Electronic Supplementary Material (ESI) for ChemComm.

Supporting Information

Contents

1. General Information

Reactions were carried out under an atmosphere of nitrogen unless stated otherwise. Temperatures of 0 °C were obtained using an ice/water bath. Heating was achieved using an oil bath equipped with a contact thermometer.

Anhydrous CH_2Cl_2 and dimethylformamide (DMF) were purchased from Acros. All other solvents and reagents were used as supplied without prior purification.

Thin layer chromatography was performed on Merck Kieselgel 60 F_{254} 0.25 mm pre-coated aluminium plates. Product spots were visualized under UV light (λ = 254 nm) and/or by staining with potassium permanganate solution. Flash chromatography was performed using VWR silica gel 60 (40-63 µm particle size) using head pressure by means of a nitrogen line.

^{1}H, ^{13}C, and ^{19}F NMR spectra were recorded using a Bruker Avance III 300 MHz, Bruker Avance II 400 MHz, Bruker Avance 500 MHz, or a Bruker Avance III HD 700 MHz, in the deuterated solvent stated, using the residual non-deuterated solvent signal as an internal reference. Chemical shifts are quoted in ppm with signal splittings recorded as singlet (s), doublet (d), triplet (t), quartet (q), quintet (qn), sextet (sext), septet (sept), octet (oct), nonet (non) and multiplet (m). The abbreviation br denotes broad. Coupling constants, *J*, are measured to the nearest 0.1 Hz and are presented as observed.

Infrared spectra were recorded on a PerkinElmer UATR Two spectrometer with attenuated total reflectance. Absorption maxima (λ_{max}) are reported in wavenumbers (cm^{-1}).

HRMS was recorded on a Waters Xevo G2-XS Quadrupole Time-of-Flight (QToF) spectrometer equipped with a Waters Acquity UPLC i-Class LC system, under conditions of electrospray ionisation (ESI). The mass reported is that containing the most abundant isotopes, with each value rounded to 4 decimal places and within 10 ppm of the calculated mass.

Chiral normal phase HPLC was performed on a Dionex Ultimate 3000 HPLC unit equipped with UV-vis diode-array detector, fitted with the appropriate Daicel Chiralpak column (dimensions: 0.46 cm ø x 25 cm) along with the corresponding guard column (0.4 cm ø x 1 cm). Wavelengths (λ) are reported in nm, retention times (t_R) are reported in minutes and solvent flow rates are reported in mL min^{-1}.

2. General procedures

2.1 General Procedure A: Chlorination of Secondary Amides

To a round bottomed flask, equipped with a stirrer bar was added trichloroisocyanuric acid (1.1 eq.) and CH_2Cl_2 (9.1 mL/mmol). The resulting stirred suspension was cooled to 0 °C and the appropriate secondary amide **1a-l** (1 eq.) was added portion wise. Following the addition, the ice-bath was removed and the reaction was stirred for 30 mins at room temperature. The reaction was then diluted with water, the layers separated, and the aqueous layer extracted twice with CH_2Cl_2. The combined organics were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude residue was purified via column chromatography (see experimental methods section for details).

2.2 General Procedure B: Determination of Racemisation Barrier

According to the literature method,[1] the appropriate racemic compound (1 mg) was dissolved in 2 mL HPLC grade *n*-hexane. The sample was subjected to semi-preparative normal-phase HPLC (100 µL injection volume) under the specified conditions using an analytical normal phase chiral column (dimensions: 0.46 cm ø x 25 cm) along with the corresponding guard column (0.4 cm ø x 1 cm). The slower eluting enantiomer was collected into a HPLC vial and the resulting solution was immediately analyzed by normal phase HPLC under identical conditions (100 µL injection volume). The enantiomeric ratio and time were recorded and taken as the reference for initial time and enantiomeric ratio. The same sample was then allowed to stand at room temperature (20 °C, 293 K) reinjecting (100 µL injection volumes) at regular intervals. The data obtained form these HPLC experiments is shown in the experimental methods section below.

A graph of ln(1/ee) was plotted against time (s) to yield the rate constant of racemisation (k_{rac}) as the gradient. The half-life of racemisation ($t_{1/2}$rac) was calculated according to equation **(1)** and the rate constant of enantiomerisation (k_{ent}) was calculated according to equation **(2)**. The barrier to racemisation was then calculated according to the Eyring equation **(3)**, where R is the gas constant (8.314 J K^{-1} mol^{-1}); T is the temperature in Kelvin; k_B is the Boltzmann constant (1.381×10^{-23} J K^{-1}) and h is Planck's constant (6.626×10^{-34} J s).

$$\textbf{(1)} \qquad t_{\frac{1}{2}}rac = \frac{\ln(2)}{k_{rac}}$$

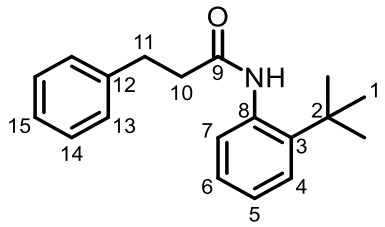
$$\textbf{(2)} \qquad k_{ent} = \frac{k_{rac}}{2}$$

$$\textbf{(3)} \qquad \Delta G^{\ddagger} = -RTln\left(\frac{k_{ent}h}{k_BT}\right)$$

3. Experimental Procedures

3.1 *Synthesis of Secondary Amide Starting Materials*

N-(2-(*tert*-Butyl)phenyl)-3-phenylpropanamide, 1a

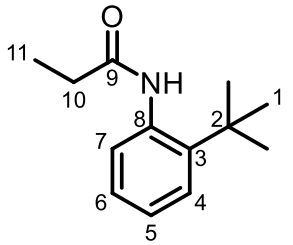


A stirred solution of hydrocinnamic acid (5.54 g, 36.9 mmol, 1.1 eq.) in $SOCl_2$ (17 mL, 230 mmol, 7 eq.) was heated to reflux for 3 hours. The solution was allowed to cool and the $SOCl_2$ was removed *in vacuo* to yield the acid chloride as a yellow oil. In a separate flask, 2-*tert*-butyl aniline (5.00 g, 33.5 mmol, 1 eq.) was dissolved in CH_2Cl_2 (115 mL) and cooled to 0 °C. Triethylamine (5.1 mL, 36.7 mmol, 1.1 eq.) was added and the acid chloride was added to the stirred solution dropwise. The solution was warmed to room temperature and stirred for 16 h. The reaction was diluted with water, the layers separated and the aqueous layer extracted twice with CH_2Cl_2. The combined organics were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude residue was purified by recrystallization (EtOAc/*n*-hexane) to afford compound **1h** as an off white solid (6.02 g, 64% yield). Spectral data is consistent with that reported previously.[2]

^{1}H NMR (400 MHz, $CDCl_3$) δ_H 7.52 (d, *J* = 7.8 Hz, 1H, H_{Ar}), 7.41 – 7.04 (m, 9H, 8H_{Ar} and N-H), 3.10 (t, *J* = 7.6 Hz, 2H, H_{10}/H_{11}), 2.71 (t, *J* = 7.6 Hz, 2H, H_{10}/H_{11}), 1.32 (s, 9H, H_1).

^{13}C NMR (101 MHz, $CDCl_3$) δ_C 170.5, 142.8, 140.8, 135.1, 128.7, 128.6, 128.2, 126.9, 126.7, 126.5, 126.3, 39.7, 34.6, 31.6, 30.8.

N-(2-(*tert*-Butyl)phenyl)propionamide, 1b



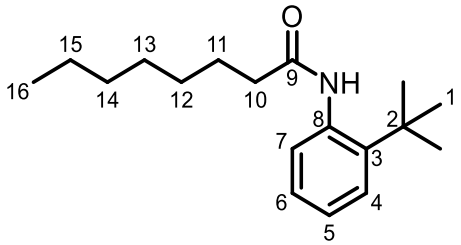
To a stirred solution of 2-*tert*-butylaniline (1.00 g, 6.70 mmol, 1 eq.) in CH_2Cl_2 (22 mL), was added triethylamine (1.0 mL, 7.2 mmol, 1.1 eq.). The mixture was cooled to 0 °C and propionyl chloride (0.64 mL, 7.3 mmol, 1.1 eq.) was added dropwise. The mixture was warmed to room temperature and stirred for 1 h. Water was then added, the layers separated, and aqueous layer extracted twice with CH_2Cl_2. The combined organic extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by recrystallization (EtOAc/ petrol 40-60) to afford compound **1b** as a white solid (995 mg, 72% yield).

Spectral data is consistent with that previously reported.[3]

^{1}H NMR (300 MHz, CDCl3) δ_H 7.59 (d, J = 7.7 Hz, 1H, H_{Ar}), 7.41 (d, J = 7.6 Hz, 1H, H_{Ar}), 7.33 – 7.09 (m, 3H, 2H_{Ar} and N-H), 2.46 (q, J = 7.5 Hz, 2H, H_{10}), 1.43 (s, 9H, H_1), 1.31 (t, J = 7.6 Hz, 3H, H_{11}).

^{13}C NMR (75 MHz, CDCl3) δ_C 171.9, 142.5, 135.2, 128.1, 126.8, 126.5, 126.1, 34.6, 30.8, 30.7, 9.8.

N-(2-(*tert*-Butyl)phenyl)octanamide, 1c



To a stirred solution of 2-*tert*-butyl aniline (250 mg, 1.68 mmol, 1 eq.) in CH_2Cl_2 (5.5 mL) was added triethylamine (0.26 mL, 1.8 mmol, 1.1 eq.). The mixture was cooled to 0 °C and octanoyl chloride (0.31 mL, 1.8 mmol, 1.1 eq.) was added dropwise. The reaction was warmed to room temperature and allowed to stir for 2 hours. The reaction was diluted with water, the layers separated, and the aqueous layer extracted twice with CH_2Cl_2. The combined organics were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude residue was purified by column chromatography (25% Et_2O/ petrol 40-60) to afford **1c** as a white solid (290 mg, 63% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, *J* = 7.9 Hz, 1H, H_4), 7.39 (d, *J* = 7.9 Hz, 1H, H_7), 7.26 – 7.11 (m, 3H, H_5 and H_6 and N-H), 2.39 (t, *J* = 7.6 Hz, 2H, H_{10}), 1.75 (qn, *J* = 7.7 Hz, 2H, H_{11}), 1.50 – 1.18 (m, 17H, H_1, H_{12}, H_{13}, H_{14}, H_{15}), 0.88 (t, *J* = 5.9 Hz, 3H, H_{16}).

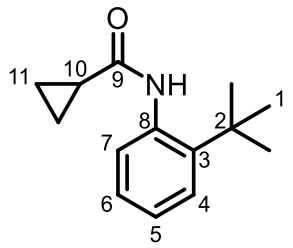
^{13}C NMR (75 MHz, $CDCl_3$) δ_C 171.5, 142.5, 135.4, 128.1, 127.0, 126.6, 126.2, 38.0, 34.7, 31.8, 30.9, 29.5, 29.2, 25.8, 22.7, 14.2.

HRMS (ESI$^+$): m/z calcd. for $C_{18}H_{30}NO^+$ $[M+H]^+$ 276.2322; found 276.2308, Δ 5.1 ppm.

FTIR (neat) v/cm^{-1}: 3262, 2958, 2915, 2849, 1649, 1517, 1286, 1182, 1052, 756, 698, 561.

Melting point (°C): 82-84.

N-(2-(*tert*-Butyl)phenyl)cyclopropanecarboxamide, 1d



A stirred solution of 2-*tert*-butylaniline (1.00 g, 6.70 mmol, 1 eq.) and triethylamine (1.0 mL, 7.4 mmol, 1.1 eq.) in CH_2Cl_2 (22 mL) was cooled to 0 °C. Cyclopropane carbonyl chloride (0.66 mL, 7.4 mmol, 1.1 eq.) was added dropwise and the mixture was stirred at room temperature for 16 hours. The reaction was diluted with water, the layers separated and the aqueous layer was extracted twice with CH_2Cl_2. The combined organics were dried

over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude residue was recrystallised (EtOAc/*n*-Hexane) to afford **1d** as white crystals (1.22 g, 84 % yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ_H 7.67 – 7.33 (m, 2H, $2H_{Ar}$), 7.27 – 7.11 (m, 3H, $2H_{Ar}$ and N-H), 1.61 – 1.34 (m, 10H, H_1, H_{10}), 1.14 – 0.57 (m, 4H, H_{11}).

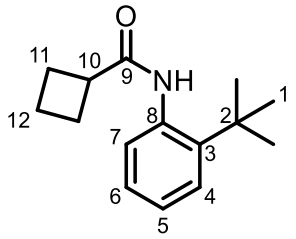
^{13}C NMR (75 MHz, $CDCl_3$) δ_C 171.9, 142.4, 135.6, 128.1, 126.9, 126.6, 126.0, 30.8, 15.9, 8.7, 7.6.

HRMS (ESI$^+$): m/z calc'd for $C_{14}H_{20}NO^+$ $[M+H]^+$ 218.1539; found 218.1554, Δ 6.9 ppm.

FTIR (neat) ν/cm^{-1} = 3242, 3004, 2957, 1650, 1524, 1199, 755.

Melting point (°C) 151-154.

N-(2-(*tert*-Butyl)phenyl)cyclobutanecarboxamide, 1e



2-*tert*-butylaniline (1.00 g, 6.70 mmol, 1.0 eq.) and cyclobutanecarboxylic acid (1.0 mL, 10 mmol, 1.5 eq.) were dissolved in CH_2Cl_2 (7 mL). The stirred solution was cooled to 0 °C and *N*-(3-dimethylaminopropyl)-*N*'-ethylcarbodiimide hydrochloride (1.94 g, 10.1 mmol, 1.5 eq.) was charged portion wise. The mixture was warmed to room temperature and stirred for 16 h. The reaction was then poured into water, the layers separated, and the aqueous layer extracted twice with CH_2Cl_2. The combined organics were sequentially washed with $NaHCO_3$, 1M HCl and brine. The combined organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude residue was recrystallised (EtOAc/*n*-hexane) to yield **1e** as a white solid (850 mg, 55% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.65 (d, *J* = 7.8 Hz, 1H, H_{Ar}), 7.37 (d, *J* = 7.6 Hz, 1H, H_{Ar}), 7.25 – 6.87 (m, 3H, $2H_{Ar}$ and N-H), 3.21 (qn, *J* = 8.6 Hz, 1H, H_{10}), 2.51 – 2.17 (m, 4H, H_{11}), 2.13 – 1.83 (m, 2H, H_{12}), 1.40 (s, 9H, H_1).

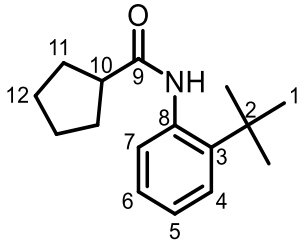
^{13}C NMR (75 MHz, $CDCl_3$) δ_C 173.0, 142.1, 135.5, 127.5, 126.9, 126.6, 125.9, 41.0, 34.7, 30.8, 25.4, 18.2.

HRMS (ESI$^+$): m/z calc'd for $C_{15}H_{21}NNaO^+$ $[M+Na]^+$ 254.1515; found 254.1494, Δ 8.3 ppm.

FTIR (neat) ν/cm^{-1} = 3244, 2998, 2966, 2865, 1640, 1515, 1250, 1228, 746, 671, 488.

Melting point (°C): 138-140.

N-(2-(*tert*-Butyl)phenyl)cyclopentanecarboxamide, 1f



A stirred solution of 2-*tert*-butylaniline (1.00 g, 6.70 mmol, 1 eq.) and triethylamine (1.0 mL, 7.4 mmol, 1.1 eq.) in CH_2Cl_2 (22 mL) was cooled to 0 °C. Cyclopentanecarbonyl chloride (0.90 mL, 7.4 mmol, 1.1 eq.) was added dropwise and the mixture was warmed to room temperature and stirred for 16 h. The reaction was diluted with water, the layers separated and the aqueous layer was extracted twice with CH_2Cl_2 . The combined organics were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude residue was recrystallised (EtOAc/*n*-hexane) to afford **1f** as a white solid (826 mg, 50 % yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.64 (d, *J* = 7.8 Hz, 1H, H_{Ar}), 7.38 (dd, *J* = 7.8, 1.7 Hz, 1H, H_{Ar}), 7.29 – 7.08 (m, 3H, $2H_{Ar}$ and N-H), 2.73 (qn, *J* = 8.1 Hz, 1H, H_{10}), 2.13 – 1.55 (m, 8H, H_{11} and H_{12}), 1.41 (s, 9H, H_1).

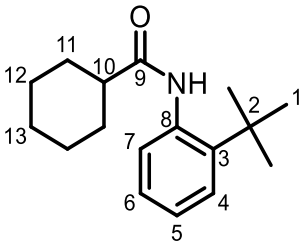
^{13}C NMR (75 MHz, $CDCl_3$) δ 174.3, 142.1, 135.6, 127.7, 126.9, 126.6, 125.9, 47.2, 34.7, 30.8, 30.4, 26.0.

HRMS (ESI$^+$): m/z calc'd for $C_{16}H_{23}NNaO^+$ $[M+Na]^+$ 268.1672; found 268.1651, Δ 7.8 ppm.

FTIR (neat) ν/cm^{-1}: 3242, 2953, 2866, 1648, 1520, 756, 706.

Melting point(°C): 148-149.

N-(2-(*tert*-Butyl)phenyl)cyclohexanecarboxamide, 1g

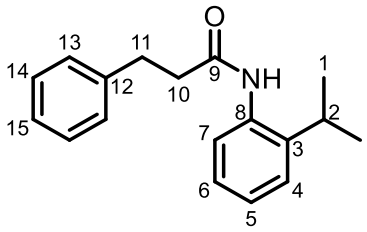


2-*tert*-Butyl aniline (1.00 g, 6.70 mmol, 1 eq.) and cyclohexanecarboxylic acid (1.3 mL, 10 mmol, 1.5 eq.) were dissolved in CH_2Cl_2 (6.7 mL). The stirred solution was cooled to 0 °C and *N*-(3-dimethylaminopropyl)-*N*'-ethylcarbodiimide hydrochloride (1.94 g, 10.1 mmol, 1.5 eq.) was charged portion wise. The mixture was warmed to room temperature and stirred for 16 h. The reaction was then poured into water, the layers separated, and the aqueous layer extracted twice with CH_2Cl_2. The combined organics were washed sequentially with $NaHCO_3$, 1M HCl and brine. The combined organics were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude residue was recrystallised (EtOAc/*n*-hexane) to yield **1g** as white crystals (442 mg, 25 % yield). Spectral data is consistent with that reported previously.[2]

^{1}H NMR (400 MHz, $CDCl_3$) δ_H 7.62 (d, *J* = 7.8 Hz, 1H, H_{Ar}), 7.40 (d, *J* = 7.7 Hz, 1H, H_{Ar}), 7.29 – 7.12 (m, 3H, $2H_{Ar}$ and N-H), 2.31 (tt, *J* = 11.9, 3.3 Hz, 1H, H_{10}), 2.11 – 1.20 (m, 10H, H_{11}, H_{12} and H_{13}) 1.44 (s, 9H, H_1).

^{13}C NMR (75 MHz, $CDCl_3$) δ_C 174.2, 142.5, 135.5, 128.0, 126.9, 126.6, 126.0, 46.7, 34.7, 30.8, 29.8, 25.9, 25.9.

N-(2-isopropylphenyl)-3-phenylpropanamide, 1h



A stirred solution of 2-isopropylaniline (450 mg, 3.33 mmol, 1 eq.) and triethylamine (0.51 mL, 3.7 mmol, 1.1 eq.) in CH_2Cl_2 (11.3 mL) was cooled to 0 °C. Freshly prepared hydrocinnamoyl chloride (0.55 mL, 3.7 mmol, 1.1 eq.) was added dropwise and the mixture was warmed to room temperature and stirred for 16 hours. After this time, the reaction was diluted with H_2O and CH_2Cl_2, the layers separated, and the aqueous layer was extracted with CH_2Cl_2 twice. The combined organics were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude residue was purified by column chromatography (50% Et_2O/ petrol 40-60) to yield **1h** as an off-white solid (739 mg, 83% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ_H 7.61 – 7.53 (m, 1H, H_7), 7.36 – 7.12 (m, 8H, H_{Ar}), 6.91 (s, 1H, N-H), 3.08 (t, J = 7.4 Hz, 2H, H_{11}), 2.78 – 2.64 (m, 3H, H_2 + H_{10}), 1.13 (d, J = 6.9 Hz, 6H, H_1).

Diagnostic signals for the minor amide isomer were observed at; 2.99-2.89 (m, H_{11}) 2.43-2.35 (m, H_{10}),

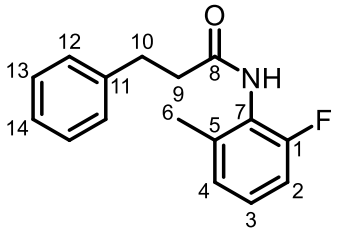
^{13}C NMR (101 MHz, $CDCl_3$) δ_C 170.9, 140.9, 140.7, 133.9, 128.8, 128.5, 126.5, 126.4, 126.3, 125.7, 125.2, 39.3, 31.8, 27.8, 23.2.

HRMS (ESI+): m/z calc'd for $C_{18}H_{21}NONa^+$ $[M+Na]^+$ 290.1515; found 290.1526, Δ 3.8 ppm.

IR (cm^{-1}): 3250, 2963, 1641, 1525, 753, 698

m.p (°C): 87-89

N-(2-Fluoro-6-methylphenyl)-3-phenylpropanamide, 1i



A stirred solution of 2-fluoro-6-methylaniline (416 mg, 3.33 mmol, 1 eq.) and triethylamine (0.51 mL, 3.7 mmol, 1.1 eq.) in CH_2Cl_2 (11.3 mL) was cooled to 0 °C. Freshly prepared hydrocinnamoyl chloride (0.55 mL, 3.7 mmol, 1.1 eq.) was added dropwise and the mixture was warmed to room temperature and stirred for 16 hours. After this time, the reaction was diluted with H_2O and CH_2Cl_2, the layers separated, and the aqueous layer was extracted with CH_2Cl_2 twice. The combined organics were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude residue was purified by column chromatography (50% Et_2O/petrol 40-60) to yield **1i** as an off-white solid (643 mg, 75% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ_H 7.35 – 7.18 (m, 5H, H_{12} + H_{13} + H_{14}), 7.15 – 7.05 (m, 1H, H_3), 7.00 – 6.87 (m, 2H, H_2 + H_4), 6.81 (s, 1H, N-H), 3.06 (t, J = 7.6 Hz, 2H, H_{10}), 2.72 (t, J = 7.6 Hz, 2H, H_9), 2.11 (s, 3H, H_6).

Diagnostic signals for the minor amide isomer were observed at; 2.93 (s, H_9/H_{10}), 2.15 (s, H_6).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.0, 157.7 (d, *J* = 246.9 Hz), 140.7, 138.0, 128.7, 128.5, 127.9 (d, *J* = 8.9 Hz), 126.5, 125.9 (d, *J* = 3.4 Hz), 123.2 (d, *J* = 13.1 Hz), 113.2 (d, *J* = 20.5 Hz), 38.3, 31.8, 18.1.

^{19}F NMR (376 MHz, $CDCl_3$) δ_F -121.94 (dd, *J* = 9.6, 5.5 Hz).

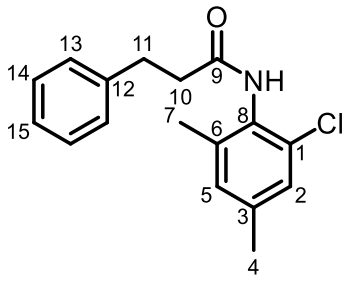
A diagnostic signal for the minor amide isomer was observed at; -120.29 (s)

HRMS (ESI+): m/z calc'd for $C_{16}H_{17}FNO^+$ $[M+H]^+$ 258.1289; found 258.1291, Δ 0.8ppm.

IR (cm^{-1}): 3243, 3029, 1657, 1525, 1275,774

m.p (°C): 117-119

N-(2-Chloro-4,6-dimethylphenyl)-3-phenylpropanamide, 1j



A stirred solution of hydrocinnamic acid (849 mg, 5.65 mmol, 1.1 eq.) in $SOCl_2$ (2.6 mL, 36 mmol, 7 eq.) was heated to reflux for 3 hours. The solution was allowed to cool and the $SOCl_2$ was removed *in vacuo* to yield the acid chloride as a yellow oil. In a separate flask, 2-chloro-4,6-dimethylaniline (800 mg, 5.14 mmol, 1 eq.) was dissolved in CH_2Cl_2 (18 mL) and cooled to 0 °C. Triethylamine (0.79 mL, 5.7 mmol, 1.1 eq.) was added and the acid chloride was added to the stirred solution dropwise. The solution was warmed to room temperature and stirred for 16 h. The reaction was diluted with water, the layers separated and the aqueous layer extracted twice with CH_2Cl_2. The combined organics were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude residue was purified by column chromatography (40% Et_2O/ petrol 40-60) to yield **1j** as an off white solid (677 mg, 46% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ_H 7.33 – 7.19 (m, 5H, H_{Ar}), 7.06 – 7.04 (m, 1H, H_2), 6.93 – 6.91 (m, 1H, H_5), 6.86 (br, 1H, N-H), 3.08 (t, *J* = 7.7 Hz, 2H, H_{10}), 2.76 – 2.70 (m, 2H, H_{11}), 2.26 (s, 3H, H_4), 2.11 (s, 3H, H_7).

Diagnostic signals for the minor amide isomer were observed at; 7.14 – 7.08 (m, H_{Ar}), 6.95 (s, H_2/H_5) 6.60 (br s, N-H), 2.99 – 2.86 (m, H_{10}/H_{11}), 2.29 (s, H_4/H_7).

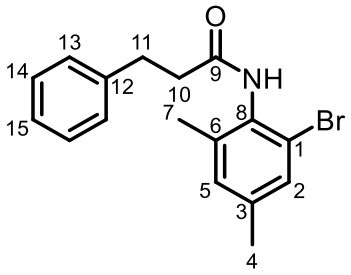
^{13}C NMR (75 MHz, $CDCl_3$) δ_C 170.9, 140.7, 138.2, 137.8, 131.1, 130.1, 129.9, 128.7, 128.6, 127.5, 126.4, 38.3, 31.7, 20.9, 18.9.

HRMS (ESI$^+$) m/z calcd. For $C_{17}H_{19}ClNO^+$ $[M+H]^+$ 288.1150; found 288.1134, Δ 5.6 ppm.

FTIR (neat) ν/cm^{-1}: 3239, 3025, 2928, 1660, 1518, 971, 848, 696, 485.

Melting point (°C): 164-166.

N-(2-Bromo-4,6-dimethylphenyl)-3-phenylpropanamide, 1k



A stirred solution of 2-bromo-4,6-dimethylaniline (666 mg, 3.33 mmol, 1 eq.) and triethylamine (0.51 mL, 3.7 mmol, 1.1 eq.) in CH_2Cl_2 (11.3 mL) was cooled to 0 °C. Hydrocinnamoyl chloride (0.55 mL, 3.7 mmol, 1.1 eq.) was added dropwise and the mixture was warmed to room temperature and stirred for 16 hours. After this time, the reaction was diluted with H_2O and CH_2Cl_2, the layers separated, and the aqueous layer was extracted with CH_2Cl_2 twice. The combined organics were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude residue was purified by column chromatography (1:1 Et_2O/petrol 40-60) to yield **1k** as an off-white solid (297 mg, 27% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ_H 7.38 – 7.17 (m, 6H, H_{Ar}), 6.99 – 6.95 (m, 1H, H_5), 6.84 (s, 1H, N-H), 3.09 (t, J = 7.7 Hz, 2H, H_{11}), 2.80 – 2.69 (m, 2H, H_{10}), 2.27 (s, 3H, H_4), 2.14 (s, 3H, H_7).

Diagnostic signals for the minor amide isomer were observed at; 7.14 – 7.08 (m, H_{Ar}), 7.00 (s, H_5), 6.62 (s, N-H).

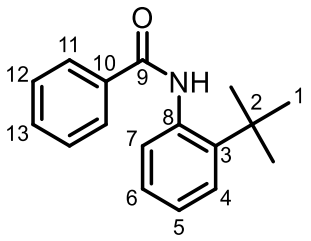
^{13}C NMR (101 MHz, $CDCl_3$) δ_C 170.7, 140.7, 138.7, 137.9, 131.3, 130.9, 130.7, 128.7, 128.6, 126.5, 121.9, 38.4, 31.7, 20.8, 19.2.

HRMS (ESI+): m/z calc'd for $C_{17}H_{18}NOBrNa^+$ $[M+Na]^+$ 354.0464; found 354.0464, Δ 0.1 ppm.

IR (cm^{-1}): 3243, 3060, 1657, 1519, 1234, 697

m.p (°C): 157-160

N-(2-(*tert*-Butyl)phenyl)benzamide, 1l

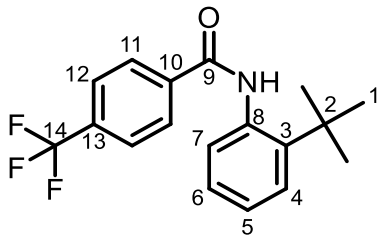


A stirred solution of 2-*tert*-butylaniline (0.957 g, 6.41 mmol, 1 eq.) in EtOAc (6.4 mL) was cooled to 0 °C. Benzoyl chloride (0.74 mL, 6.4 mmol, 1 eq.) was added dropwise followed by the dropwise addition of a saturated solution of aqueous Na_2CO_3 (3.2 mL). The reaction mixture was warmed to room temperature and stirred for 2 hours and then the reaction mixture was diluted with water and extracted three times with EtOAc. The combined organics were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude solid was recrystallised (EtOAc/ petrol 40-60) affording the title compound **1l** as a white solid (1.14 g, 70%). Spectral data is consistent with that previously reported.[4]

^{1}H NMR (300 MHz, $CDCl_3$): δ_H 7.96 – 7.88 (m, 3H, $2H_{Ar}$ + N-H), 7.74 (d, *J* = 7.8 Hz, 1H, H_{Ar}), 7.62 – 7.47 (m, 3H, $3H_{Ar}$), 7.45 (dd, *J* = 7.8, 1.7 Hz, 1H, H_{Ar}), 7.34 – 7.16 (m, 2H, H_{Ar}), 1.46 (s, 9H, H_1).

^{13}C NMR (75 MHz, $CDCl_3$): δ_C 165.8, 142.8, 135.4, 135.1, 132.0, 129.0, 128.0, 127.1, 127.1, 126.8, 126.4, 34.8, 30.9.

N-(2-(*tert*-Butyl)phenyl)-4-trifluoromethylbenzamide, 1m



para-Trifluoromethylbenzoic acid (1.40 g, 7.37 mmol, 1.1 eq.) was suspended in $SOCl_2$ (3.8 mL, 52 mmol, 7.0 eq.) and heated to reflux for 3 hours, with stirring. The solution was allowed to cool and the $SOCl_2$ was removed *in vacuo* to yield the acid chloride as a yellow oil. In a separate flask, 2-*tert*-butylaniline (1.00 g, 6.70 mmol, 1.0 eq.) was dissolved in CH_2Cl_2 (25 mL) and cooled to 0 °C. Triethylamine (1.0 mL, 7.4 mmol, 1.1 eq.) was added and the acid chloride was added to the stirred solution dropwise. The reaction was warmed to room temperature and stirred for 16 h. The reaction was diluted with water, the layers separated and the aqueous layer extracted twice with CH_2Cl_2. The combined organics were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude residue was purified by column chromatography (10% EtOAc/ petrol 40-60) to yield **1m** as an off white solid (403 mg, 19% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 8.02 (d, *J* = 8.1 Hz, 2H, $2H_{Ar}$), 7.90 (s, 1H, N-H), 7.79 (d, *J* = 8.2 Hz, 2H, $2H_{Ar}$), 7.76 – 7.66 (m, 1H H_{Ar}), 7.46 (dd, *J* = 7.8, 1.8 Hz, 1H, H_{Ar}), 7.34 – 7.27 (m, 1H, H_{Ar}), 7.28 – 7.17 (m, 1H, H_{Ar}), 1.45 (s, 9H, H_1).

^{13}C NMR (176 MHz, $CDCl_3$) δ_C 164.5, 142.8, 138.4, 135.0, 133.7 (q, *J*= 33.6 Hz), 130.7, 128.0, 127.6, 127.2, 126.9 (q, *J* = 16.1 Hz), 126.2, 123.8 (q, *J* = 272.4 Hz), 34.8, 31.0.

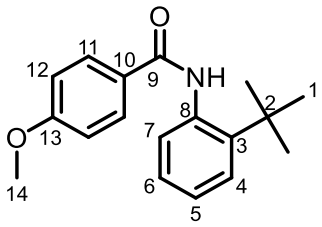
^{19}F NMR (282 MHz, $CDCl_3$) δ_F – 63.0.

HRMS (ESI^+): m/z calc'd for $C_{18}H_{18}F_3NNaO^+[M+Na]^+$ 344.1233; found 344.1211, Δ -6.4.

FTIR (neat) ν/cm^{-1} = 3252, 2992, 2965, 1649, 1529, 1316, 1125, 758.

Melting point (°C) 252-254.

N-(2-(*tert*-Butyl)phenyl)-4-methoxybenzamide, 1n



4-Methoxybenzoic acid (1.12 g, 7.37 mmol, 1.10 eq.) was dissolved in $SOCl_2$ (3.8 mL, 52 mmol, 7.0 eq.) and heated to reflux for 3 hours, with stirring. After this time, the mixture was allowed to cool and the $SOCl_2$ was

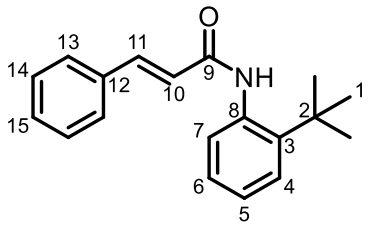
removed *in vacuo* to yield the acid chloride as a yellow oil. A stirred solution of 2-*tert*-butylaniline (1.00 g, 6.70 mmol, 1.0 eq.) and triethylamine (1.0 mL, 7.4 mmol, 1.1 eq.) in CH_2Cl_2 (25 mL) was cooled to 0 °C and the acid chloride was added dropwise. The solution was stirred at room temperature for 16 h. The reaction was diluted with water, the layers separated, and the aqueous layer extracted twice with CH_2Cl_2. The combined organics were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude residue was purified by column chromatography (20% EtOAc/ petrol 40-60) to yield **1n** as a white solid (1.39 g, 73% yield).

Spectral data is consistent with that previously reported in the literature.[5]

^{1}H NMR (300 MHz, d_6-DMSO) δ_H 9.66 (s, 1H, N-H), 7.99 (d, *J* = 8.3 Hz, 2H, H_{Ar}), 7.50 – 7.41 (m, 1H, H_{Ar}), 7.32 – 7.21 (m, 2H, H_{Ar}), 7.14 – 6.99 (m, 3H, H_{Ar}), 3.84 (s, 3H, H_{14}), 1.34 (s, 9H, H_1).

^{13}C NMR (75 MHz, d_6-DMSO) δ_C 165.6, 161.8, 147.1, 136.4, 132.2, 129.4, 127.1, 126.8, 126.7, 126.4, 113.6, 55.4, 34.9, 30.9.

N-(2-(*tert*-Butyl)phenyl)cinnamamide, 1o



To a stirred solution of 2-*tert*-butylaniline (957 mg, 6.41 mmol, 1.00 eq.) in CH_2Cl_2 (21 ml) was added triethylamine (1.0 ml, 7.1 mmol, 1.1 eq.). The solution was cooled to 0 °C and *trans*-cinnamoyl chloride (1.2 g, 7.1 mmol, 1.1 eq.) was added in small portions to the reaction. The reaction was stirred at room temperature for 16 h. The reaction was then diluted with water, the layers separated, and the aqueous layer was extracted twice with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude residue was purified by recrystallisation (EtOAc/ petrol 40-60) to afford **1o** as a white solid (1.29 g, 72 % yield).

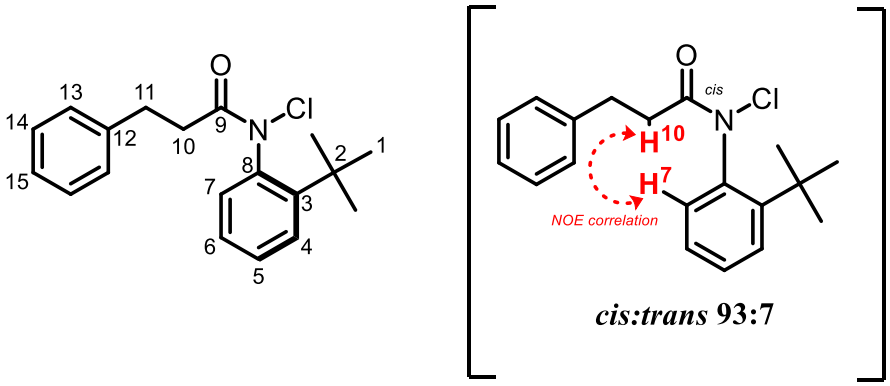
Spectral data is consistent with that previously reported.[2]

^{1}H NMR (300 MHz, $CDCl_3$): δ_H 7.79 (d, J = 15.6 Hz, 1H, H_{11}), 7.73 – 7.18 (m, 10H, H_{Ar} and N-H), 6.61 (d, J = 15.6 Hz, 1H, H_{10}), 1.47 (s, 9H, H_1)

^{13}C NMR (75 MHz, $CDCl_3$): δ_C 164.3, 142.8, 142.4, 135.2, 134.7, 130.0, 128.9, 128.2, 128.0, 126.9, 126.7, 126.4, 121.0, 34.8, 30.8.

3.2 *Synthesis of Chloroamides and Evaluation of Configurational Stability*

***rac*-N-(2-(*tert*-Butyl)phenyl)-N-chloro-3-phenylpropanamide, 2a**



According to a modification of general procedure A, a stirred suspension of trichloroisocyanuric acid (1.82 g, 7.82 mmol, 1.1 eq.) in CH_2Cl_2 (70 mL) was cooled to 0 ˚C and a solution of secondary amide **1a** (2.00 g, 7.11 mmol, 1.0 eq.) in CH_2Cl_2 (30 mL) was added dropwise. Following the addition, the ice-bath was removed and the reaction was stirred for 30 mins at room temperature. The reaction was then diluted with water, the layers separated, and the aqueous layer extracted twice with CH_2Cl_2. The combined organics were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude residue was purified via column chromatography (15% Et_2O/petrol 40-60) afforded **2a** as an off white solid (2.14 g, 95% yield).

^{1}H NMR (700 MHz, 298 K, $CDCl_3$) δ_H 7.50 (d, *J* = 8.1 Hz, 1H, H_4), 7.35 (t, *J* = 7.7 Hz, 1H, H_5), 7.26 – 7.16 (m, 4H, H_{14}, H_{15} and H_6), 7.09 – 7.05 (m, 2H, H_{13}), 6.90 (d, *J* = 7.8 Hz, 1H, H_7), 3.07 – 2.88 (m, 2H, H_{11}), 2.42 – 2.37 (m, 2H, H_{10}), 1.40 (s, 9H).

^{13}C NMR (176 MHz, 298 K, $CDCl_3$) δ_C 171.2, 148.2, 141.4, 140.5, 131.9, 130.6, 129.3, 128.7, 128.6, 128.0, 126.4, 37.5, 36.3, 31.9, 31.7.

^{1}H NMR (700 MHz, 273 K, $CDCl_3$) δ_H δ 7.50 (dd, *J* = 8.1, 1.5 Hz, 1H, H_4), 7.36 (ddd, *J* = 8.2, 7.3, 1.5 Hz, 1H, H_5), 7.27 – 7.22 (m, 2H, H_{14}), 7.21 – 7.16 (m, 2H, H_{15} and H_6), 7.07 (d, *J* = 7.1 Hz, 2H, H_{13}), 6.88 (dd, *J* = 7.8, 1.5 Hz, 1H, H_7), 3.01 (dt, *J* = 13.9, 7.9 Hz, 1H, H_{11}), 2.91 (ddd, *J* = 14.2, 8.4, 6.7 Hz, 1H, H_{11}'), 2.43 – 2.35 (m, 2H, H_{10}), 1.39 (s, 9H, H_1). Diagnostic signals for the minor *trans*-isomer were observed at; 7.48 – 7.44 (m, H_4), 7.34 – 7.28 (m, H_{13} and H_{Ar}), 7.16 – 7.13 (m, H_7), 3.16 – 3.08 (m, H_{10}), 1.35 (s, H_1). The identity of the major geometrical isomer was assigned as *cis*- on the basis of NOE correlations between H_{10} and H_7 (see spectra). A ratio of 93:7 *cis*/*trans* was measured from ^{1}H NMR data collected at 233 K.

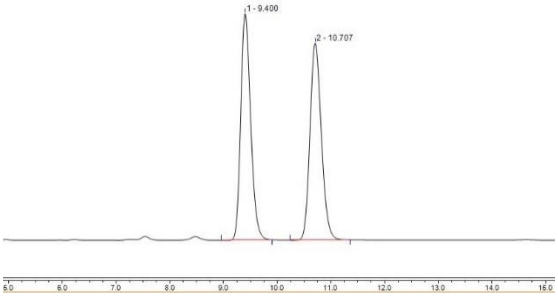
^{13}C NMR (176 MHz, 273 K, $CDCl_3$) δ_C ^{13}C NMR (176 MHz, $CDCl_3$) δ 176.0 (min.), 171.3 (maj.), 148.3 (min.), 148.0 (maj.), 142.6 (min.), 141.2 (maj.), 140.7 (min.), 140.4 (maj.), 131.8 (maj.), 131.6 (min.), 130.6 (maj.), 129.8 (min.), 129.3 (maj.) , 128.7 (min.), 128.7 (maj.), 128.6 (maj.), 128.5 (min.), 128.2 (min.), 128.1 (maj.), 128.0 (min.), 126.4 (maj.), 126.4 (min.), 37.6 (maj.), 36.3 (min.), 36.2 (maj.), 35.7 (min.), 31.9 (maj.), 31.6 (maj.), 31.3 (min.), 30.9 (min.)

HRMS (ESI$^+$): m/z calc'd for $C_{19}H_{23}ClNO^+$ $[M+H]^+$ 316.1463; found 316.1452, Δ -3.5 ppm.

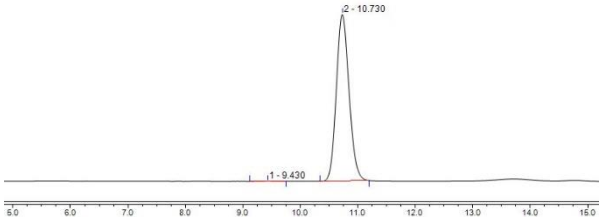
FTIR (neat) ν/cm^{-1} = 3252, 2992, 2965, 1649, 1529, 1316, 1125, 758.

Melting point (˚C) 63-64.

Chiral HPLC: Chiralpak-IC column. Solvent ratio = 90:10 *n*-hexane: ^{i}PrOH. Temperature = 25 °C. Flow rate = 1 ml/min, λ= 240 nm, τ_{ret} = 9.4 min and 10.7 min.



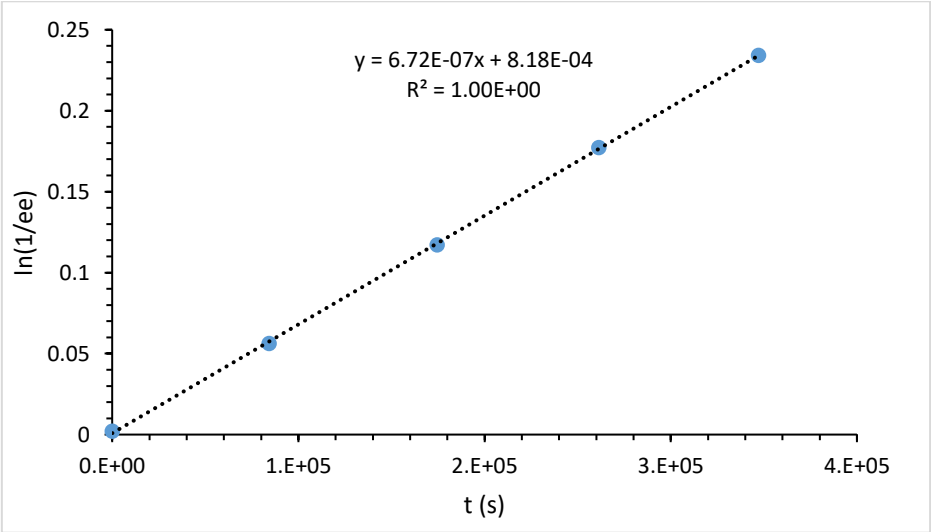
Ret.Time min	Amount n.a.	Rel.Area %	Area mAU*min	Height mAU
9.400	n.a.	50.04	91.8826	430.11
10.707	n.a.	49.96	91.7304	374.00



Ret.Time min	Amount n.a.	Rel.Area %	Area mAU*min	Height mAU
9.430	n.a.	0.10	0.0605	0.29
10.730	n.a.	99.90	58.4978	228.49

Racemization study for 2a: According to general procedure B, and using the conditions specified immediately above, an analytical quantity of the slower eluting enantiomer was collected by semipreparative HPLC and reinjected successively over time intervals, shown below, to calculate the rate of racemization.

Time (s)	% maj. enantiomer	% min. enantiomer	ln(1/ee)
0.00	99.90	0.10	0.00200
84240	97.27	2.73	0.0561
174480	94.47	5.53	0.117
261360	91.88	8.12	0.177
347160	89.56	10.44	0.234

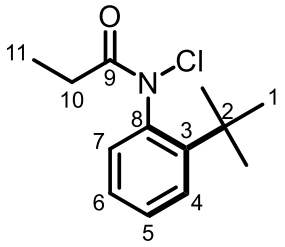


$$k_{rac} = 6.72 \times 10^{-7}\ s^{-1}$$

$$t_{\frac{1}{2}} rac = \mathbf{11.9\ days}$$

$$\Delta G^{\ddagger} = \mathbf{108.0\ kJ/mol}$$

***rac*-N-(2-(*tert*-Butyl)phenyl)-N-chloro-propionamide, 2b**



Synthesised from **1b** (110 mg, 0.536 mmol, 1.00 eq.), trichloroisocyanuric acid (137 mg, 0.589 mmol, 1.10 eq.) and CH_2Cl_2 (4.8 mL) according to general procedure A. Column Chromatography (5% EtOAc/petrol 40-60) afforded **2b** as a yellow solid (117 mg, 91% yield).

^{1}H NMR (300 MHz, $CDCl_3$, 298 K) δ_H ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53 (d, *J* = 8.1 Hz, 1H, H_4), 7.38 (t, *J* = 7.7 Hz, 1H, H_5), 7.31 – 7.24 (m, 1H, H_6), 7.17 (dd, *J* = 7.8, 1.6 Hz, 1H, H_7), 2.22 – 2.01 (m, 2H, H_{10}) 1.43 (s, 9H, H_1), 1.17 – 1.06 (m, 3H, H_{11}).

^{13}C NMR (126 MHz, $CDCl_3$, $CDCl_3$, 298 K) δ_C 172.9, 148.3, 141.7, 131.8, 130.5, 129.3, 128.0, 36.3, 31.7, 28.9, 9.8.

^{1}H NMR (500 MHz, $CDCl_3$, 263 K) δ_H 7.53 (dd, *J* = 8.1, 1.5 Hz, 1H, H_4), 7.48 – 7.36 (m, 1H, H_5), 7.36 – 7.23 (m, 1H, H_6), 7.18 (dd, *J* = 7.8, 1.6 Hz, 1H, H_7), 2.11 (m, 2H, H_{10} + H_{10}'), 1.42 (s, 9H, H_1), 1.09 (t, *J* = 7.4 Hz, 3H, H_{11}). Diagnostic peaks for the minor *trans* isomer were observed at 7.50 – 7.43 (m, H_{Ar}), 7.35-7.31 (m, H_{Ar}), 2.87 – 2.68 (m, H_{10} + H_{10}'), 1.36 (s, H_1), 1.21 (t, J = 7.2 Hz, H_{11}). A ratio of 88:12 *cis*/*trans* was measured from the ^{1}H NMR data collected at 263 K.

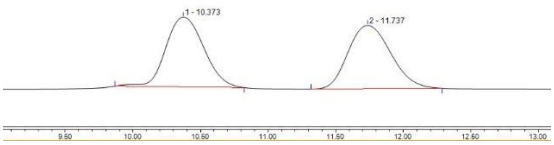
^{13}C NMR (126 MHz, $CDCl_3$, 263 K) δ_C 177.7 (min.), 173.1 (maj.), 148.2 (min.), 147.9 (maj.), 142.8 (min.), 141.4 (maj.), 131.7 (maj.), 131.5 (min.), 130.6 (maj.), 129.7 (min.), 129.3 (maj.), 128.1 (min.), 128.1 (maj.), 128.0 (min.), 36.3 (maj.), 35.6 (min.), 31.6 (maj.), 31.2 (min.), 29.0 (maj.), 28.0 (min.), 9.9 (maj.), 9.2 (min.).

FTIR (cm^{-1}): 3059, 2992, 2970, 2875, 1692, 1458.

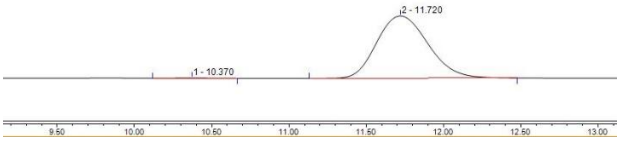
HRMS (ESI): m/z calc'd for $C_{13}H_{19}ClNO^+[M+H]^+$ 240.1150; found 240.1161, Δ 4.6 ppm.

Melting point (°C): 45-47.

Chiral HPLC: Chiralpak-IC column with guard; solvent ratio = 90:10 *n*-hexane: ^{i}PrOH. Temperature = 25 °C. Flow rate = 1 ml/min, λ= 240 nm, τ_{ret} = 10.4 min and 11.7 min.



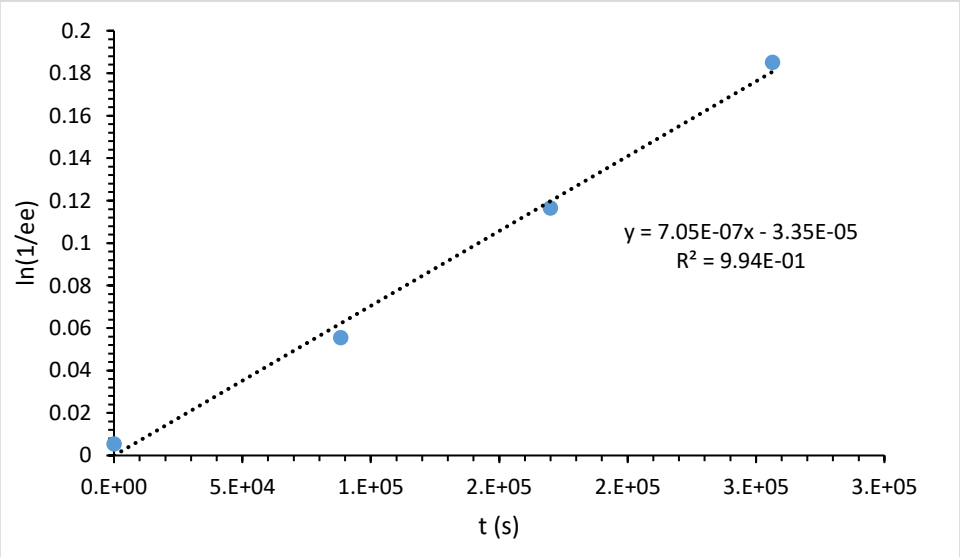
Ret.Time min	Amount n.a.	Rel.Area %	Area mAU*min	Height mAU
10.373	n.a.	49.50	38.8659	119.42
11.737	n.a.	50.50	39.6491	108.40



Ret.Time min	Amount n.a.	Rel.Area %	Area mAU*min	Height mAU
10.370	n.a.	0.27	0.0986	0.35
11.720	n.a.	99.73	35.7892	93.24

Racemization study for 2b: According to general procedure B, and using the conditions specified immediately above, an analytical quantity of the slower eluting enantiomer was collected by semipreparative HPLC and reinjected successively over time intervals shown below to calculate the rate of racemization.

Time (s)	% maj. enantiomer	% min. enantiomer	ln(1/ee)
0	99.73	0.27	0.00542
88260	97.30	2.70	0.0555
168820	94.50	5.50	0.117
256440	91.55	8.45	0.185

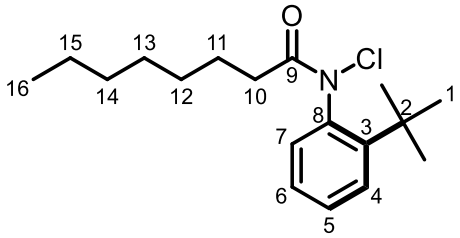


$$k_{rac} = 7.05 \times 10^{-7}\ s^{-1}$$

$$t_{\frac{1}{2}}rac = \mathbf{11.4\ days}$$

$$\Delta G^{\ddagger} = \mathbf{107.9\ kJ/mol}$$

***rac*-N-(2-(*tert*-Butyl)phenyl)-N-chloro-octanamide, 2c**



Synthesised from **1c** (250 mg, 0.908 mmol, 1.00 eq.), trichloroisocyanuric acid (232 mg, 1.00 mmol, 1.10 eq.) and CH_2Cl_2 (8.3 mL) according to general procedure A. Column chromatography (10% Et_2O/ petrol 40-60) afforded **2c** as a yellow oil (218 mg, 78% yield).

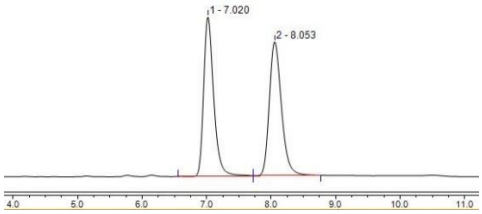
^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 7.53 (m, 1H, H_4), 7.38 (m, 1H, H_5), 7.27 (td, *J* = 7.5, 1.6 Hz, 1H, H_6), 7.16 (dd, *J* = 7.8, 1.6 Hz, 1H, H_7), 2.08 (br s, 2H, H_{10}), 1.69 – 1.56 (m, 2H, H_{11}), 1.44 (s, 9H, H_1), 1.30 – 1.11 (m, 8H, H_{12} + H_{13} + H_{14} + H_{15}), 0.88 – 0.82 (m, 3H, H_{16}).

^{13}C NMR (126 MHz, $CDCl_3$) δ_C: ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.0, 148.1, 141.6, 131.8, 130.5, 129.3, 127.9, 36.2, 35.3, 31.6, 31.6, 29.2, 28.9, 25.5, 22.6, 14.1.

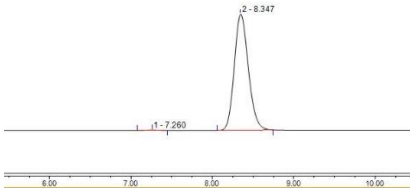
HRMS (ESI$^+$): m/z calc'd for $C_{18}H_{28}ClNNaO^+$ $[M+Na]^+$ 332.1752; found 332.1758, Δ 1.8 ppm.

FTIR (neat) ν/cm^{-1}: 2957, 2926, 2855, 1692, 1485, 1364, 1159, 1051, 756.

Chiral HPLC: Chiralpak-IC column with guard; solvent ratio = 90:10 *n*-hexane: ^{i}PrOH. Temperature = 25 °C. Flow rate = 1 ml/min, λ= 240 nm, τ_{ret} = 7.0 min and 8.1 min.



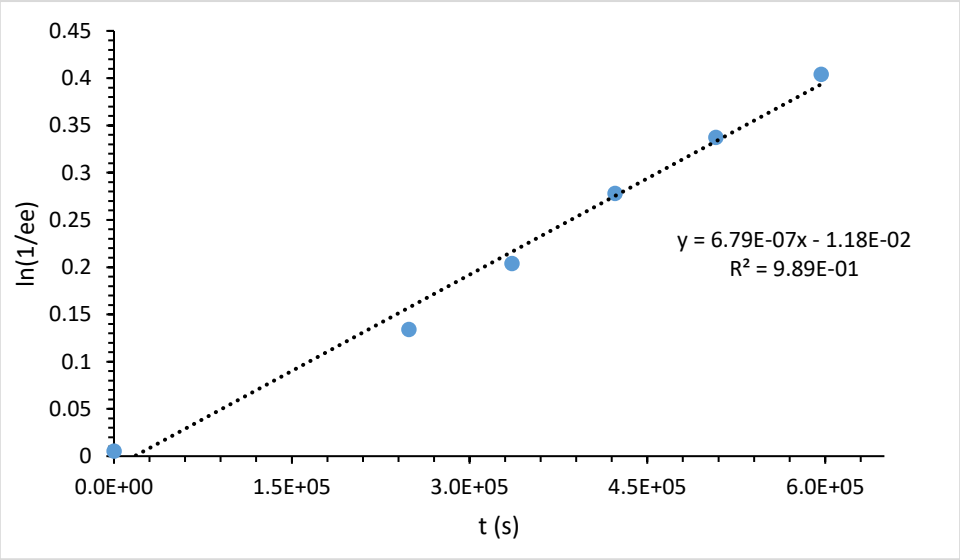
Ret.Time min	Amount n.a.	Rel.Area %	Area mAU*min	Height mAU
7.020	n.a.	49.55	81.6236	452.89
8.053	n.a.	50.45	83.1033	380.51



Ret.Time min	Amount n.a.	Rel.Area %	Area mAU*min	Height mAU
7.260	n.a.	0.27	0.1421	0.86
8.347	n.a.	99.73	51.6451	257.91

Racemization study for 2c: According to general procedure B, and using the conditions specified immediately above, an analytical quantity of the slower eluting enantiomer was collected by semipreparative HPLC and reinjected successively over time intervals shown below to calculate the rate of racemization.

Time (s)	% maj. enantiomer	% min. enantiomer	ln(1/ee)
0.00	99.73	0.27	0.00541
248640	93.72	6.28	0.134
335640	90.77	9.23	0.204
422580	87.86	12.14	0.278
507660	85.68	14.32	0.337
596460	83.38	16.62	0.404

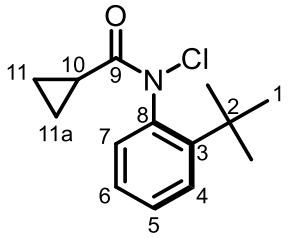


Therefore; $k_{rac} = 6.79 \times 10^{-7}\ s^{-1}$

$$t_{\frac{1}{2}}rac = \mathbf{11.8\ days}$$

$$\Delta G^{\ddagger} = \mathbf{108.0\ kJ/mol}$$

***rac*-N-(2-(*tert*-Butyl)phenyl)-N-chloro-cyclopropanecarboxamide, 2d**



Synthesised from **1d** (100 mg, 0.460 mmol, 1.00 eq.), trichloroisocyanuric acid (118 mg, 0.506 mmol, 1.10 eq.) and CH_2Cl_2 (4.2 mL) according to the general procedure A. Column chromatography (10% EtOAc/ petrol 40-60) afforded **2d** as an off white solid (100 mg, 86% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 7.47 (d, *J* = 8.0 Hz, 1H, H_{Ar}), 7.32 (t, *J* = 7.9 Hz, 1H, H_{Ar}), 7.25 – 7.17 (m, 2H, H_{Ar}), 1.40 (s, 9H, H_1), 1.25 (m, 1H, H_{10}), 1.15 – 0.95 (m, 2H, H_{11} and H_{11a}), 0.66 (m, 2H, H_{11}' and H_{11a}').

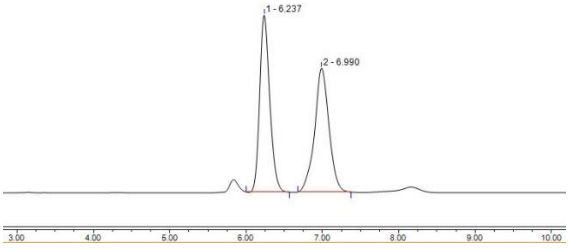
^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 173.5, 148.8, 142.0, 132.4, 130.4, 129.0, 128.1, 36.3, 31.7, 14.3, 10.4, 10.0.

HRMS (ESI$^+$): m/z calc'd for $C_{14}H_{18}ClNNaO^+$ $[M+Na]^+$ 274.0969; found 274.0963, Δ 2.2 ppm.

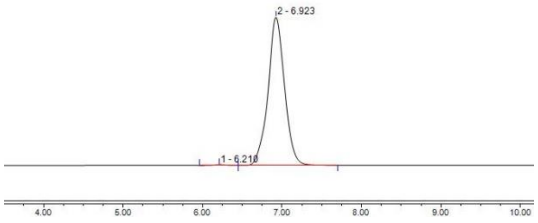
FTIR (neat) ν/cm^{-1} 2996, 2948, 2870, 1680, 1483, 1163, 760, 523.

Melting point (°C) 92-94.

Chiral HPLC: Chiralpak-IH column with guard; solvent ratio = 95:5 *n*-hexane: ^{i}PrOH. Temperature = 25 °C. Flow rate = 1 ml/min, λ= 240 nm, τ_{ret} = 6.2 min and 7.0 min.



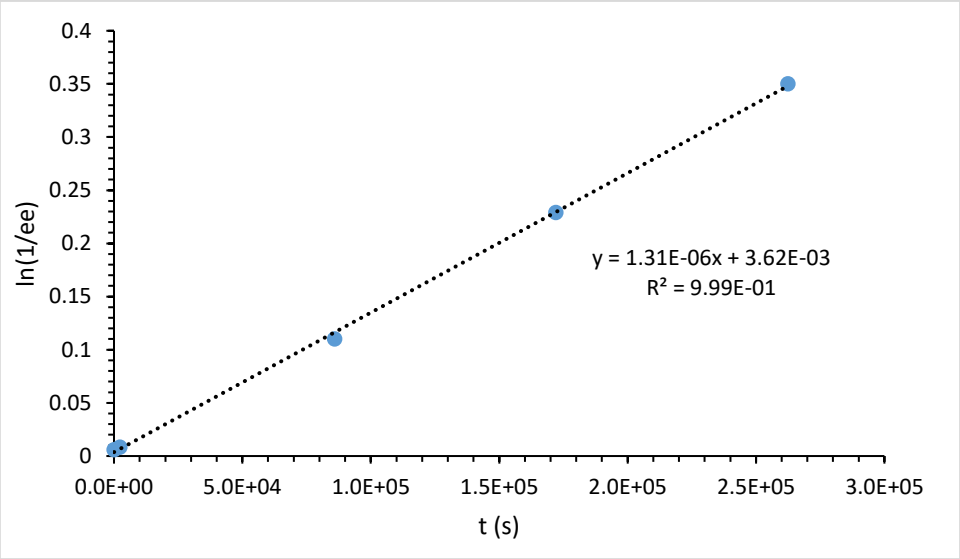
Ret.Time min	Amount n.a.	Rel.Area %	Area mAU*min	Height mAU
6.237	n.a.	49.95	53.5679	350.93
6.990	n.a.	50.05	53.6718	245.61



Ret.Time min	Amount n.a.	Rel.Area %	Area mAU*min	Height mAU
6.210	n.a.	0.28	0.1907	1.18
6.923	n.a.	99.72	67.9289	281.58

Racemization study for 2d: According to general procedure B, and using the conditions specified immediately above, an analytical quantity of the slower eluting enantiomer was collected by semipreparative HPLC and reinjected successively over time intervals shown below to calculate the rate of racemization.

Time (s)	% maj. enantiomer	% min. enantiomer	ln(1/ee)
0.00	99.72	0.28	0.00602
2220.00	99.58	0.42	0.00844
85860.00	94.79	5.21	0.110
171960.00	89.76	10.24	0.229
262380.00	85.23	14.77	0.350

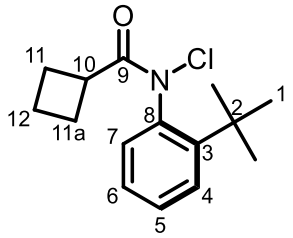


$$k_{rac} = 1.31 \times 10^{-6}\ s^{-1}$$

$$t_{\frac{1}{2}}rac = \mathbf{6.1\ days}$$

$$\Delta G^{\ddagger} = \mathbf{106.4\ kJ/mol}$$

***rac*-N-(2-(*tert*-Butyl)phenyl)-N-chloro-cyclobutanecarboxamide, 2e**



Synthesised from **1e** (150 mg, 0.649 mmol, 1.00 eq.), trichloroisocyanuric acid (166 mg, 0.714, mmol, 1.10 eq.) and CH_2Cl_2 (5.9 mL) according to the general procedure A. Column chromatography (10% EtOAc/ petrol 40-60) yielded **2e** as an off white solid (93 mg, 54% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ_H: 7.53 (m, 1H, H_4), 7.38 (m, 1H, H_5), 7.25 (ddd, *J* = 7.7, 7.2, 1.6 Hz, 1H, H_6), 7.06 (m, 1H, H_7), 3.05 – 2.85 (m, 1H, H_{10}), 2.63 – 2.44 (m, 1H, H_{11}), 2.36 – 2.15 (m, 1H, H_{11a}), 1.99 – 1.71 (m, 4H, H_{11}', $H_{11a'}$ and H_{12}), 1.41 (s, 9H, H_1).

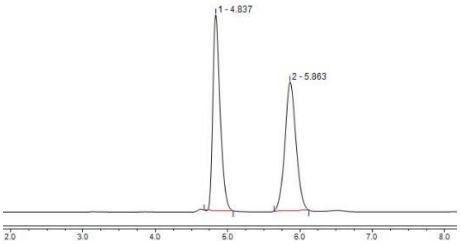
^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 174.1, 148.2, 141.6, 132.0, 130.5, 129.1, 127.8, 38.5, 36.3, 31.7, 27.7, 24.8, 18.1.

HRMS (ESI$^+$): m/z calc'd for $C_{15}H_{20}ClNNaO^+$ $[M+Na]^+$ 288.1126; found 288.1102, Δ –8.3 ppm.

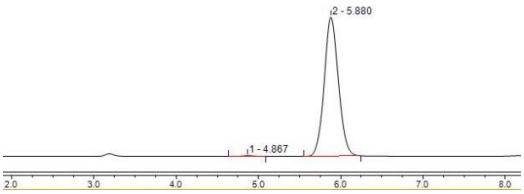
FTIR (neat) ν/cm^{-1} 2997, 2947, 2871, 1681, 1483, 1249, 1162, 760, 693, 524.

Melting point (°C): 80-82.

Chiral HPLC: Chiralpak-IC column with guard; solvent ratio = 90:10 *n*-hexane: ^{i}PrOH. Temperature = 25 °C. Flow rate = 1 ml/min, λ= 240 nm, τ_{ret} = 4.8 min and 5.9 min.



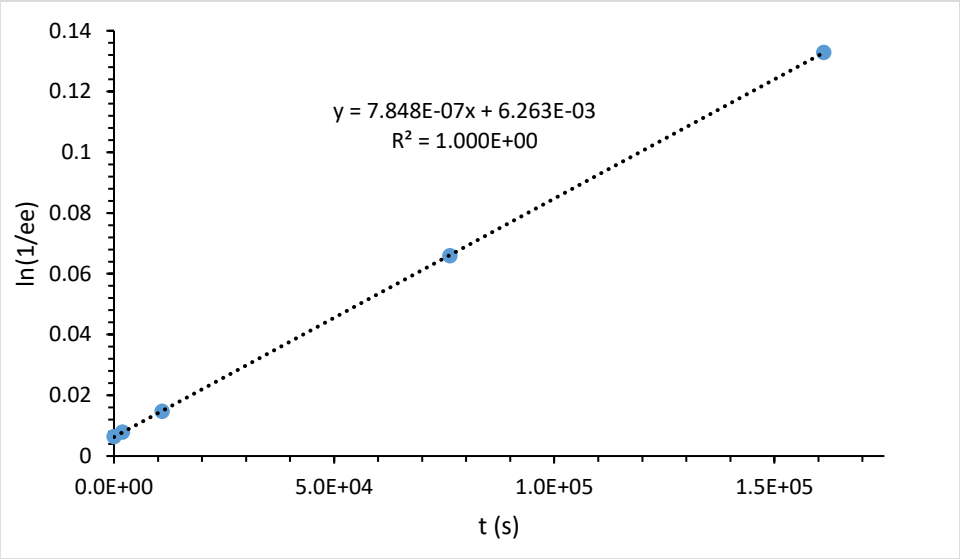
Ret.Time min	Amount n.a.	Rel.Area %	Area mAU*min	Height mAU
4.837	n.a.	50.03	62.4230	533.16
5.863	n.a.	49.97	62.3567	351.25



Ret.Time min	Amount n.a.	Rel.Area %	Area mAU*min	Height mAU
4.867	n.a.	0.32	0.2167	1.55
5.880	n.a.	99.68	66.5150	332.85

Racemization study for 2e: According to general procedure B, and using the conditions specified immediately above, an analytical quantity of the slower eluting enantiomer was collected by semipreparative HPLC and reinjected successively over time intervals shown below to calculate the rate of racemization.

Time (s)	% maj. enantiomer	% min. enantiomer	ln(1/ee)
0	99.68	0.32	0.00642
1920	99.61	0.39	0.00783
10920	99.27	0.73	0.0147
76260	96.81	3.19	0.0659
161160	93.78	6.22	0.133

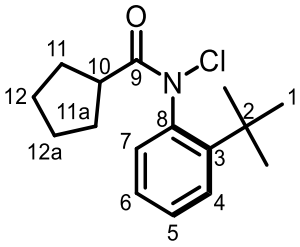


$$k_{rac} = 7.85 \times 10^{-7}\ s^{-1}$$

$$t_{\frac{1}{2}}rac = \mathbf{10.2\ days}$$

$$\Delta G^{\ddagger} = \mathbf{107.7\ kJ/mol}$$

***rac*-N-(2-(*tert*-Butyl)phenyl)-N-chloro-cyclopentanecarboxamide, 2f**



Synthesised from **1f** (300 mg, 1.22 mmol, 1.00 eq.), trichloroisocyanuric acid (311 mg, 1.34 mmol, 1.10 eq.) and CH_2Cl_2 (11 mL) according to the general procedure A. Column chromatography (10% EtOAc/ petrol 40-60) yielded **2f** as a white solid (215 mg, 63% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ_H: 7.53 (m, 1H, H_4), 7.38 (m, 1H, H_5), 7.27 (td, *J* = 7.5, 1.6 Hz, 1H, H_6), 7.17 (dd, *J* = 7.8, 1.6 Hz, 1H, H_7), 2.48 (s, 1H, H_{10}), 2.15 – 1.53 (m, 7H, H_{11} + H_{11}' + H_{11a} + H_{11a}' + H_{12} + H_{12}' + H_{12a}), 1.53 – 1.32 (m, 10H, H_1 + H_{12a}').

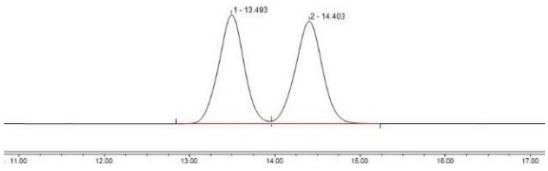
^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 176.6, 148.2, 141.9, 132.1, 130.4, 129.2, 127.8, 43.7, 36.4, 32.3, 31.7, 31.0, 26.4, 26.3.

HRMS (ESI$^+$): m/z calc'd for $C_{16}H_{23}ClNO$ $[M+H]^+$ 280.1463; found 280.1443, Δ –7.1 ppm.

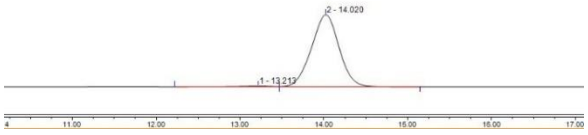
FTIR (neat) ν/cm^{-1} 2962, 2872, 1682, 1483, 1363, 1145, 760, 526.

Melting point (°C): 72-74.

Chiral HPLC: Chiralpak-IC column with guard; solvent ratio = 97:3 *n*-hexane: ^{i}PrOH. Temperature = 25 °C. Flow rate = 1 ml/min, λ= 240 nm, τ_{ret} = 13.5 min and 14.4 min.



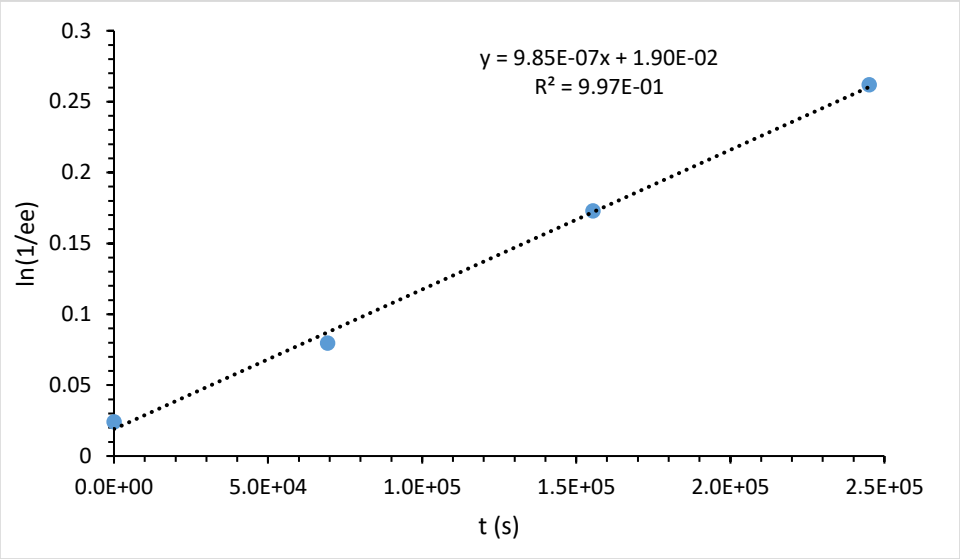
Ret.Time min	Amount n.a.	Rel.Area %	Area mAU*min	Height mAU
13.493	n.a.	49.94	47.9895	138.17
14.403	n.a.	50.06	48.0952	129.99



Ret.Time min	Amount n.a.	Rel.Area %	Area mAU*min	Height mAU
13.213	n.a.	1.19	0.3979	0.81
14.020	n.a.	98.81	32.9172	85.91

Racemization study for 2f: According to general procedure B, and using the conditions specified immediately above, an analytical quantity of the slower eluting enantiomer was collected by semipreparative HPLC and reinjected successively over time intervals shown below to calculate the rate of racemization.

Time (s)	% maj. enantiomer	% min. enantiomer	ln(1/ee)
0	98.81	1.19	0.0240
69300	96.17	3.83	0.0797
155400	92.06	7.94	0.173
245040	88.48	11.52	0.262

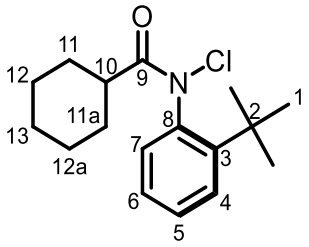


$$k_{rac} = 9.85 \times 10^{-7}\ s^{-1}$$

$$t_{\frac{1}{2}}rac = \mathbf{8.1\ days}$$

$$\Delta G^{\ddagger} = \mathbf{107.1\ kJ/mol}$$

***rac*-N-(2-(*tert*-Butyl)phenyl)-N-chloro-cyclohexanecarboxamide, 2g**



Synthesised from **1g** (100 mg, 0.386 mmol, 1 eq.), trichloroisocyanuric acid (99 mg, 0.42 mmol, 1.1 eq.) and CH_2Cl_2 (3.5 mL) according to the general procedure A. Column chromatography (4% EtOAc/ petrol 40-60) yielded **2g** as a white solid (43 mg, 38% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ_H: 7.53 (m, 1H, H_4), 7.38 (m, 1H, H_5), 7.26 (td, *J* = 7.7, 1.4 Hz, 1H, H_6), 7.18 (d, *J* = 7.8 Hz, 1H, H_7), 2.17 – 1.98 (m, 1H, H_{10}), 1.83 – 1.55 (m, 6H, $H_{11,}$ + H_{11}' + H_{11a} + H_{11a}'+H_{12} + H_{12}'), 1.54 – 1.34 (m, 10H, H_1 + H_{12a}), 1.33 – 0.72 (m, 3H, H_{13} + H_{12a}').

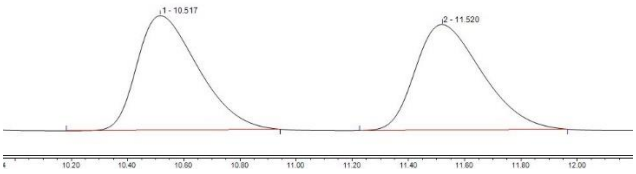
^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 175.0, 148.1, 141.5, 131.7, 130.4, 129.2, 127.6, 43.3, 36.3, 31.7, 29.8, 29.0, 25.6, 25.5, 25.3.

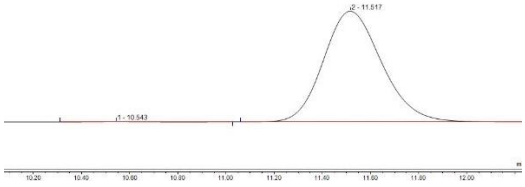
HRMS (ESI$^+$): m/z calc'd for $C_{17}H_{24}ClNNaO^+$ $[M+Na]^+$ 316.1439; found 316.1416, Δ –7.3 ppm.

FTIR (neat) ν/cm^{-1}: 2935, 2848, 1693, 1483, 1319, 1248, 1158, 763, 693.

Melting point (°C): 89-91.

Chiral HPLC: Chiralpak-IG column with guard; solvent ratio = 97:3 *n*-hexane: ^{i}PrOH. Temperature = 25 °C. Flow rate = 1 ml/min, λ= 240 nm, τ_{ret} = 10.5 min and 11.5 min.



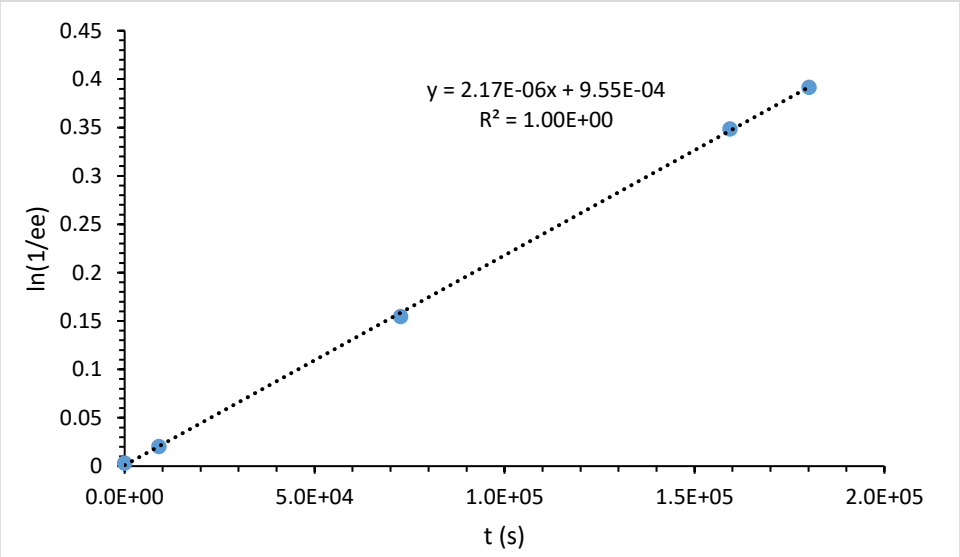


Ret.Time min	Amount n.a.	Rel.Area %	Area mAU*min	Height mAU
10.517	n.a.	49.90	429.8618	1703.08
11.520	n.a.	50.10	431.5424	1569.16

Ret.Time min	Amount n.a.	Rel.Area %	Area mAU*min	Height mAU
10.543	n.a.	0.15	0.0661	0.35
11.517	n.a.	99.85	45.4818	162.80

Racemization study for 2g: According to general procedure B, and using the conditions specified immediately above, an analytical quantity of the slower eluting enantiomer was collected by semipreparative HPLC and reinjected successively over time intervals shown below to calculate the rate of racemization.

Time (s)	% maj. enantiomer	% min. enantiomer	ln(1/ee)
0.00	99.85	0.15	0.00301
9000	98.99	1.01	0.0204
72600	92.83	7.17	0.155
159300	85.29	14.71	0.348
180120	83.80	16.20	0.392

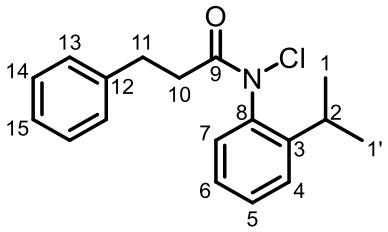


$$k_{rac} = 2.17 \times 10^{-6}\, s^{-1}$$

$$t_{\frac{1}{2}} rac = \mathbf{3.7\ days}$$

$$\Delta G^{\ddagger} = \mathbf{105.2\ kJ/mol}$$

***rac*-N-Chloro-N-(2-isopropylphenyl)-3-phenylpropanamide, 2h**



Synthesised from **1h** (100 mg, 0.374 mmol, 1.00 eq.), trichloroisocyanuric acid (96 mg, 0.41, mmol, 1.1 eq.) and CH_2Cl_2 (3.4 mL) according to the general procedure A. Column chromatography (CH_2Cl_2) yielded **2h** as a clear oil (99 mg, 88% yield).

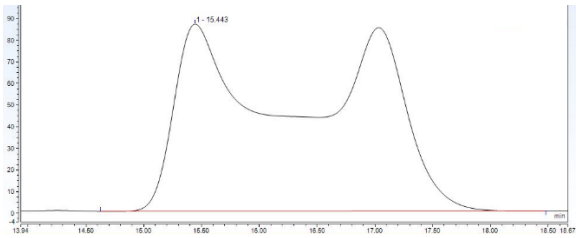
^{1}H NMR (400 MHz, $CDCl_3$) δ_H 7.44 – 7.34 (m, 2H, H_4 + H_5), 7.28 – 7.14 (m, 4H, H_{14} + H_{15} + H_6), 7.10 – 7.00 (m, 3H, H_{13} + H_7), 3.19 – 3.07 (m, 1H, H_2), 3.04 – 2.88 (m, 2H, H_{11}), 2.49 – 2.36 (m, 1H, H_{10}), 2.37 – 2.25 (m, 1H, $H_{10'}$), 1.25 (d, J = 6.8 Hz, 3H, H_1), 1.16 (d, J = 6.9 Hz, 3H, $H_{1'}$).

^{13}C NMR (101 MHz, $CDCl_3$) δ_C 170.1, 147.9, 140.6, 140.2, 131.0, 129.4, 128.7, 128.6, 127.6, 127.4, 126.5, 36.4, 31.9, 28.0, 24.2, 23.3.

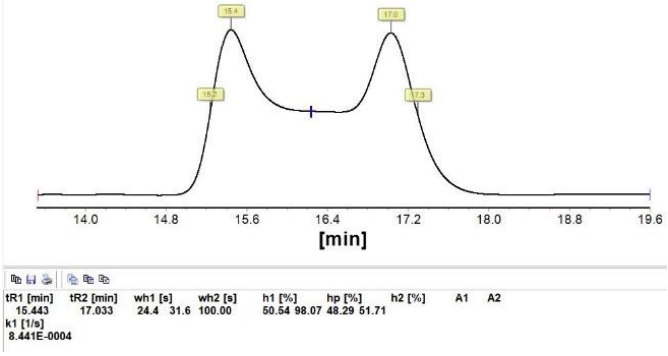
HRMS (ESI+): m/z calc'd for $C_{18}H_{20}ClNONa^+$ $[M+Na]^+$ 324.1126; found 324.1126, Δ < 0.1 ppm.

IR (cm^{-1}): 2929, 2965, 1690, 1487, 1363, 757, 700

Chiral HPLC: Chiralpak-IC column with guard; solvent ratio: 97:3 *n*-hexane: ^{i}PrOH. Temperature = 5 °C. Flow rate = 1 ml/min, λ = 240 nm, τ_{ret} = 15.4 min and 17.0 min.



Racemization Barrier: The HPLC data was processed using DCXPlorer to obtain k_{ent}:[1,6]



$$k_{ent} = \mathbf{8.441} \times \mathbf{10^{-4}}\ s^{-1}(\mathbf{5}\ ^\circ\mathrm{C})\ \text{from DCXplorer}$$

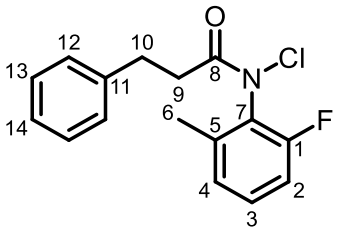
$$\Delta G^{\ddagger} = \mathbf{84.3\ kJ/mol}\ (\mathbf{5}\ ^\circ\mathrm{C})$$

Assuming $\Delta G^{\ddagger}$ is invariant with temperature:

$$k_{rac} = \mathbf{1.151} \times \mathbf{10}^{-2}\ s^{-1}(\mathbf{20}\ ^\circ\mathrm{C})$$

$$t_{\frac{1}{2}} rac \approx \mathbf{1\ minute}\ (\mathbf{20}\ ^\circ\mathrm{C})$$

***rac*-N-Chloro-N-(2-fluoro-6-methylphenyl)-3-phenylpropanamide, 2i**



Synthesised from **1i** (100 mg, 0.389 mmol, 1.00 eq.), trichloroisocyanuric acid (99 mg, 0.43, mmol, 1.1 eq.) and CH_2Cl_2 (3.5 mL) according to the general procedure A. Column chromatography (CH_2Cl_2) yielded **2i** as a clear oil (55 mg, 48% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ_H δ 7.34 – 7.28 (m, 1H, H_3), 7.27 – 7.14 (m, 3H, H_{13} + H_{14}), 7.10 – 6.98 (m, 4H, H_2 + H_4 + H_{12}), 3.03 – 2.90 (m, 2H, H_{10}), 2.45 (ddd, J = 15.2, 9.0, 5.9 Hz, 1H, H_9), 2.35 – 2.25 (m, 1H, $H_{9'}$), 2.22 (s, 3H, H_6). Diagnostic signals for the minor amide isomer were observed at; 7.35 – 7.32 (m, H_{Ar}), 3.12 – 3.05 (m, H_9/H_{10}), 2.26 (s, H_6).

^{13}C NMR (101 MHz, $CDCl_3$) δ_C 170.0, 159.2 (d, *J* = 253.2 Hz), 140.4 (d, *J* = 16.6 Hz), 131.7 (d, *J* = 8.7), 129.5 (d, *J* = 13.2 Hz), 128.7, 128.5, 126.8 (d, *J* = 3.5 Hz), 126.5, 114.4 (d, *J* = 20.0 Hz), 35.4, 31.6, 17.1 (d, *J* = 2.4 Hz).

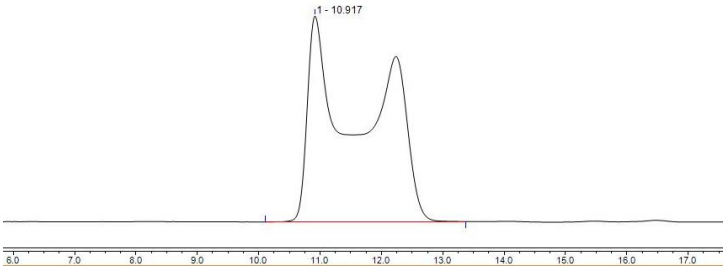
N.B. One aromatic ^{13}C signal is not observed due to overlapping peaks.

^{19}F NMR (376 MHz, $CDCl_3$) δ_F -119.30 (dd, *J* = 9.0, 5.5 Hz).

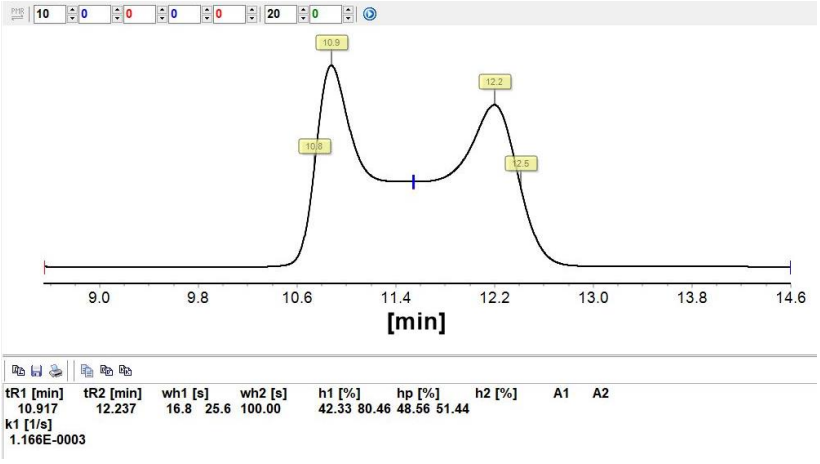
HRMS (ESI+): m/z calc'd for $C_{16}H_{15}ClFNONa^+$ $[M+Na]^+$ 314.0718; found 314.0714, Δ 1.3 ppm.

IR (cm^{-1}): 3033, 2925, 1694, 1473, 1177, 701

Chiral HPLC: Chiralpak-IH column with guard; solvent ratio: 95:5 *n*-hexane: ^{i}PrOH. Temperature = 20 °C. Flow rate = 1 ml/min, λ = 240 nm, τ_{ret} = 10.9 min and 12.2 min.



Racemization Barrier: The HPLC data was processed using DCXPlorer to ontain k_{ent}:[1,6]

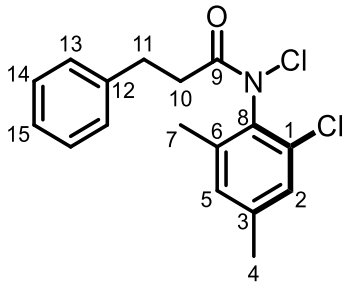


$$k_{ent} = \mathbf{1.166} \times \mathbf{10^{-3}}\ s^{-1}\ from\ DCXplorer$$

$$\Delta G^{\ddagger} = \mathbf{88.2\ kJ/mol}$$

$$t_{\frac{1}{2}} rac = \mathbf{5.0\ minutes}$$

***rac*-N-Chloro-N-(2-chloro-4,6-dimethylphenyl)-3-phenylpropanamide, 2j**



Synthesised from **1j** (100 mg, 0.347 mmol, 1.0 eq.), trichloroisocyanuric acid (89 mg, 0.38 mmol, 1.1 eq.) and CH_2Cl_2 (3.1 mL) according to the general procedure A. Column chromatography (15% Et_2O/ petrol 40:60) afforded **2j** as a colourless oil (102 mg, 91% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ_H: δ 7.33 – 7.16 (m, 3H, H_{Ar}), 7.15 (s, 1H, H_2), 7.12 – 7.07 (m, 2H, H_{Ar}), 6.98 (s, 1H, H_5), 3.04 – 2.93 (m, 2H, H_{11}), 2.49 – 2.36 (m, 1H, H_{10}), 2.34 (s, 3H, H_4) 2.32 – 2.21 (m, 1H, H_{10}'), 2.17 (s, 3H, H_7).

^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 169.8, 142.1, 140.7, 139.8, 136.0, 134.5, 130.7, 128.9, 128.6, 128.6, 126.4, 35.5, 31.6, 21.2, 17.9.

^{1}H NMR (700 MHz, C_6D_6) δ_H 7.04 – 7.00 (m, 2H, H_{Ar}), 7.00 – 6.94 (m, 3H, H_{Ar}), 6.66 (s, 1H, H_2), 6.30 (s, 1H, H_5), 3.08 (dt, *J* = 13.9, 7.8 Hz, 1H, H_{11}), 2.87 (ddd, *J* = 13.9, 8.0, 6.0 Hz, 1H, $H_{11'}$), 2.38 (ddd, *J* = 16.1, 8.0, 6.0 Hz, 1H, $H_{10'}$), 2.13 (dt, *J* = 15.9, 7.8 Hz, 1H, H_{10}), 1.80 (s, 3H, H_7), 1.70 (s, 3H, H_4).

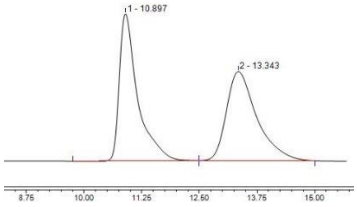
Diagnostic signals for the minor *trans*-isomer were observed at: δ 7.15 – 7.13 (m, H_{Ar}), 7.10 – 7.06 (m, H_{Ar}), 6.80 (s, 1H, H_2), 6.44 (s, 1H, H_5), 2.03 (s, H_7), 1.76 (s, H_4). The identity of the major geometrical isomer was assigned as *cis*- on the basis of NOE correlations between H_7 and H_{10} (see spectra). A ratio of 85:15 *cis*/*trans* was measured from the ^{1}H NMR data collected in C_6D_6.

^{13}C NMR (125 MHz, C_6D_6) δ_C 172.6 (min.), 168.7 (maj.), 141.5 (maj.), 141.2 (maj.), 141.2 (min.), 140.7 (min.), 140.0 (maj.), 139.5 (min.), 137.2 (min.), 136.7 (maj.), 134.7 (maj.), 134.1 (min.), 130.6 (maj.), 130.2 (min.), 128.9 (min.), 128.8 (maj.), 128.8 (maj.), 128.8 (maj.), 128.4 (min.), 126.5 (maj.), 35.8 (maj.), 35.0 (min.), 31.9 (maj.), 31.2 (min.), 20.7 (maj.), 17.9 (min.), 17.6 (min.), 17.5 (maj.). N.B. Two aromatic ^{13}C signals for the minor isomer were not observed, presumably as a result of overlap with the residual solvent peak for benzene.

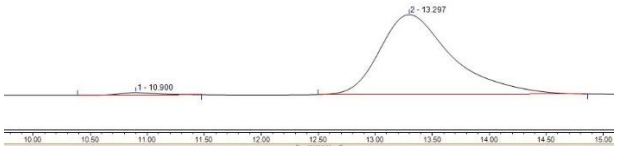
HRMS (ESI$^+$): m/z calc'd for $C_{17}H_{18}Cl_2NO^+$ $[M+H]^+$ 322.0760; found 322.0776, Δ 5.0 ppm.

FTIR (neat) ν/cm^{-1}: 3028, 2924, 1697, 1452, 1358, 1296, 1181, 851, 739, 699, 569.

Chiral HPLC: Chiralpak-IA column with guard; solvent ratio = 97.5:2.5 *n*-hexane: ^{i}PrOH. Temperature = 25 °C. Flow rate = 1 ml/min, λ= 240 nm, τ_{ret} = 10.9 min and 13.3 min.



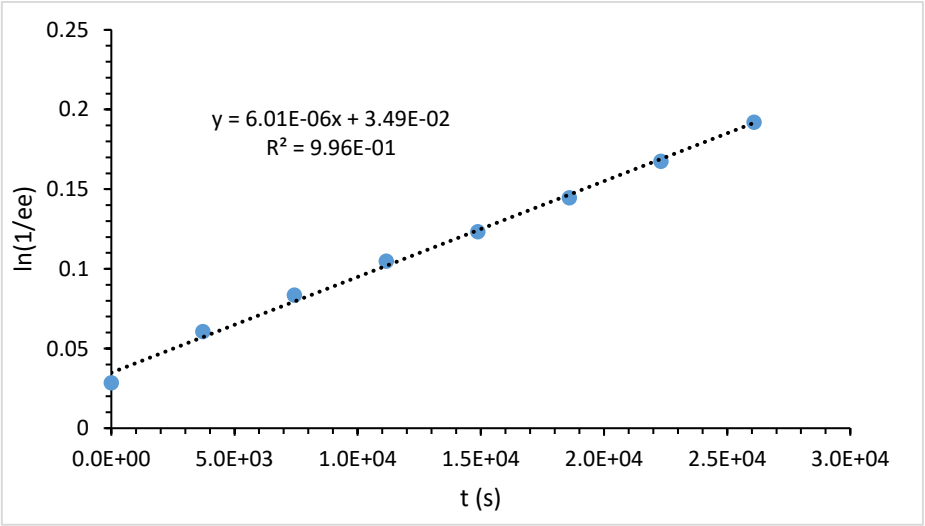
Ret.Time min	Amount n.a.	Rel.Area %	Area mAU*min	Height mAU
10.897	n.a.	49.82	466.9409	1010.62
13.343	n.a.	50.18	470.3918	612.78



Ret.Time min	Amount n.a.	Rel.Area %	Area mAU*min	Height mAU
10.900	n.a.	1.41	0.3621	0.97
13.297	n.a.	98.59	25.3116	34.55

Racemization study for 2j: According to general procedure B, and using the conditions specified immediately above, an analytical quantity of the slower eluting enantiomer was collected by semipreparative HPLC and reinjected successively over time intervals shown below to calculate the rate of racemization.

Time (s)	% maj. enantiomer	% min. enantiomer	ln(1/ee)
0	98.59	1.41	0.0286
3720	97.06	2.94	0.0606
7440	95.99	4.01	0.0836
11160	95.02	4.98	0.105
14880	94.20	5.80	0.123
18600	93.27	6.73	0.145
22320	92.29	7.71	0.167
26100	91.26	8.74	0.192

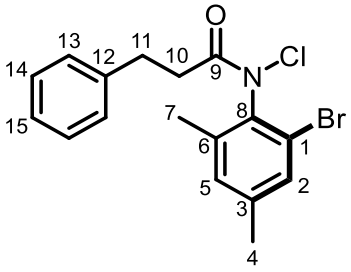


$$k_{rac} = 6.01 \times 10^{-6}\ s^{-1}$$

$$t_{\frac{1}{2}} rac = \mathbf{32\ hours}$$

$$\Delta G^{\ddagger} = \mathbf{102.7\ kJ/mol}$$

***rac*-N-(2-Bromo-4,6-dimethylphenyl)-N-chloro-3-phenylpropanamide, 2k**



Synthesised from **1k** (100 mg, 0.302 mmol, 1.0 eq.), trichloroisocyanuric acid (77 mg, 0.33 mmol, 1.1 eq.) and CH_2Cl_2 (2.8 mL) according to the general procedure A. Column chromatography (CH_2Cl_2) afforded **2k** as a colourless oil (89 mg, 80% yield).

1H NMR (400 MHz, $CDCl_3$) δ_H 7.35 – 7.31 (m, 1H, H_2), 7.27 – 7.20 (m, 2H, H_{14}), 7.20 – 7.14 (m, 1H, H_{15}), 7.13 – 7.07 (m, 2H, H_{13}), 7.04 – 6.98 (m, 1H, H_5), 3.04 – 2.91 (m, 2H, H_{11}), 2.49 – 2.39 (m, 1H, H_{10}), 2.32 (s, 3H, H_4), 2.30 – 2.18 (m, 1H, $H_{10'}$), 2.18 (s, 3H, H_7).

Diagnostic peaks for the minor amide isomer were observed at; 7.30 (s, H_2), 3.08 – 3.04 (m, H_{10}/H_{11}), 2.30 (s, H_4), 2.24 (s, H_7).

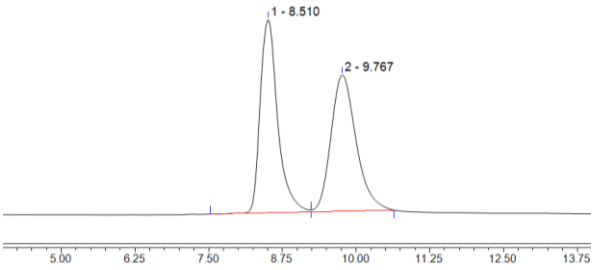
^{13}C NMR (101 MHz, $CDCl_3$) δ_C 169.6, 142.4, 140.7, 140.0, 137.4, 132.2, 131.5, 128.6, 126.4, 125.0, 35.8, 31.7, 21.1, 18.3.

N.B. Two ^{13}C signals are overlapping at 128.6 ppm

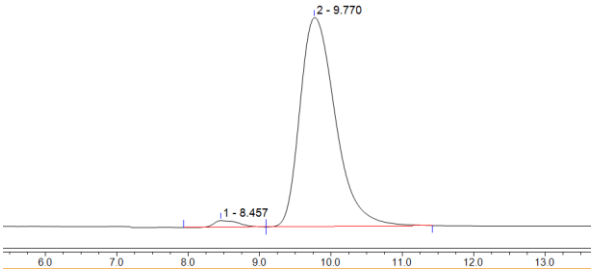
HRMS (ESI$^+$): m/z calc'd for $C_{17}H_{18}BrClNO^+$ $[M+H]^+$ 366.0255; found 366.0244, Δ 3.0 ppm.

FTIR (neat) ν/cm^{-1}: 3027, 2922, 1695, 1307, 699

Chiral HPLC: Chiralpak-IA column; solvent ratio = 95:5 *n*-hexane: ^{i}PrOH. Temperature = 25 °C. Flow rate = 1 ml/min, λ= 240 nm, τ_{ret} = 8.5 min and 9.7 min.



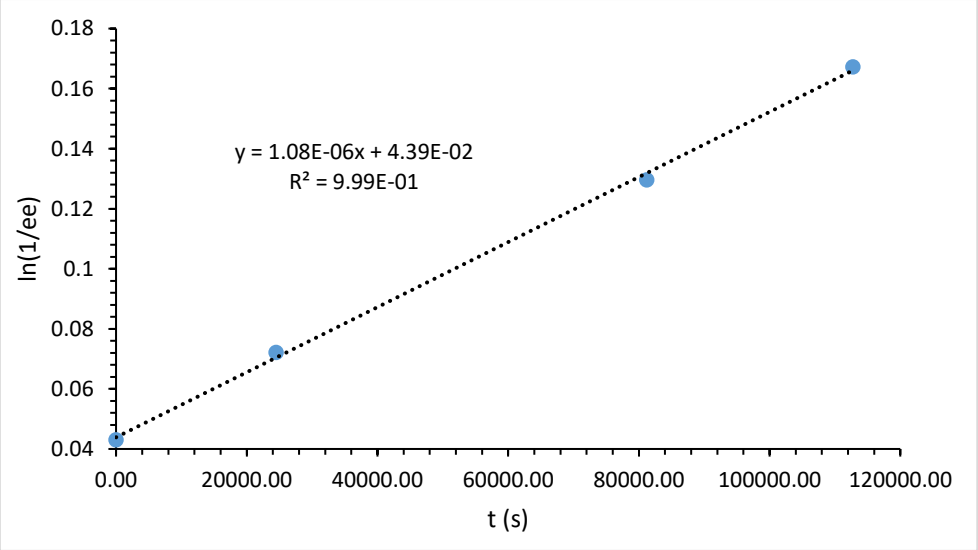
Ret.Time min	Amount n.a.	Rel.Area %	Area mAU*min	Height mAU
8.510	n.a.	49.67	36.4270	105.75
9.767	n.a.	50.33	36.9178	74.64



Ret.Time min	Amount n.a.	Rel.Area %	Area mAU*min	Height mAU
8.457	n.a.	2.11	0.5409	1.41
9.770	n.a.	97.89	25.1059	43.60

Racemization study for 2k According to general procedure B, and using the conditions specified immediately above, an analytical quantity of the slower eluting enantiomer was collected by semipreparative HPLC and reinjected successively over time intervals shown below to calculate the rate of racemization.

Time (s)	% maj. enantiomer	% min. enantiomer	ln(1/ee)
0.00	97.89	2.11	0.0431
24480	96.52	3.48	0.0721
81180	93.92	6.08	0.130
112740	92.3	7.7	0.167

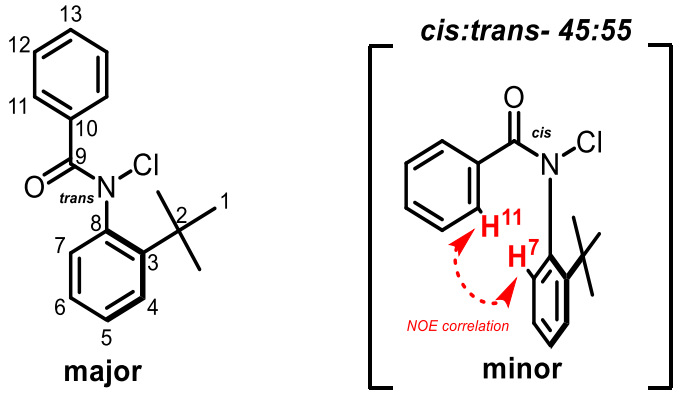


$$k_{rac} = 1.08 \times 10^{-6}\ s^{-1}$$

$$t_{\frac{1}{2}}rac = \mathbf{7.4\ days}$$

$$\Delta G^{\ddagger} = \mathbf{106.9\ kJ/mol}$$

***rac*-N-(2-(*tert*-Butyl)phenyl)-N-chloro-benzamide, 2l**



Synthesised from **1l** (250 mg, 0.987 mmol, 1.00 eq.), trichloroisocyanuric acid (252 mg, 1.09 mmol, 1.10 eq.), and CH_2Cl_2 (9.0 mL), according to general procedure A. Column Chromatography (10% EtOAc/ pentane) afforded **2l** as a yellow solid (277 mg, 98% yield).

^{1}H NMR (400 MHz, $CDCl_3$, 298 K) δ_H 7.69 – 7.53 (m, 2H, H_{Ar}), 7.48 (dd, *J* = 8.1, 1.6 Hz, 1H, H_{Ar}), 7.44 – 7.23 (m, 6H, H_{Ar}), 1.45 (s, 9H, H_1).

^{13}C NMR (75 MHz, $CDCl_3$, 298 K) δ_C 148.0, 142.6, 133.5, 132.3, 131.2, 130.0, 129.1, 129.1, 128.1, 127.8, 36.2, 31.7. (N.B. ^{13}C signal for C=O not observed due to signal broadening)

^{1}H NMR (500 MHz, $CDCl_3$, 218 K) δ_H: 7.91 –7.83 (m, 2H, $H_{11Maj.}$), 7.63 –7.57 (m, 1H, $H_{13Maj.}$), 7.57 –7.51 (m, 3H, $H_{12Maj.}$ + $H_{4Maj.}$), 7.49 (dd, J = 8.2, 1.5 Hz, 1H, $H_{4Min.}$), 7.47 –7.42 (m, 3H, $H_{5Maj.}$, $H_{6Maj.}$, $H_{7Maj.}$), 7.39 –7.31 (m, 4H, $H_{5Min.}$, $H_{11Min.}$, and $H_{13Min.}$), 7.26 (dd, J = 7.9, 1.6 Hz, 1H, $H_{7Min.}$), 7.24 –7.16 (m, 3H, $H_{6Min.}$ and $H_{12Min.}$), 1.49 (s, 9H, $H_{1Maj.}$), 1.35 (s, 9H, $H_{1Min.}$)

The identity of the *minor* geometrical isomer was assigned as *cis*- on the basis of NOE correlations between H_{11} and H_7 (see spectra). A ratio of 45:55 *cis*/*trans* was measured from the ^{1}H NMR data collected at 218 K.

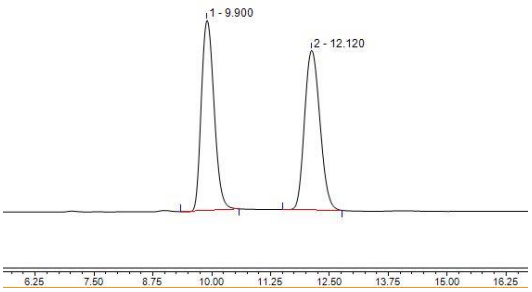
^{13}C NMR (126 MHz, $CDCl_3$, 218 K): δ_C 175.7 (maj.), 167.5 (min.), 147.3 (maj.), 147.0 (min.), 142.7 (maj.), 140.7 (min.), 132.7 (maj.), 132.3 (min.), 132.2 (maj.), 132.0 (min.), 131.3 (maj.), 130.9 (min.), 130.5 (maj.), 130.2 (min.), 129.8 (maj.), 129.3 (maj.), 128.8 (min.), 128.3 (min.), 128.2 (maj.), 127.9 (maj.), 127.7 (min.), 127.4 (min.), 36.6 (min.), 35.4 (maj.), 31.7 (min.), 30.8 (maj.).

FTIR (neat) v/cm^{-1} 3059, 2992, 2970, 2875, 1692, 1458

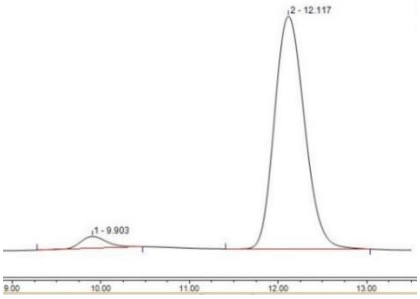
HRMS (ESI): m/z calc'd for $C_{17}H_{19}ClNO^+[M+H]^+$ 288.1150; found 288.1142 Δ –2.8 ppm

Melting Point (°C): 46-48

Chiral HPLC: Chiralpak-IC column with guard; solvent ratio = 90:10 *n*-hexane: ^{i}PrOH. Temperature = 25 °C. Flow rate = 1 ml/min, λ= 240 nm, τ_{ret} = 9.9 min and 12.1 min.



Ret.Time min	Amount n.a.	Rel.Area %	Area mAU*min	Height mAU
9.900	n.a.	49.67	103.6940	330.63
12.120	n.a.	50.33	105.0745	277.65

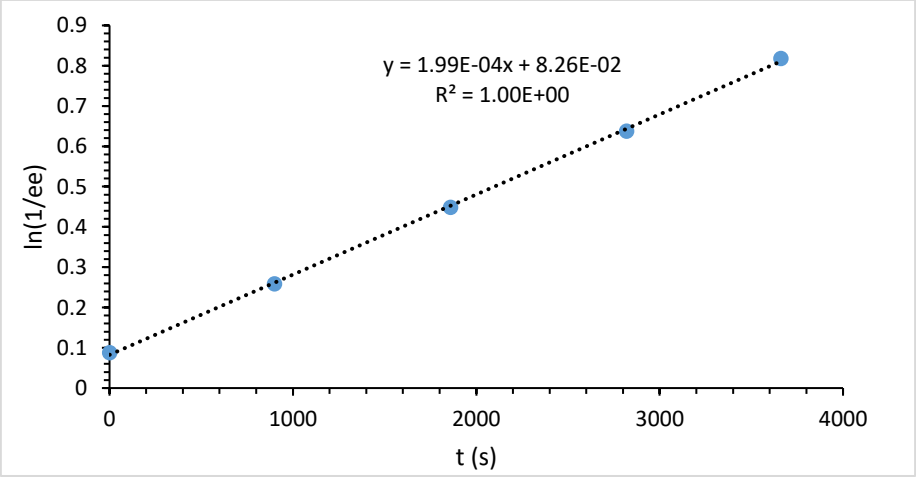


Ret.Time min	Amount n.a.	Rel.Area %	Area mAU*min	Height mAU
9.903	n.a.	4.22	2.8987	8.48
12.117	n.a.	95.78	65.7343	167.57

Racemization study for 2l: According to general procedure B, and using the conditions specified immediately above, an analytical quantity of the slower eluting enantiomer was collected by semipreparative HPLC and reinjected successively over time intervals shown below to calculate the rate of racemization.

Data from run 1:

Time (s)	% maj. enantiomer	% min. enantiomer	ln(1/ee)
0	95.78	4.22	0.0882
900	88.61	11.39	0.259
1860	81.93	18.07	0.448
2820	76.42	23.58	0.638
3660	72.07	27.93	0.818



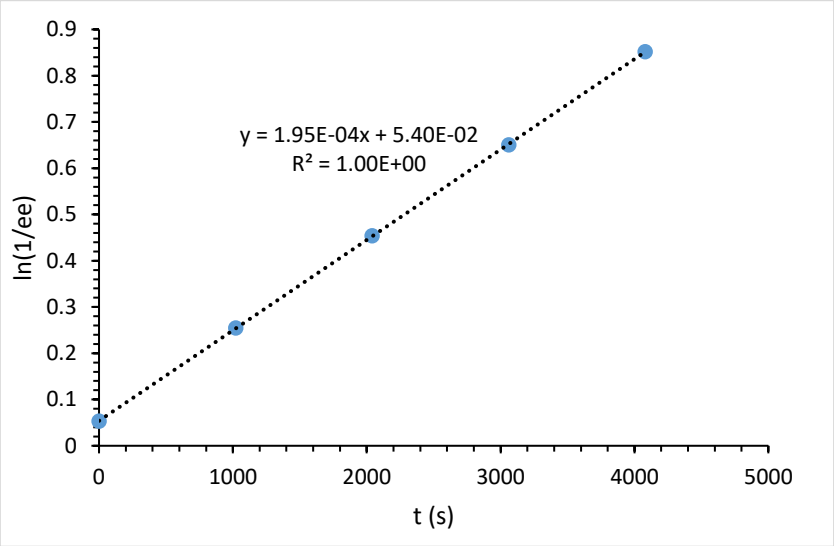
$$k_{rac} = 1.99 \times 10^{-4}\ s^{-1}$$

$$t_{\frac{1}{2}}rac = \mathbf{58\ minutes}$$

$$\Delta G^{\ddagger} = \mathbf{94.2\ kJ/mol}$$

Data from run 2:

Time (s)	% maj. enantiomer	% min. enantiomer	ln(1/ee)
0	97.43	2.57	0.052768
1020	88.76	11.24	0.254634
2040	81.75	18.25	0.45413
3060	76.1	23.9	0.650088
4080	71.33	28.67	0.851908

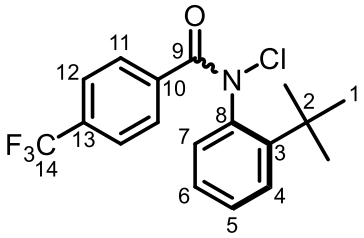


$$k_{rac} = 1.95 \times 10^{-4}\ s^{-1}$$

$$t_{\frac{1}{2}} rac = \mathbf{59\ minutes}$$

$$\Delta G^{\ddagger} = \mathbf{94.2\ kJ/mol}$$

***rac*-N-(2-(*tert*-Butyl)phenyl)-N-chloro-4-(trifluoromethyl)benzamide, 2m**



Synthesised from **1m** (150 mg, 0.467 mmol, 1.0 eq.), trichloroisocyanuric acid (119 mg, 0.513 mmol, 1.10 eq.) and CH_2Cl_2 (4.3 mL), according to general procedure A. Column chromatography (5% EtOAc/ petrol 40-60) afforded **2m** as a white solid (130 mg, 78% yield).

^{1}H NMR (500 MHz, $CDCl_3$, 218 K) δ_H: δ 7.96 (d, *J* = 8.0 Hz, 2H, $H_{11Maj.}$), 7.79 (d, *J* = 8.0 Hz, 2H, $H_{12Maj.}$), 7.56 – 7.34 (m, 10H, H_{Ar}), 7.30 – 7.19 (m, 2H, H_{Ar}), 1.49 (s, 9H $H_{Maj.}$), 1.36 (s, 9H, $H_{1Min.}$).

^{13}C NMR (126 MHz, $CDCl_3$, 218 K): δ_C 174.2 (Maj.), 166.1 (Min.), 147.4 (Maj.), 147.1 (Min.), 142.1 (Maj.), 140.1 (Min.), 136.4 (Maj.), 135.9 (Min.), 132.7 (q, *J* = 32.7 Hz, Maj.), 132.2 (Maj.), 131.8 (q, *J* = 32.7 Hz, Min.), 131.2 (Min.), 130.7 (Min.), 130.7 (Maj.), 130.1 (Min.), 129.7 (Maj.), 129.0 (Min.), 128.3z (Maj.), 127.9 (Min.), 127.6 (Maj.), 125.3 (q, *J* = 3.6 Hz Min.), 125.0 (q, *J* = 3.6 Hz, Maj.), 123.4 (q, *J* = 272.9 Hz, Maj.), 123.2 (q, *J* = 272.9 Hz, Min.), 36.6 (Min.), 35.4 (Maj.), 31.7 (Min.), 30.9 (Maj.).

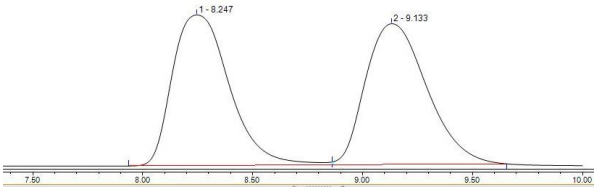
^{19}F NMR (282 MHz, $CDCl_3$, 298 K): δ_F –63.1.

FTIR (neat) ν/cm^{-1}: 2962, 1673, 1619, 1580, 1514, 1484, 1316, 1167, 851, 757.

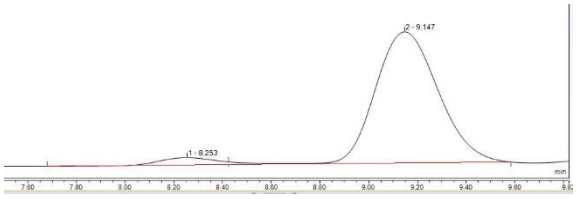
HRMS (ESI): m/z calc'd for $C_{18}H_{18}ClF_3NO^+[M+H]^+$ 356.1024; found 356.1006. Δ –5.1 ppm.

Melting Point (°C): 66-68.

Chiral HPLC: Chiralpak-IC column with guard; solvent ratio = 97.5:2.5 *n*-hexane: ^{i}PrOH. Temperature = 25 °C. Flow rate = 1 ml/min, λ= 240 nm, τ_{ret} = 9.9 min and 12.1 min.



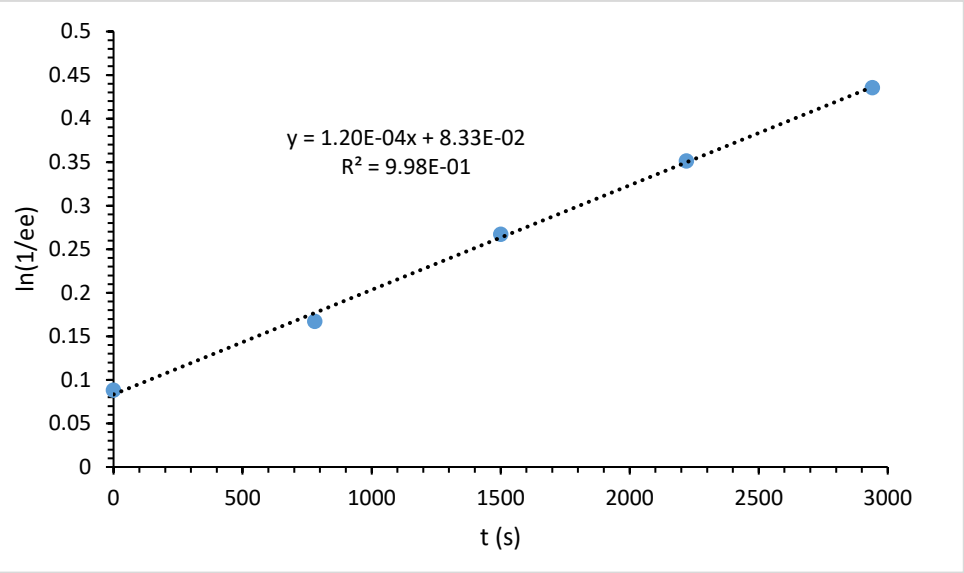
Ret.Time min	Amount n.a.	Rel.Area %	Area mAU*min	Height mAU
8.247	n.a.	49.96	910.2829	3019.65
9.133	n.a.	50.04	911.6783	2822.26



Ret.Time min	Amount n.a.	Rel.Area %	Area mAU*min	Height mAU
8.253	n.a.	4.37	4.0063	16.38
9.147	n.a.	95.63	87.7757	292.71

Racemization study for 2m: According to general procedure B, and using the conditions specified immediately above, an analytical quantity of the slower eluting enantiomer was collected by semipreparative HPLC and reinjected successively over time intervals shown below to calculate the rate of racemization.

Time (s)	% maj. enantiomer	% min. enantiomer	ln(1/ee)
0	95.78	4.22	0.0882
780	92.30	7.70	0.167
1500	88.27	11.73	0.267
2220	85.19	14.81	0.351
2940	82.34	17.66	0.436

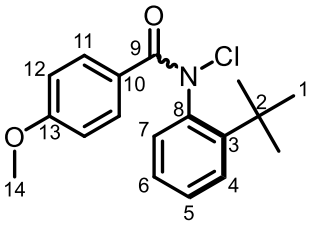


$$k_{rac} = 1.20 \times 10^{-4}\ s^{-1}$$

$$t_{\frac{1}{2}}rac = \mathbf{96\ minutes}$$

$$\Delta G^{\ddagger} = \mathbf{95.4\ kJ/mol}$$

***rac*-N-(2-(*tert*-Butyl)phenyl)-N-chloro-4-methoxybenzamide, 2n**



Synthesised from **1n** (200 mg, 0.706 mmol, 1.00 eq.), trichloroisocyanuric acid (180 mg, 0.775 mmol, 1.1 eq.) and CH_2Cl_2 (6.5 mL) according to the general procedure A. Column Chromatography (7% EtOAc/ petrol 40-60) yielded **2n** as a gummy solid (143 mg, 64% yield).

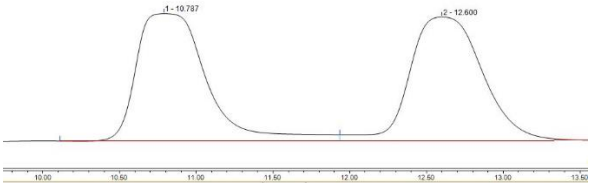
^{1}H NMR (300 MHz, $CDCl_3$) δ_H: 7.56 (d, *J* = 8.5 Hz, 2H, H_{11}), 7.49 (dd, *J* = 8.0, 1.5 Hz, 1H, H_{Ar}), 7.40 – 7.19 (m, 3H, 3 H_{Ar}), 6.81 (d, *J* = 8.5 Hz, 2H, H_{12}), 3.80 (s, 3H, H_{14}), 1.45 (s, 9H, H_1).

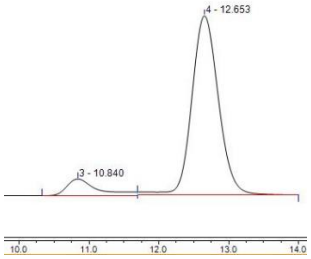
^{13}C NMR (75 MHz, $CDCl_3$): δ_C 161.9, 147.7, 143.0, 132.3, 131.5, 129.8, 128.9, 127.6, 125.2, 113.4, 113.3, 55.4, 36.1, 31.6.

FTIR (neat) ν/cm^{-1}: 2960, 2839, 1664, 1604, 1509, 1295, 1253, 1173, 758, 600.

HRMS (ESI): m/z calc'd for $C_{18}H_{21}ClNO_2^+$ $[M+H]^+$ 318.1255; found 318.1258 Δ 0.94 ppm.

Chiral HPLC: Chiralpak-IC column with guard; solvent ratio = 75:25 *n*-hexane: ^{i}PrOH. Temperature = 25 °C. Flow rate = 1 ml/min, λ= 240 nm, τ_{ret} = 10.8 min and 12.6 min.



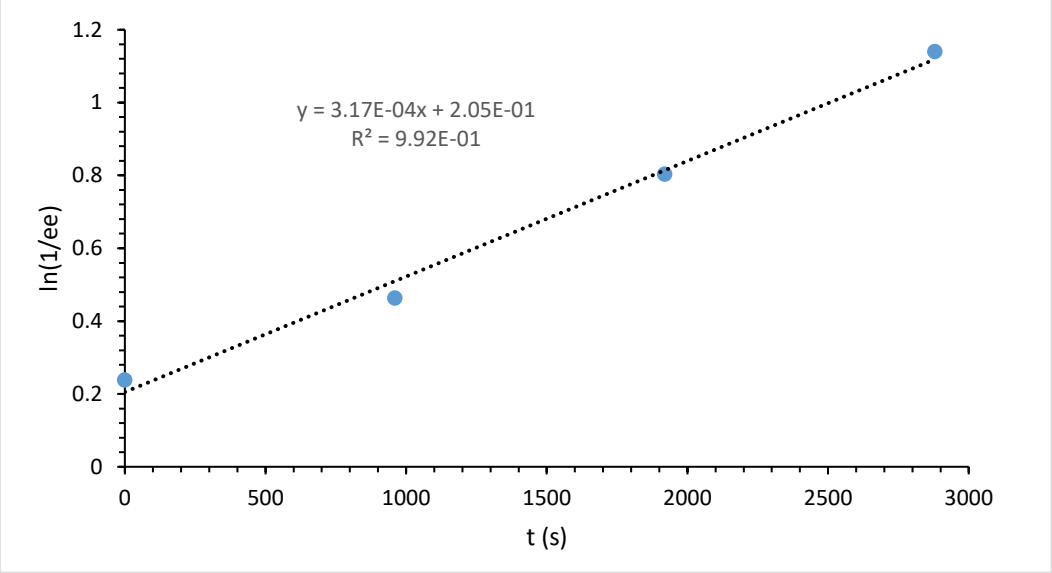


Ret.Time min	Amount n.a.	Rel.Area %	Area mAU*min	Height mAU
10.787	n.a.	49.91	1395.3131	2636.63
12.600	n.a.	50.09	1400.0818	2562.00

Ret.Time min	Amount n.a.	Rel.Area %	Area mAU*min	Height mAU
10.840	n.a.	10.63	13.5288	23.99
12.653	n.a.	89.37	113.7630	260.77

Racemization study for 2n: According to general procedure B, and using the conditions specified immediately above, an analytical quantity of the slower eluting enantiomer was collected by semipreparative HPLC and reinjected successively over time intervals shown below to calculate the rate of racemization.

Time (s)	% maj. enantiomer	% min. enantiomer	ln(1/ee)
0	89.37	10.63	0.239
960	81.44	18.56	0.464
1920	72.37	27.63	0.804
2880	65.98	34.02	1.14

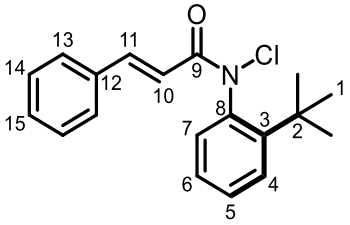


$$k_{rac} = 3.17 \times 10^{-4}\ s^{-1}$$

$$t_{\frac{1}{2}}rac = \mathbf{36\ minutes}$$

$$\Delta G^{\ddagger} = \mathbf{93.0\ kJ/mol}$$

***rac*-N-(2-(*tert*-Butyl)phenyl)-N-chloro-cinnamamide, 2o**



Synthesised from **1o** (206 mg, 0.737 mmol, 1.00 eq.), trichloroisocyanuric acid (189 mg, 0.815 mmol, 1.1 eq.) and CH_2Cl_2 (7.5 mL) according to the general procedure A. Column chromatography (10% EtOAc/ petrol 40-60) yielded **2o** as a white solid (89 mg, 38% yield).

^{1}H NMR (500 MHz, $CDCl_3$, 218 K) δ_H: 7.78 (d, *J* = 15.6 Hz, 1H, H_{11}), 7.64 – 7.59 (m, 1H, H_7), 7.52 – 7.47 (m, 1H, H_6), 7.42 – 7.31 (m, 6H, H_5, H_{13}, H_{14}, H_{15}), 7.29 – 7.23 (m, 1H, H_4), 6.15 (d, *J* = 15.6 Hz, 1H, H_{10}), 1.44 (s, 9H, H_1).

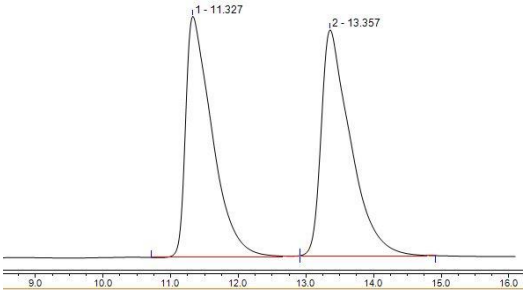
^{13}C NMR (126 MHz, $CDCl_3$, 218 K): δ_C: δ 166.0, 148.0, 143.9, 140.8, 133.7, 132.2, 130.8, 130.5, 128.9, 128.8, 128.2, 128.2, 115.7, 36.0, 31.4.

FTIR (neat) ν/cm^{-1}: 3001, 2961, 2841, 1901, 1655, 1630, 1594, 1572, 1508.

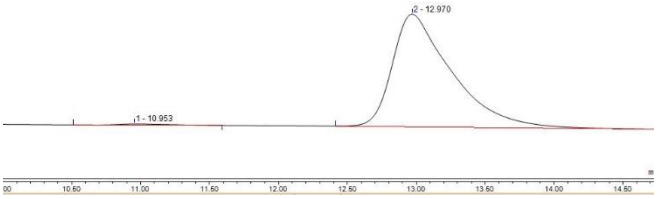
HRMS (ESI): m/z calc'd for $C_{19}H_{21}ClNO^+$ $[M+H]^+$ 314.1306; found 314.1307 Δ= 0.3 ppm.

Melting point (°C): 111-113.

Chiral HPLC: Chiralpak-IA column; solvent ratio = 95:5 *n*-hexane: ^{i}PrOH. Temperature = 25 °C, flow rate = 1 ml/min, λ= 240 nm, τ_{ret} = 11.3 min and 13.4 min.



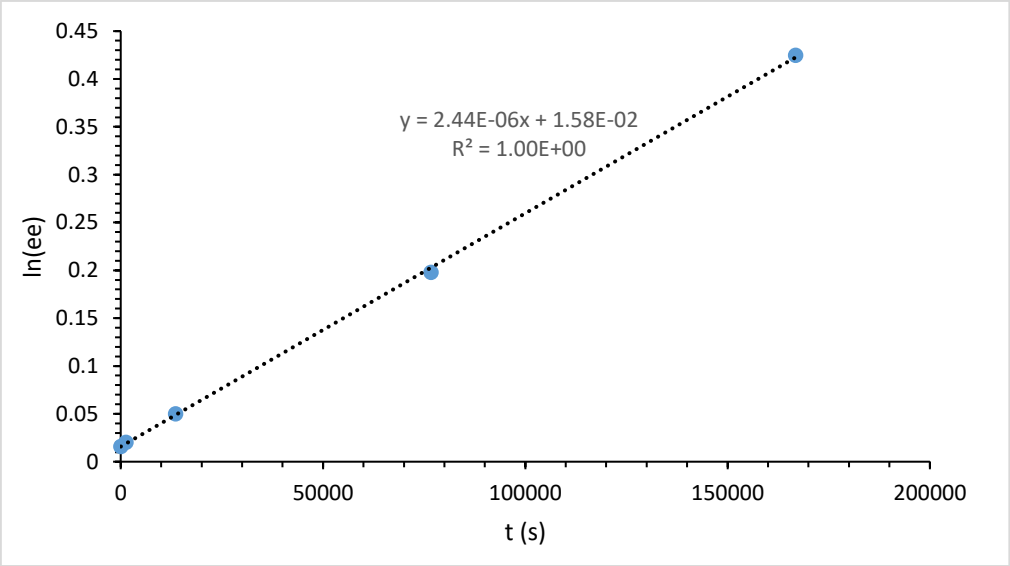
Ret.Time min	Amount n.a.	Rel.Area %	Area mAU*min	Height mAU
11.327	n.a.	48.89	681.6093	1503.68
13.357	n.a.	51.11	712.6900	1413.54



Ret.Time min	Amount n.a.	Rel.Area %	Area mAU*min	Height mAU
10.953	n.a.	0.80	0.2936	0.76
12.970	n.a.	99.20	36.4381	72.85

Racemization study for 2o: According to general procedure B, and using the conditions specified immediately above, an analytical quantity of the slower eluting enantiomer was collected by semipreparative HPLC and reinjected successively over time intervals shown below to calculate the rate of racemization.

Time (s)	% maj. enantiomer	% min. enantiomer	ln(1/ee)
0	99.20	0.80	0.0161
1291	99.00	1.00	0.0202
13536	97.56	2.44	0.0500
76693	91.02	8.98	0.198
166802	82.70	17.30	0.444



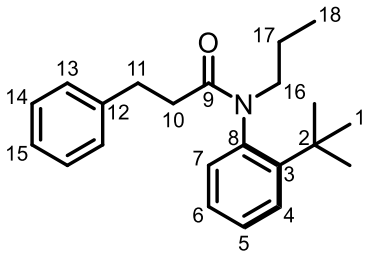
$$k_{rac} = 2.44 \times 10^{-6}\ s^{-1}$$

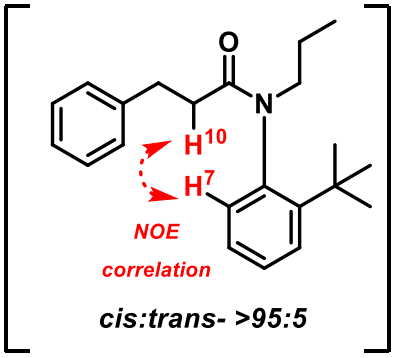
$$t_{\frac{1}{2}} rac = \mathbf{3.3\ days}$$

$$\Delta G^{\ddagger} = \mathbf{104.9\ kJ/mol}$$

3.3 Synthesis of N-alkyl amides

***rac*-N-(2-(*tert*-Butyl)phenyl)-3-phenyl-N-propylpropanamide, 3a**





NaH (60% dispersion in mineral oil, 17 mg, 0.43 mmol, 1.2 eq.) was suspended in dry DMF (0.35 mL) and cooled to 0 °C. A solution of **1a** (100 mg, 0.356 mmol, 1.00 eq.) in dry DMF (1.8 mL) was added dropwise and the solution was stirred at 0 °C for 15 minutes. After this time, 1-iodopropane (0.10 mL, 1.0 mmol, 3.0 eq.) was added dropwise and the solution was allowed to warm to room temperature and stirred for 16 hours. The reaction was diluted with water and EtOAc. The layers were separated and the aqueous layer was extracted twice with EtOAc. The combined organics were washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude residue was purified via column chromatography (7% EtOAc/petrol 40-60) to yield **3a** as a white solid (61 mg, 53% yield, >95:5 *cis*/*trans*).

^{1}H NMR (400 MHz, $CDCl_3$) δ_H 7.53 (dd, *J* = 8.1, 1.5 Hz, 1H, H_4), 7.32 – 7.25 (m, 1H, H_6), 7.25 – 7.20 (m, 2H, H_{14}), 7.18 – 7.13 (m, 1H, H_{15}), 7.13 – 7.06 (m, 3H, H_{13} & H_5), 6.65 (dd, *J* = 7.7, 1.6 Hz, 1H, H_7), 4.25 (ddd, *J* = 13.0, 11.1, 5.3 Hz, 1H, H_{16}), 2.98 (ddd, *J* = 13.7, 9.3, 6.9 Hz, 1H, H_{11}), 2.86 (ddd, *J* = 13.8, 9.0, 6.0 Hz, 1H, $H_{11'}$), 2.68 (ddd, *J* = 13.0, 11.0, 4.8 Hz, 1H, $H_{16'}$), 2.36 – 2.15 (m, 2H, H_{10}), 1.85 – 1.68 (m, 1H, H_{17}), 1.59 – 1.40 (m, 1H, $H_{17'}$), 1.33 (s, 9H, H_1), 0.88 (t, *J* = 7.4 Hz, 3H, H_{18}).

The identity of the <u>*major*</u> geometrical isomer was assigned as <u>*cis-*</u> on the basis of NOE correlations between H_7-H_{10} (see spectra).

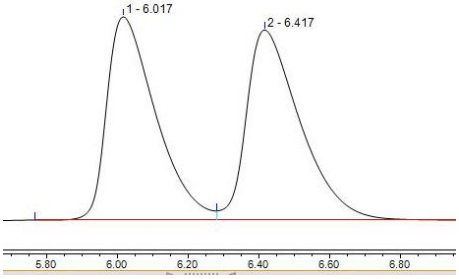
^{13}C NMR (75 MHz, $CDCl_3$): δ_C: 172.2, 146.4, 141.6, 140.0, 131.7, 130.3, 128.8, 128.5, 128.4, 126.9, 126.1, 53.0, 37.5, 36.3, 32.3, 31.7, 20.4, 11.6.

FTIR (neat) ν/cm^{-1}: 2965, 2932, 2874, 1645, 1403, 753, 701, 510.

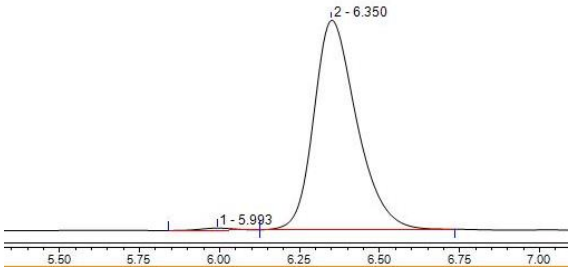
HRMS (ESI): m/z calc'd for $C_{22}H_{30}NO^+[M+H]^+$ 324.2322; found 324.2327 Δ= 1.5 ppm.

Melting Point (°C): 82-84.

Chiral HPLC: Chiralpak-IB column; solvent ratio = 97:3 *n*-hexane: ^{i}PrOH. Temperature = 25 °C, flow rate = 1 ml/min, λ= 240 nm, τ_{ret} = 6.00 min and 6.40 min.



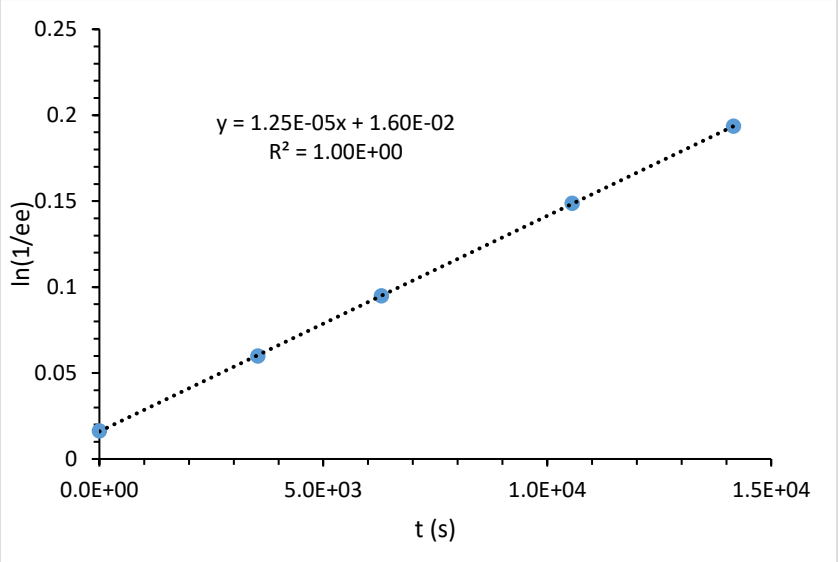
Ret.Time min	Amount n.a.	Rel.Area %	Area mAU*min	Height mAU
6.017	n.a.	49.28	344.9285	2156.34
6.417	n.a.	50.72	354.9716	2017.59



Ret.Time min	Amount n.a.	Rel.Area %	Area mAU*min	Height mAU
5.993	n.a.	0.84	0.2581	2.03
6.350	n.a.	99.16	30.3370	195.16

Racemization study for 3a: According to a modification of general procedure B, *rac*-**3a** (1 mg) was dissolved in 2 mL HPLC grade *n*-hexane. The sample was subjected to semi-preparative normal-phase HPLC (100 µL injection volume) under the conditions specified immediately above using an analytical Daicel IB column (dimensions: 0.46 cm ø x 25 cm) along with the corresponding guard column (0.4 cm ø x 1 cm) and the slower eluting enantiomer was collected. The solvent was removed under a stream of nitogen and the residue was redissolved in isoctane. The sample was heated to 100 °C in a preheated oil bath, and 100 µL aliquots were removed and analyzed by chiral HPLC (under identical conditions) at the time intervals shown below to calculate the rate of racemization.

Time (s)	% maj. enantiomer	% min. enantiomer	ln(1/ee)
0	99.16	0.84	0.0169
3540	97.09	2.91	0.0600
6300	95.47	4.53	0.0950
10560	93.09	6.91	0.149
14160	91.20	8.80	0.194



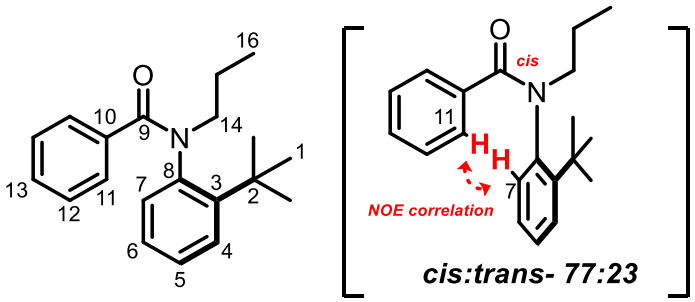
$$k_{rac} = 1.25 \times 10^{-5}\ s^{-1}\ (100\ °C)$$

$$t_{\frac{1}{2}} rac = \mathbf{15.4\ \ hours\ (100\ °C)}$$

$$\Delta G^{\ddagger} = \mathbf{129.2\ kJ/mol\ (100\ °C)}$$

Assuming $\Delta G^{\ddagger}$ is invariant with temperature, $t_{\frac{1}{2}}\ rac \approx \mathbf{200\ years\ (20\ °C)}$

***rac*-N-(2-(*tert*-Butyl)phenyl)-N-propylbenzamide, 3b**



A suspension of sodium hydride (60% dispersion in mineral oil, 47 mg, 1.2 mmol, 1.2 eq.) in dry DMF (1.3 mL) was cooled to 0 ˚C and a solution of **1i** (250 mg, 0.987 mmol, 1.0 eq.) in DMF (4.2 mL) was added. The mixture was stirred for 15 minutes at 0 °C. Propyl iodide (0.3 mL, 3.0 mmol, 3.0 eq.) was added dropwise and the mixture was warmed to room temperature and stirred for 2 h. After this time, water and EtOAc were added, the layers separated, and the aqueous layer extracted twice with EtOAc. The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography (eluent: gradient from 5% Et_2O in petrol 40-60 to 100% Et_2O) to afford **3b** as a white solid (79 mg, 27% yield).

^{1}H NMR (700 MHz, $CDCl_3$) δ_H; 7.62 – 7.57 (m, 3H, $H_{4min.}$ and $H_{11min.}$), 7.51 – 7.44 (m, 4H, $H_{4maj.}$, $H_{13min.}$ and $H_{12min.}$), 7.35 – 7.34 (m, 1H, $H_{5min.}$), 7.33 – 7.31 (m, 2H, $H_{11maj.}$), 7.31 – 7.28 (m, 1H, $H_{6min.}$), 7.27 – 7.24 (m, 1H, $H_{5maj.}$), 7.23

– 7.19 (m, 1H, $H_{13maj.}$), 7.17 (dd, J = 7.7, 1.6 Hz, 1H, $H_{7min.}$), 7.15 – 7.12 (m, 2H, $H_{12maj.}$), 7.12 – 7.09 (m, 1H, $H_{6maj.}$), 7.01 (dd, J = 7.8, 1.5 Hz, 1H, $H_{7maj.}$), 4.44 (ddd, J = 13.0, 11.1, 5.3 Hz, 1H, $H_{14maj.}$), 3.77 (ddd, J = 14.4, 11.3, 5.3 Hz, 1H, $H_{14min.}$), 3.17 (ddd, J = 14.4, 11.2, 4.8 Hz, 1H, $H_{14'min.}$), 2.93 (ddd, J = 13.0, 11.1, 4.8 Hz, 1H, $H_{14'maj.}$), 2.16 – 1.89 (m, 1H, $H_{15maj.}$), 1.76 – 1.63 (m, 2H, $H_{15'maj.}$ and $H_{15min.}$), 1.51 (s, 10H, $H_{1min.}$ and $H_{15min.}$), 1.33 (s, 9H, $H_{1maj.}$), 0.98 (t, J = 7.4 Hz, 3H, $H_{16maj.}$), 0.66 (t, J = 7.4 Hz, 3H, $H_{16min.}$).

The identity of the ***major*** geometrical isomer was assigned as ***cis-*** on the basis of NOE correlations between H_{11} and H_7 (see spectra). A ratio of 77:23 *cis*/*trans* was measured from the ^{1}H NMR data collected at 218 K.

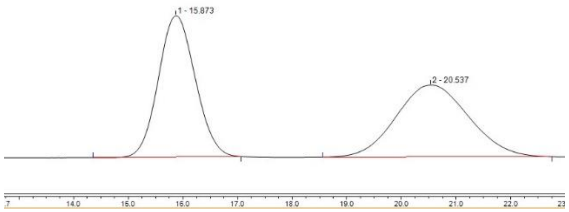
^{13}C NMR (176 MHz, $CDCl_3$) δ_C = 172.3 (min.), 168.8 (maj.), 146.5 (min.), 146.1 (maj.), 140.1 (maj.), 139.9 (min.), 137.1 (min.), 136.2 (maj.), 132.5 (maj.), 131.9 (min.), 130.8 (maj.), 129.5 (min.), 129.4 (maj.), 129.3 (min.), 129.1 (maj.), 128.5 (min.), 128.1 (maj.), 128.0 (min.), 127.4 (maj.), 126.8 (min.), 126.5 (min.), 126.2 (maj.), 55.9 (min.), 54.8 (maj.), 36.3 (maj.), 36.1 (min.), 32.3 (maj.), 31.9 (min.), 22.4 (min.), 20.2 (maj.), 11.6 (maj.), 11.2 (min.)

FTIR (neat) ν/cm^{-1}: 3060, 2951, 2925, 2867, 1626, 1593, 1489, 1403, 1319, 774, 658, 609.

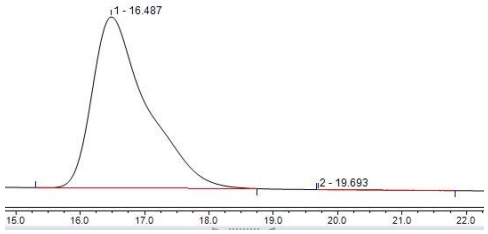
HRMS (ESI): m/z calc'd for $C_{20}H_{26}NO^+$ $[M+H]^+$ 296.2009; found 296.2027 Δ 6.1 ppm.

Melting Point (°C): 92-96.

Chiral HPLC: Chiralpak-IC column; solvent ratio = 92:8 *n*-hexane: ^{i}PrOH. Temperature = 25 °C, flow rate = 1 ml/min, λ= 254 nm, τ_{ret} = 15.9 min and 20.5 min.



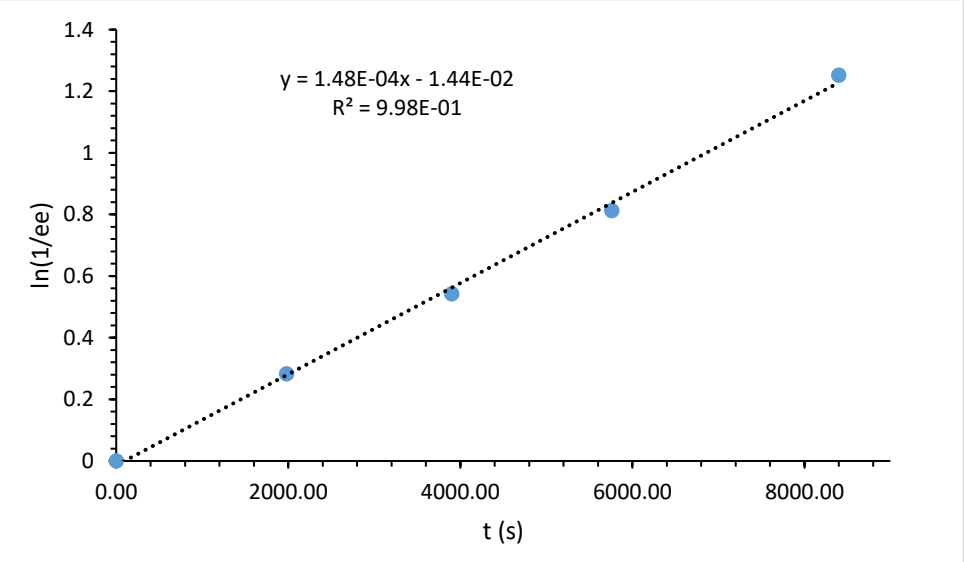
Ret.Time min	Amount n.a.	Rel.Area %	Area mAU*min	Height mAU
15.873	n.a.	49.91	768.4869	980.87
20.537	n.a.	50.09	771.1462	499.23



Ret.Time min	Amount n.a.	Rel.Area %	Area mAU*min	Height mAU
16.487	n.a.	99.99	179.9279	183.01
19.693	n.a.	0.01	0.0117	0.01

Racemization study for 3b: According to a modification of general procedure B, *rac*-**3b** (1 mg) was dissolved in 2 mL HPLC grade *n*-hexane. The sample was subjected to semi-preparative normal-phase HPLC (100 µL injection volume) under the conditions specified immediately above using an analytical Daicel IC column (dimensions: 0.46 cm ø x 25 cm) along with the corresponding guard column (0.4 cm ø x 1 cm). The slower eluting enantiomer was collected. The solvent was removed under a stream of nitogen and the residue was redissolved in isoctane. The sample was heated to 70 °C in a preheated oil bath, and 100 µL aliquots were removed and analyzed by chiral HPLC (under identical conditions) at the time intervals shown below to calculate the rate of racemization.

Time (s)	% maj. enantiomer	% min. enantiomer	ln(1/ee)
0	99.99	0.01	0.0002
1980	87.67	12.33	0.283
3900	79.06	20.94	0.543
5760	72.17	27.83	0.813
8400	64.29	35.71	1.25



$$k_{rac} = 1.48 \times 10^{-4}\ s^{-1}\ (70\ °C)$$

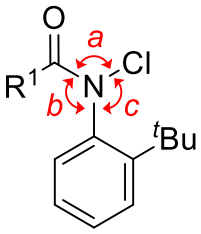
$$t_{\frac{1}{2}}\ rac = \mathbf{1.3\ h}\ \mathbf{(70\ °C)}$$

$$\Delta G^{\ddagger} = \mathbf{111.5\ kJ/mol}\ \mathbf{(70\ °C)}$$

Assuming $\Delta G^{\ddagger}$ is invariant with temperature, $t_{\frac{1}{2}}\ rac \approx \mathbf{60\ days}\ \mathbf{(20\ °C)}$

3.4 *Correlation of Racemization Rates with Charton Parameters and* θ

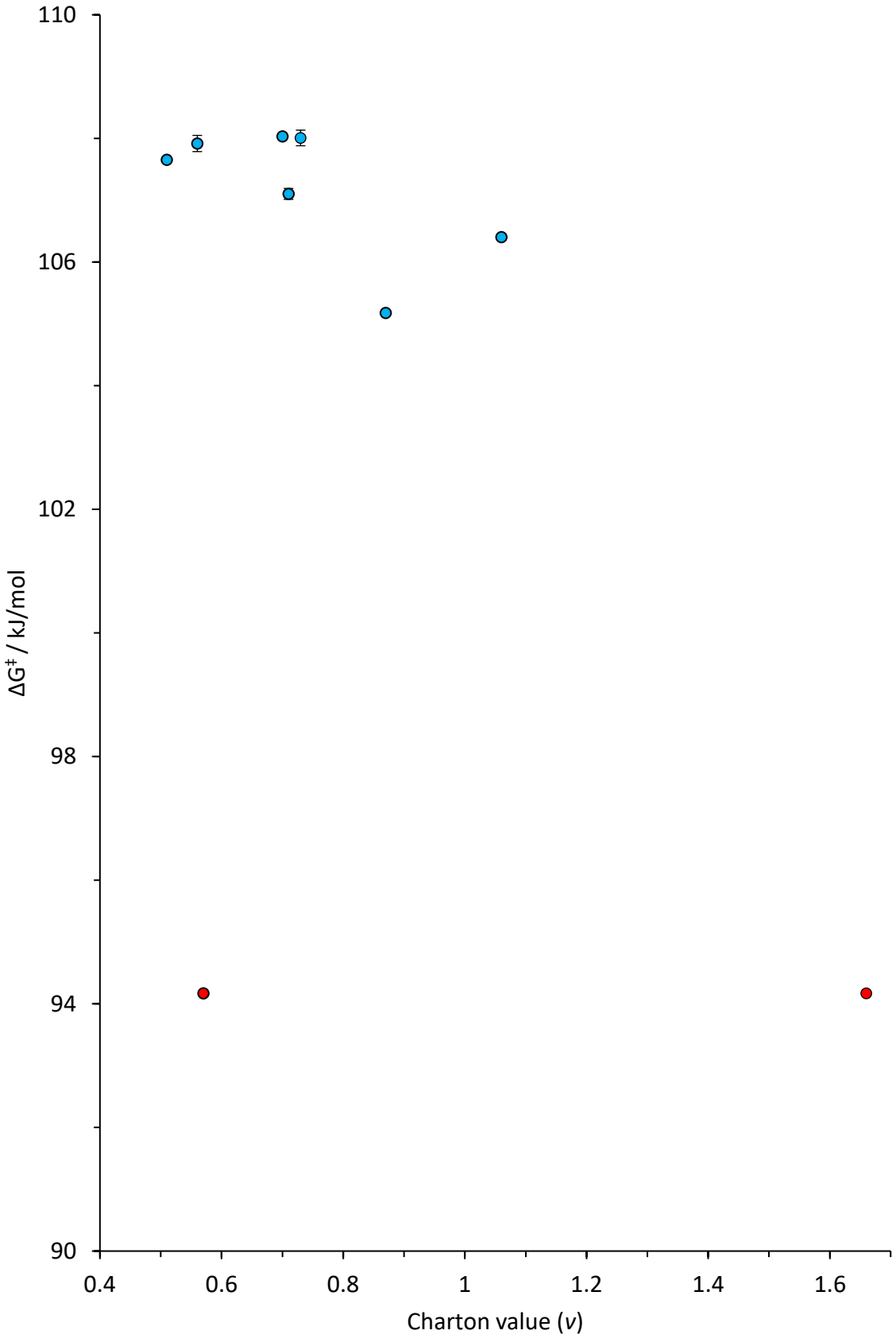
The table below summarises the experimentally detemined values of $\Delta G^{\ddagger}$ for compounds **2a-g** and **2l-n** along with Charton values (*v*) reported in the literature,[7,8,9] Taft-Dubois steric parameter (E_S') reported in the literature, [10] and angle parameters θ calculated from the X-ray crystal structures. Uncertainties in θ were estimated by propagating individual standard deviations of angles a, b and c obtained from analysis of X-ray diffraction data. Uncertianties in $\Delta G^{\ddagger}$ were estimated by propagating standard errors in k_{rac} obtained via linear regression analysis.



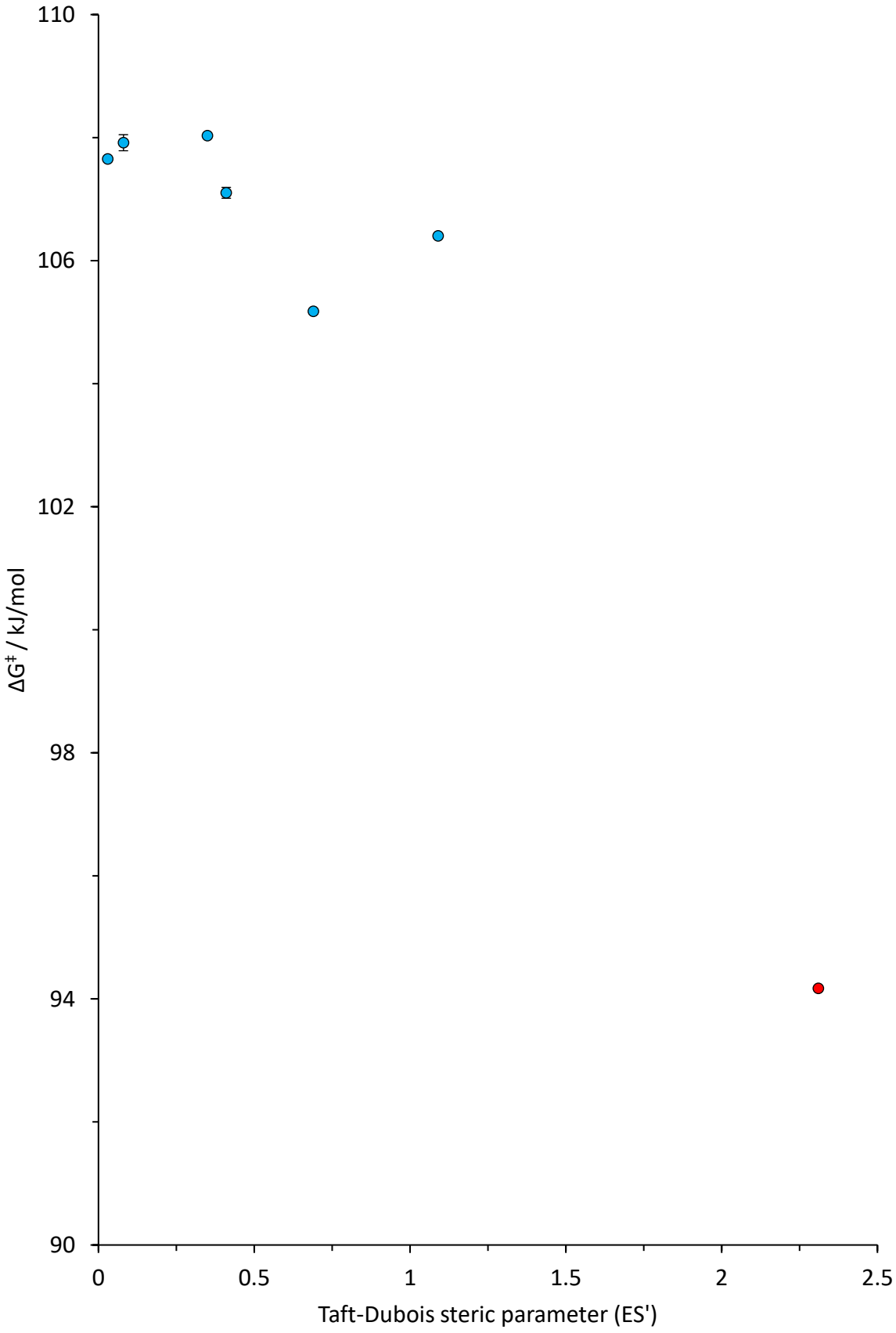
θ = a + b + c

Compound [R^1]	angle *a* / ° (CO-N-Cl)	angle *b* / ° (CO-N-Ar)	angle *c* / ° (Ar-N-Cl)	θ / ° (*a*+*b*+*c*)	*v*	$-E_S'$	$\Delta G^{\ddagger}$ / kJ/mol
2a [$PhCH_2CH_2$]	116.63	127.11	112.88	356.62 ± 0.23	0.70[7]	0.35[10]	108.03 ± 0.02
2b [Et]	115.43	124.39	113.64	353.46 ± 0.15	0.56[7]	0.08[10]	107.92 ± 0.13
2c [^{n}Hept]	–	–	–	–	0.73[8]	–	108.01 ± 0.13
2d [^{c}Pr]	114.12	123.90	111.84	349.86 ± 0.31	1.06[8]	1.09[10]	106.40 ± 0.03
2e [^{c}Bu]	115.43	125.11	113.72	354.26 ± 0.16	0.51[8]	0.03[10]	107.66 ± 0.004
2f [^{c}Pent]	114.12	123.88	112.26	350.26 ± 0.25	0.71[8]	0.41[10]	107.10 ± 0.09
2g [^{c}Hex]	113.61	121.01	111.44	346.06 ± 0.17	0.87[8]	0.69[10]	105.18 ± 0.02
2l [Ph]	117.33	118.06	114.06	349.45 ± 0.23	0.57 *or* 1.66[9]	2.31[10]	94.17 ± 0.03 94.21 ± 0.01
2m [*p*-$CF_3C_6H_4$]	117.92	120.50	112.99	351.41 ± 0.18	–	–	95.39 ± 0.10
2n [*p*-$OMeC_6H_4$]	116.57	119.15	112.22	347.94 ± 0.20	–	–	93.03 ± 0.16

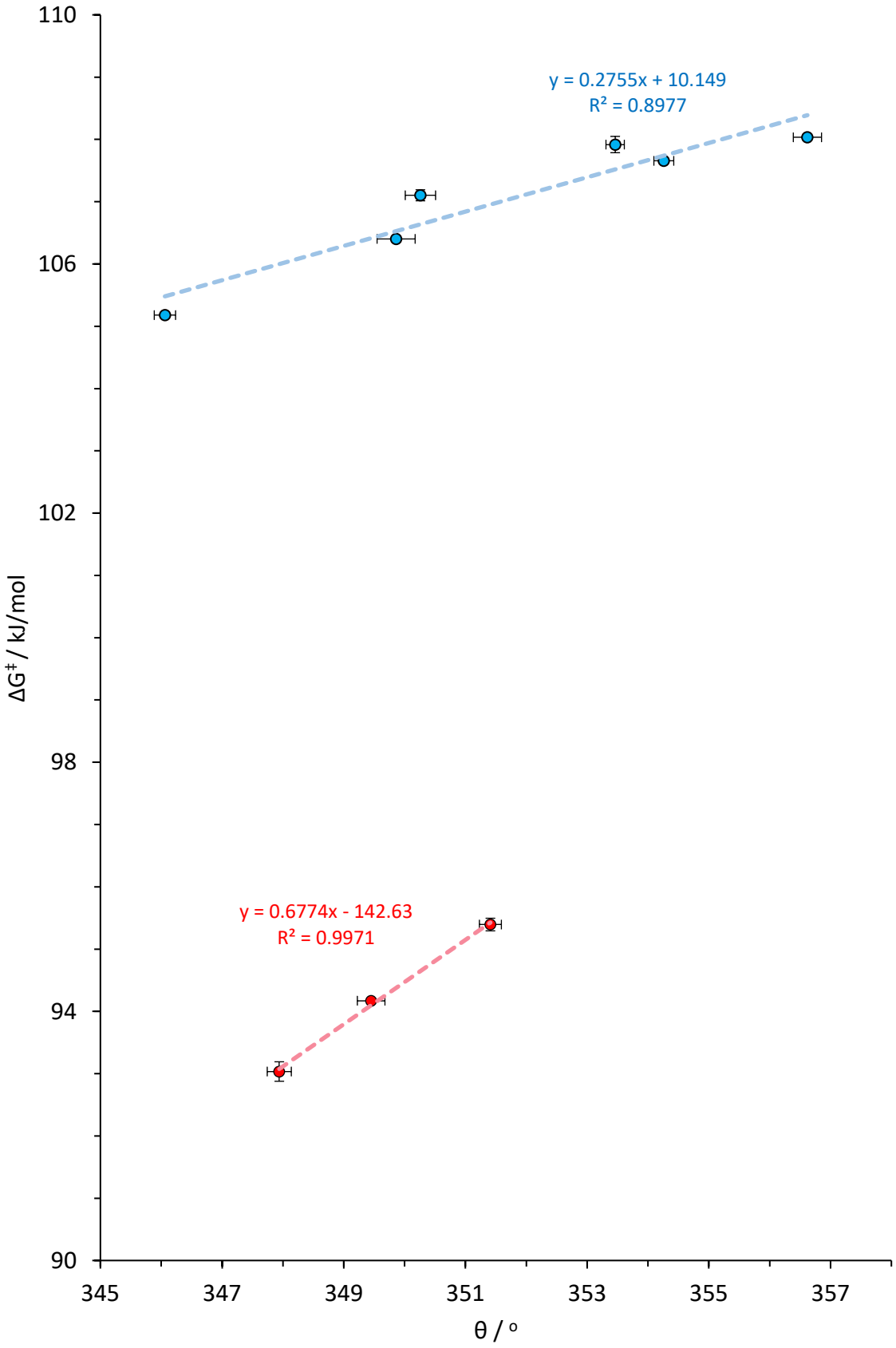
Plotting the values for Charton parameter against $\Delta G^{\ddagger}$ gave the following graph. Error bars represent uncertainties in $\Delta G^{\ddagger}$ as described above.



Plotting the values for the Taft-Dubois steric parameter against $\Delta G^{\ddagger}$ gave the following graph. Error bars represent uncertainties in $\Delta G^{\ddagger}$ as described above.



Plotting the values for θ against $\Delta G^{\ddagger}$ gave the following graph. Error bars represent uncertainties in θ and $\Delta G^{\ddagger}$ as described above.



4. X-Ray Crystallography

4.1 *Experimental*

Single crystal diffraction data were collected on a XtaLAB Synergy HyPix-Arc 100 diffractometer using copper radiation ($\lambda_{CuK\alpha}$ = 1.54184 Å). Data were collected at 150 K using an Oxford Cryosystems CryostreamPlus open-flow N_2 cooling device.

Intensities were corrected for absorption using a multifaceted crystal model created by indexing the faces of the crystal for which data were collected. [11] Cell refinement, data collection and data reduction were undertaken via the software CrysAlisPro.[12]

All structures were solved using XT[13] and refined by XL[14] using the Olex2 interface.[15] All non-hydrogen atoms were refined anisotropically and hydrogen atoms were positioned with idealised geometry, with the exception of those bound to heteroatoms, the positions of which were located using peaks in the Fourier difference map. The displacement parameters of the hydrogen atoms were constrained using a riding model with $U_{(H)}$ set to be an appropriate multiple of the U_{eq} value of the parent atom.

4.2 Crystal data and structure refinement for 2a

Empirical formula	$C_{19}H_{22}ClNO$
Formula weight	315.82
Temperature/K	150.0(2)
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	16.7373(9)
b/Å	6.1891(2)
c/Å	18.0916(11)
α/°	90
β/°	110.509(6)
γ/°	90
Volume/Å^3	1755.30(17)
Z	4
ρ_{calc}g/cm^3	1.195
μ/mm^{-1}	1.923
F(000)	672.0
Crystal size/mm^3	0.26 × 0.06 × 0.05
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	8.926 to 155.896
Index ranges	-20 ≤ h ≤ 21, -7 ≤ k ≤ 7, -21 ≤ l ≤ 22
Reflections collected	20357
Independent reflections	3493 [R_{int} = 0.0320, R_{sigma} = 0.0217]

Data/restraints/parameters	3493/234/233
Goodness-of-fit on F^2	1.148
Final R indexes [I>=2σ (I)]	R_1 = 0.0428, wR_2 = 0.1167
Final R indexes [all data]	R_1 = 0.0509, wR_2 = 0.1354
Largest diff. peak/hole / e $Å^{-3}$	0.31/-0.44

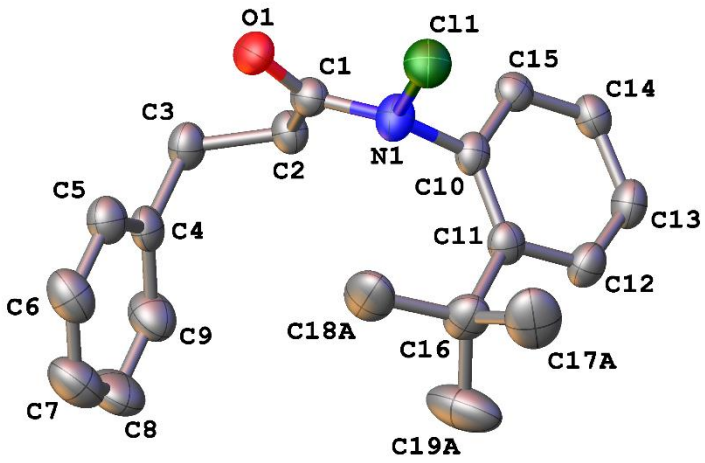


*Figure 1: The structure of **2a** with probability ellipsoids drawn at the 50% probability level. Only the disorder component with the highest occupancy is shown and hydrogen atoms have been omitted for clarity*

4.3 Crystal data and structure refinement for 2b

Empirical formula	$C_{13}H_{18}ClNO$
Formula weight	239.746
Temperature/K	150.0(2)
Crystal system	triclinic
Space group	P-1
a/Å	6.66649(19)
b/Å	9.4285(3)
c/Å	10.2117(3)
α/°	93.580(2)
β/°	96.362(2)
γ/°	93.083(2)
Volume/$Å^3$	635.47(3)
Z	2
$\rho_{calc}g/cm^3$	1.253
μ/mm^{-1}	2.486
F(000)	257.4
Crystal size/mm^3	0.19 × 0.18 × 0.06
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	8.74 to 155.2
Index ranges	-8 ≤ h ≤ 8, -11 ≤ k ≤ 11, -12 ≤ l ≤ 12
Reflections collected	13900
Independent reflections	2505 [R_{int} = 0.0347, R_{sigma} = 0.0219]

Data/restraints/parameters	2505/0/150
Goodness-of-fit on F^2	1.039
Final R indexes [I>=2σ (I)]	R_1 = 0.0304, wR_2 = 0.0794
Final R indexes [all data]	R_1 = 0.0323, wR_2 = 0.0812
Largest diff. peak/hole / e $Å^{-3}$	0.23/-0.21

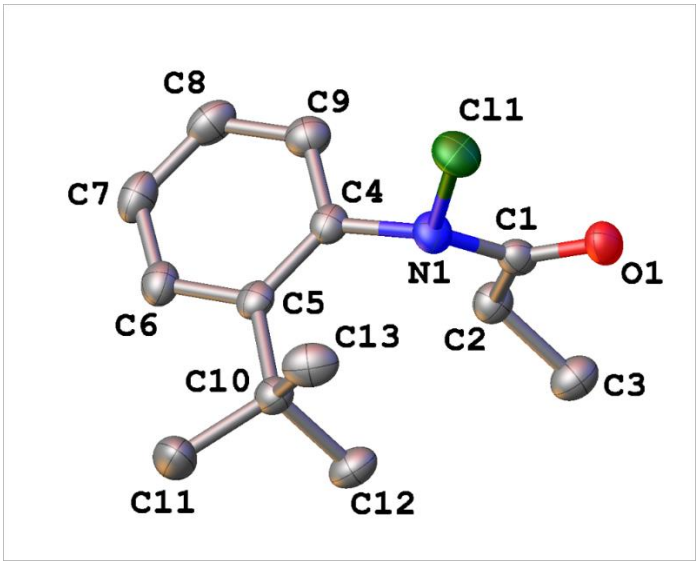


*Figure 2: The structure of **2b** with probability ellipsoids drawn at the 50% probability level. Hydrogen atoms have been omitted for clarity*

4.4 Crystal data and structure refinement for 2d

Empirical formula	$C_{14}H_{18}ClNO$
Formula weight	251.74
Temperature/K	150.0(2)
Crystal system	monoclinic
Space group	I2/a
a/Å	18.5653(4)
b/Å	6.36990(10)
c/Å	23.6434(5)
α/°	90
β/°	108.817(2)
γ/°	90
Volume/$Å^3$	2646.61(9)
Z	8
$\rho_{calc}g/cm^3$	1.264
μ/mm^{-1}	2.414
F(000)	1072.0
Crystal size/mm^3	0.27 × 0.1 × 0.03
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	7.9 to 155.126
Index ranges	-22 ≤ h ≤ 22, -7 ≤ k ≤ 7, -28 ≤ l ≤ 29
Reflections collected	14323
Independent reflections	2651 [R_{int} = 0.0384, R_{sigma} = 0.0270]
Data/restraints/parameters	2651/0/157
Goodness-of-fit on F^2	1.051

Final R indexes [I>=2σ (I)]	R_1 = 0.0607, wR_2 = 0.1564
Final R indexes [all data]	R_1 = 0.0668, wR_2 = 0.1619
Largest diff. peak/hole / e Å^{-3}	1.65/-0.78

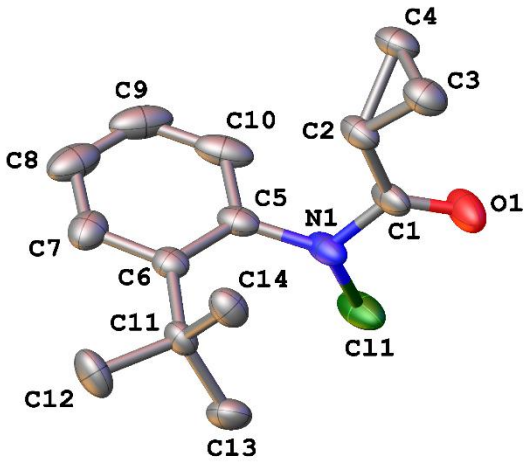


*Figure 3: The structure of **2d** with probability ellipsoids drawn at the 50% probability level. Hydrogen atoms have been omitted for clarity*

4.5 Crystal data and structure refinement for 2e

Empirical formula	$C_{15}H_{20}ClNO$
Formula weight	265.77
Temperature/K	150.0(2)
Crystal system	monoclinic
Space group	C2/c
a/Å	17.0047(5)
b/Å	6.6560(2)
c/Å	24.7570(8)
α/°	90
β/°	92.075(3)
γ/°	90
Volume/Å^3	2800.24(15)
Z	8
ρ_{calc}g/cm^3	1.261
μ/mm^{-1}	2.308
F(000)	1136.0
Crystal size/mm^3	0.19 × 0.16 × 0.1
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	7.146 to 156.44
Index ranges	-20 ≤ h ≤ 19, -8 ≤ k ≤ 8, -30 ≤ l ≤ 30
Reflections collected	12518
Independent reflections	2785 [R_{int} = 0.0331, R_{sigma} = 0.0243]
Data/restraints/parameters	2785/0/166
Goodness-of-fit on F^2	1.066

Final R indexes [I>=2σ (I)]	R_1 = 0.0330, wR_2 = 0.0886
Final R indexes [all data]	R_1 = 0.0372, wR_2 = 0.0928
Largest diff. peak/hole / e Å^{-3}	0.22/-0.27

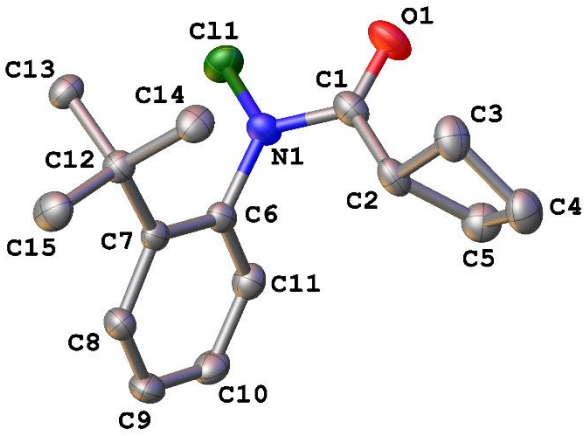


*Figure 4: The structure of **2e** with probability ellipsoids drawn at the 50% probability level. Hydrogen atoms have been omitted for clarity*

4.6 Crystal data and structure refinement for 2f

Empirical formula	$C_{16}H_{22}ClNO$
Formula weight	279.79
Temperature/K	150.0(2)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	12.6132(6)
b/Å	6.8258(4)
c/Å	17.3255(8)
α/°	90
β/°	93.319(4)
γ/°	90
Volume/Å^3	1489.13(14)
Z	4
ρ_{calc}g/cm^3	1.248
μ/mm^{-1}	2.195
F(000)	600.0
Crystal size/mm^3	0.21 × 0.09 × 0.02
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	7.02 to 156.434
Index ranges	-11 ≤ h ≤ 15, -7 ≤ k ≤ 8, -21 ≤ l ≤ 22
Reflections collected	13974
Independent reflections	2982 [R_{int} = 0.0307, R_{sigma} = 0.0235]
Data/restraints/parameters	2982/0/175
Goodness-of-fit on F^2	1.046

Final R indexes [I>=2σ (I)]	R_1 = 0.0445, wR_2 = 0.1230
Final R indexes [all data]	R_1 = 0.0557, wR_2 = 0.1337
Largest diff. peak/hole / e Å^{-3}	0.32/-0.24

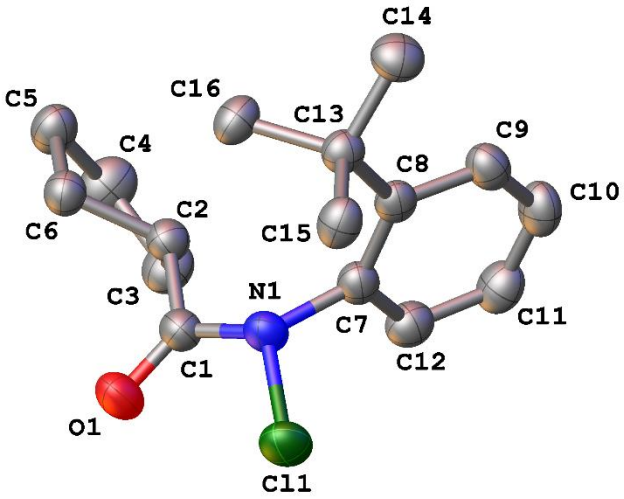


*Figure 5: The structure of **2f** with probability ellipsoids drawn at the 50% probability level. Hydrogen atoms have been omitted for clarity*

4.7 Crystal data and structure refinement for 2g

Empirical formula	$C_{17}H_{24}ClNO$
Formula weight	293.82
Temperature/K	150.0(2)
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	9.22350(10)
b/Å	7.00790(10)
c/Å	25.1221(4)
α/°	90
β/°	94.528(2)
γ/°	90
Volume/Å^3	1618.76(4)
Z	4
ρ_{calc}g/cm^3	1.206
μ/mm^{-1}	2.041
F(000)	632.0
Crystal size/mm^3	0.1 × 0.08 × 0.03
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	7.06 to 156.672
Index ranges	-11 ≤ h ≤ 11, -8 ≤ k ≤ 6, -30 ≤ l ≤ 31
Reflections collected	15611
Independent reflections	3262 [R_{int} = 0.0309, R_{sigma} = 0.0237]
Data/restraints/parameters	3262/0/184

Goodness-of-fit on F^2	1.044
Final R indexes [I>=2σ (I)]	R_1 = 0.0368, wR_2 = 0.0961
Final R indexes [all data]	R_1 = 0.0433, wR_2 = 0.1014
Largest diff. peak/hole / e $Å^{-3}$	0.52/-0.27

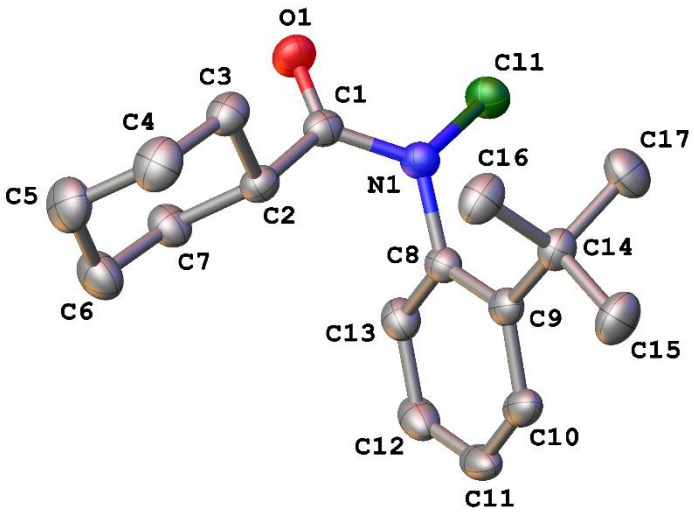


*Figure 6: The structure of **2g** with probability ellipsoids drawn at the 50% probability level. Hydrogen atoms have been omitted for clarity*

4.8 Crystal data and structure refinement for 2l

Empirical formula	$C_{17}H_{18}ClNO$
Formula weight	287.77
Temperature/K	150.0(2)
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å	7.63450(10)
b/Å	9.62950(10)
c/Å	20.4737(2)
α/°	90
β/°	90
γ/°	90
Volume/$Å^3$	1505.15(3)
Z	4
$\rho_{calc}g/cm^3$	1.270
μ/mm^{-1}	2.194
F(000)	608.0
Crystal size/mm^3	0.22 × 0.15 × 0.08
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	8.638 to 156.91
Index ranges	-9 ≤ h ≤ 8, -10 ≤ k ≤ 12, -24 ≤ l ≤ 24
Reflections collected	19192
Independent reflections	3057 [R_{int} = 0.0346, R_{sigma} = 0.0202]
Data/restraints/parameters	3057/0/185

Goodness-of-fit on F^2	1.046
Final R indexes [I>=2σ (I)]	R_1 = 0.0252, wR_2 = 0.0649
Final R indexes [all data]	R_1 = 0.0259, wR_2 = 0.0654
Largest diff. peak/hole / e $Å^{-3}$	0.17/-0.17
Flack parameter	-0.010(5)

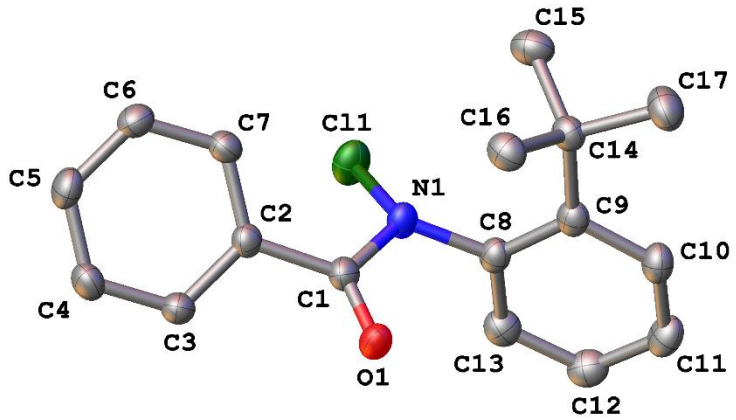


*Figure 7: The structure of **2l** with probability ellipsoids drawn at the 50% probability level. Hydrogen atoms have been omitted for clarity*

4.9 Crystal data and structure refinement for 2m

Empirical formula	$C_{18}H_{17}ClF_3NO$
Formula weight	355.77
Temperature/K	150.0(2)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	6.21560(10)
b/Å	11.1571(3)
c/Å	24.7517(6)
α/°	90
β/°	92.551(2)
γ/°	90
Volume/$Å^3$	1714.78(7)
Z	4
$\rho_{calc}g/cm^3$	1.378
μ/mm^{-1}	2.295
F(000)	736.0
Crystal size/mm^3	0.23 × 0.04 × 0.04
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	7.15 to 157.838
Index ranges	-7 ≤ h ≤ 7, -13 ≤ k ≤ 13, -30 ≤ l ≤ 30

Reflections collected	18811
Independent reflections	3491 [R_{int} = 0.0350, R_{sigma} = 0.0235]
Data/restraints/parameters	3491/420/275
Goodness-of-fit on F^2	1.092
Final R indexes [I>=2σ (I)]	R_1 = 0.0361, wR_2 = 0.0986
Final R indexes [all data]	R_1 = 0.0406, wR_2 = 0.1026
Largest diff. peak/hole / e $Å^{-3}$	0.31/-0.26

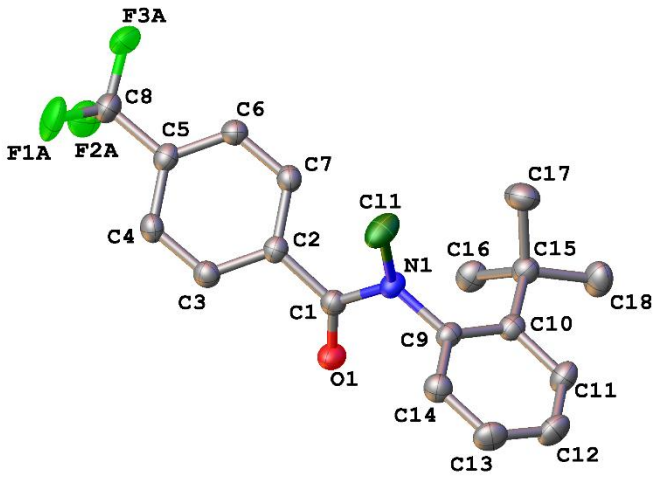


*Figure 8: The structure of **2m** with probability ellipsoids drawn at the 50% probability level. . Only the disorder component with the highest occupancy is shown and hydrogen atoms have been omitted for clarity*

4.10 Crystal data and structure refinement for 2n

Empirical formula	$C_{18}H_{20}ClNO_2$
Formula weight	317.80
Temperature/K	150.0(2)
Crystal system	triclinic
Space group	P-1
a/Å	8.35130(10)
b/Å	13.4596(2)
c/Å	15.5830(2)
α/°	77.9650(10)
β/°	76.1000(10)
γ/°	77.2070(10)
Volume/$Å^3$	1635.64(4)
Z	4
$\rho_{calc}g/cm^3$	1.291
μ/mm^{-1}	2.116
F(000)	672.0
Crystal size/mm^3	0.27 × 0.09 × 0.05
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	5.922 to 157.166
Index ranges	-9 ≤ h ≤ 10, -17 ≤ k ≤ 17, -19 ≤ l ≤ 19

Reflections collected	43178
Independent reflections	6442 [R_{int} = 0.0342, R_{sigma} = 0.0208]
Data/restraints/parameters	6442/0/406
Goodness-of-fit on F^2	1.065
Final R indexes [I>=2σ (I)]	R_1 = 0.0395, wR_2 = 0.1056
Final R indexes [all data]	R_1 = 0.0431, wR_2 = 0.1083
Largest diff. peak/hole / e $Å^{-3}$	0.45/-0.46

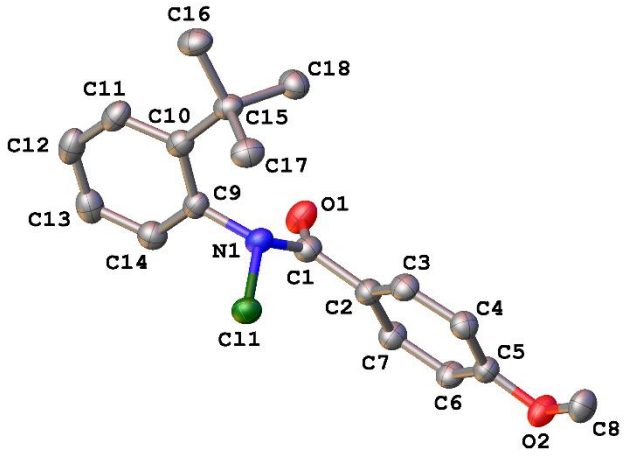


*Figure 9: The structure of **2n** with probability ellipsoids drawn at the 50% probability level. Hydrogen atoms have been omitted for clarity*

5. Computational Modelling

5.1 Computational Methods

All conformational searches were performed using MacroModel (Version 13.6)[14] in the gas phase utilizing the MMFF force field[15-20] and a mixture of Low Mode following and Monte Carlo search algorithms.[21,22] Quantum mechanical calculations were carried out using ORCA 5.0.2.[23] The molecular geometries were optimized using the PBE0-D3 functional[24,25] with the def2-TZVP basis set[26,27]. The optimisations were using the implicit SMD solvent model.[28] All single-point energies were separately calculated using ωB97M-V functional[29] and def2-QZVPP[26,27] basis set using the SMD solvent model. Frequency calculations were performed on all structures and confirmed to contain no imaginary frequencies or just one imaginary frequency for ground states and transition states, respectively. Full set of DFT output files with optimized structures, frequencies and high-level single-point energies are provided in the accompanied archive. The archive structure is shown below in section 5.3.

5.2 Investigation of solvent effect on racemization and amide rotation barriers

To investigate the influence of a different solvent on the racemization barriers, single point energy calculations using SMD(DCM) solvent model were repeated for all structures (see below). This revealed that all of the free energy trends remained similar in DCM solvent, but the racemization free activation energies all were 1.7 – 3.2 kJ/mol higher in DCM compared to hexane. This may be due to more efficient ground state stabilization in the more polar solvent. All reported energies are in kJ/mol.

amide	G_{rel} *trans* vs *cis* (hexane)	G_{rel} *trans* vs *cis* (DCM)	$\Delta G^{‡}$ calc. (hexane)	$\Delta G^{‡}$ calc. (DCM)
2b (Et)	+2.1	+2.1	117.2	120.4
2d (cPr)	+4.3	+5.3	115.0	116.7
2l (Ph)	–3.4	-1.5	100.7	103.2
2n (PMP)	–4.8	-3.7	97.8	100.2

5.3 Summary of additional geometrical parameters

For comparison purposes, key additional geometrical parameters (bond lengths and angles) at the transition states for racemization and *cis-trans* isomerization are identified below:

Racemization transition states:

amide	Bond lengths (in Å)			Bond angles (in degrees)		
	C(O)-N	**N-Cl**	**N-Ar**	**C(O)-N-Cl**	**Cl-N-Ar**	**Ar-N-CO**
2b (Et)	1.47	1.71	1.42	103.6	126.5	116.6
2d (cPr)	1.47	1.71	1.42	103.2	125.7	116.1
2l (Ph)	1.46	1.72	1.43	101.8	125	118.1
2n (PMP)	1.47	1.72	1.43	102.2	125.1	117.3

Cis-trans isomerization transition states:

amide	Bond lengths (in Å)			Bond angles (in degrees)		
	C(O)-N	**N-Cl**	**N-Ar**	**C(O)-N-Cl**	**Cl-N-Ar**	**Ar-N-CO**
2b (Et)	1.48	1.76	1.44	104.8	111.6	115.7
2d (cPr)	1.47	1.76	1.44	106.3	110.8	115
2l (Ph)	1.47	1.76	1.45	106.6	110.5	114.8
2n (PMP)	1.47	1.76	1.45	106.6	110.1	114.7

5.4 Summary of the associated computational dataset contents

This dataset contains ORCA DFT output files of the key ground-states and transition state DFT optimized structures. The dataset contains 160 files in total. The data is organized by the chloroamide studies, covering substrates **2b**, **2l**, **2d**, **2n**. Each of the substrate folders contain subfolders for the ground state calculations, racemization transition states and the cis-trans isomerization transition states. Each of the lower level folders contain the output of the final optimization calculation (*opt*.out), frequency calculation (*freq.out) as well as single point calculation (*_sp.out). All optimized geometries are also provided as *.xyz files for even better usability. The full dataset structure is shown below.

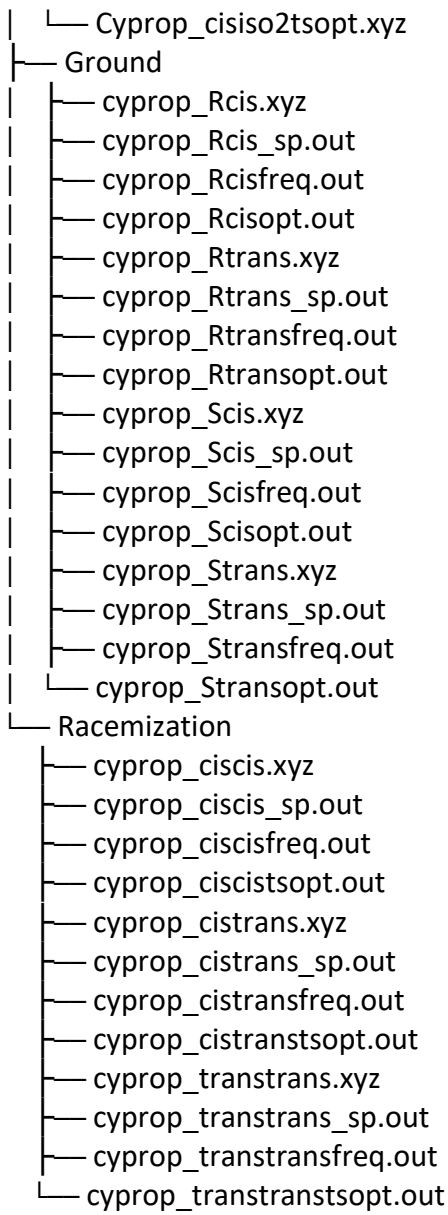
All of the files can be opened in any text editor. ORCA output structures can be viewed and the frequency modes visualised in Avogadro, jmol and in most other molecular viewers/editors. *.xyz files can be viewed in essentially all 3D molecular editors and viewers.

```
├── Et (2b)
│   ├── Cis-trans isomerization
│   │   ├── Et_cisiso1_sp.out
│   │   ├── Et_cisiso1freq.out
```

```
│   │   ├── Et_cisiso1tsopt.out
│   │   ├── Et_cisiso1tsopt.xyz
│   │   ├── Et_cisiso2_sp.out
│   │   ├── Et_cisiso2freq.out
│   │   ├── Et_cisiso2tsopt.out
│   │   └── Et_cisiso2tsopt.xyz
│   ├── Ground
│   │   ├── Etciscis_end.xyz
│   │   ├── Etciscis_end_sp.out
│   │   ├── Etciscis_endfreq.out
│   │   ├── Etciscis_endopt.out
│   │   ├── Etciscis_start.xyz
│   │   ├── Etciscis_start_sp.out
│   │   ├── Etciscis_startfreq.out
│   │   ├── Etciscis_startopt.out
│   │   ├── Etcistrans_end.xyz
│   │   ├── Etcistrans_end_sp.out
│   │   ├── Etcistrans_endfreq.out
│   │   ├── Etcistrans_endopt.out
│   │   ├── Etcistrans_start.xyz
│   │   ├── Etcistrans_start_sp.out
│   │   ├── Etcistrans_startfreq.out
│   │   ├── Etcistrans_startopt.out
│   │   ├── Ettranstrans_end.xyz
│   │   ├── Ettranstrans_end_sp.out
│   │   ├── Ettranstrans_endfreq.out
│   │   ├── Ettranstrans_endopt.out
│   │   ├── Ettranstrans_start.xyz
│   │   ├── Ettranstrans_start_sp.out
│   │   ├── Ettranstrans_startfreq.out
│   │   └── Ettranstrans_startopt.out
│   └── Racemization
│       ├── Etciscis.xyz
│       ├── Etciscis_sp.out
│       ├── Etciscisfreq.out
│       ├── Etciscistsoptd.out
│       ├── Etcistrans.xyz
│       ├── Etcistrans_sp.out
│       ├── Etcistransfreq.out
│       ├── Etcistranstsopt.out
│       ├── Ettranstrans.xyz
│       ├── Ettranstrans_sp.out
│       ├── Ettranstransfreq.out
│       └── Ettranstranstsopt.out
├── PMP (2n)
│   ├── Cis-trans isomerization
│   │   ├── PMP_transiso1_sp.out
```

```
│   │   ├── PMP_transiso1freq.out
│   │   ├── PMP_transiso1tsopt.out
│   │   ├── PMP_transiso1tsopt.xyz
│   │   ├── PMP_transiso2_sp.out
│   │   ├── PMP_transiso2freq.out
│   │   ├── PMP_transiso2tsopt.out
│   │   └── PMP_transiso2tsopt.xyz
│   ├── Ground
│   │   ├── PMP_Rcis.xyz
│   │   ├── PMP_Rcis_sp.out
│   │   ├── PMP_Rcisfreq.out
│   │   ├── PMP_Rcisopt.out
│   │   ├── PMP_Rtrans.xyz
│   │   ├── PMP_Rtrans_sp.out
│   │   ├── PMP_Rtransfreq.out
│   │   ├── PMP_Rtransopt.out
│   │   ├── PMP_Scis.xyz
│   │   ├── PMP_Scis_sp.out
│   │   ├── PMP_Scisfreq.out
│   │   ├── PMP_Scisopt.out
│   │   ├── PMP_Strans.xyz
│   │   ├── PMP_Strans_sp.out
│   │   ├── PMP_Stransfreq.out
│   │   └── PMP_Stransopt.out
│   └── Racemization
│       ├── PMPciscis.xyz
│       ├── PMPciscis_sp.out
│       ├── PMPciscisfreq.out
│       ├── PMPciscistsopt.out
│       ├── PMPcistrans.xyz
│       ├── PMPcistrans_sp.out
│       ├── PMPcistransfreq.out
│       ├── PMPcistranstsoptb.out
│       ├── PMPtranstrans.xyz
│       ├── PMPtranstrans_sp.out
│       ├── PMPtranstransfreq.out
│       └── PMPtranstranstsoptb.out
├── Ph (2l)
│   ├── Cis-trans isomerization
│   │   ├── Ph_transiso1_sp.out
│   │   ├── Ph_transiso1freq.out
│   │   ├── Ph_transiso1tsopt.out
│   │   ├── Ph_transiso1tsopt.xyz
│   │   ├── Ph_transiso2_sp.out
│   │   ├── Ph_transiso2freq.out
│   │   ├── Ph_transiso2tsopt.out
│   │   └── Ph_transiso2tsopt.xyz
```

```
│   ├── Ground
│   │   ├── Ph_ciscis_end.xyz
│   │   ├── Ph_ciscis_end_sp.out
│   │   ├── Ph_ciscis_endfreq.out
│   │   ├── Ph_ciscis_endopt.out
│   │   ├── Ph_ciscis_start.xyz
│   │   ├── Ph_ciscis_start_sp.out
│   │   ├── Ph_ciscis_startfreq.out
│   │   ├── Ph_ciscis_startopt.out
│   │   ├── Ph_trans_cis_start.xyz
│   │   ├── Ph_trans_cis_start_sp.out
│   │   ├── Ph_trans_cis_startfreq.out
│   │   ├── Ph_trans_cis_startopt.out
│   │   ├── Ph_trans_trans_end.xyz
│   │   ├── Ph_trans_trans_end_sp.out
│   │   ├── Ph_trans_trans_endfreq.out
│   │   ├── Ph_trans_trans_endopt.out
│   │   ├── Ph_trans_trans_start.xyz
│   │   ├── Ph_trans_trans_start_sp.out
│   │   ├── Ph_trans_trans_startfreq.out
│   │   ├── Ph_trans_trans_startopt.out
│   │   ├── Ph_transcis_end.xyz
│   │   ├── Ph_transcis_end_sp.out
│   │   ├── Ph_transcis_endfreq.out
│   │   └── Ph_transcis_endopt.out
│   └── Racemization
│       ├── Ph_ciscis_sp.out
│       ├── Ph_ciscisfreq.out
│       ├── Ph_ciscistsoptb.out
│       ├── Ph_ciscistsoptb.xyz
│       ├── Ph_trans_cis_sp.out
│       ├── Ph_trans_cisfreq.out
│       ├── Ph_trans_cistsopt.out
│       ├── Ph_trans_cistsopt.xyz
│       ├── Ph_trans_trans_sp.out
│       ├── Ph_trans_transfreq.out
│       ├── Ph_trans_transtsoptb.out
│       └── Ph_trans_transtsoptb.xyz
└── cPr (2d)
    ├── Cis-trans isomerization
    │   ├── Cyprop_cisiso1_sp.out
    │   ├── Cyprop_cisiso1freq.out
    │   ├── Cyprop_cisiso1tsopt.out
    │   ├── Cyprop_cisiso1tsopt.xyz
    │   ├── Cyprop_cisiso2_sp.out
    │   ├── Cyprop_cisiso2freq.out
    │   ├── Cyprop_cisiso2tsopt.out
```


Cyprop_cisiso2tsopt.xyz
Ground
cyprop_Rcis.xyz
cyprop_Rcis_sp.out
cyprop_Rcisfreq.out
cyprop_Rcisopt.out
cyprop_Rtrans.xyz
cyprop_Rtrans_sp.out
cyprop_Rtransfreq.out
cyprop_Rtransopt.out
cyprop_Scis.xyz
cyprop_Scis_sp.out
cyprop_Scisfreq.out
cyprop_Scisopt.out
cyprop_Strans.xyz
cyprop_Strans_sp.out
cyprop_Stransfreq.out
cyprop_Stransopt.out
Racemization
cyprop_ciscis.xyz
cyprop_ciscis_sp.out
cyprop_ciscisfreq.out
cyprop_ciscistsopt.out
cyprop_cistrans.xyz
cyprop_cistrans_sp.out
cyprop_cistransfreq.out
cyprop_cistranstsopt.out
cyprop_transtrans.xyz
cyprop_transtrans_sp.out
cyprop_transtransfreq.out
cyprop_transtranstsopt.out

6. References

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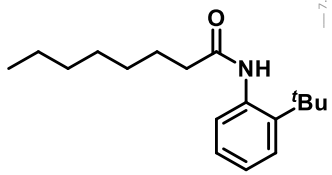
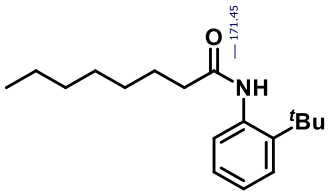
7. NMR Spectra



1c

^{1}H NMR, $CDCl_3$

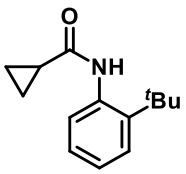
400 MHz, 298K



1c

^{13}C NMR, $CDCl_3$

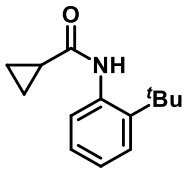
75 MHz, 298K



1d

^{1}H NMR, $CDCl_3$

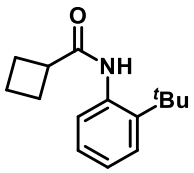
400 MHz, 298K



1d

^{13}C NMR, $CDCl_3$

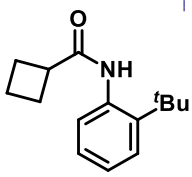
75 MHz, 298K



1e

^{1}H NMR, $CDCl_3$

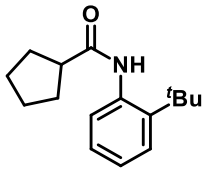
300 MHz, 298K



1e

^{13}C NMR, $CDCl_3$

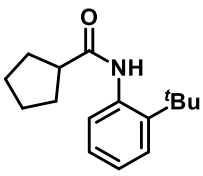
75 MHz, 298K



1f

^{1}H NMR, $CDCl_3$

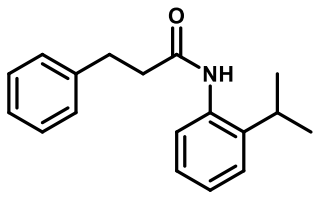
300 MHz, 298K



1f

^{13}C NMR, $CDCl_3$

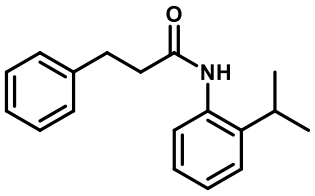
75 MHz, 298K



1h

^{1}H NMR, $CDCl_3$

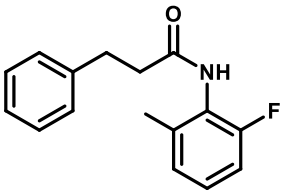
400 MHz, 298K



1h

^{13}C NMR, $CDCl_3$

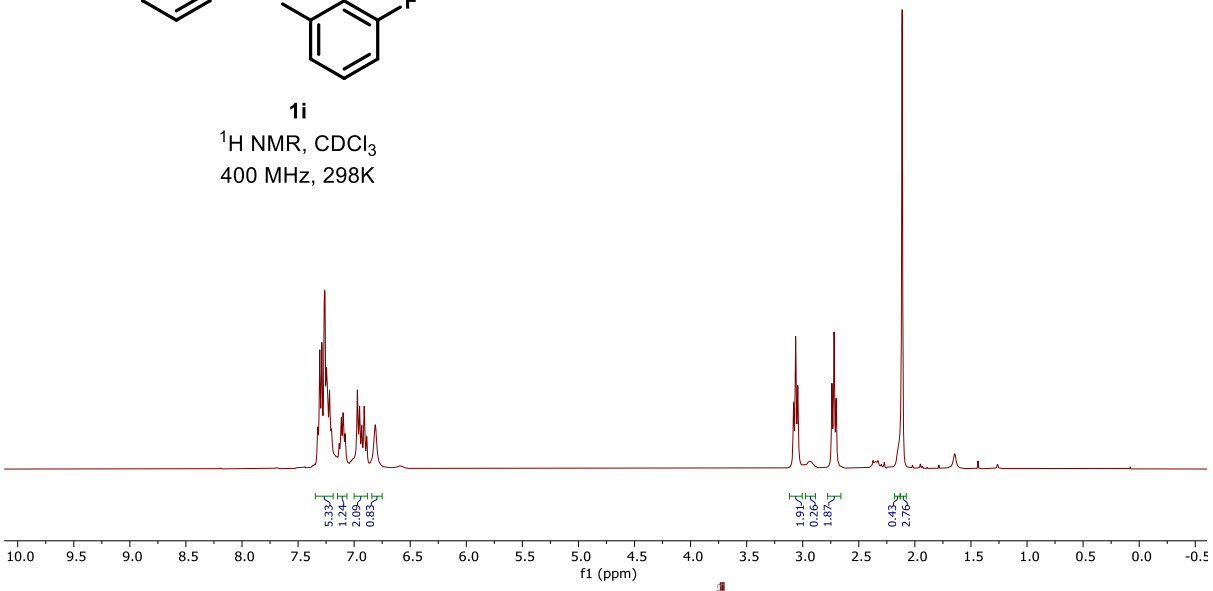
101 MHz, 298K

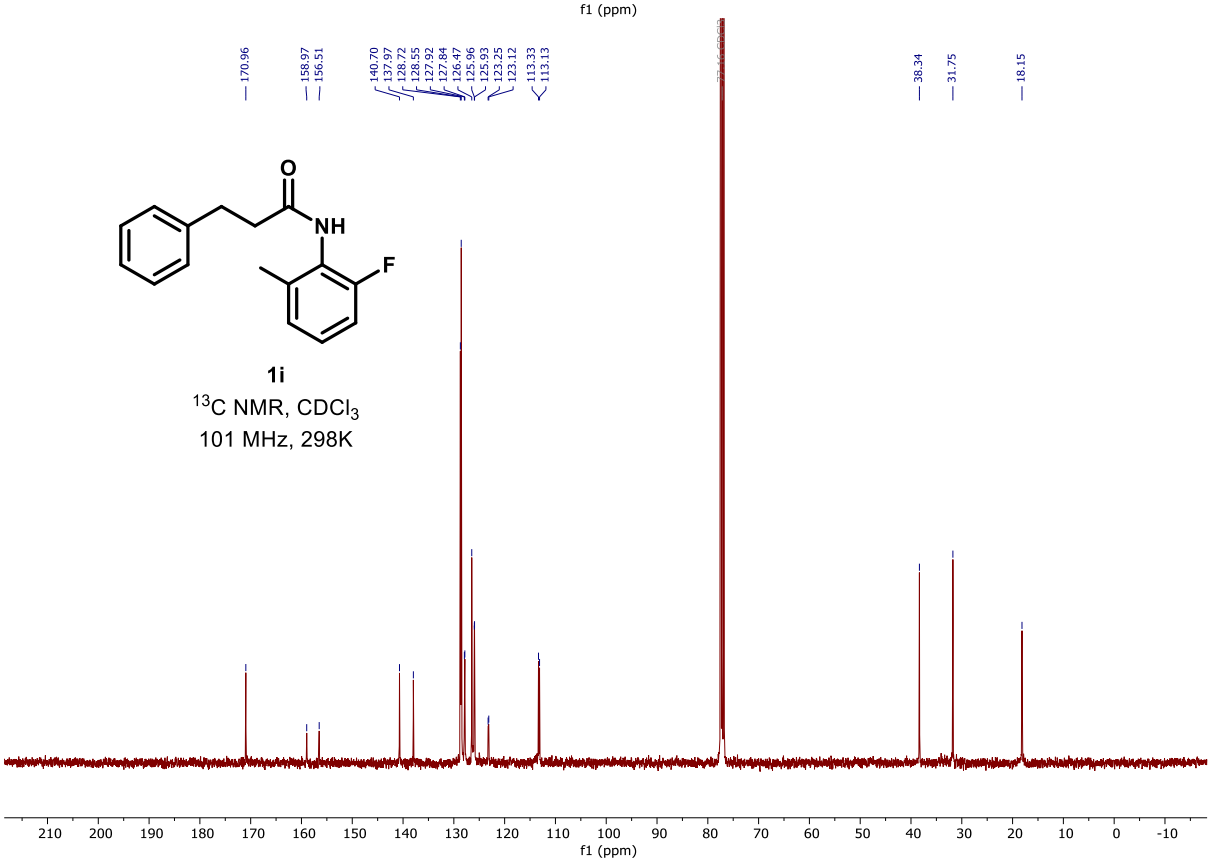


1i

^{1}H NMR, $CDCl_3$

400 MHz, 298K

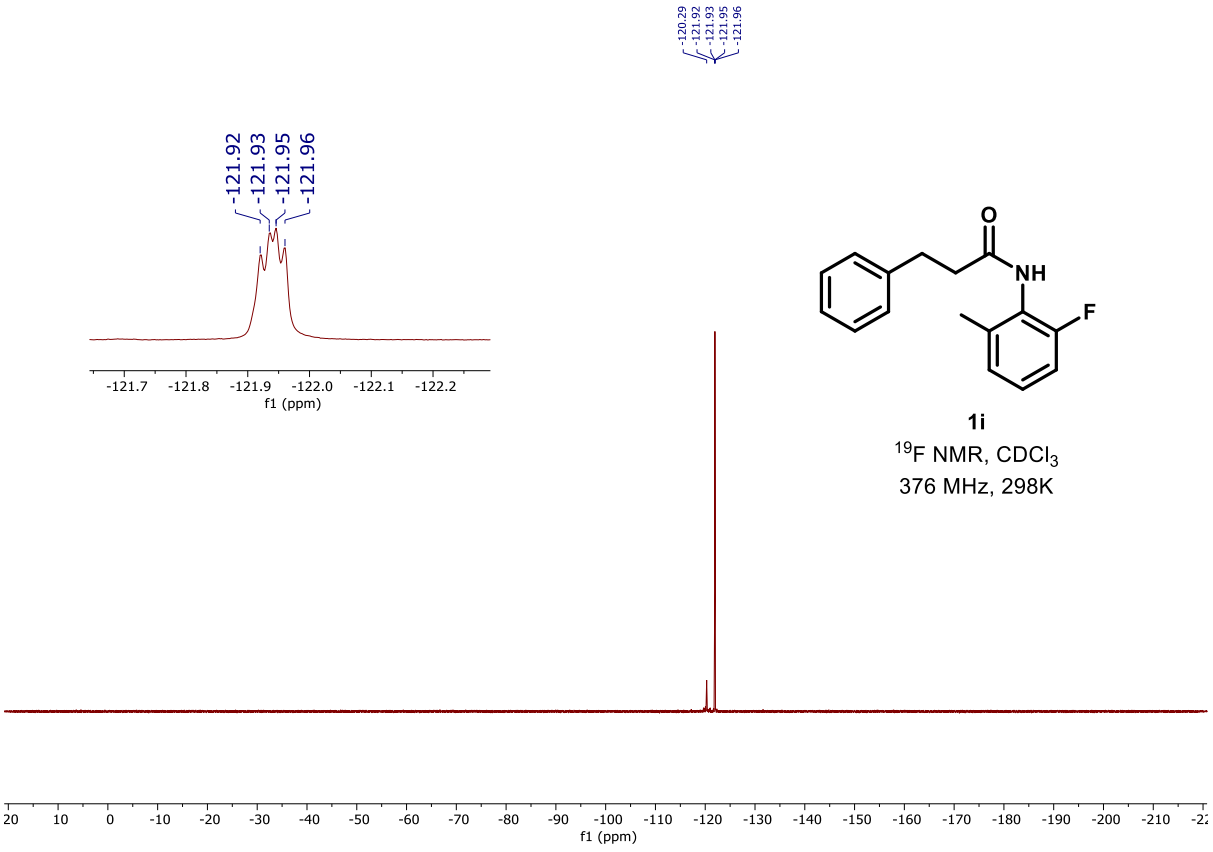


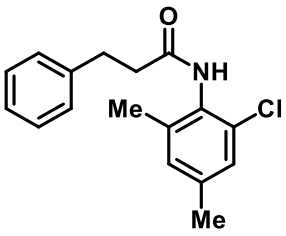


1i

^{13}C NMR, $CDCl_3$

101 MHz, 298K

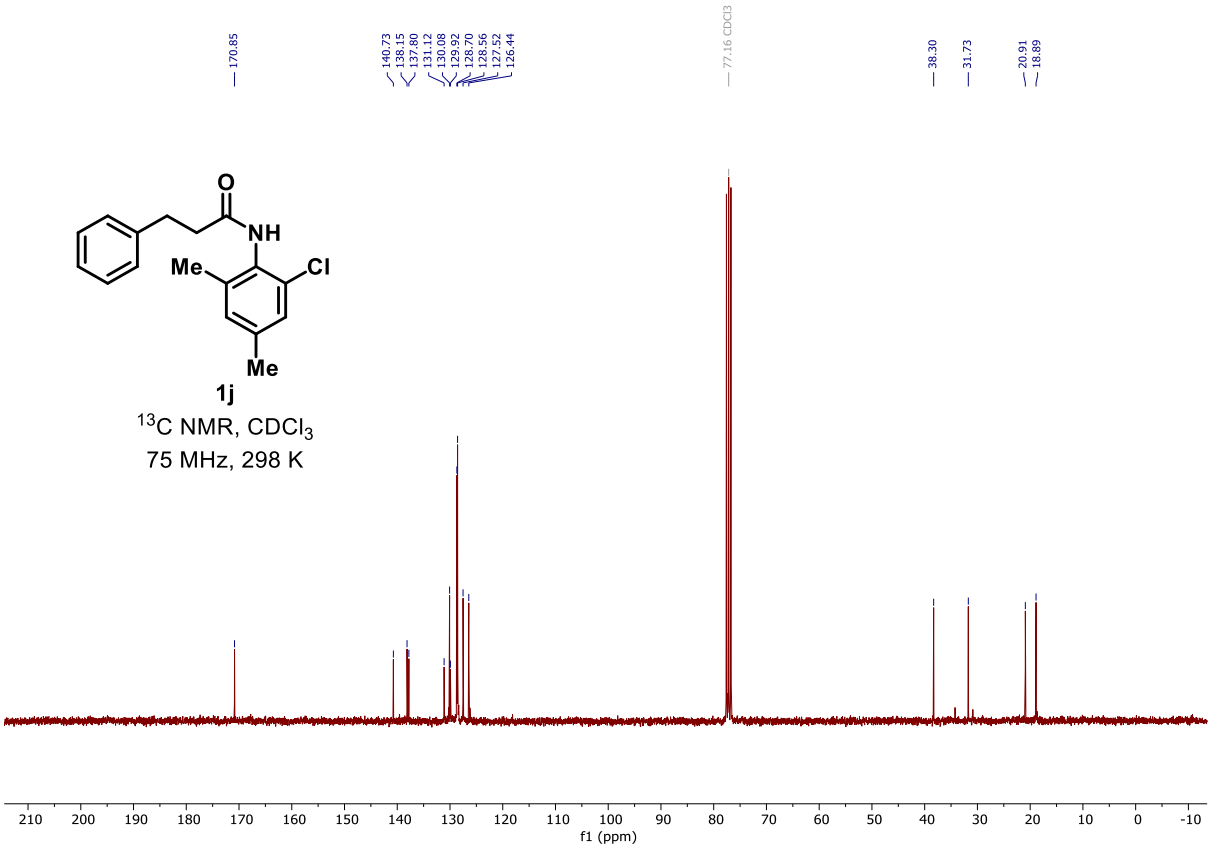

-120.29
-121.92
-121.93
-121.95
-121.96
-121.92
-121.93
-121.95
-121.96
-121.7
-121.8
-121.9
-122.0
-122.1
-122.2
f1 (ppm)
O
NH
F
1i
19F NMR, CDCl3
376 MHz, 298K
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)



1j

^{1}H NMR, $CDCl_3$

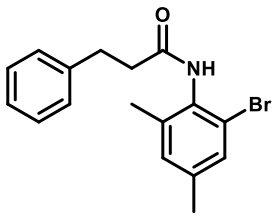
400 MHz, 298 K



1j

^{13}C NMR, $CDCl_3$

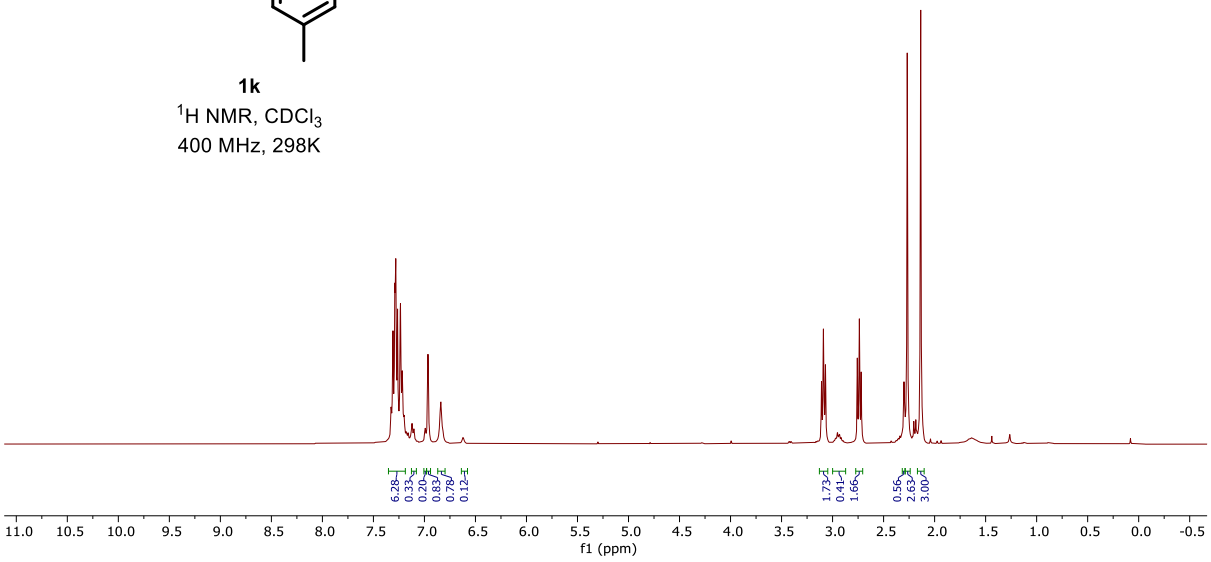
75 MHz, 298 K

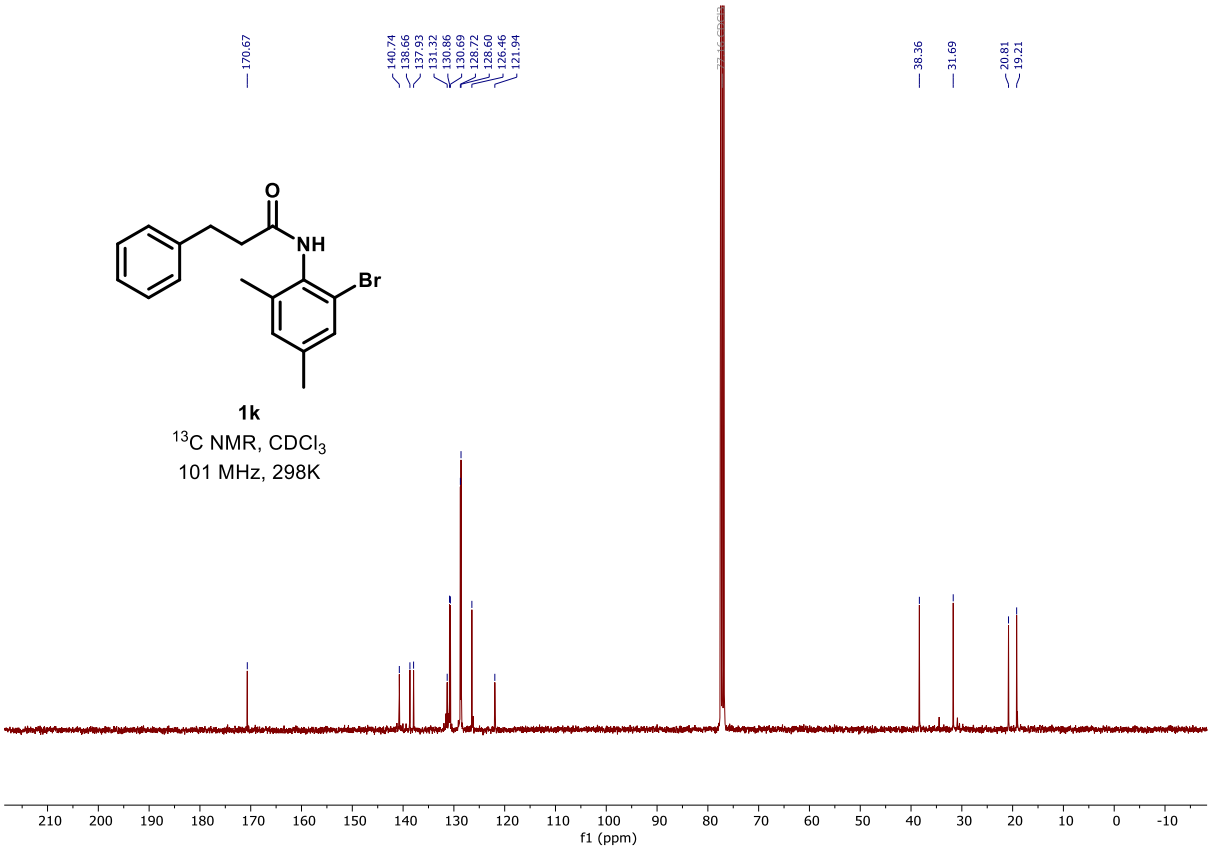


1k

^{1}H NMR, $CDCl_3$

400 MHz, 298K

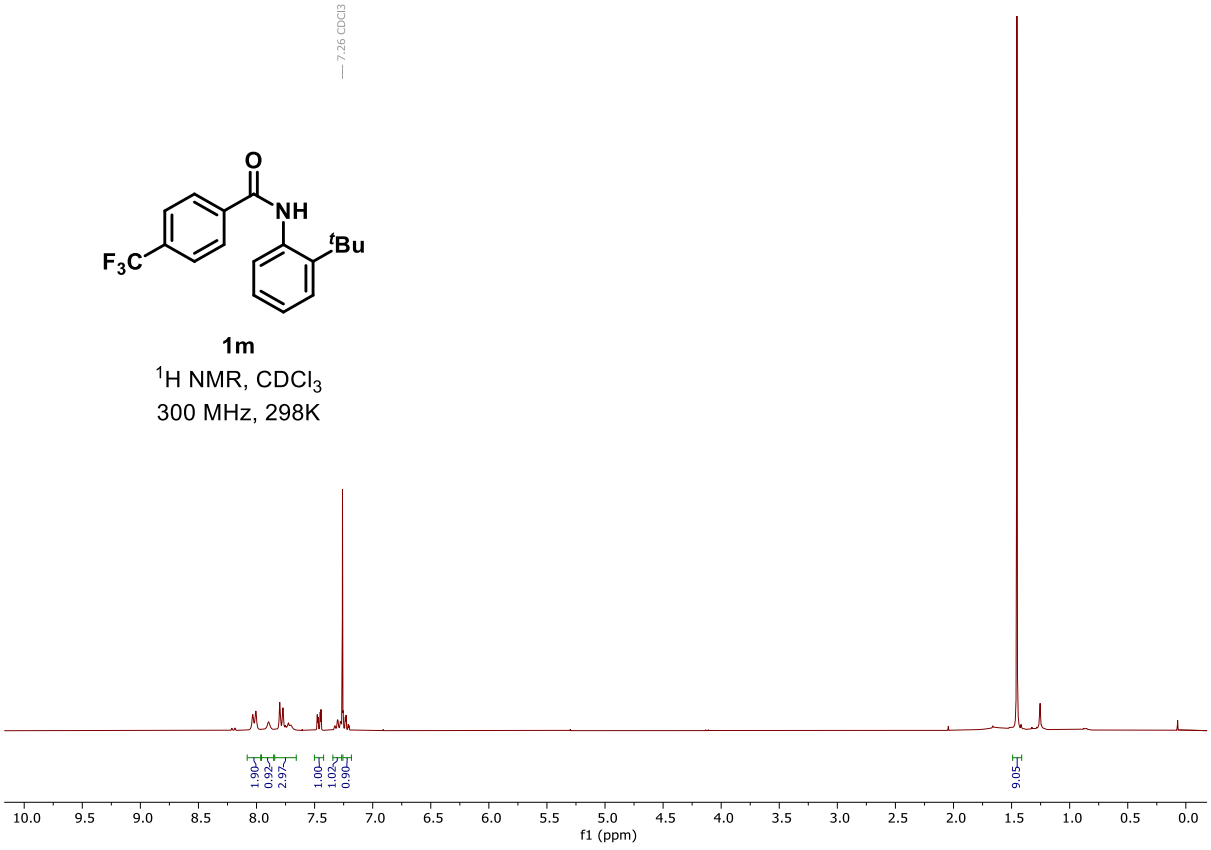




1k

^{13}C NMR, $CDCl_3$

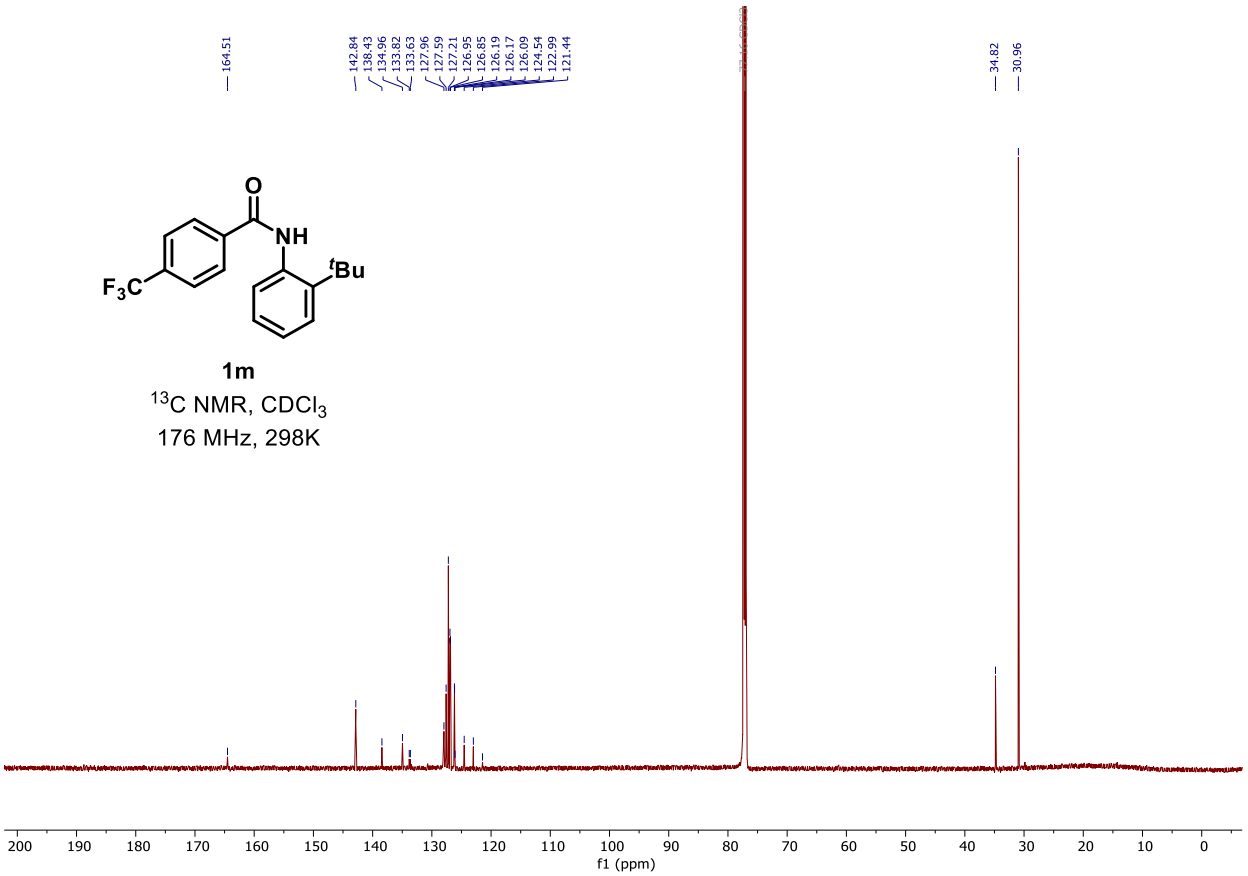
101 MHz, 298K



1m

^{1}H NMR, $CDCl_3$

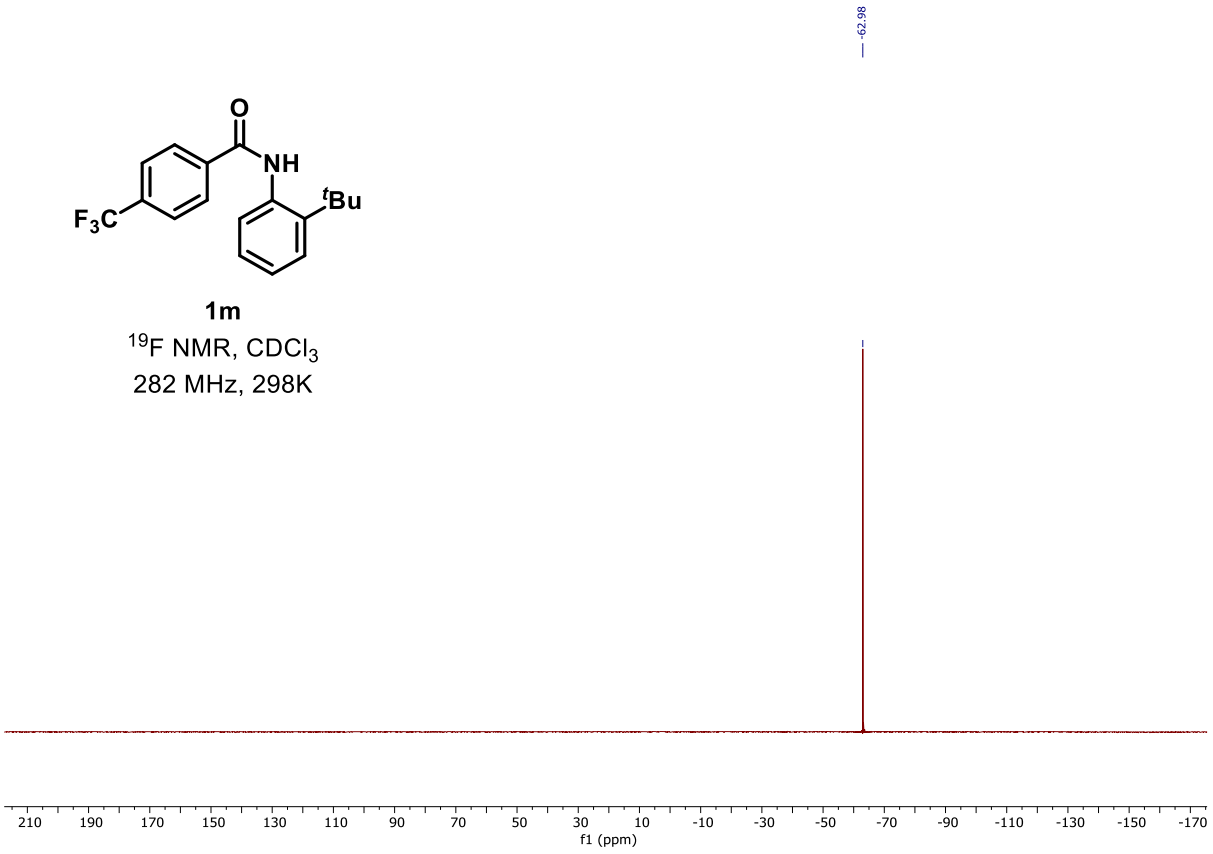
300 MHz, 298K



1m

^{13}C NMR, $CDCl_3$

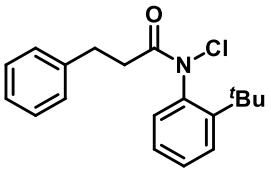
176 MHz, 298K



1m

^{19}F NMR, $CDCl_3$

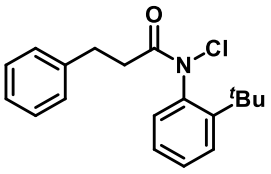
282 MHz, 298K



2a

^{1}H NMR, $CDCl_3$

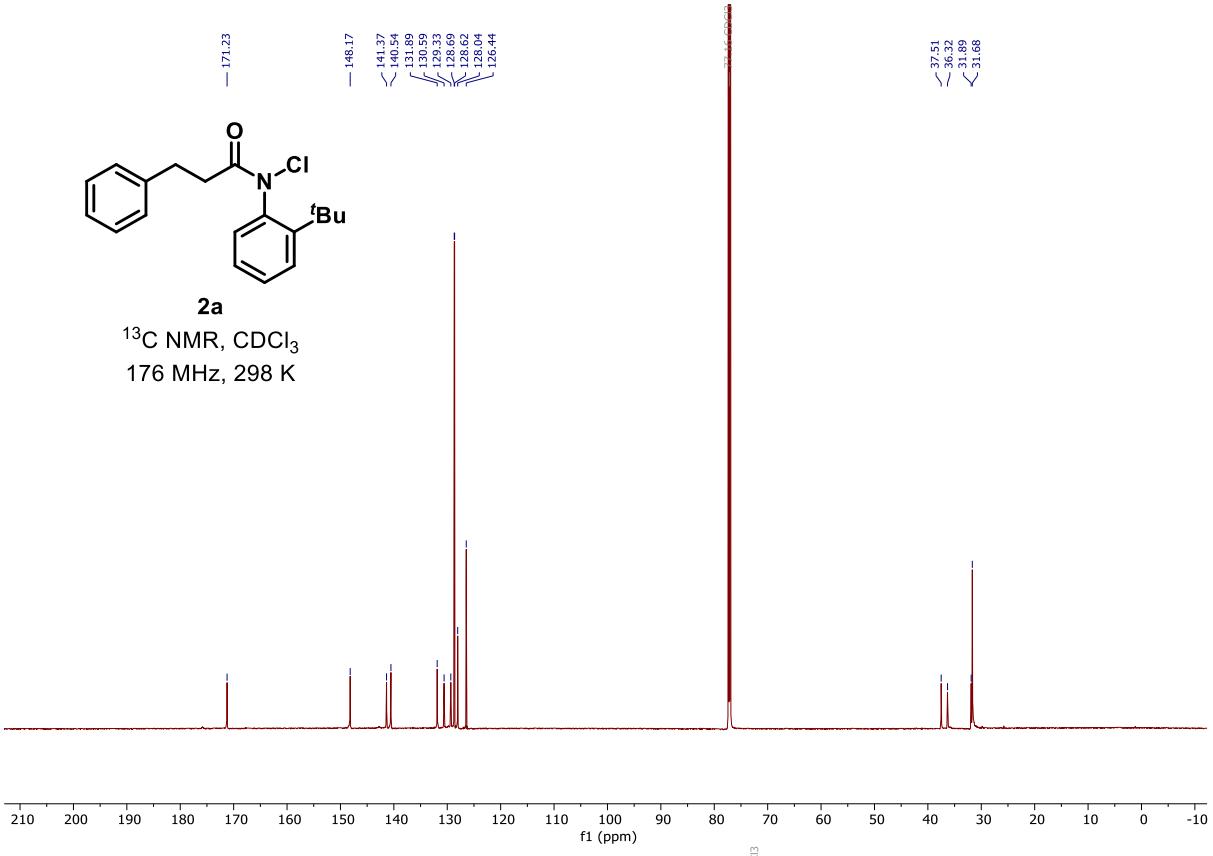
700 MHz, 298 K



2a

^{1}H NMR, $CDCl_3$

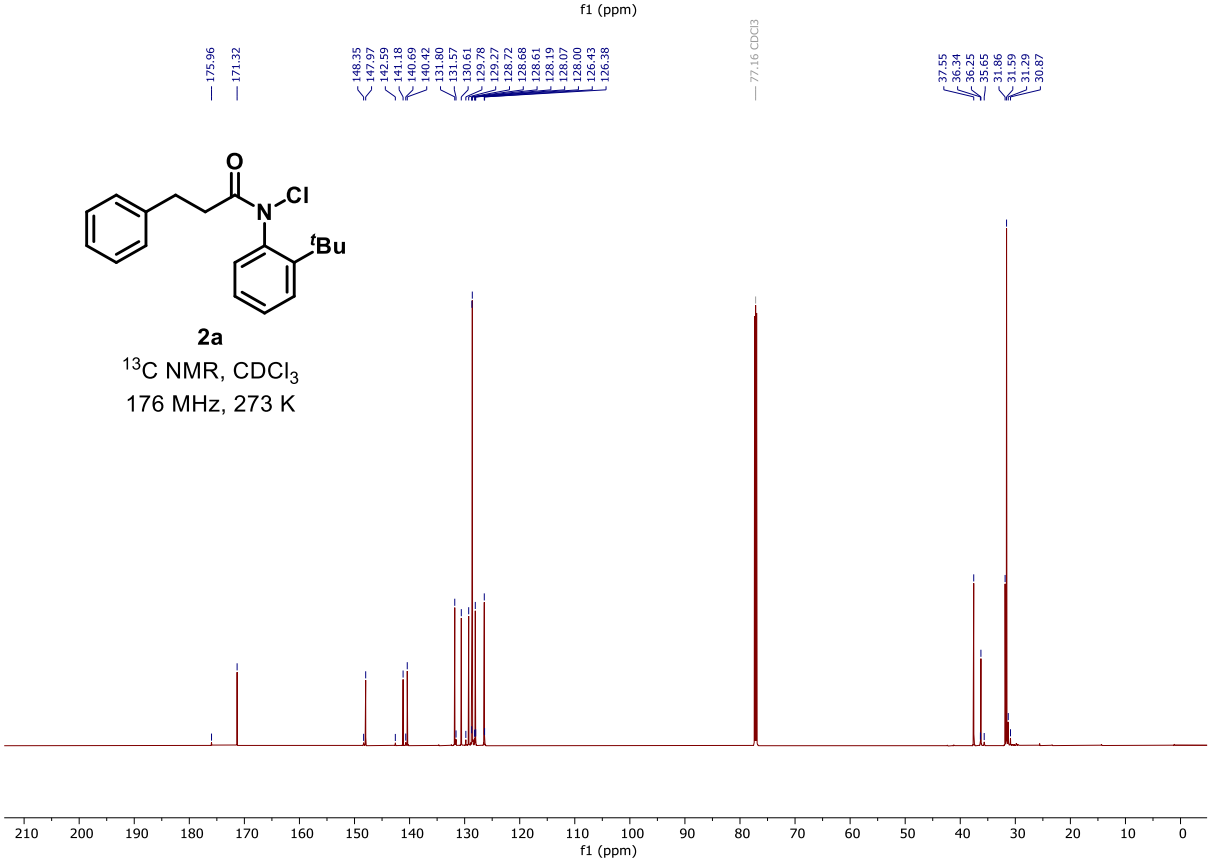
700 MHz, 273 K



2a

^{13}C NMR, $CDCl_3$

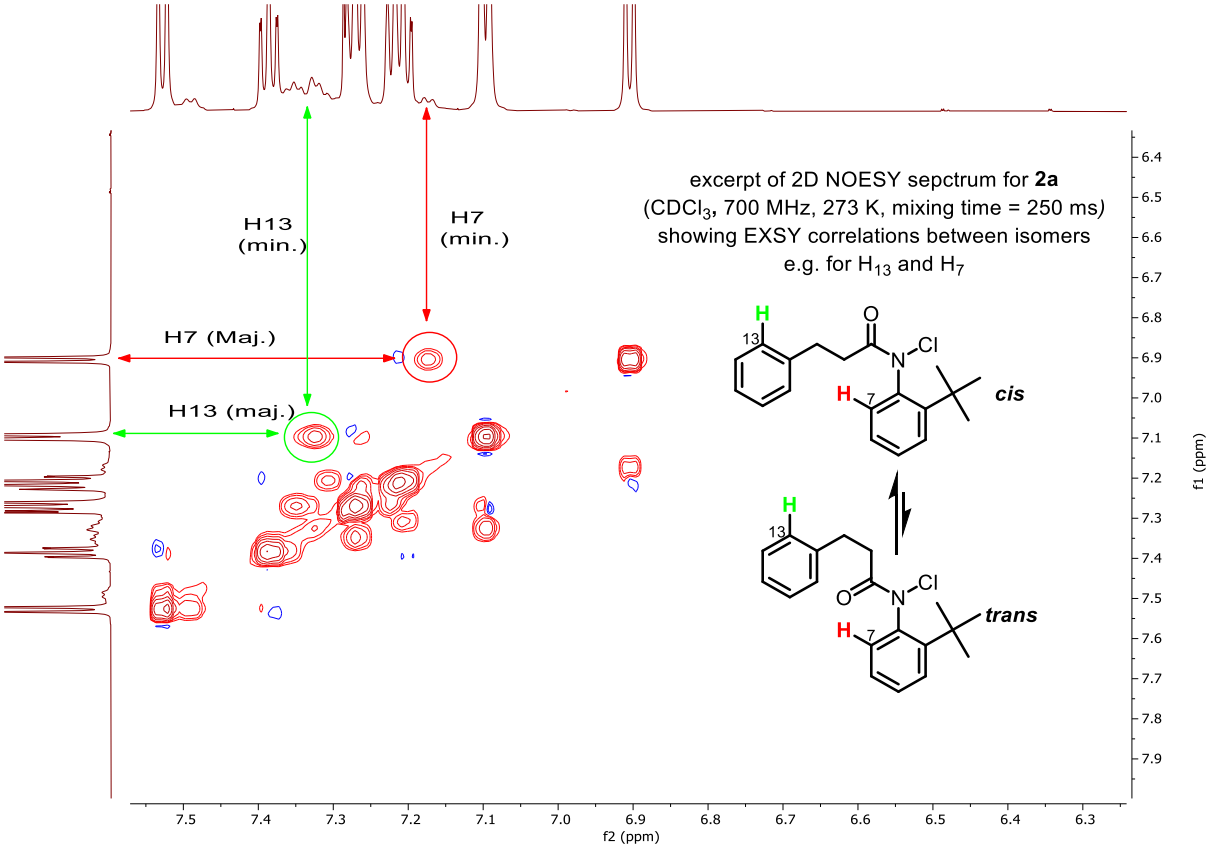
176 MHz, 298 K

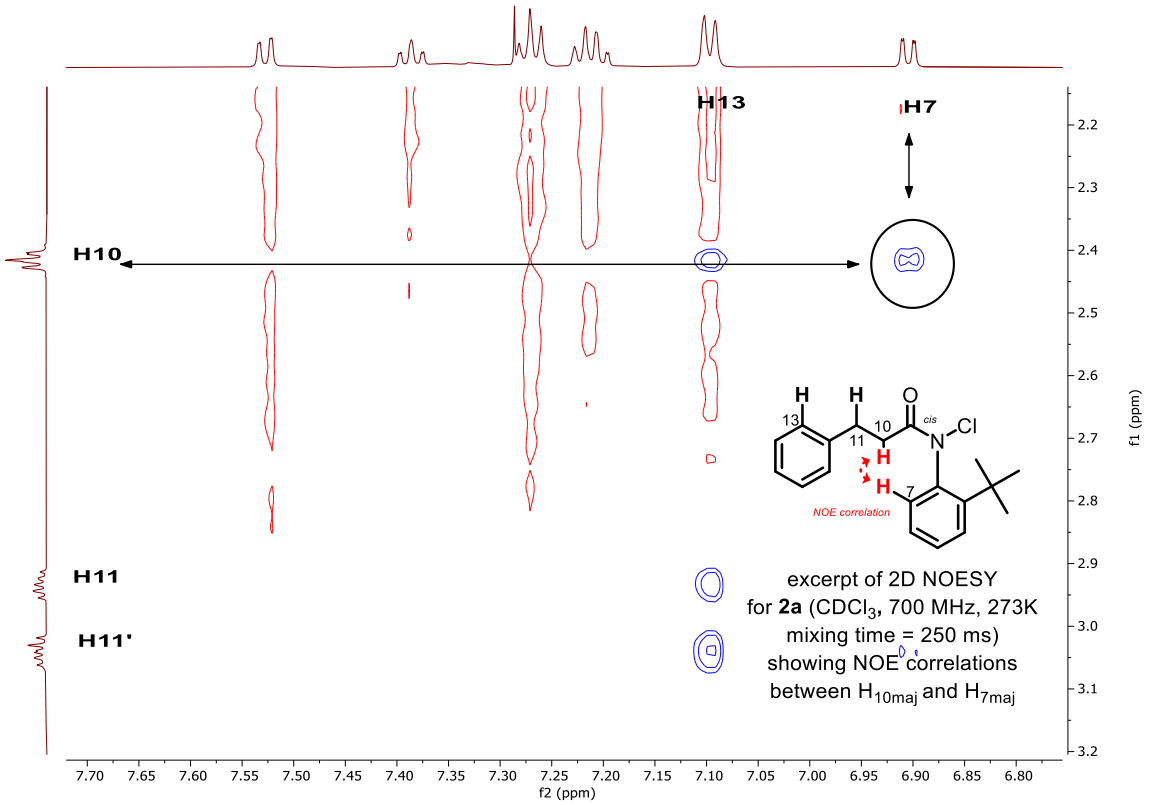


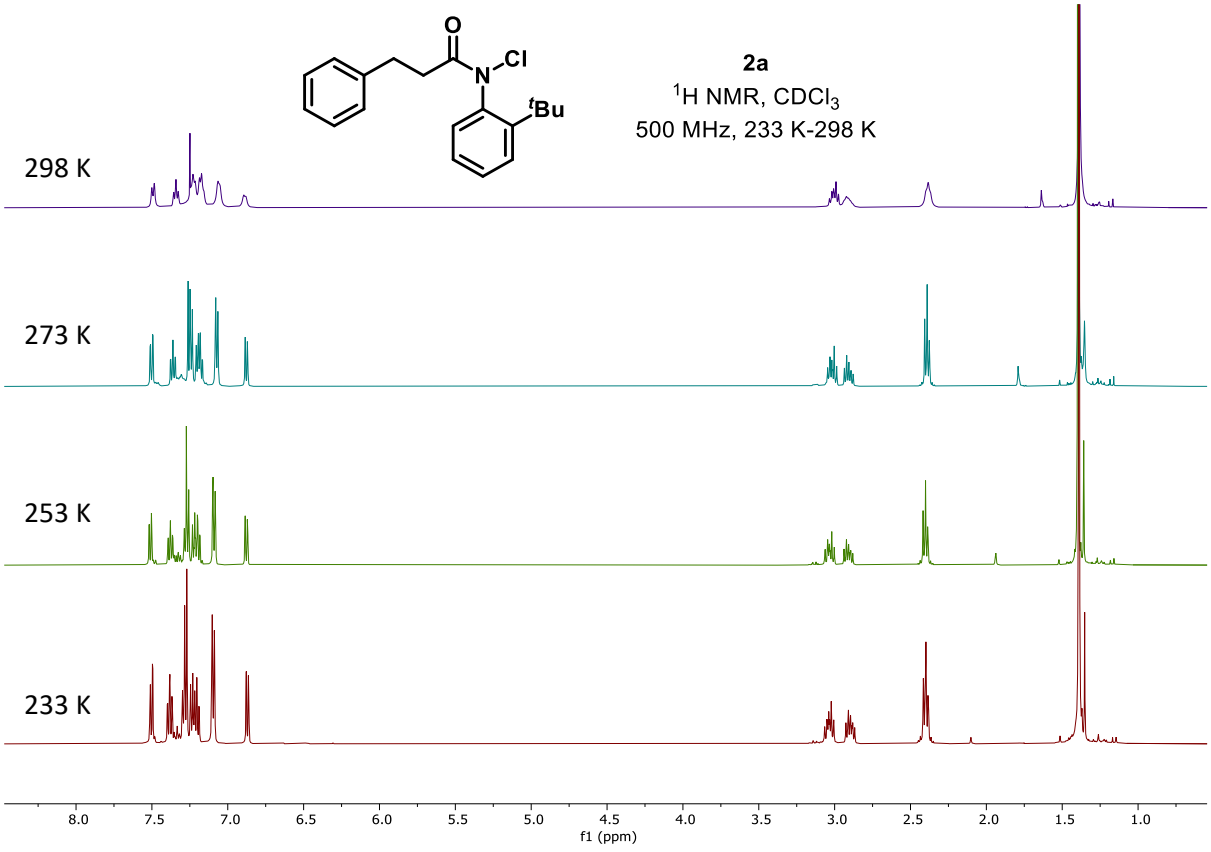
2a

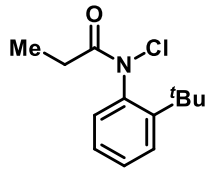
^{13}C NMR, $CDCl_3$

176 MHz, 273 K


H13 (min.)
H7 (min.)
H7 (Maj.)
H13 (maj.)
excerpt of 2D NOESY sepctrum for 2a
(CDCl3, 700 MHz, 273 K, mixing time = 250 ms)
showing EXSY correlations between isomers
e.g. for H13 and H7
cis
trans
f2 (ppm)
f1 (ppm)


H13
H7
H10
H11
H11'
NOE correlation
excerpt of 2D NOESY
for 2a (CDCl3, 700 MHz, 273K
mixing time = 250 ms)
showing NOE correlations
between H10maj and H7maj
f2 (ppm)
f1 (ppm)

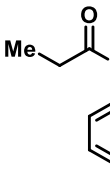

O
N
Cl
tBu
2a
1H NMR, CDCl3
500 MHz, 233 K-298 K
298 K
273 K
253 K
233 K
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)



2b

^{1}H NMR, $CDCl_3$

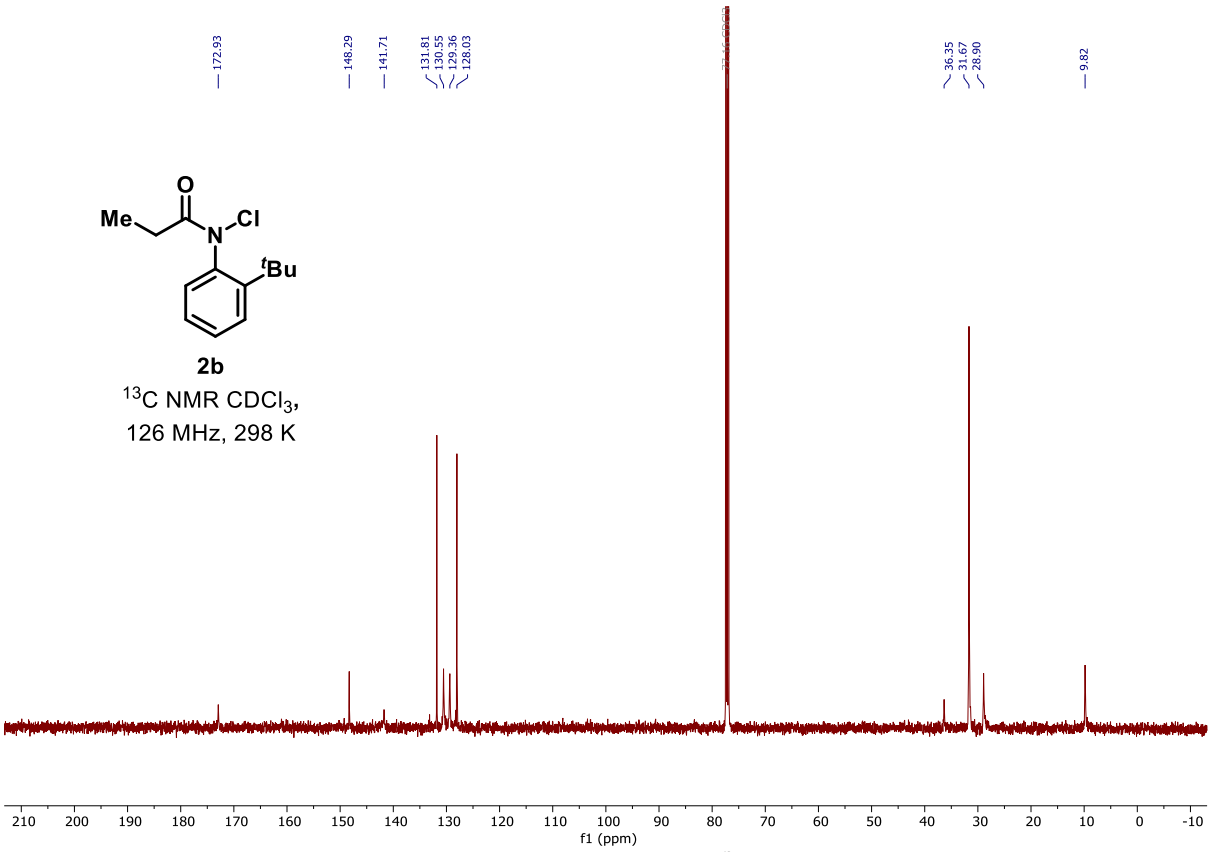
300 MHz, 298 K



2b

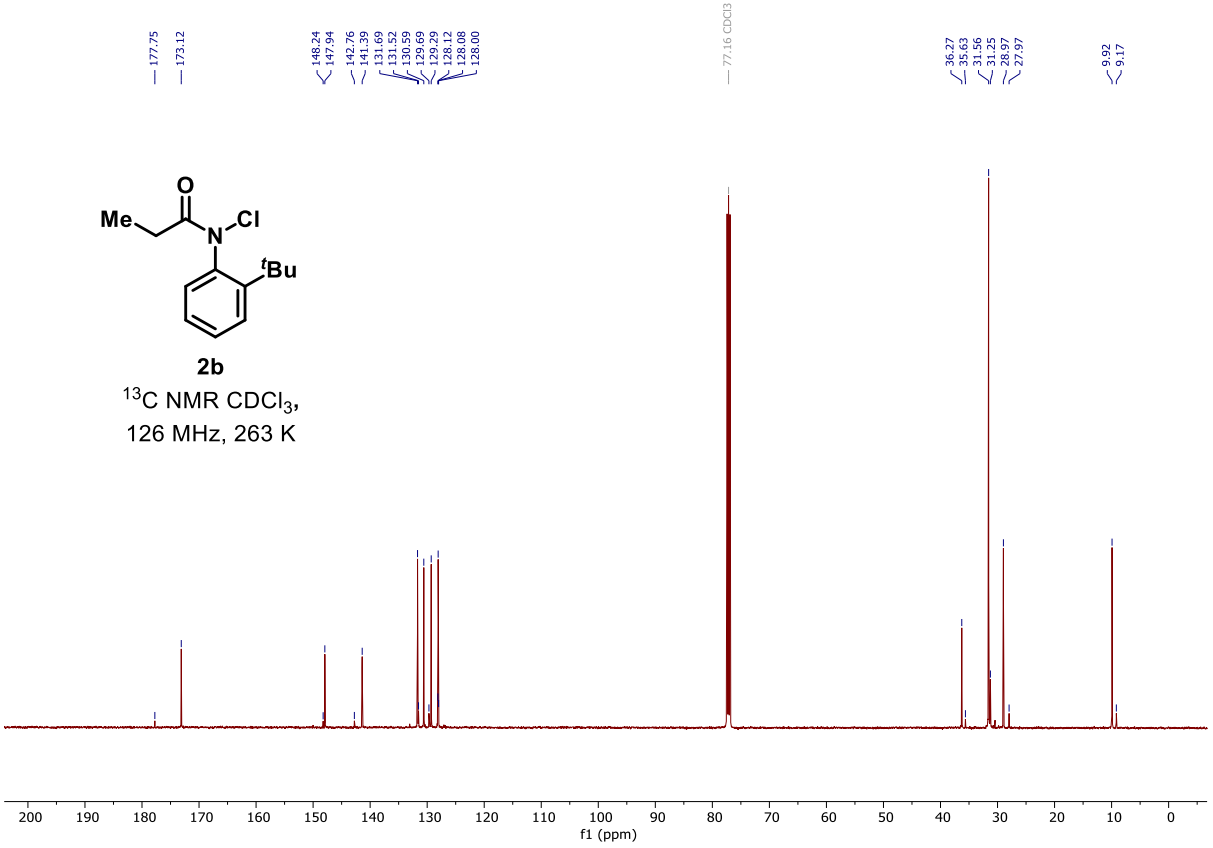
^{1}H NMR $CDCl_3$,

500 MHz, 263 K



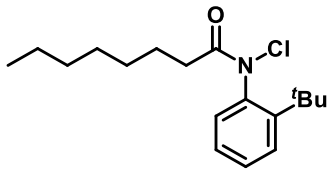
2b

^{13}C NMR $CDCl_3$,
126 MHz, 298 K



2b

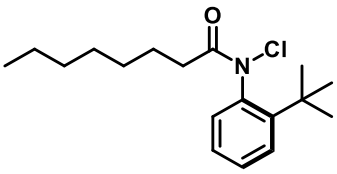
^{13}C NMR $CDCl_3$,
126 MHz, 263 K



2c

^{1}H NMR, $CDCl_3$

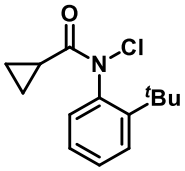
400 MHz, 298 K



2c

^{13}C NMR, $CDCl_3$

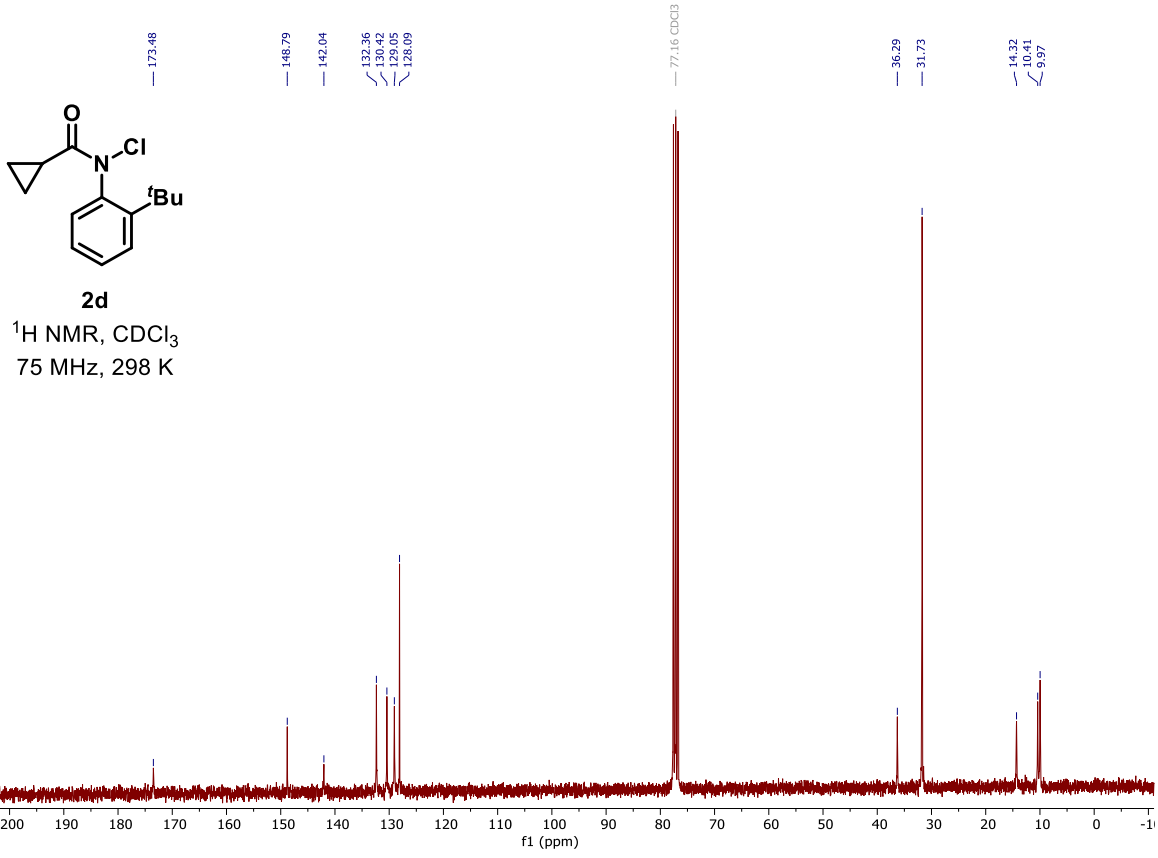
126 MHz, 298 K



2d

^{1}H NMR, $CDCl_3$

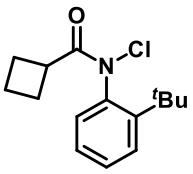
300 MHz, 298 K



2d

^{1}H NMR, $CDCl_3$

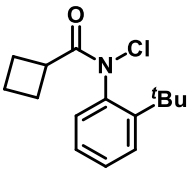
75 MHz, 298 K



2e

^{1}H NMR, $CDCl_3$

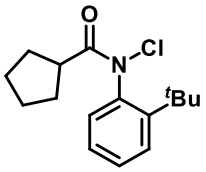
300 MHz, 298 K



2e

^{13}C NMR, $CDCl_3$

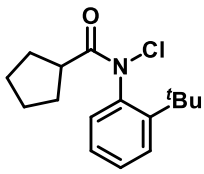
75 MHz, 298 K



2f

^{1}H NMR, $CDCl_3$

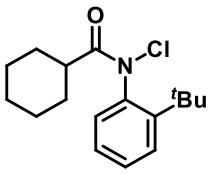
300 MHz, 298 K



2f

^{13}C NMR, $CDCl_3$

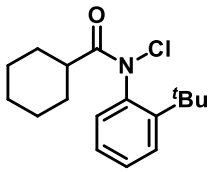
75 MHz, 298 K



2g

^{1}H NMR, $CDCl_3$

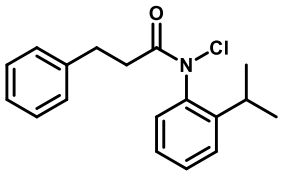
300 MHz, 298 K



2g

^{13}C NMR, $CDCl_3$

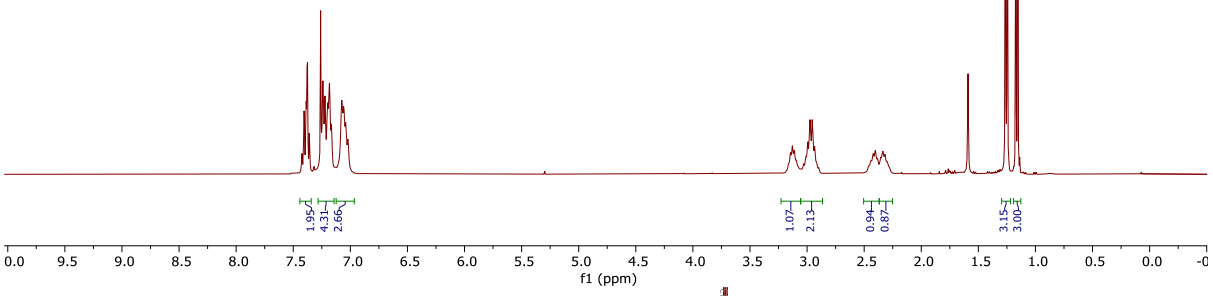
75 MHz, 298 K

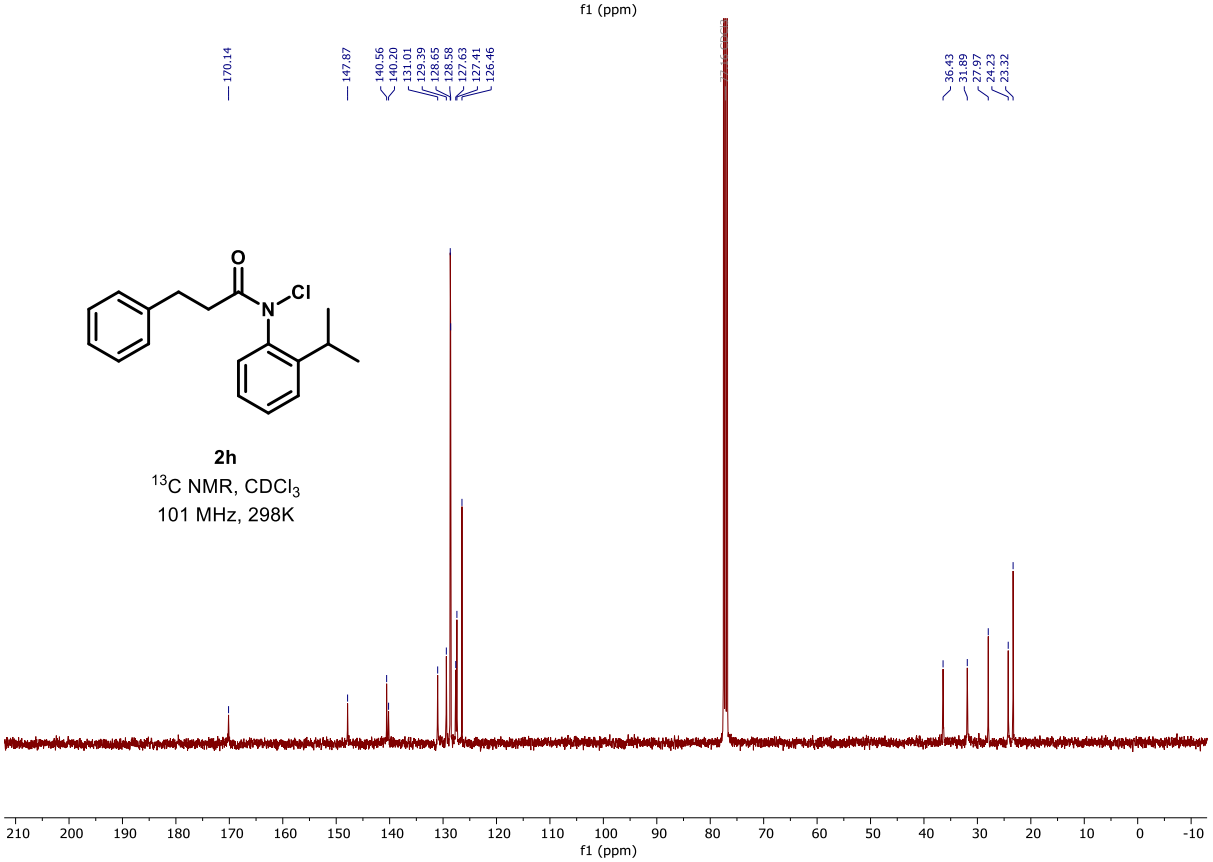


2h

^{1}H NMR, $CDCl_3$

400 MHz, 298K

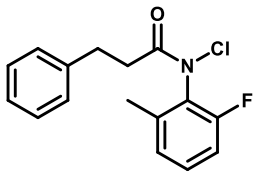




2h

^{13}C NMR, $CDCl_3$

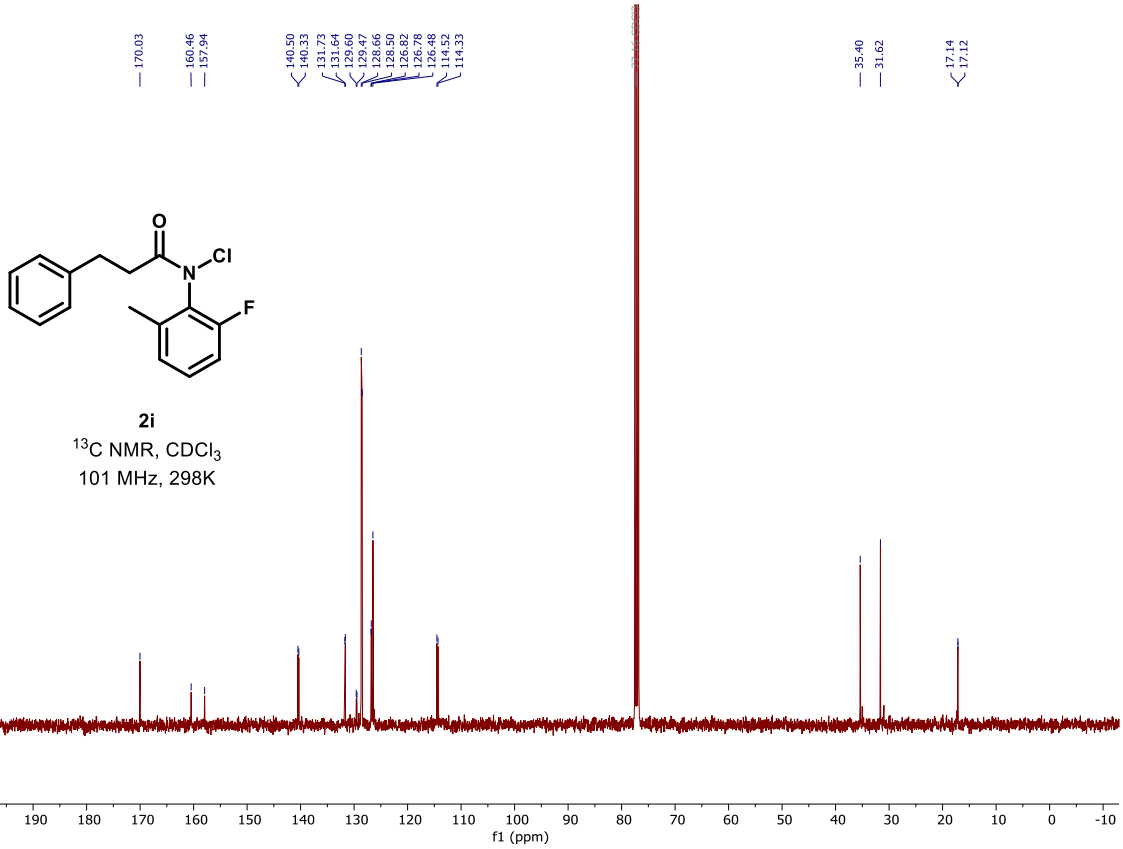
101 MHz, 298K



2i

^{1}H NMR, $CDCl_3$

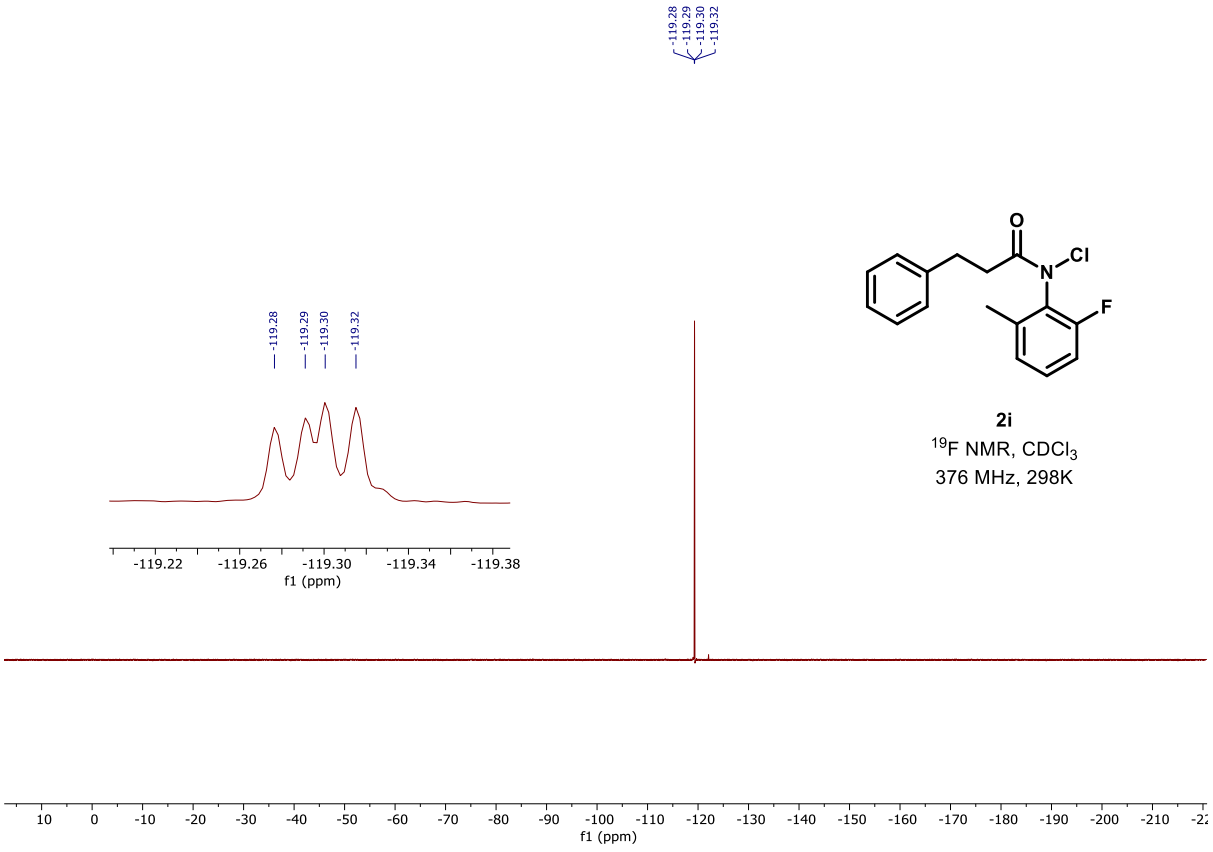
400 MHz, 298K



2i

^{13}C NMR, $CDCl_3$

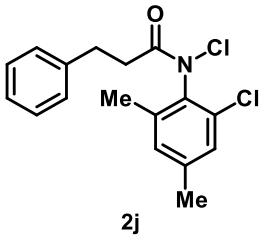
101 MHz, 298K



2i

^{19}F NMR, $CDCl_3$

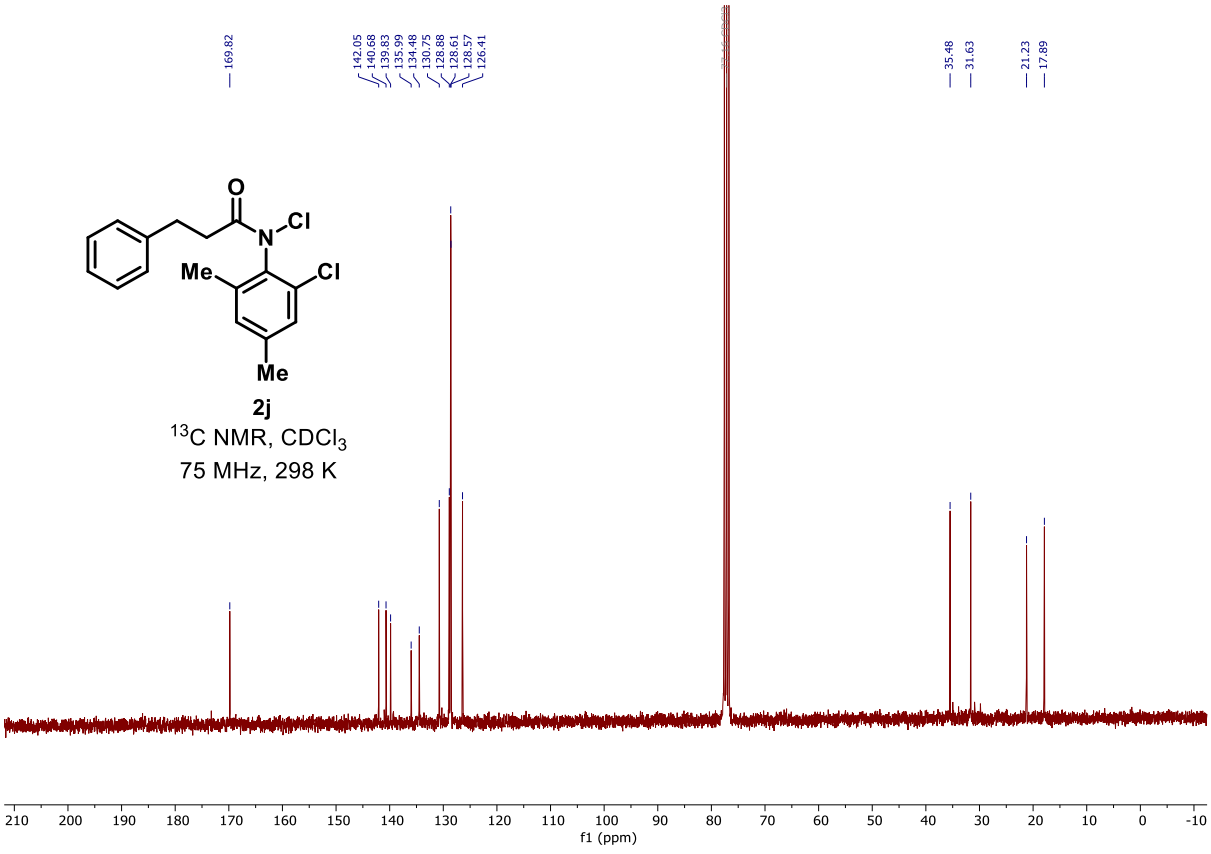
376 MHz, 298K



2j

^{1}H NMR, $CDCl_3$

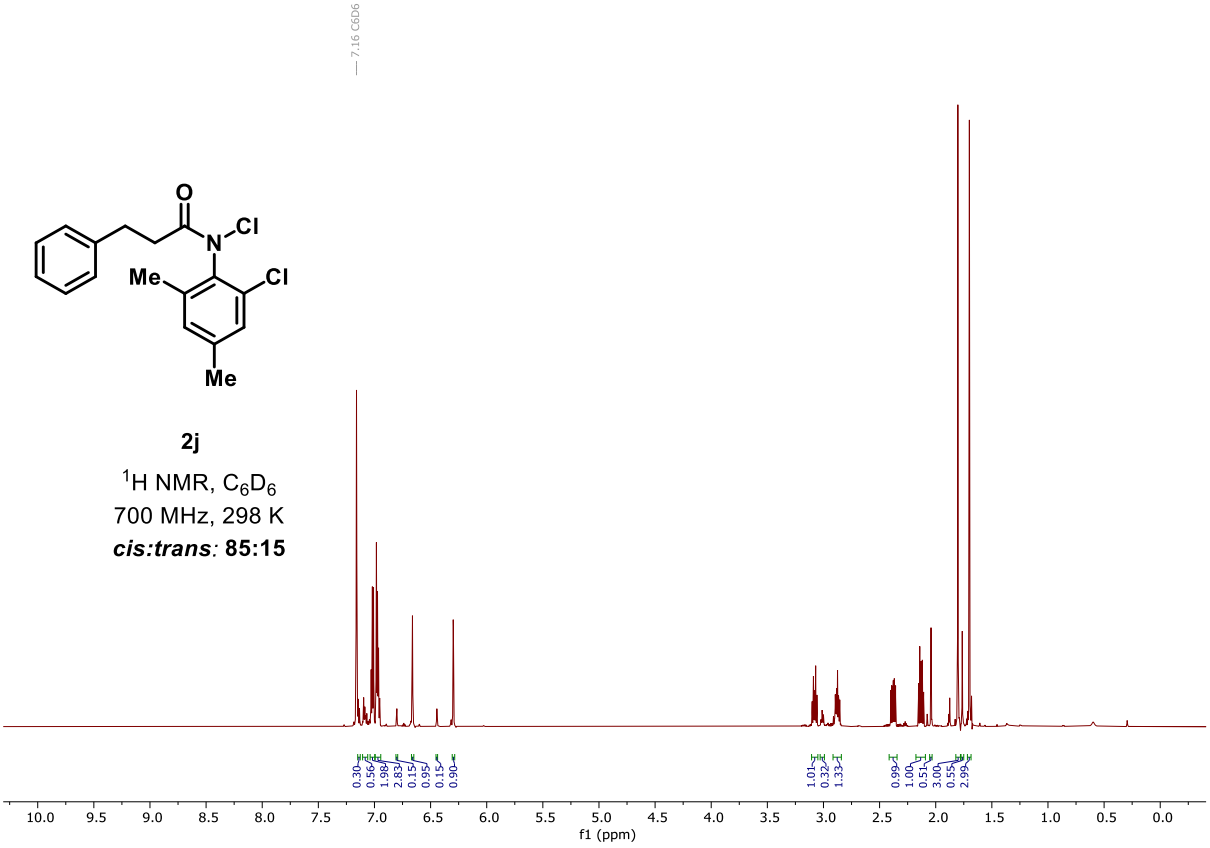
300 MHz, 298 K



2j

^{13}C NMR, $CDCl_3$

75 MHz, 298 K

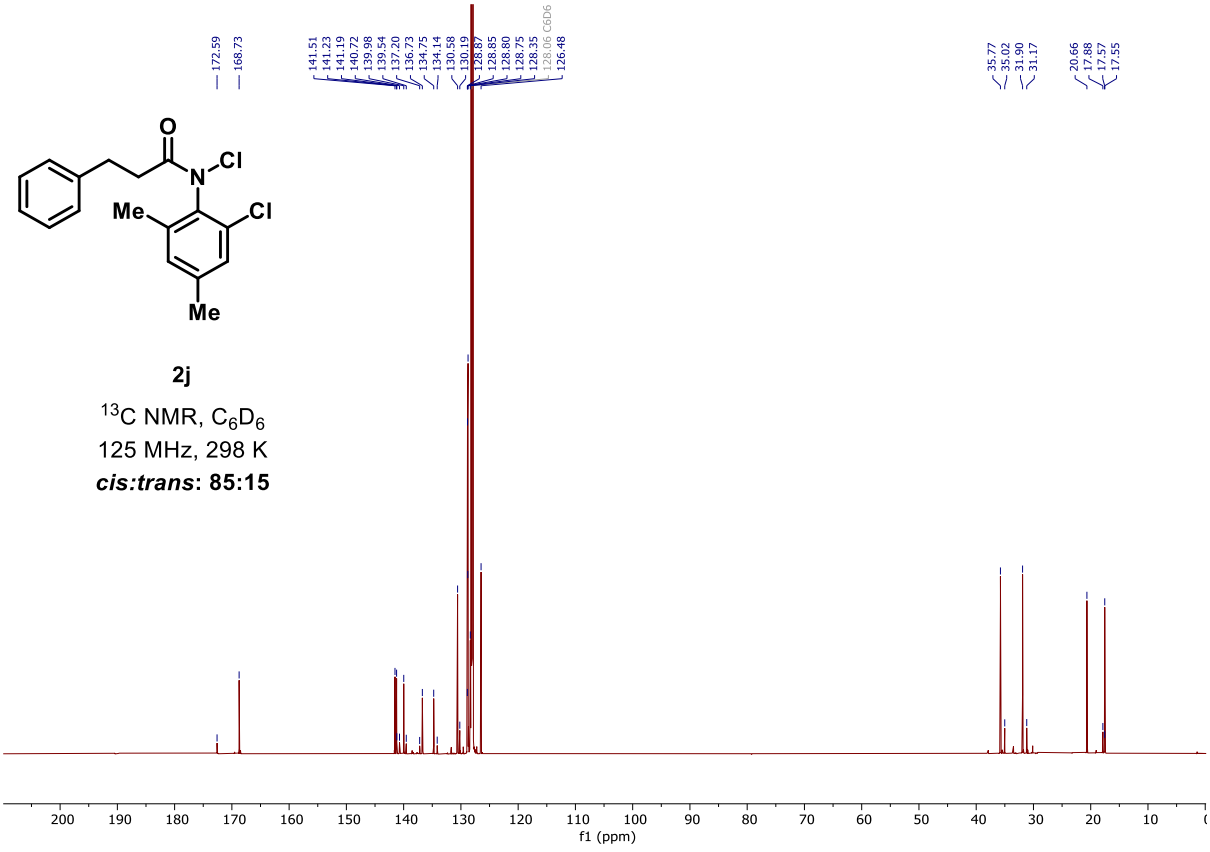


2j

^{1}H NMR, C_6D_6

700 MHz, 298 K

***cis:trans*: 85:15**

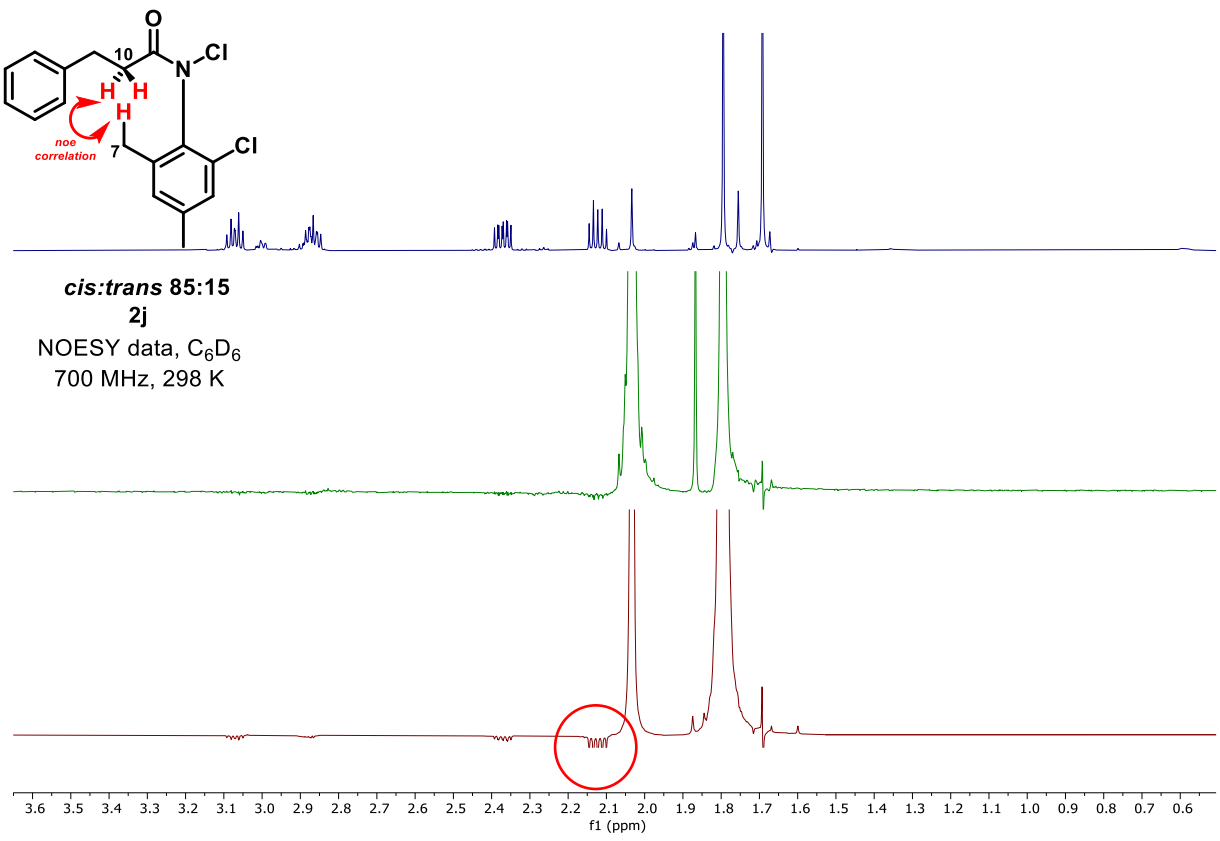


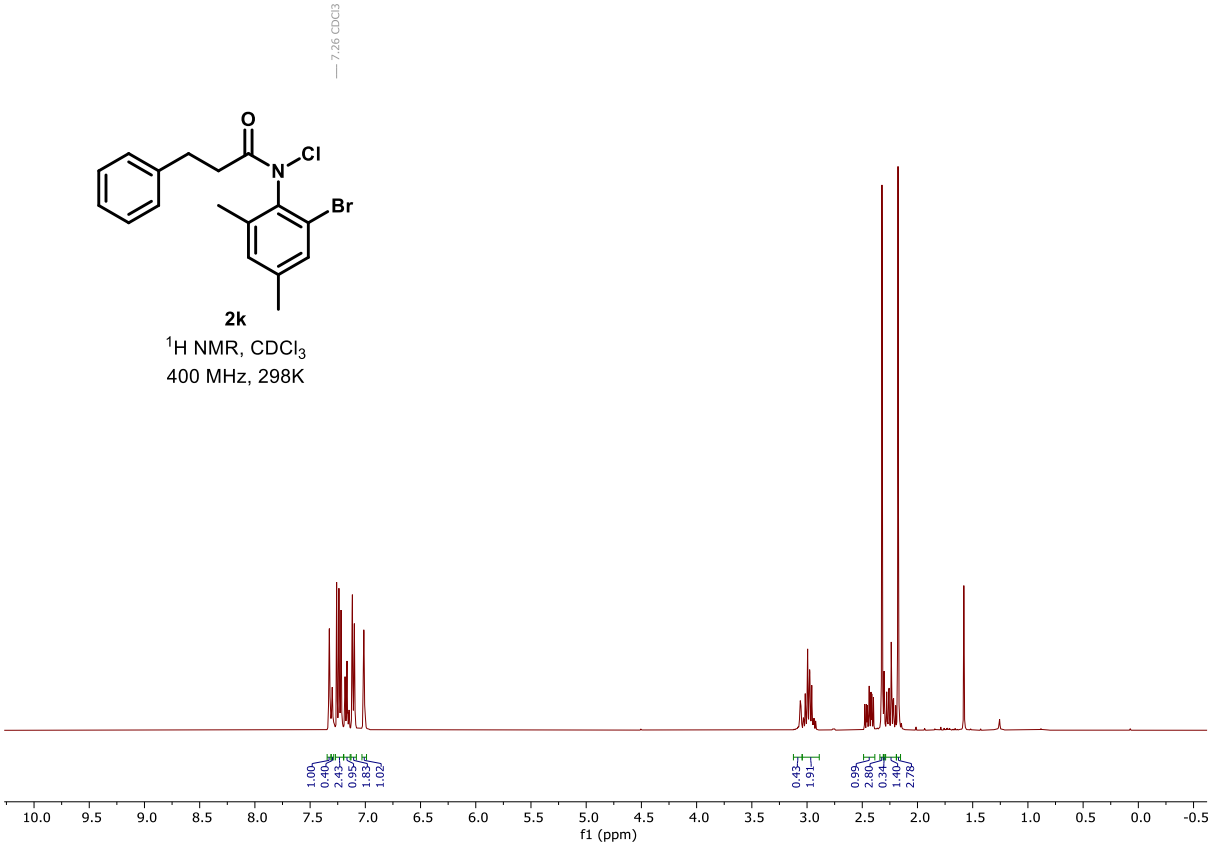
2j

^{13}C NMR, C_6D_6

125 MHz, 298 K

***cis:trans*: 85:15**

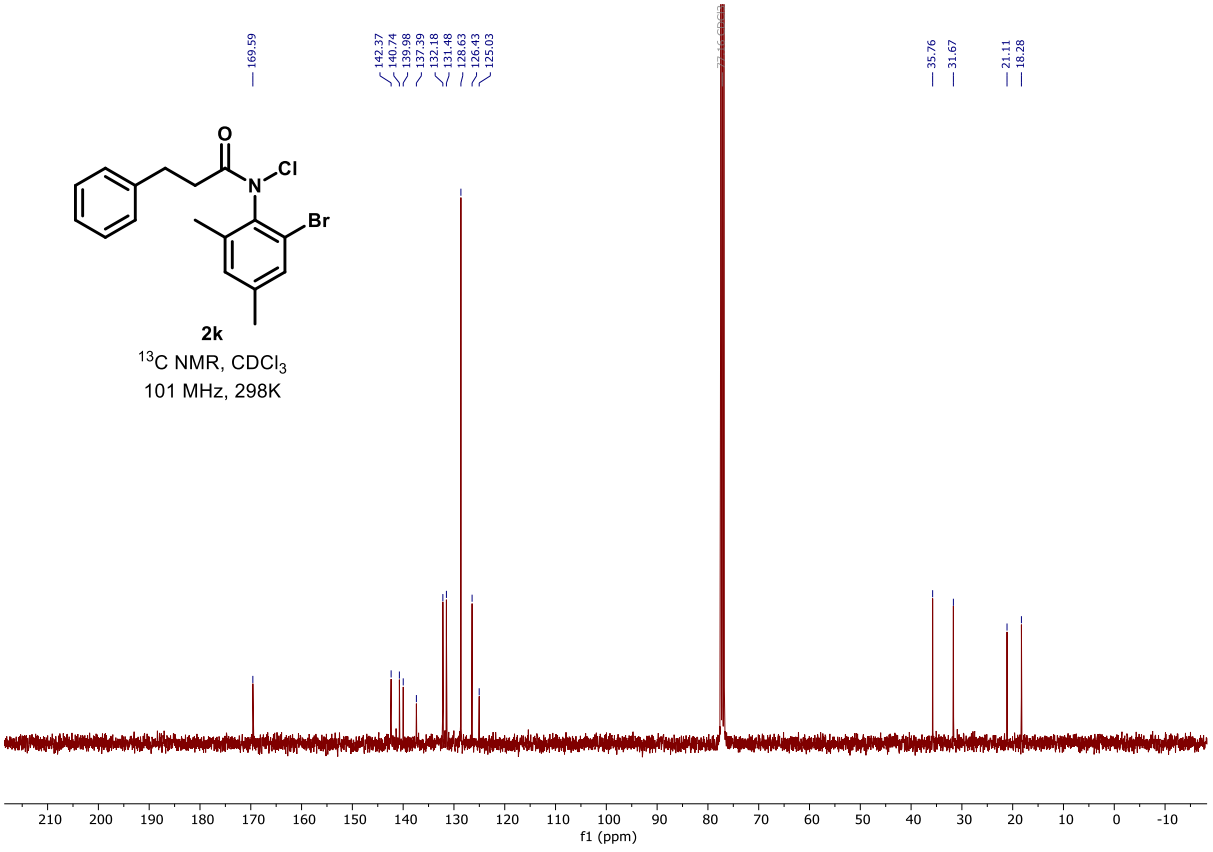

O
10
N
Cl
H
H
H
noe
correlation
7
Cl
cis:trans 85:15
2j
NOESY data, C6D6
700 MHz, 298 K
3.6 3.5 3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 2.6 2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.8 1.7 1.6 1.5 1.4 1.3 1.2 1.1 1.0 0.9 0.8 0.7 0.6
f1 (ppm)



2k

^{1}H NMR, $CDCl_3$

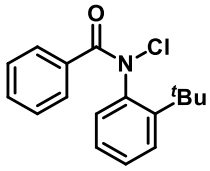
400 MHz, 298K



2k

^{13}C NMR, $CDCl_3$

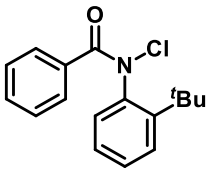
101 MHz, 298K



2l

^{1}H NMR, $CDCl_3$

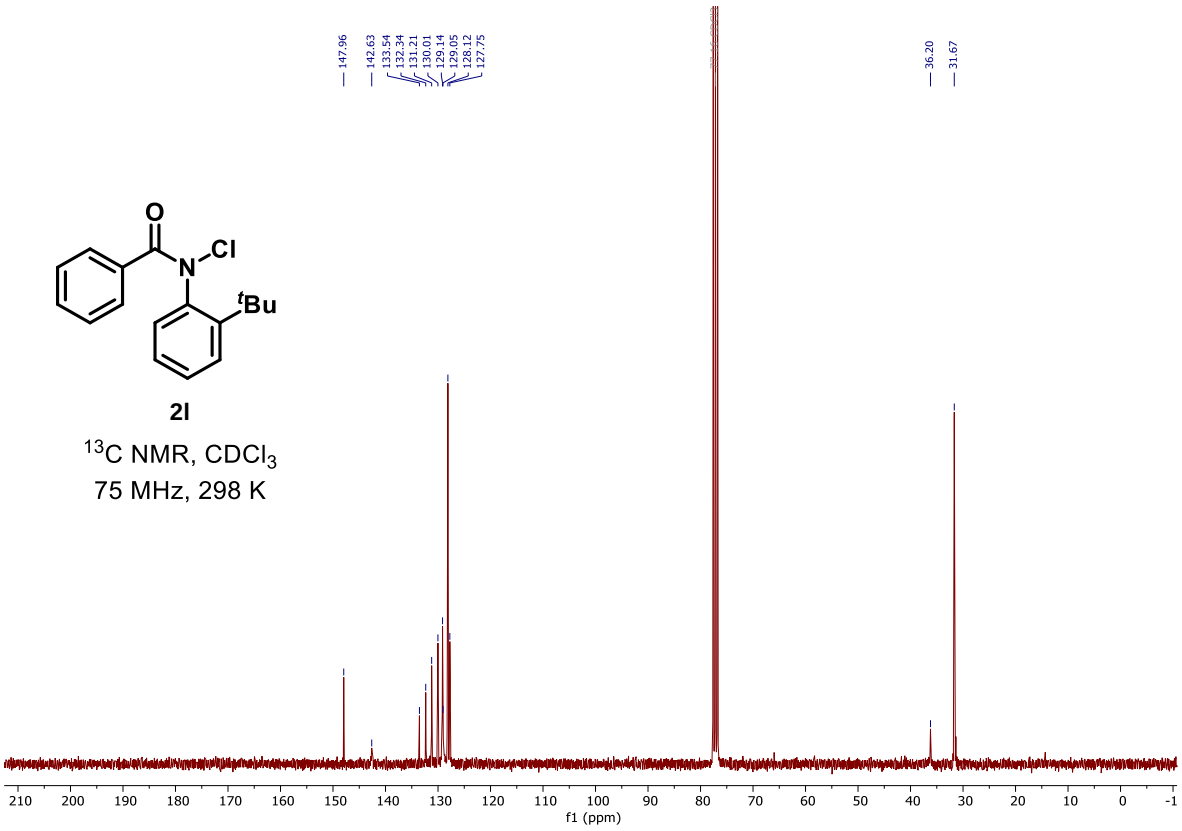
400 MHz, 298 K



2l

^{1}H NMR, $CDCl_3$

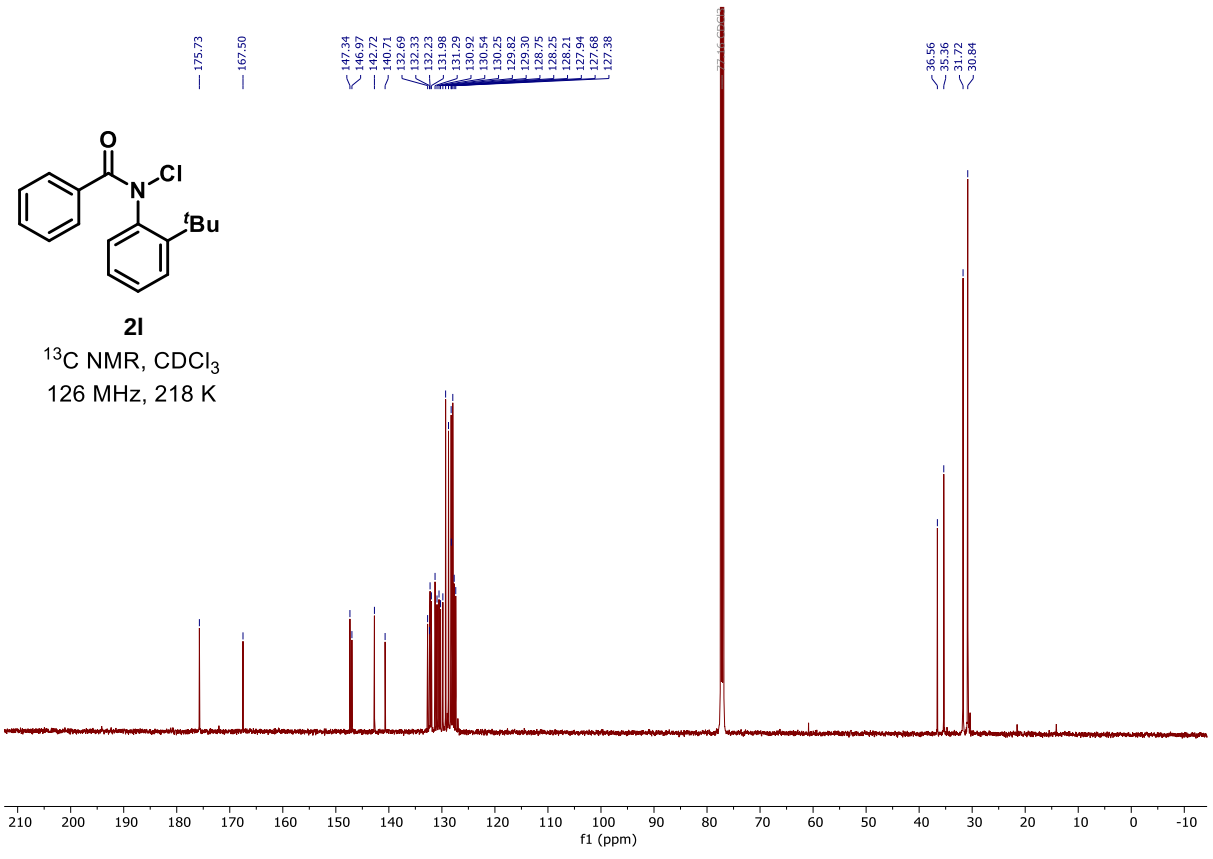
500 MHz, 218K



2l

^{13}C NMR, $CDCl_3$

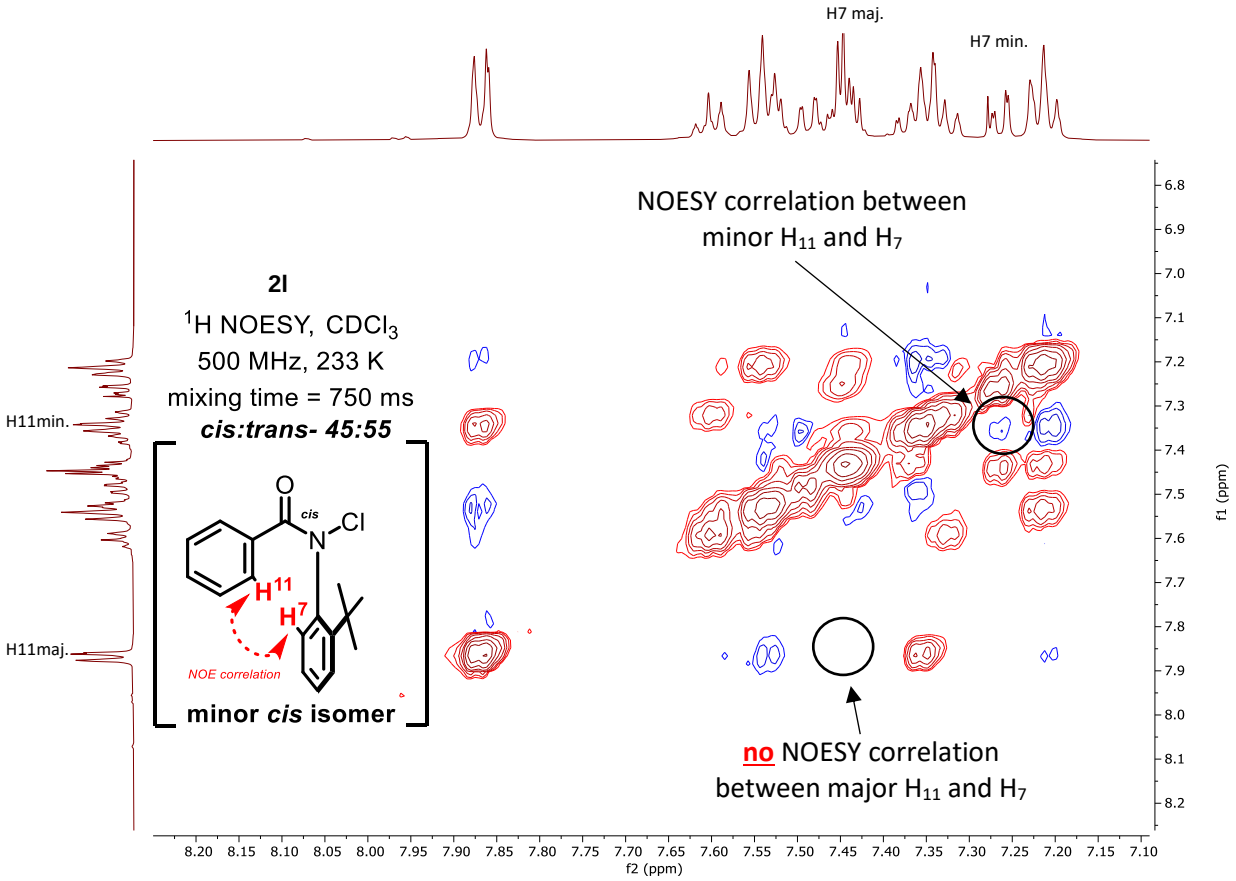
75 MHz, 298 K

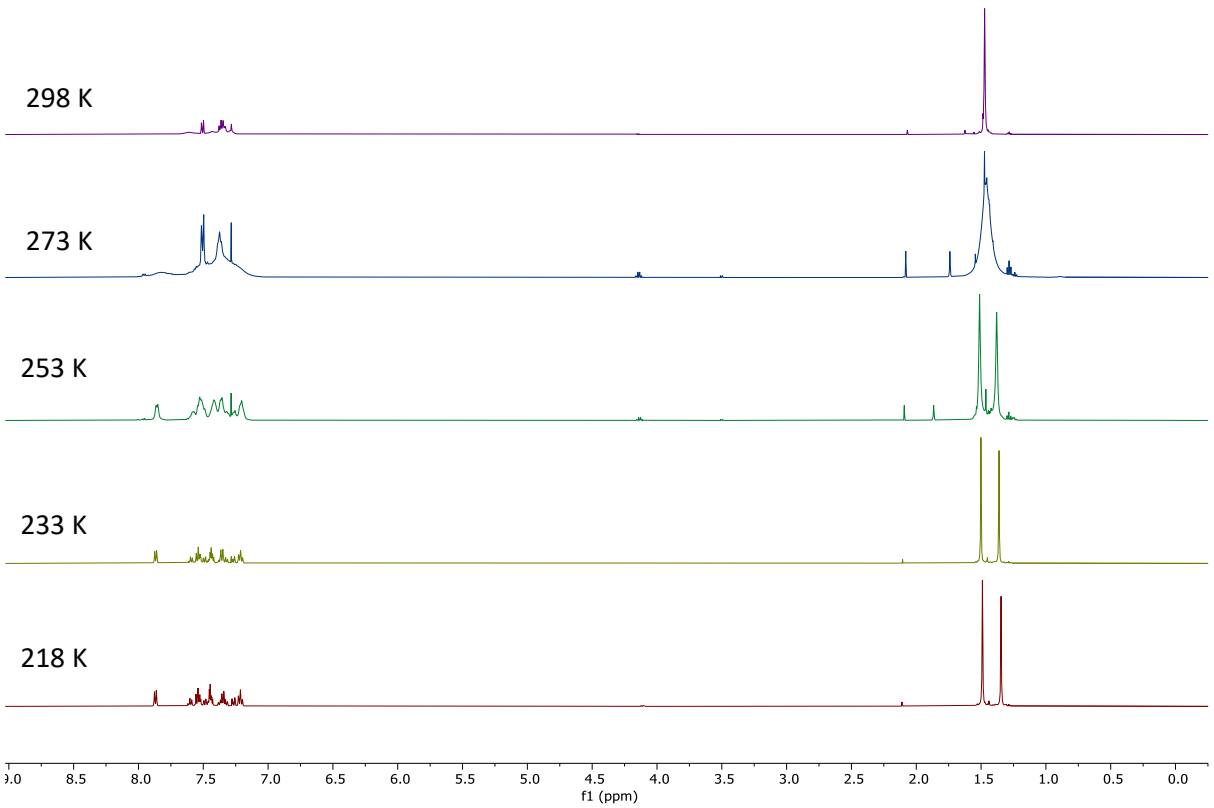


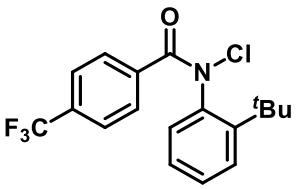
2l

^{13}C NMR, $CDCl_3$

126 MHz, 218 K


H7 maj.
H7 min.
H11min.
H11maj.
2l
^{1}H NOESY, $CDCl_3$
500 MHz, 233 K
mixing time = 750 ms
cis:trans- 45:55
cis
Cl
H11
H7
NOE correlation
minor cis isomer
NOESY correlation between minor H_{11} and H_7
no NOESY correlation between major H_{11} and H_7
f1 (ppm)
f2 (ppm)

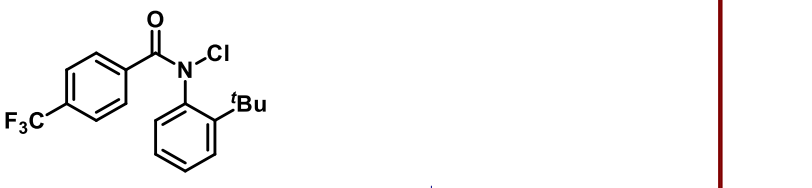

298 K
273 K
253 K
233 K
218 K
f1 (ppm)



2m

^{1}H NMR, $CDCl_3$

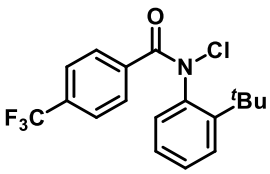
500MHz, 218 K



2m

^{13}C NMR, $CDCl_3$

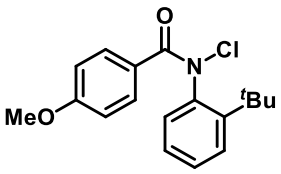
126 MHz, 218 K



2m

^{19}F NMR, $CDCl_3$

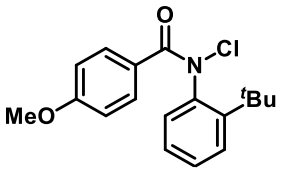
282 MHz, 298 K



2n

^{1}H NMR, $CDCl_3$

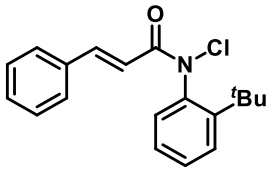
300 MHz, 298K



2n

^{13}C NMR, $CDCl_3$

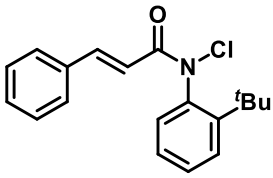
75 MHz, 298K



2o

^{1}H NMR, $CDCl_3$

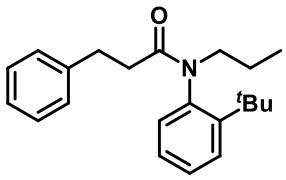
500 MHz, 218K



2o

^{13}C NMR, $CDCl_3$

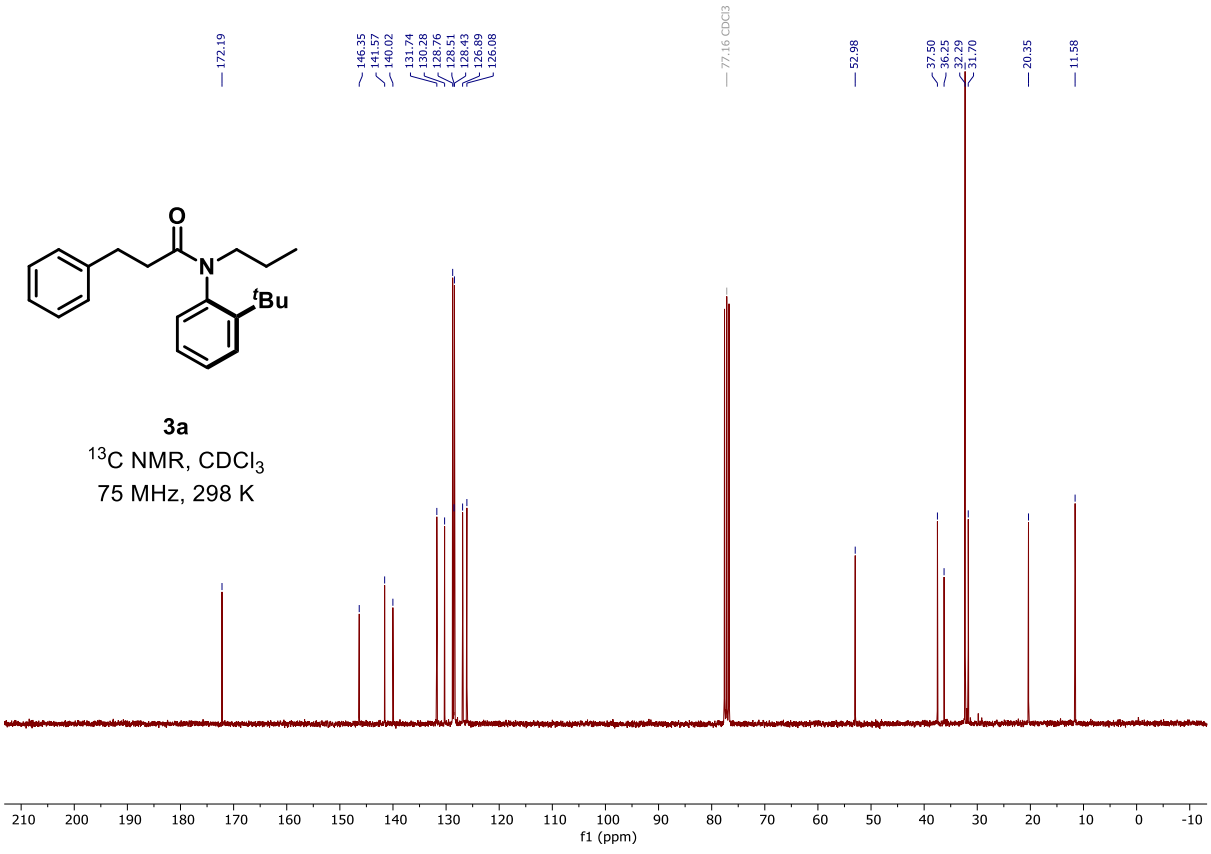
126 MHz, 218K



3a

^{1}H NMR, $CDCl_3$

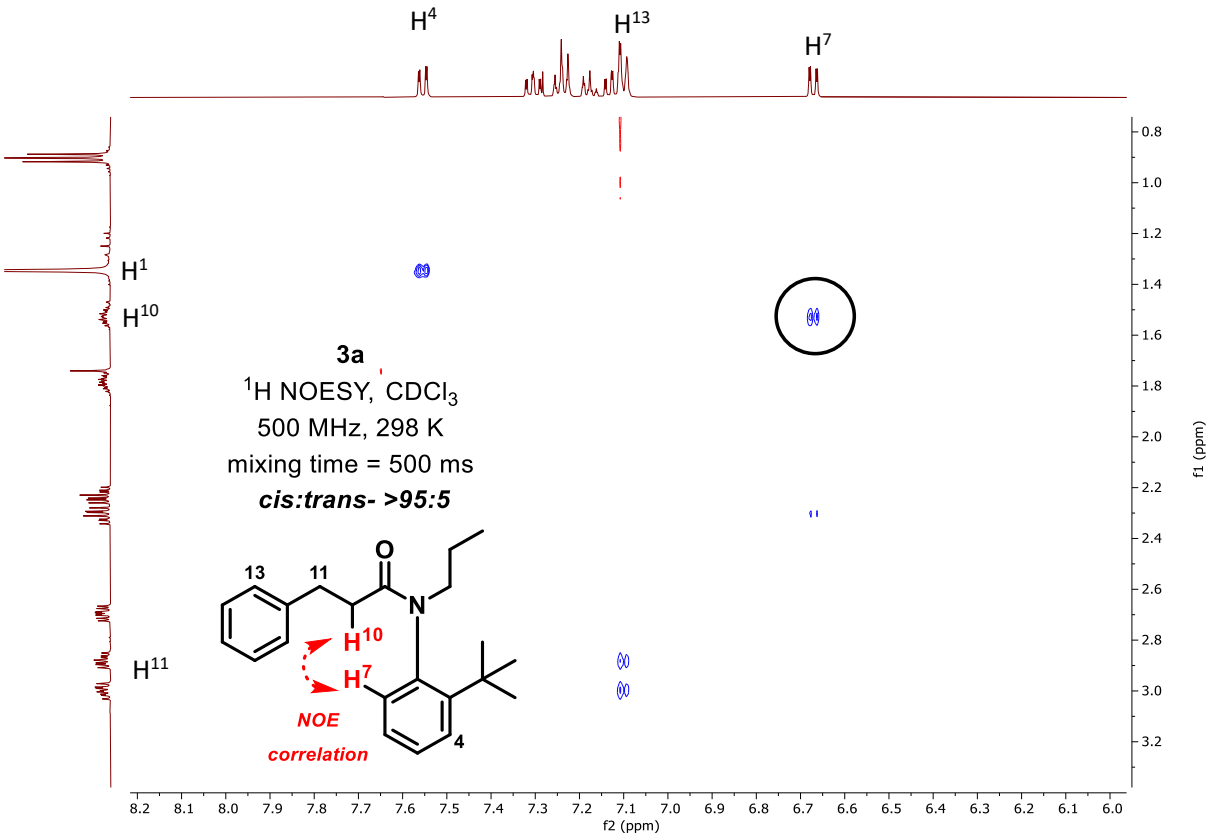
400 MHz, 298K

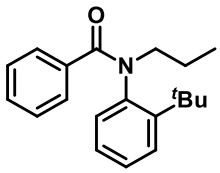


3a

^{13}C NMR, $CDCl_3$

75 MHz, 298 K


H4
H13
H7
H1
H10
H11
3a
1H NOESY, CDCl3
500 MHz, 298 K
mixing time = 500 ms
cis:trans- >95:5
13
11
O
N
H10
H7
4
NOE
correlation
f2 (ppm)
f1 (ppm)

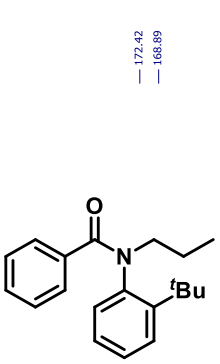


3b

^{1}H NMR, $CDCl_3$

700 MHz, 298K

77:23 *cis:trans*

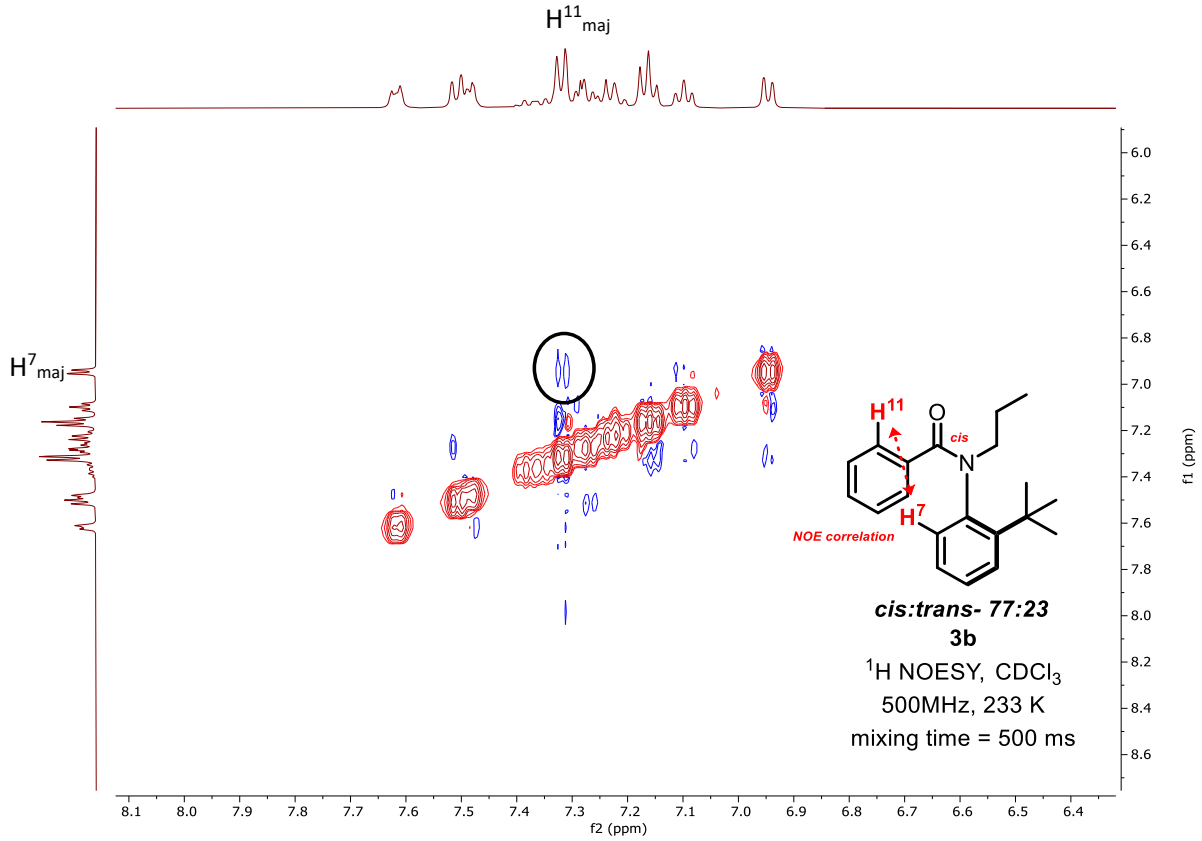


3b

^{13}C NMR, $CDCl_3$

176 MHz, 298K

cis/trans: 77:23


H11maj
H7maj
f2 (ppm)
f1 (ppm)
H11
H7
O
N
cis
NOE correlation
cis:trans- 77:23
3b
1H NOESY, CDCl3
500MHz, 233 K
mixing time = 500 ms