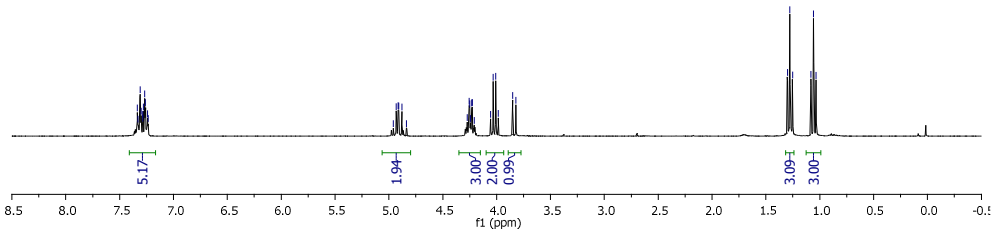
6


155.31
140.19
138.76
131.74
112.45
108.83
99.56
66.91
53.62
39.73
33.23
29.62
25.09
24.26
21.27
NH2
H
N
N
N
H
NMe2
6
f1 (ppm)


7.33
7.33
7.31
7.30
7.29
7.28
7.28
7.27
7.26
7.24
7.24
4.96
4.93
4.92
4.91
4.88
4.84
4.27
4.26
4.25
4.24
4.23
4.23
4.21
4.06
4.03
4.01
3.98
3.85
3.82
1.30
1.28
1.25
1.08
1.06
1.03

O
O
EtO
OEt
NO2

3a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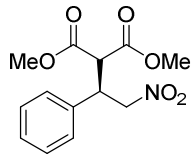
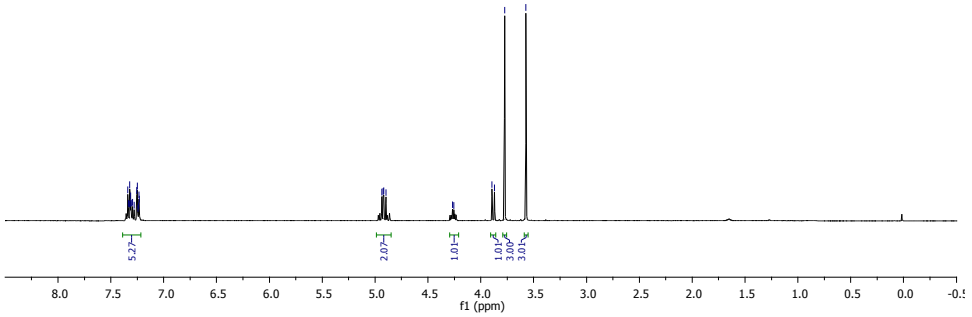
1.94
3.00
2.00
0.99
3.09
3.00
f1 (ppm)


O
O
MeO
OMe
NO2

3b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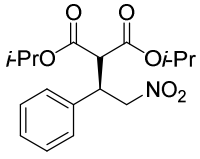
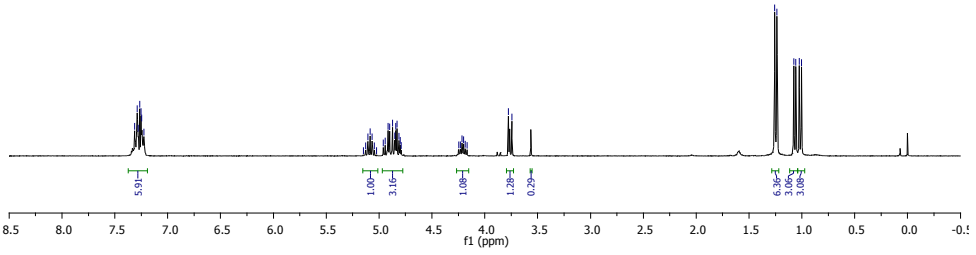
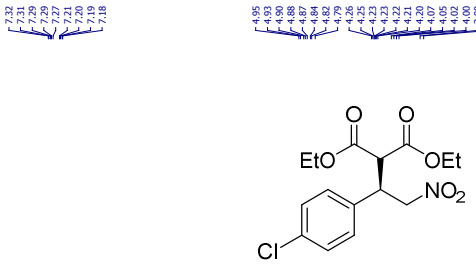
2.07
1.01
1.01
3.00
3.01
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

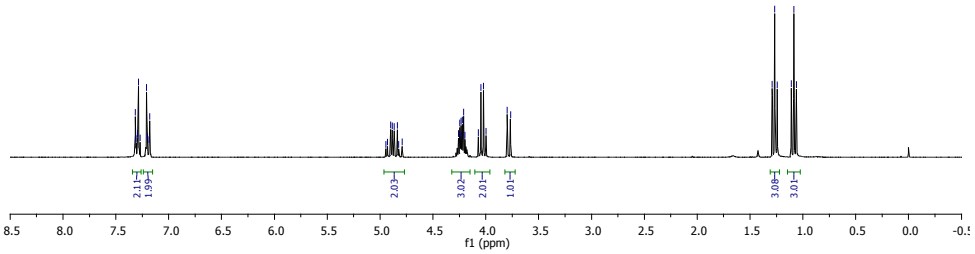

O
O
i-PrO
Oi-Pr
NO2

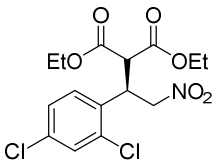
3c


5.91
1.00
3.16
1.08
1.28
0.29
6.36
3.06
3.08
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

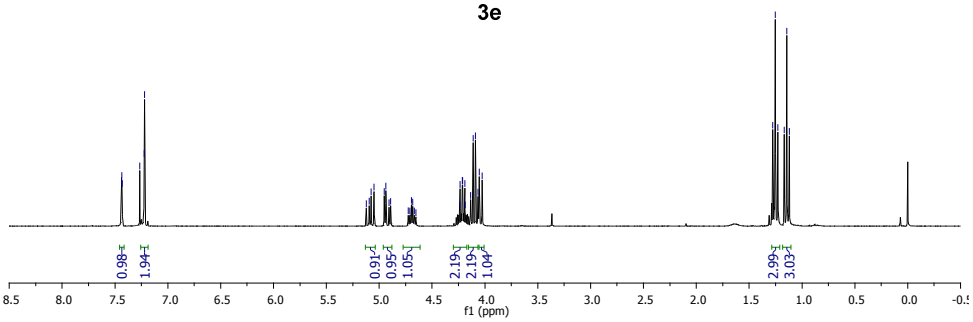


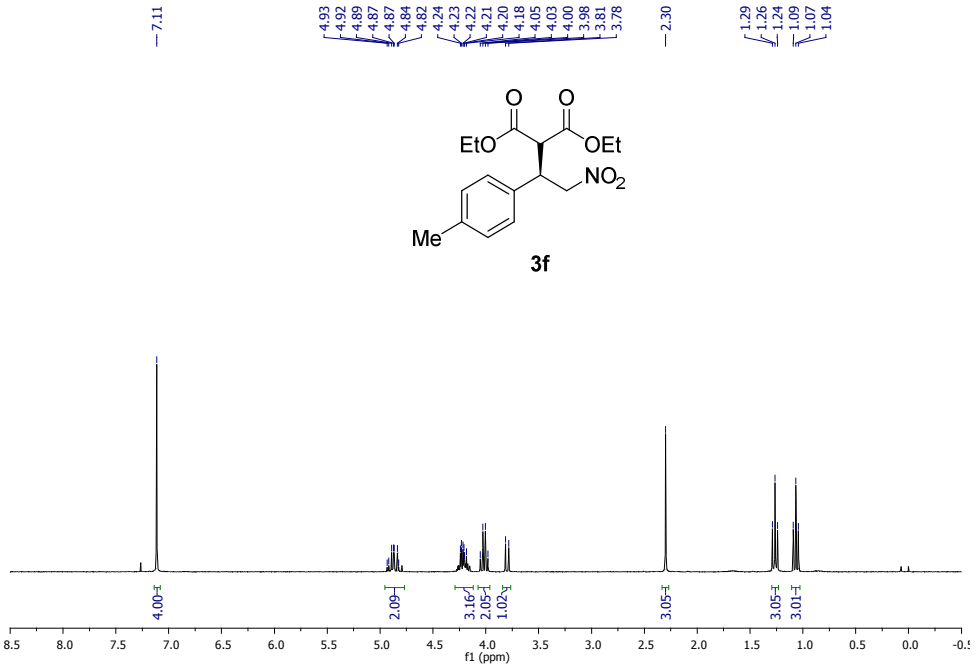
3d



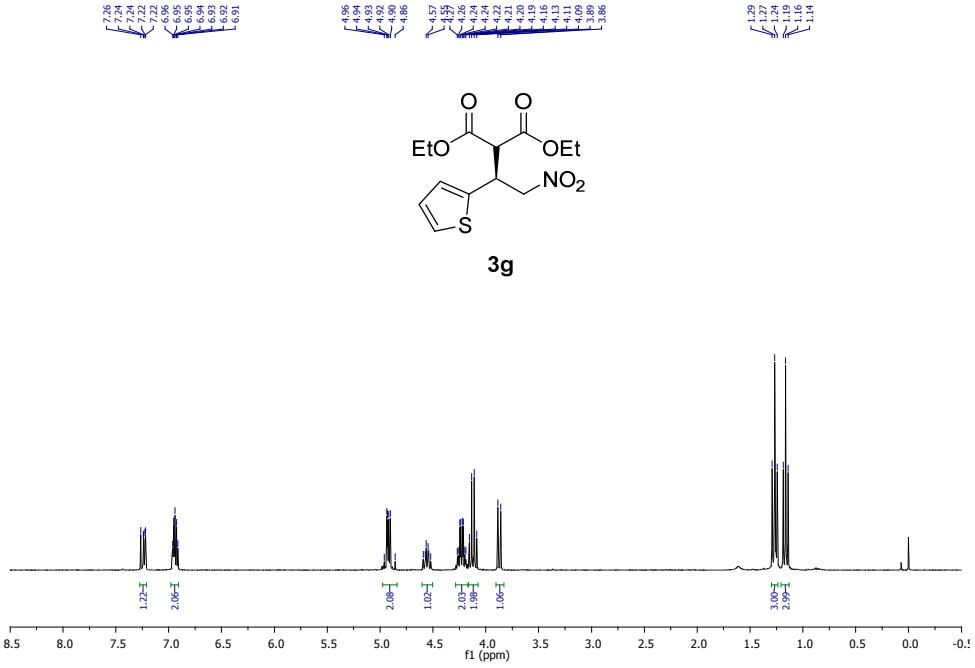


3e

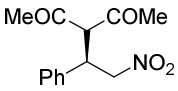



7.11
4.93
4.92
4.89
4.87
4.87
4.84
4.82
4.24
4.23
4.22
4.21
4.20
4.18
4.05
4.03
4.00
3.98
3.81
3.78
2.30
1.29
1.26
1.24
1.09
1.07
1.04
O
O
EtO
OEt
NO2
Me
4.00
2.09
3.16
2.05
1.02
3.05
3.05
3.01
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

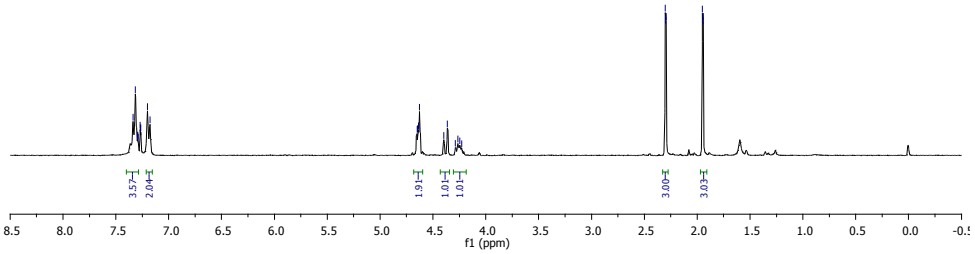
3f

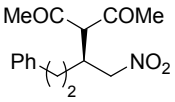

7.26
7.24
7.24
7.22
7.22
6.96
6.95
6.95
6.94
6.93
6.92
6.91
4.96
4.94
4.93
4.92
4.90
4.86
4.57
4.55
4.26
4.24
4.24
4.22
4.21
4.20
4.19
4.16
4.13
4.11
4.09
3.89
3.86
1.29
1.27
1.24
1.19
1.16
1.14
O
O
EtO
OEt
NO2
S
1.22
2.06
2.08
1.02
2.03
1.98
1.06
3.00
2.99
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

3g

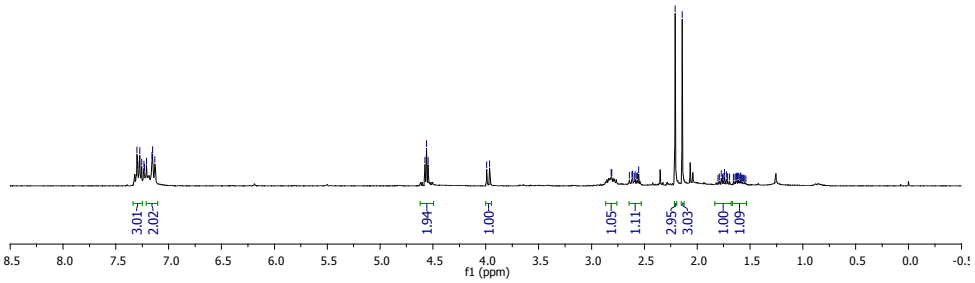

MeOC
COMe
Ph
NO2

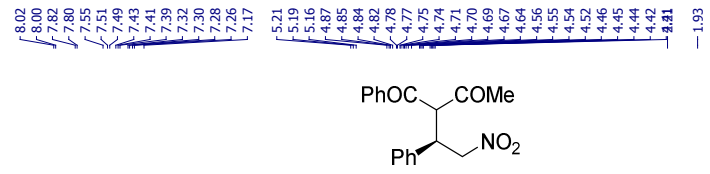
3h


3.57
2.04
1.91
1.01
1.01
3.00
3.03
f1 (ppm)


MeOC
COMe
Ph
2
NO2

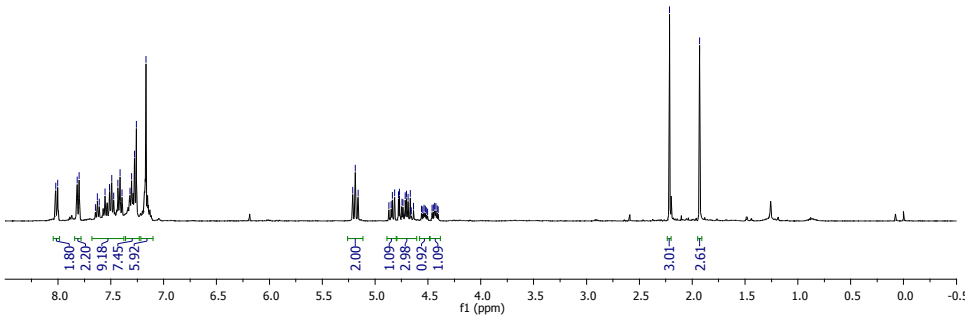
3i

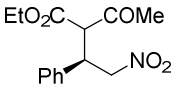

3.01
2.02
1.94
1.00
1.05
1.11
2.95
3.03
1.00
1.09
f1 (ppm)



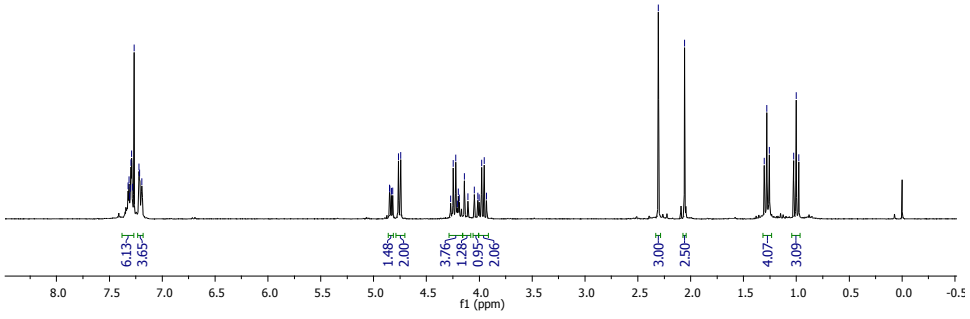
PhOC
COMe
NO2
Ph

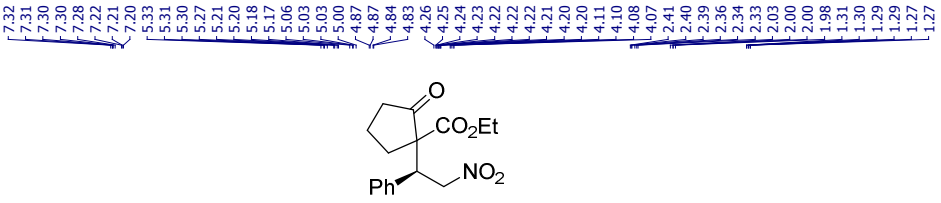
3j


1.80
2.20
9.18
7.45
5.92
2.00
1.09
2.98
0.92
1.09
3.01
2.61
f1 (ppm)


EtO2C
COMe
NO2
Ph

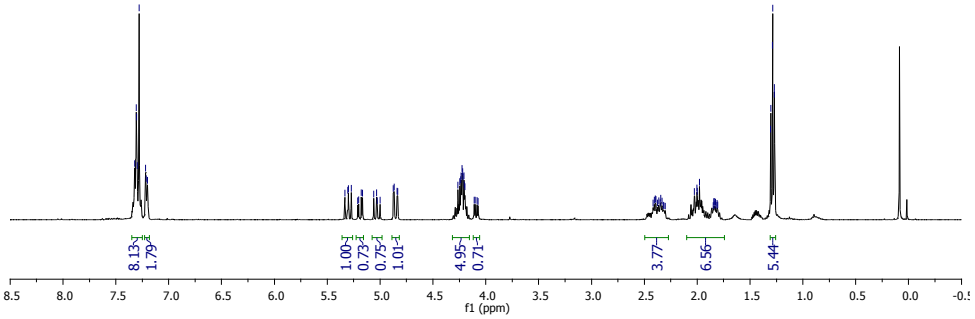
3k

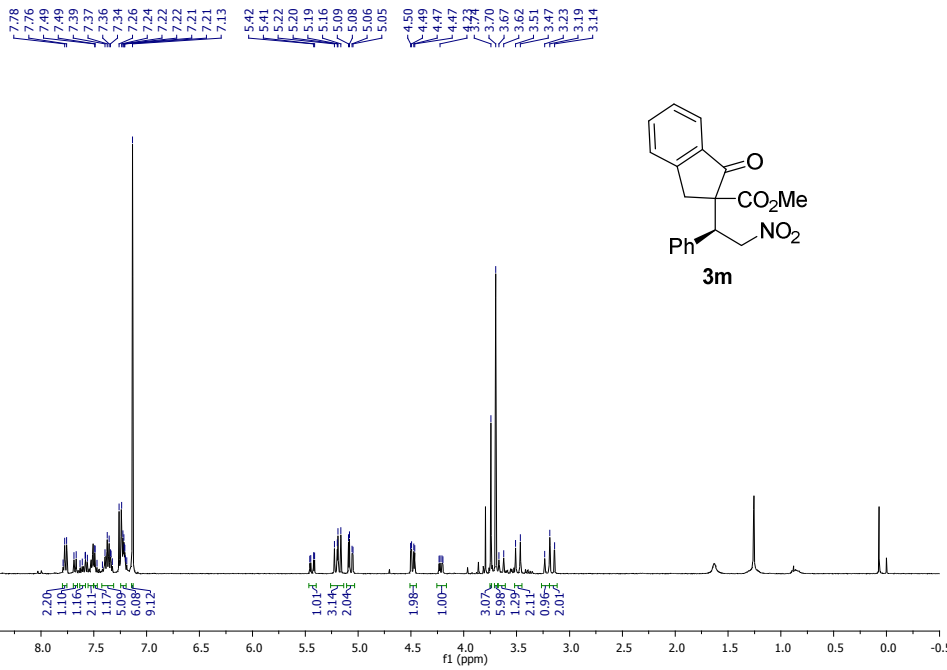

6.13
3.65
1.48
2.00
3.76
1.28
0.95
2.06
3.00
2.50
4.07
3.09
f1 (ppm)



O
CO2Et
NO2
Ph

3l


8.13
1.79
1.00
0.73
0.75
1.01
4.95
0.71
3.77
6.56
5.44
f1 (ppm)

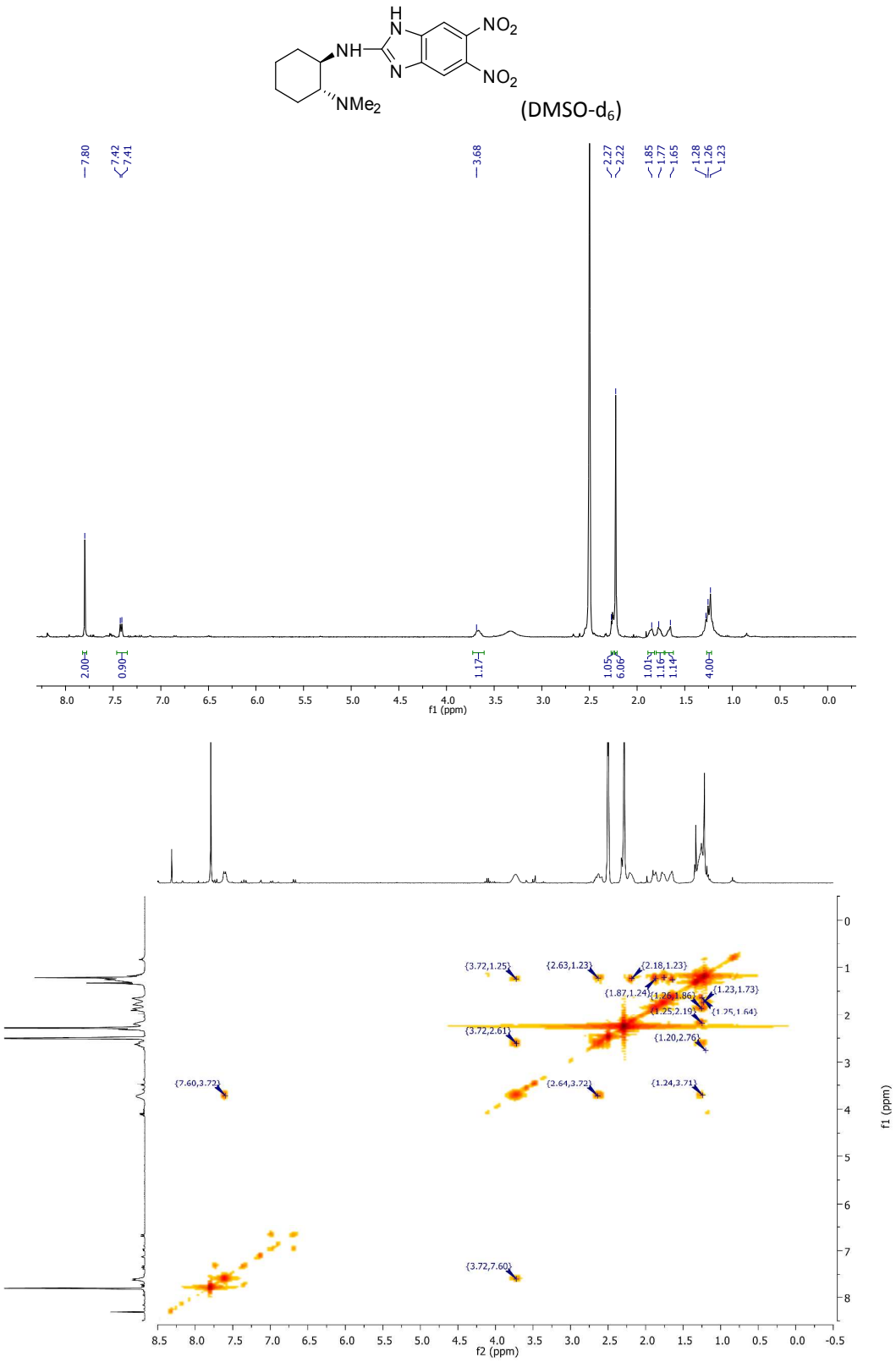


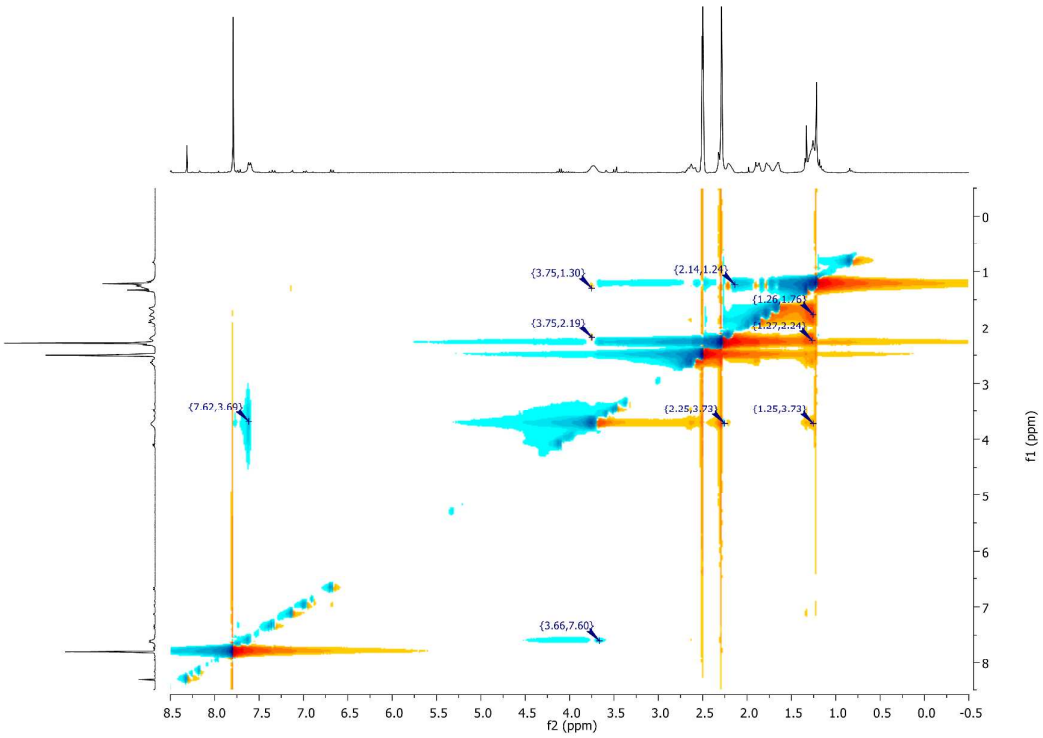
O
CO2Me
NO2
Ph

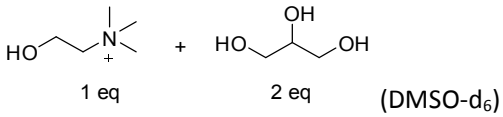
3m

f1 (ppm)

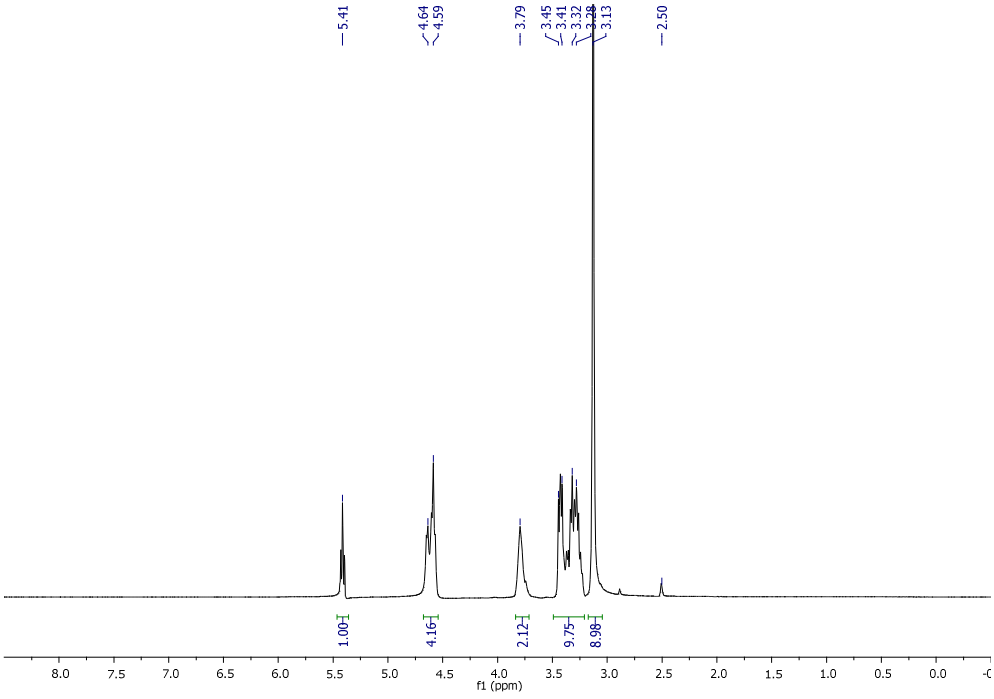
8. NMR studies for the DES-Organocatalyst interaction

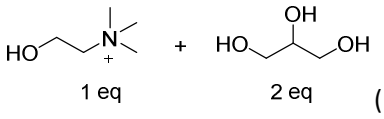



{3.75,1.30}
{2.14,1.24}
{1.26,1.76}
{3.75,2.19}
{1.27,2.24}
{7.62,3.60}
{2.25,3.73}
{1.25,3.73}
{3.66,7.60}
f2 (ppm)
f1 (ppm)

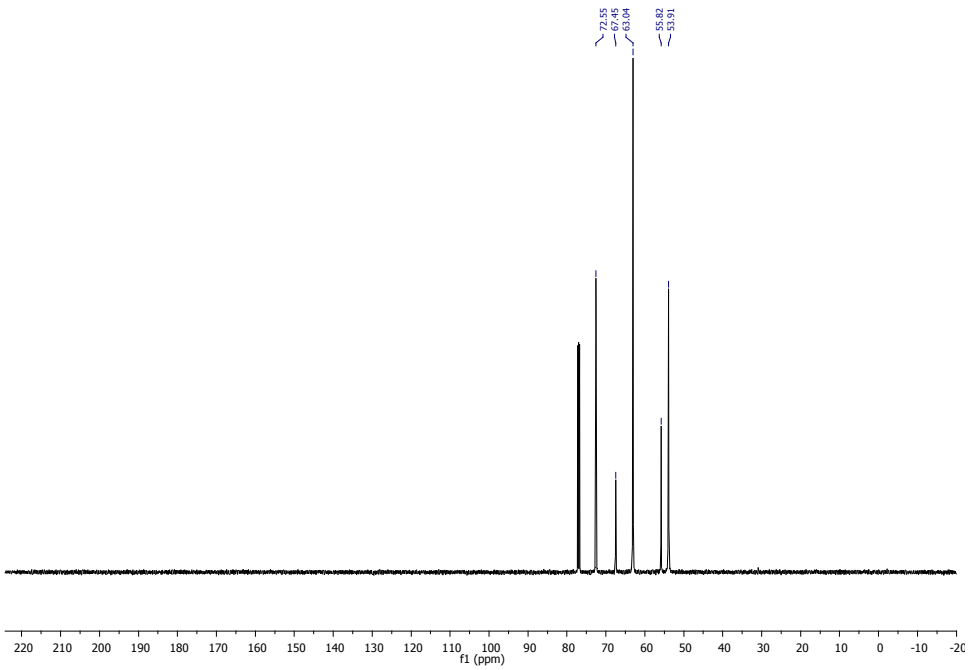

HO
N
+
HO
OH
OH
1 eq
2 eq

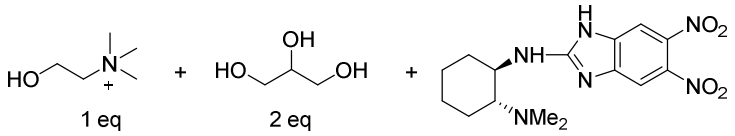
(DMSO-d_6)


5.41
4.64
4.59
3.79
3.45
3.41
3.32
3.28
3.13
2.50
1.00
4.16
2.12
9.75
8.98
f1 (ppm)



1 eq 2 eq (DMSO-d_6)





1 eq 2 eq (DMSO-d_6)

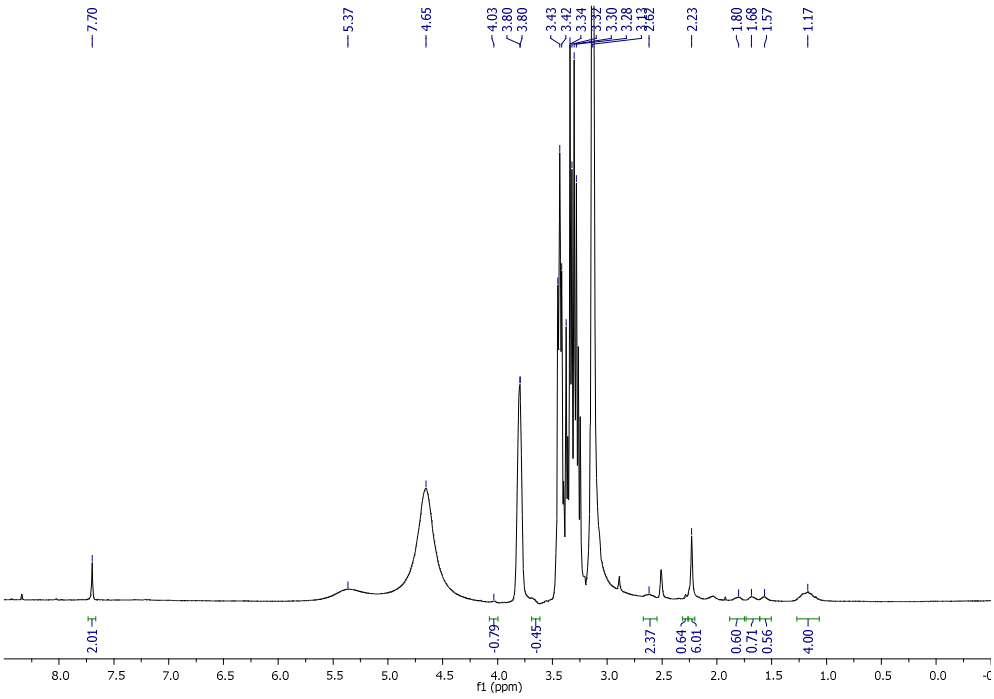
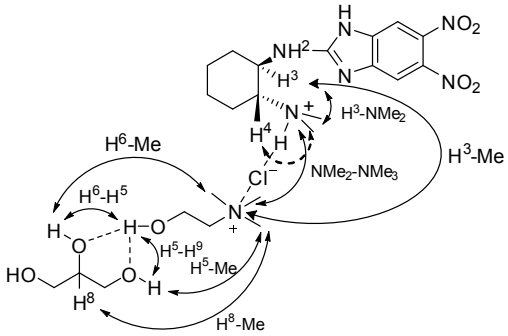
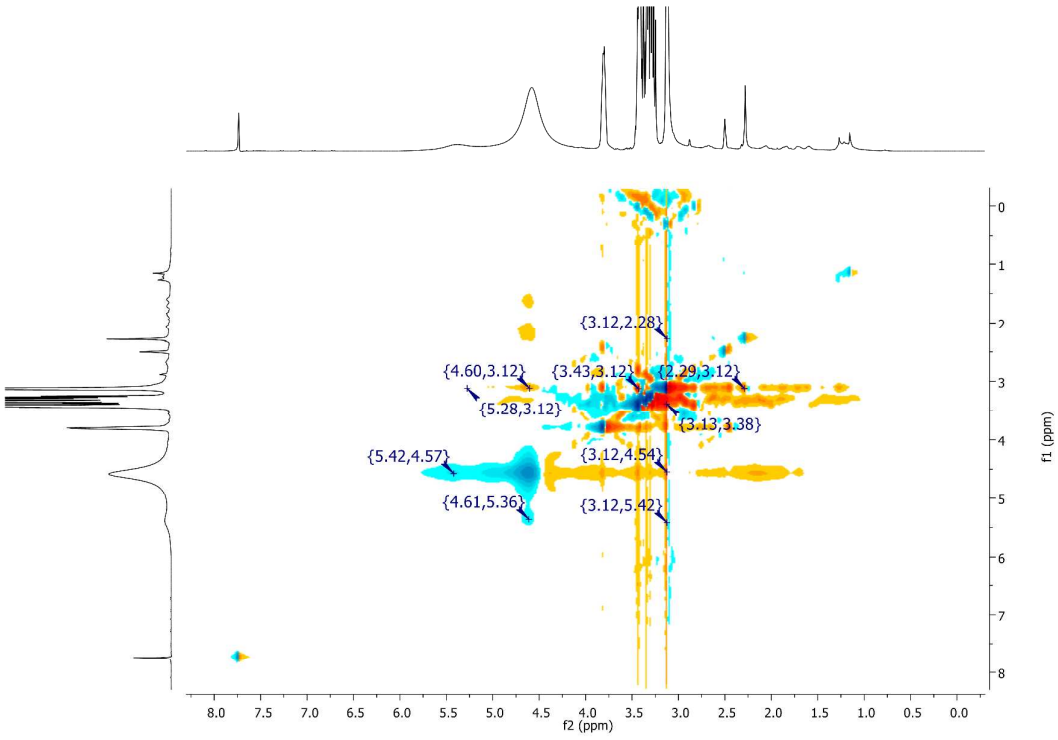


Table S2. Chemical shifts and interactions found by NOESY and NOE experiments



Group	δ_H (ppm)	Interaction	δ_H (ppm)
NMe_2	2.29	$NMe_2 - NMe_3$	2.29 – 3.12
NMe_3	3.12	$NMe_2 - H^3$	2.29 – 3.74
H^2	7.55	$NMe_2 - H^4$	2.29 – 2.58
H^3	3.74	$NMe_3 - H^3$	3.12 – 3.74
H^4	2.58	$NMe_3 - H^5$	3.12 – 5.48
H^5	5.48	$NMe_3 - H^6$	3.12 – 4.58
H^6	4.58	$NMe_3 - H^8$	3.12 – 3.43
H^8	3.43	$H^6 - H^5$	4.58 – 5.48
H^9	4.58	$H^5 - H^9$	4.58 – 5.48



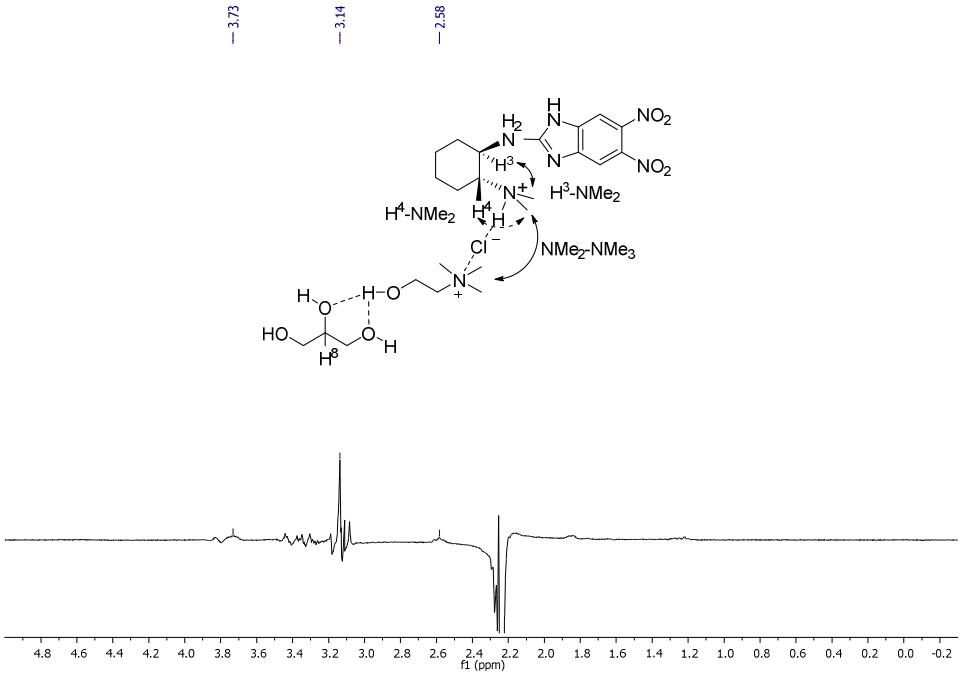


Figure S15. NOE experiment over **5**+DES with irradiation of the NMe_2 protons (δ_H = 2.28 ppm)

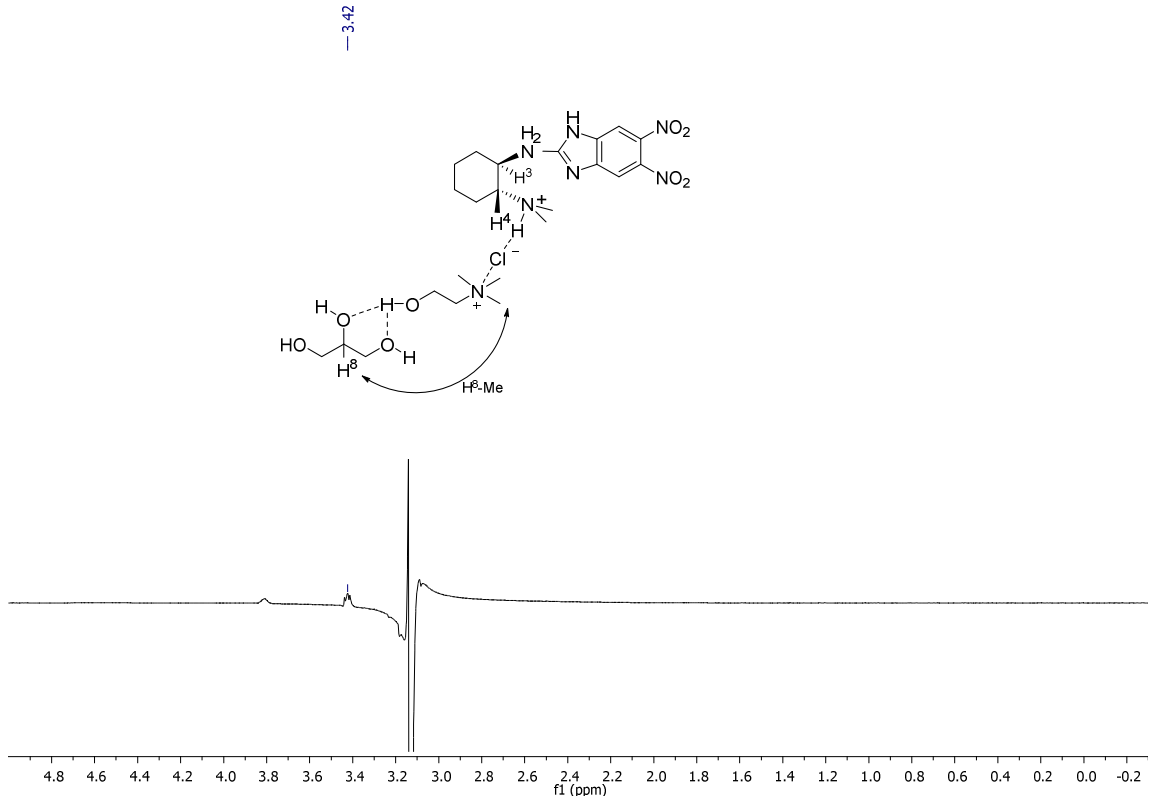


Figure S16 NOE experiment over **5**+DES with irradiation of the NMe_3 protons (δ_H = 3.13 ppm)

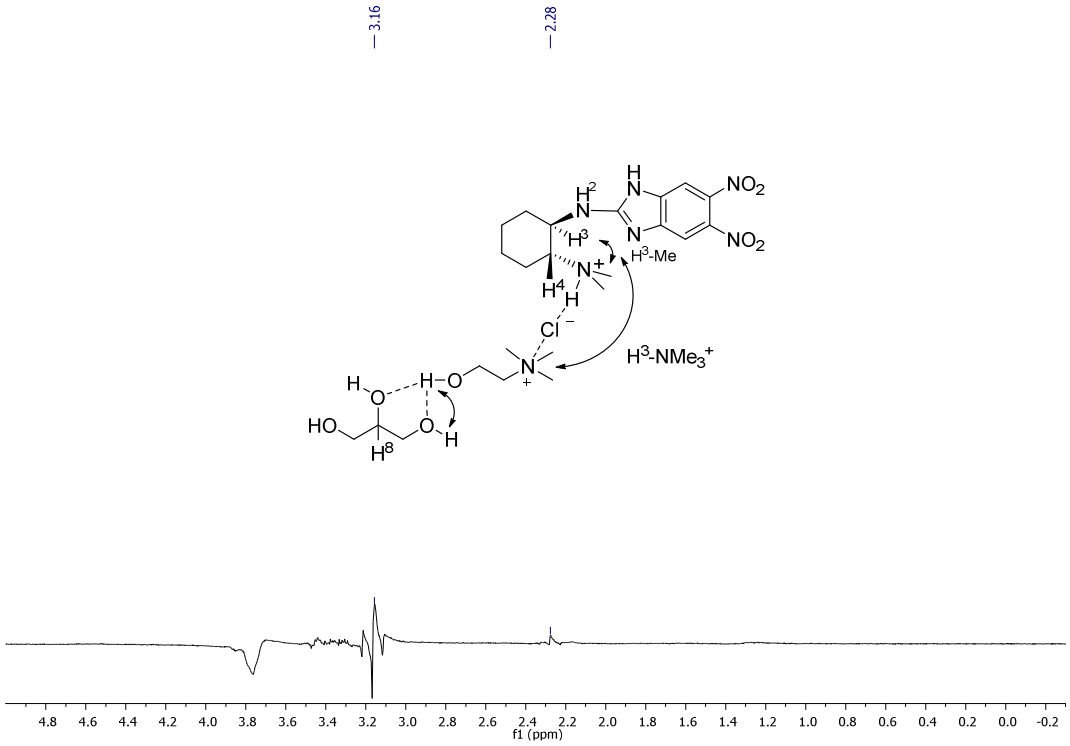


Figure S17. NOE experiment over **5**+DES with irradiation of H^3 proton (δ_H = 3.73 ppm)

(S1) Almaşi, D.; Alonso, D. A.; Gómez-Bengoa, E.; Nájera, C. *J. Org. Chem.* **2009**, *74*, 6163-6168.

(S2) Gómez-Torres, E.; Alonso, D. A.; Gómez-Bengoa, E.; Nájera, C. *Eur. J. Org. Chem.* **2013**, *2013*, 1434-1440.

(S3) Evans, D. A.; Mito, S.; Seidel, D. *J. Am. Chem. Soc.* **2007**, *129*, 11583-11592.

(S4) Okino, T.; Hoashi, Y.; Furukawa, T.; Xu, X.; Takemoto, Y. *J. Am. Chem. Soc.* **2005**, *127*, 119-125.

(S5) Ballini, R.; Maggi, R.; Palmieri, A.; Sartori, G. *Synthesis* **2007**, 3017-3020.

(S6) Luo, J.; Xu, L.-W.; Hay, R.; A., S.; Lu, Y. *Org. Lett.* **2009**, *11*, 437-440.