

Supporting information

Direct Organocatalytic Oxidation of Aldehydes to Anhydrides and Oxidative Dimerization of Primary Alcohols

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General Information

All non-aqueous reactions were carried out using oven-dried (120 °C) or heat gun dried glassware under a positive pressure of dry argon unless otherwise noted. Acetonitrile was purified by distillation and dried by passage over activated alumina under a nitrogen atmosphere (water content < 20 ppm, *Karl–Fischer* titration).

Pyridine was distilled from calcium hydride. Decanal was distilled before use. All other commercially available reagents were used without further purification. Except if indicated otherwise, reactions were magnetically stirred and monitored by thin layer chromatography using Merck Silica Gel 60 F254 plates and visualized by fluorescence quenching under UV light. In addition, TLC plates were stained using ceric ammonium molybdate and potassium permanganate. Chromatographic purification of products (flash chromatography) was performed on silica 32-63, 60 Å using a forced flow of eluent at 0.3-0.5 bar. Concentration under reduced pressure was performed by rotary evaporation at 40 °C at the appropriate pressure. Yields refer to chromatographically purified compounds.

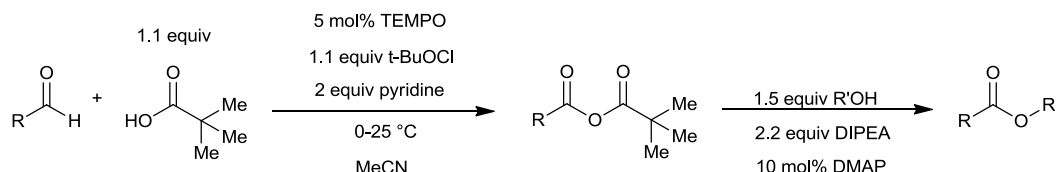
NMR spectra: NMR spectra were recorded on a Bruker Avance I 300 spectrometer operating at 300 MHz and 75 MHz for ^1H and ^{13}C acquisitions, respectively, or on Bruker Avance III 400 spectrometers operating at 400 MHz (^1H) and 101 MHz (^{13}C) or on a Bruker DPX200 spectrometer operating at 200 MHz (^1H) and 50 Mhz respectively (^{13}C). Chemical shifts (δ) are reported in ppm with the solvent resonance as the internal standard relative to chloroform (δ 7.26) ^1H , and chloroform (δ 77.0) for ^{13}C . All ^{13}C spectra were measured with complete proton decoupling. Data are reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad signal; coupling constants in Hz.

IR spectra: recorded on a Bruker FT-IR (as thin film). Absorptions are given in wavenumbers (cm^{-1}).

Mass spectra: High resolution mass spectra were recorded by the MS service at Technion. ESI-MS (m/z): was recorded on a Waters Micromass LCT premier instrument at 70eV in the positive or negative mode. APCI was recorded on the same instrument using 70% acetonitrile/30 % water at 0.2 mL flowrate.

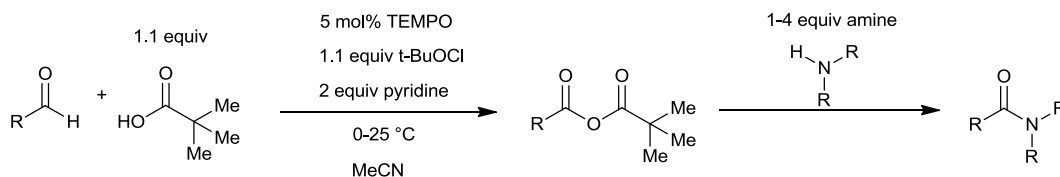
General Procedures

Synthesis of esters via mixed anhydride with pivalic acid (general procedure A)



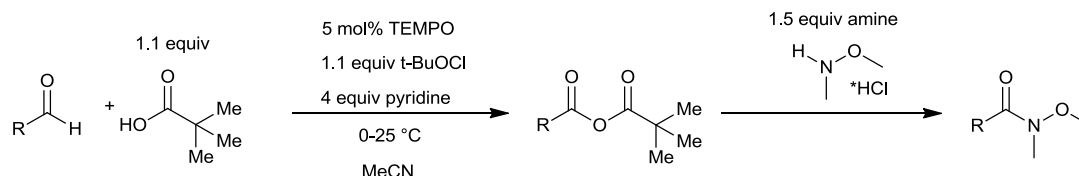
The aldehyde (1 mmol), TEMPO (7.81 mg, 0.05 mmol, 5 mol%), pivalic acid (112.3 mg, 1.1 mmol, 1.1 equiv) and pyridine (0.16 mL, 2 mmol, 2 equiv) are dissolved in 2.5 mL acetonitrile. *t*-BuOCl (0.113 mL, 1.1 mmol) was added drop-wise at 0 °C over 25 min. After complete reaction the yellow color of **2** lingered. When drop-wise addition was used the color disappeared rapidly between each drop until completion of the oxidation. The reaction was allowed to reach room temperature and then the alcohol (1.5 equiv) was added followed by DIPEA (0.392 mL, 2.2 mmol, 2.2 equiv) and DMAP (12.2 mg, 0.1 mmol, 10 mol%). The mixture was stirred until reaction was complete as judged by TLC. 25 mL sat. NaHCO₃ was added and the reaction extracted with 4x20 mL diethyl ether. The combined extractions were dried over Na₂SO₄. The product is purified by flash chromatography using ethyl acetate/hexane as the eluent. A

Synthesis of amides via mixed anhydride with pivalic acid (general procedure B)



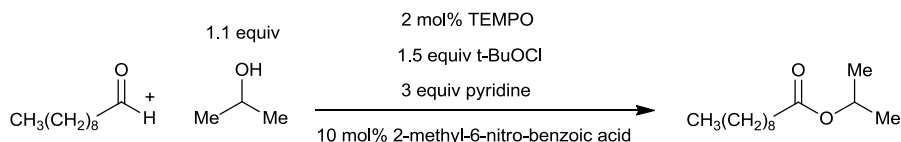
Oxidation was carried out as described in procedure A. After completion of the oxidation of aldehyde to the mixed anhydride the reaction was allowed to reach room temperature and then the amine (1–4 mmol, 1–4 equiv) was added. The mixture was stirred until the reaction was complete as judged by TLC. 25 mL sat. NaHCO₃ was added and the reaction extracted with 4x20 mL ethyl acetate. The combined extracts were dried over Na₂SO₄. The product was purified by flash chromatography using ethyl acetate/hexane as the eluent.

Synthesis of Weinreb amide via mixed anhydride with pivalic acid (general procedure C)



The aldehyde (1 mmol), TEMPO (7.81 mg, 0.05 mmol, 5 mol%), pivalic acid (112.3 mg, 1.1 mmol, 1.1 equiv) and pyridine (0.32 mL, 4 mmol, 4 equiv) are dissolved in 2.5 mL acetonitrile. *t*-BuOCl (0.113 mL, 1.1 mmol) was added either in one portion or drop-wise at 0°C. After complete reaction the yellow color of **5** lingered. When drop-wise addition was used the color disappeared rapidly between each drop until completion of the oxidation. After completion of the oxidation of aldehyde to the mixed anhydride the reaction was allowed to reach room temperature and then the N,O-dimethylhydroxylamine hydrochloride (1.5 mmol) was added. The mixture was stirred until the reaction was complete as judged by TLC. 25 mL sat. NaHCO₃ was added and the reaction extracted with 4x20 mL ethyl acetate. The combined extracts were dried over Na₂SO₄. The product was purified by flash chromatography using ethyl acetate/hexane as the eluent.

Synthesis of decanic acid 2-proyl ester from decanal and 2-propanol catalyzed by TEMPO and 2-methyl-6-nitro-benzoic acid (general procedure D).



Decanal (0.190 mL, 1 mmol), TEMPO (3.1 mg, 0.02 mmol, 2 mol%), 2-methyl-6-nitro-benzoic acid (18.1 mg, 0.1 mmol, 10 mol%) and pyridine (0.24 mL, 3 mmol, 3 equiv) were dissolved in 3 mL acetonitrile. *t*-BuOCl (0.169 mL, 1.5 mmol, 1.5 equiv) was added drop-wise at 0°C over 45 minutes at which time no aldehyde could be observed. The mixture was stirred overnight and then evaporated on to celite. The celite was loaded onto column with silica gel and the product is purified by flash chromatography using 6% ethyl acetate/hexane as the eluent to afford 154 mg (71% yield) of the product as an oil.

Identification of mixed anhydride of decanoic acid and pivalic acid by NMR

Results and Discussion

The mixed anhydrides were made by two independent methods. The first preparation involved starting from decanal and pivalic acid as described above. A sample of the reaction mixture was withdrawn and submitted to NMR spectroscopy.

In the second method the same anhydride was made by the procedure used by Shiina et al for the preparation of the anhydride of 2-methyl-6-nitro-benzoic acid.¹ First decanoic acid was converted to decanoic acid chloride by the action of oxaloyl chloride and catalytic DMF. After complete reaction the solvent and excess oxaloyl chloride was removed. Then the acid chloride was re-dissolved and pivalic acid (1.1 equiv) and pyridine (2 equiv) were added. Instantaneous formation of a precipitate was observed. The precipitate was studied by NMR.

The spectra of the crude anhydrides, made by two different methods, are almost identical, save the presence of acetonitrile in the sample of mixed anhydride prepared using the oxidative conditions. In both cases, the product contains the mixed anhydride (ca 70-80% as estimated by ¹H NMR at 2.34 ppm. In the carbon NMR signals indicative of the presence of pivalic anhydride and decanoic anhydride can be seen in the carbonyl region.² The peak heights of these signals also indicate app. 80% mixed anhydride and around 10% of each of the other two anhydrides. A paper on the stability and scrambling of benzoic anhydrides has been published by SantaLucia.³ Unfortunately, it is not possible to establish at which point the scrambling of anhydrides took place. Irrespective the fact that acylation yields in excess of 90% can be achieved is indicative that if the scrambling process takes place prior to addition of the alcohol or amine, the process is probably reversible.

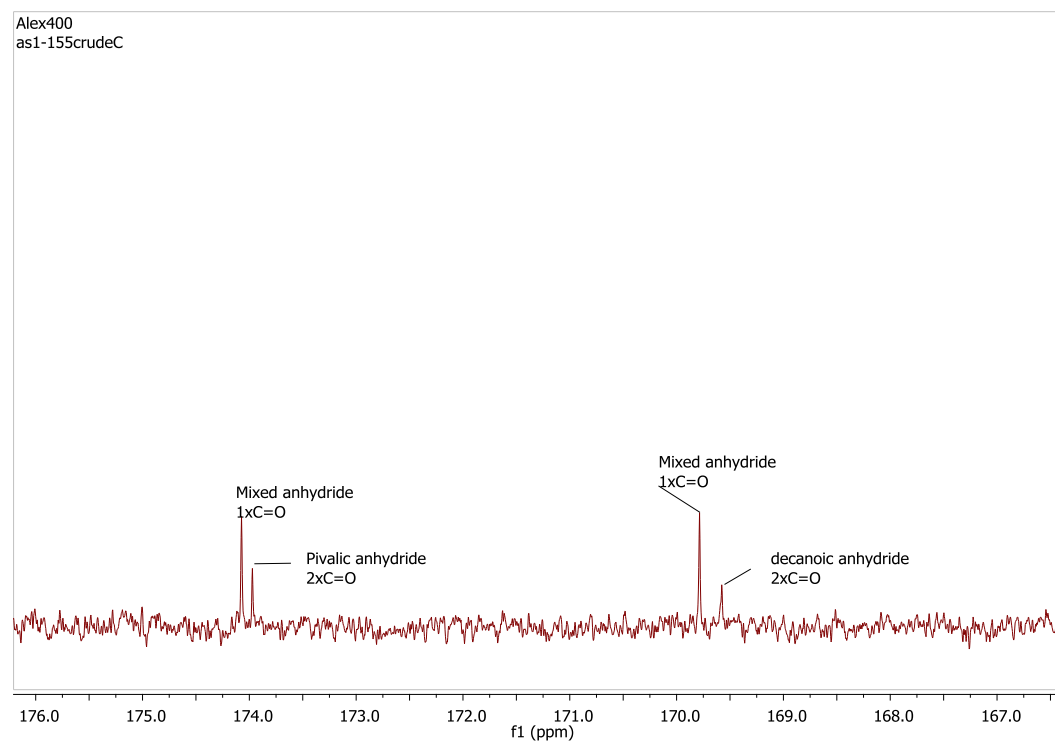
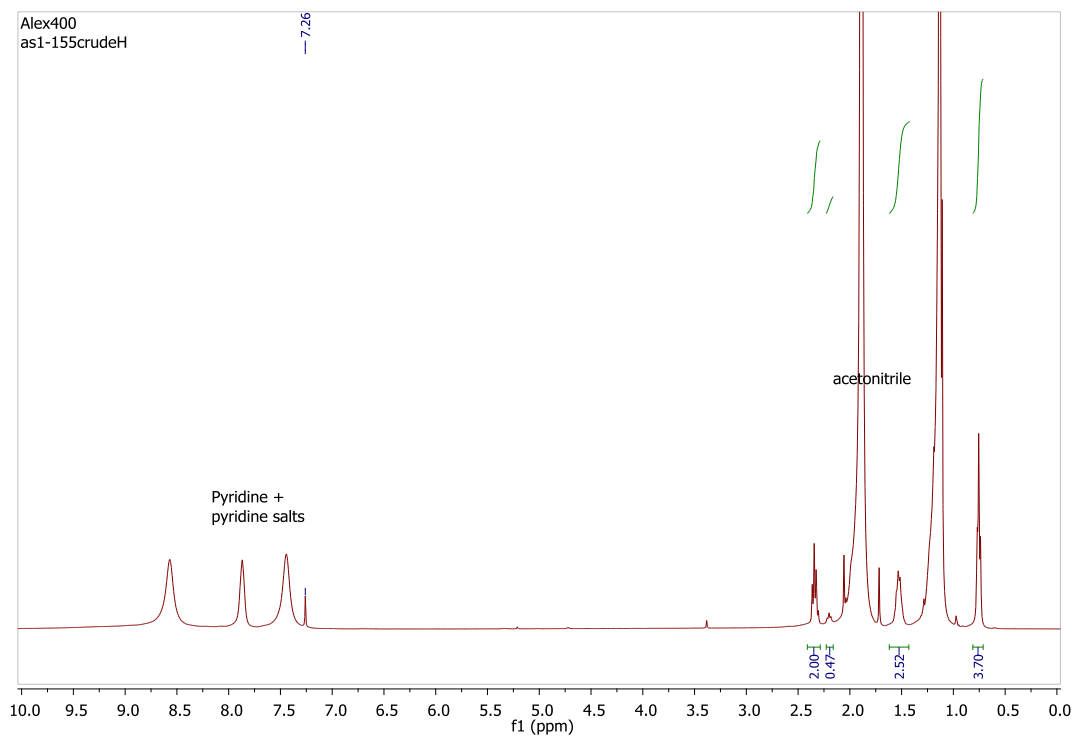
Synthesis of the anhydride from decanal and pivalic acid

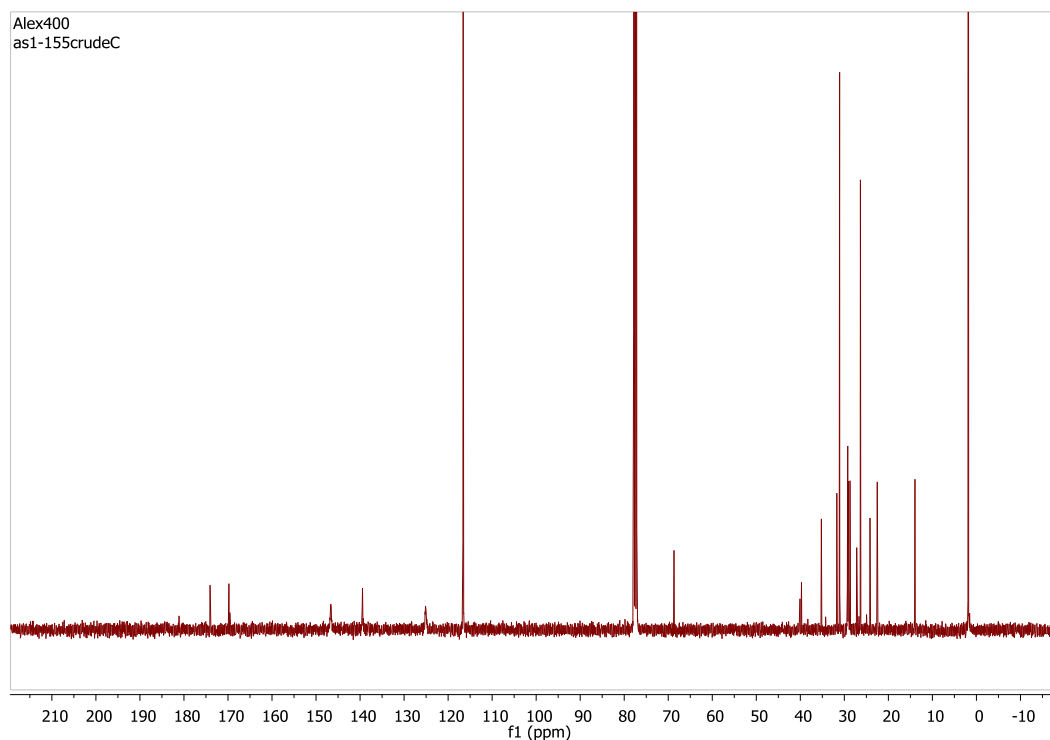
Decanal (0.190 mL, 1 mmol), TEMPO (3.1 mg, 0.02 mmol, 2 mol%), pivalic acid (112.3 mg, 1.1 mmol, 1.1 equiv) and pyridine (0.16 mL, 2 mmol, 2 equiv) were dissolved in 1 mL acetonitrile. *t*-BuOCl (0.113 mL, 1.1 mmol) was added drop-wise at 0°C at such a rate that the color of the TEMPO oxoammonium species disappeared before addition of the next drop. After 20 min addition was complete and no starting material could be observed. The reaction mixture was stirred for another hour and 0.1 mL extracted and added to a NMR tube with CDCl₃ (0.7 mL). The ¹H and ¹³C NMR was recorded.

1 I. Shiina, M. Kubota, H. Oshiumi and M. Hashizume *J. Org. Chem.*, 2004, **69**, 1822.

2 The literature values for pivalic anhydride and decanoic anhydride were taken from the online Spectral Database of Organic Compounds at this address: http://riodb01.ibase.aist.go.jp/sdbs/cgi-bin/cre_index.cgi?lang=eng

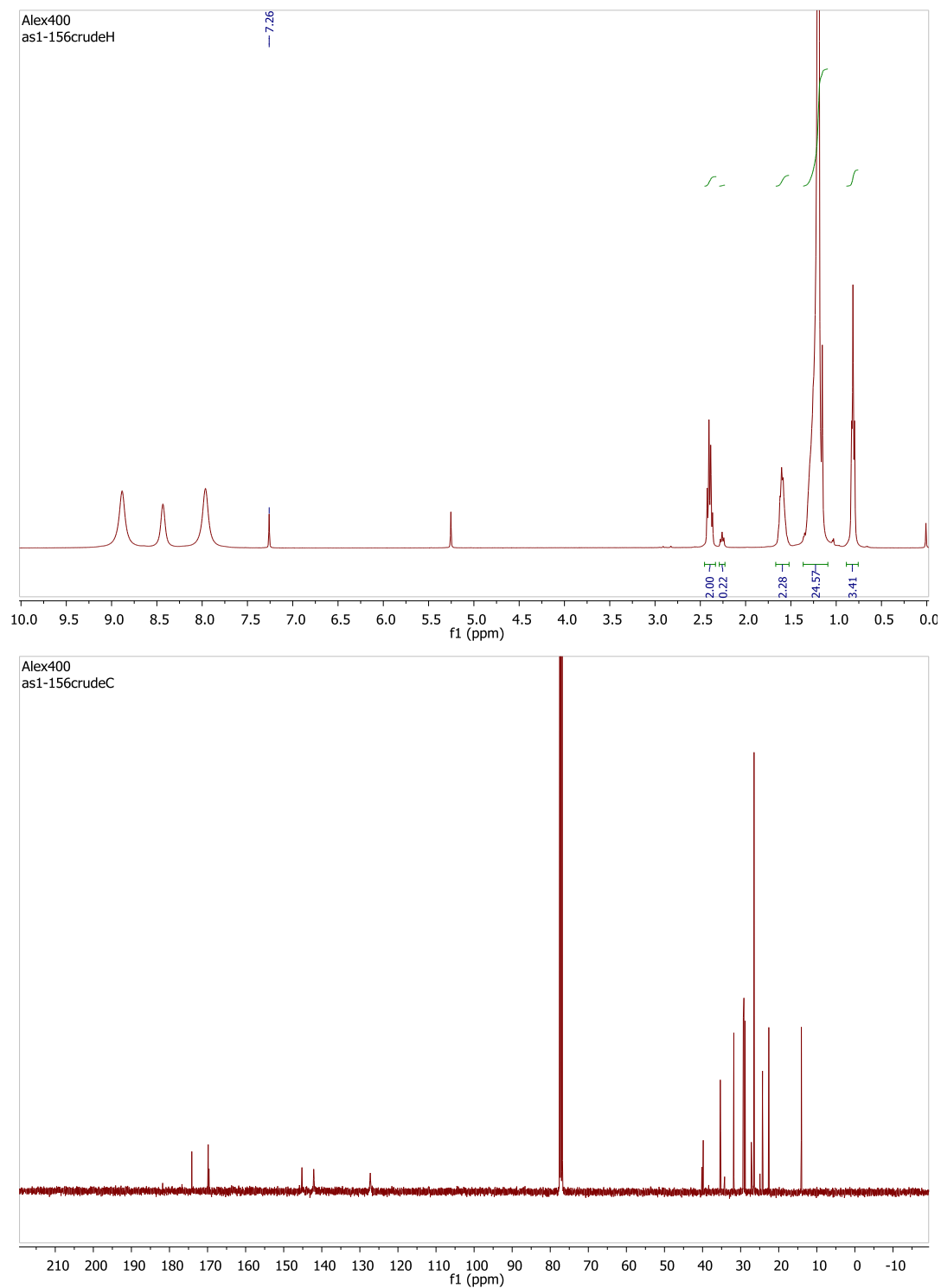
3 I. Dhimitruka and J. SantaLucia, Jr. *Org. Lett.* 2006, **8**, 47.

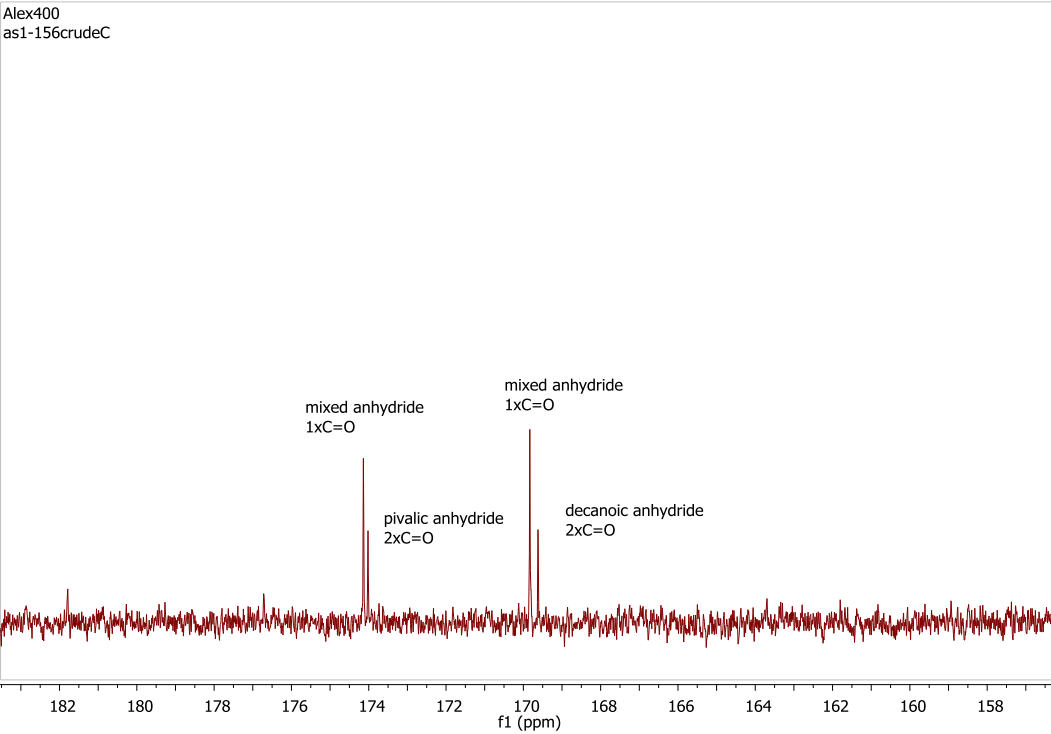




Synthesis of the mixed anhydride from decanoic acid and pivalic acid

Decanoic acid (172 mg, 1 mmol), was dissolved in dichloromethane (2 mL) and 1 drop of DMF added. To the reaction mixture was added oxaloyl chloride over 2-3 min. Gas evolution was observed for 5 minutes. Left for an additional hour and concentrated by a stream of argon. Dichloromethane (1 mL) was added followed by pivalic acid (112 mg, 1.1 mmol, 1.1 equiv). Pyridine (0.1 mL, 1.3 equiv) was added drop wise. A precipitate was formed immediately. The mixture was concentrated by a stream of argon and a portion of the precipitate submitted for 400 Mhz NMR spectroscopy as above.

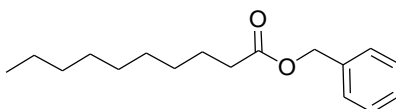




Characterization data

All known compounds had NMR spectra consistent with published data. For several known compounds full characterization was performed due to the difficulty in finding the relevant data in one literature source. For these compounds the data is given below in full and a reference containing the NMR data is given.

Benzyl decanoate⁴ (Table 1, entry 1)



The compound was prepared according to general procedure A and purified by flash chromatography (6% EtOAc/Hexane) to give the product as an oil (235 mg, 90 %).

R_f = 0.81 (20% EtOAc/Hexane).

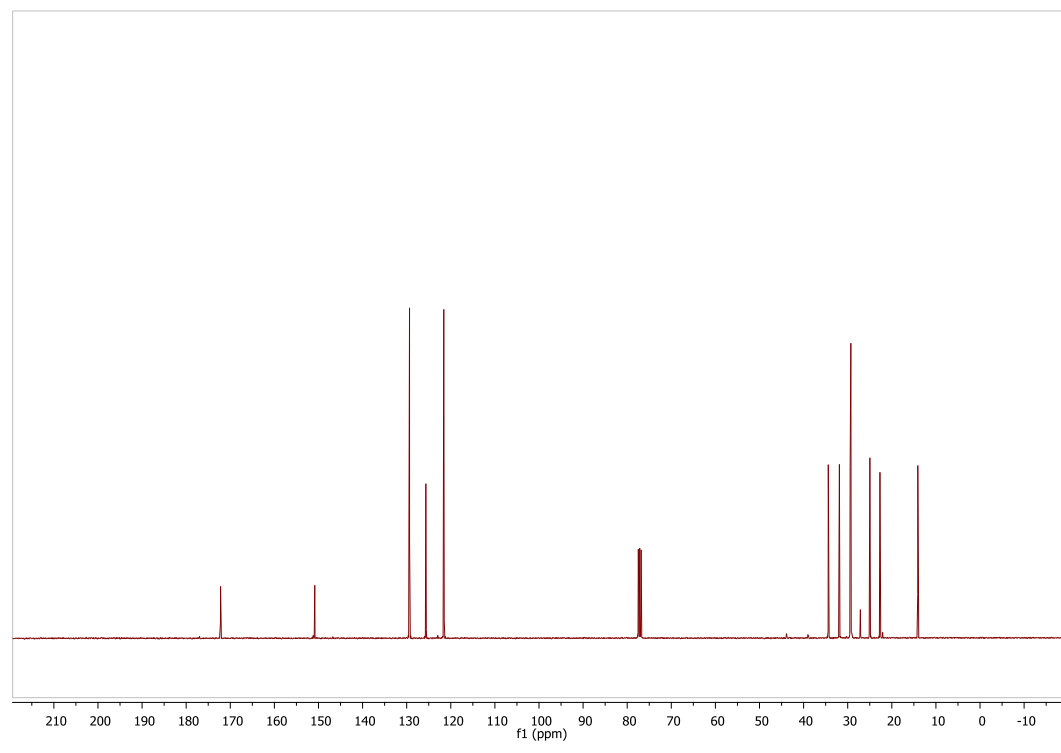
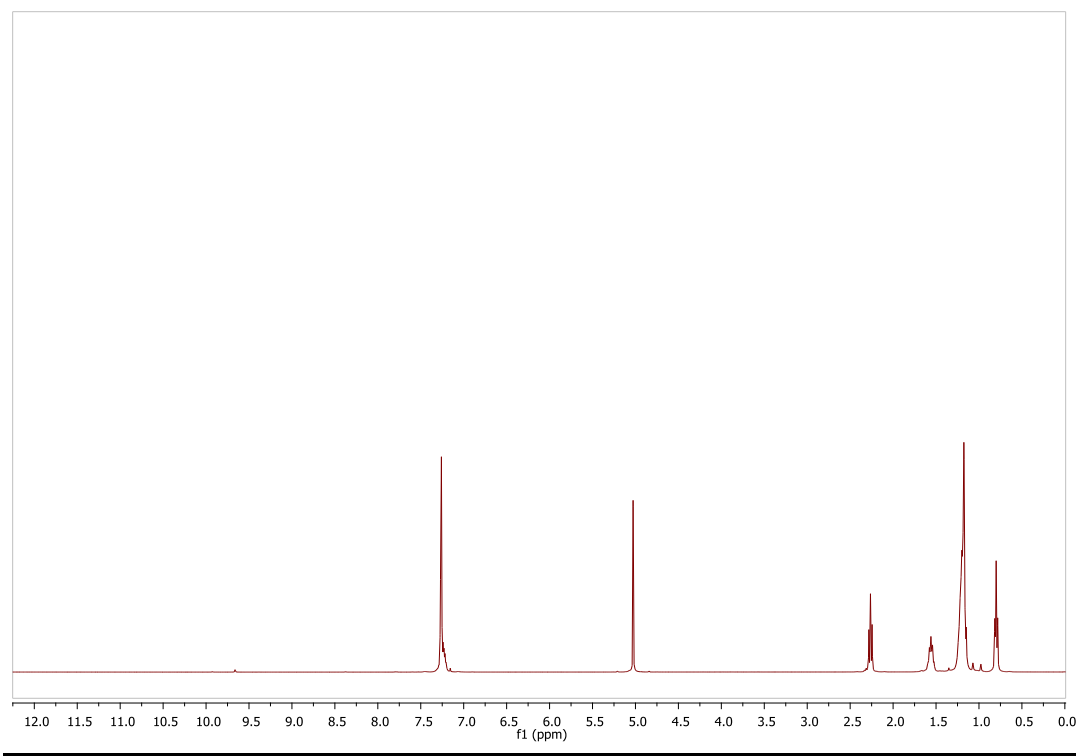
¹H NMR (400 MHz, CDCl₃) δ = 7.30 – 7.20 (m, 5H), 5.03 (s, 2H), 2.26 (t, J = 7.5 Hz, 2H), 1.61 – 1.49 (m, 2H), 1.30 – 1.10 (m, J = 9.6 Hz, 12H), 0.80 (t, J = 6.7 Hz, 3H).

¹³C NMR (101 MHz, CDCl₃) δ = 172.22 , 129.32 , 125.74 , 121.59 , 34.40 , 31.89 , 29.29 , 27.16, 24.97 , 22.69 , 14.10 .

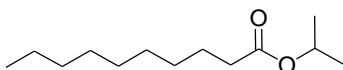
IR (thin film) ν 3039, 2927, 2858, 1730, 1639, 1458, 1377, 1350, 1244, 1230, 1161, 1111 cm⁻¹.

HRMS (ESI) m/z : calcd for C₁₇H₂₈O₂, [M+H₂O] 280.2038; found 280.2045

4 E. Eliel and R. P. Anderson, *J. Am. Chem. Soc.*, 1952, **74**, 547; For a recent synthesis see: K. Ishihara, M. Niwa and Y. Kosugi, *Y. Org. Lett.*, 2008, **10**, 2187.



2-propyl decanoate⁵ (Table 1, entry 2 and Scheme 2)



The compound was prepared according to general procedure A and purified by flash chromatography (6% EtOAc/Hexane) to give the product as an oil (207 mg, 97 %).

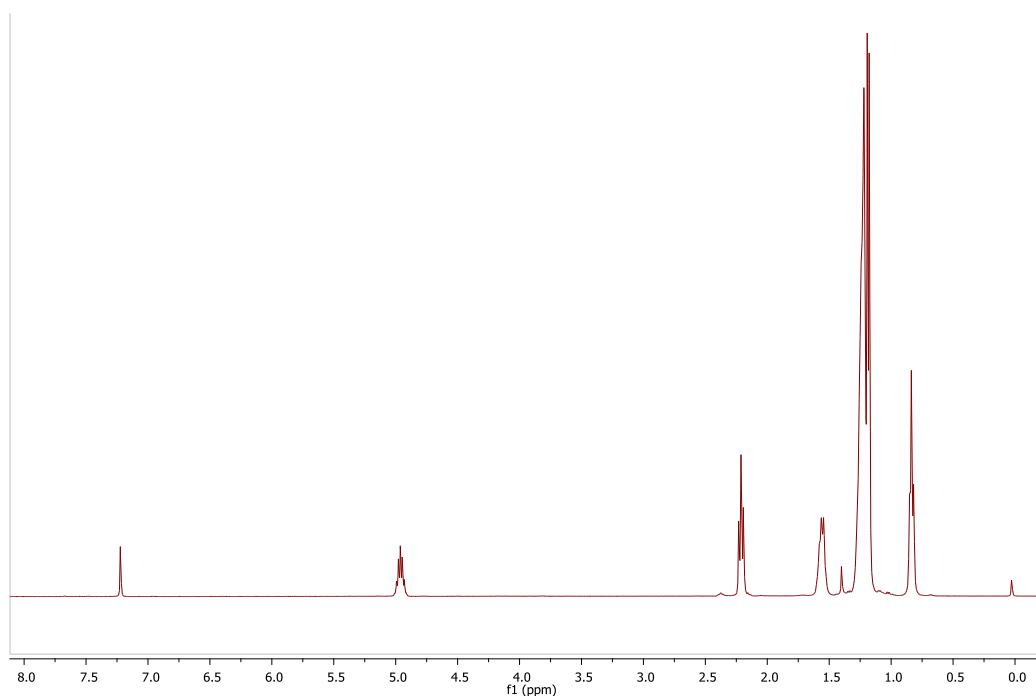
R_f = 0.88 (10% EtOAc/Hexane).

¹H NMR (400 MHz, CDCl₃) δ = 5.00 (dt, J = 12.5, 6.3 Hz, 1H), 2.25 (t, J = 7.5 Hz, 2H), 1.66 – 1.52 (m, 2H), 1.27 (m, 12H), 1.23 (s, 3H), 1.22 (s, 3H), 0.88 (t, J = 6.8 Hz, 3H).

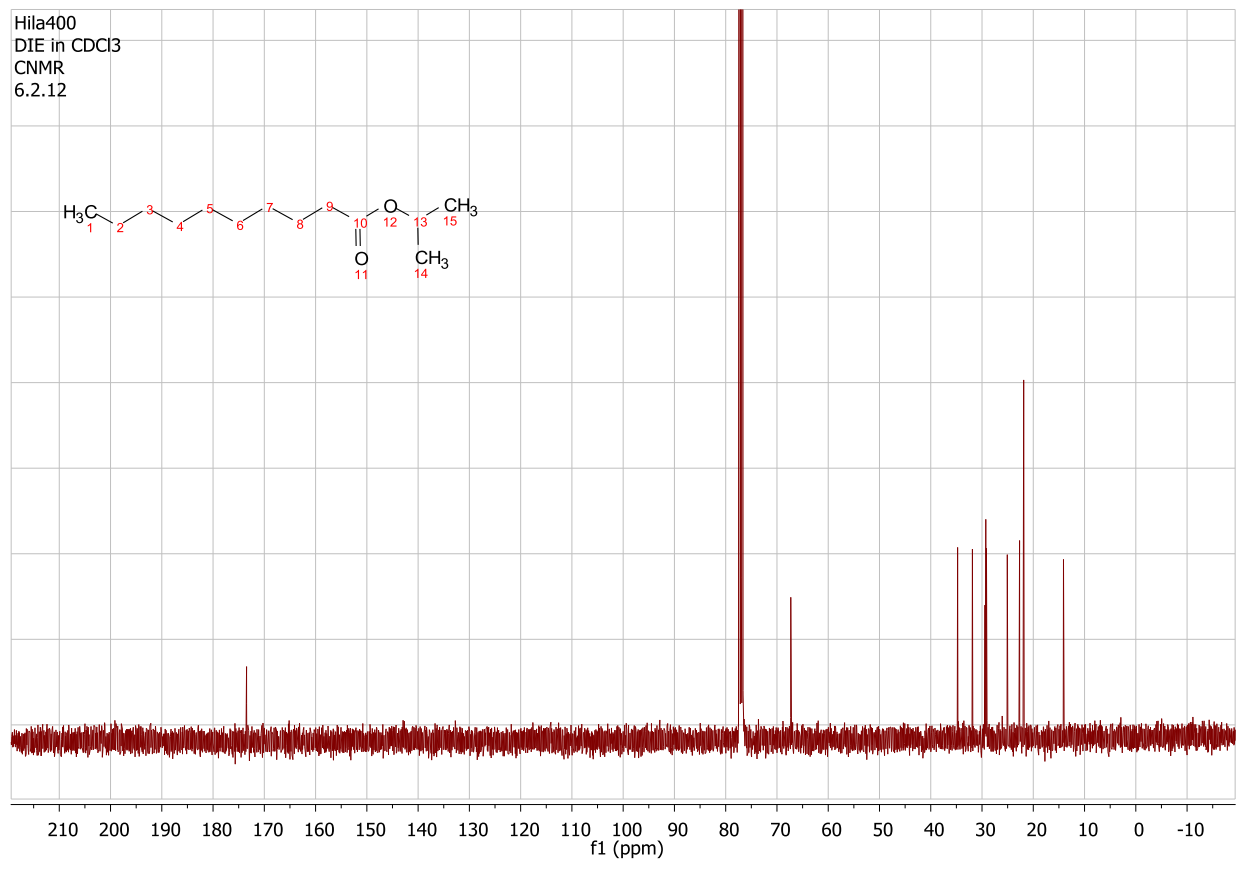
¹³C NMR (101 MHz, CDCl₃) δ = 173.64, 67.30, 34.87, 31.87, 29.55, 29.28, 29.26, 29.13, 25.20, 22.68, 21.97, 14.16.

IR: (thin film) ν 2929, 2861.84, 1718.26, 1459.85, 1375, 1263.15, 1108.87, 767.53 cm⁻¹.

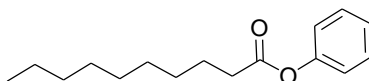
HRMS (ESI) m/z: calcd for C₁₃H₂₆O₂, [M+1], 215.2011; found 215.2022



⁵ T. Takeda, H. Watanabe and T. Kitahara, *Synlett* 1997, 1149.



phenyl decanoate⁶ (Table 1, entry 3)



The compound was prepared according to general procedure A and purified by flash chromatography (6% EtOAc/Hexane) to give the product as an oil (225 mg, 91 %).

R_f=0.82 (20% EtOAc/Hexane).

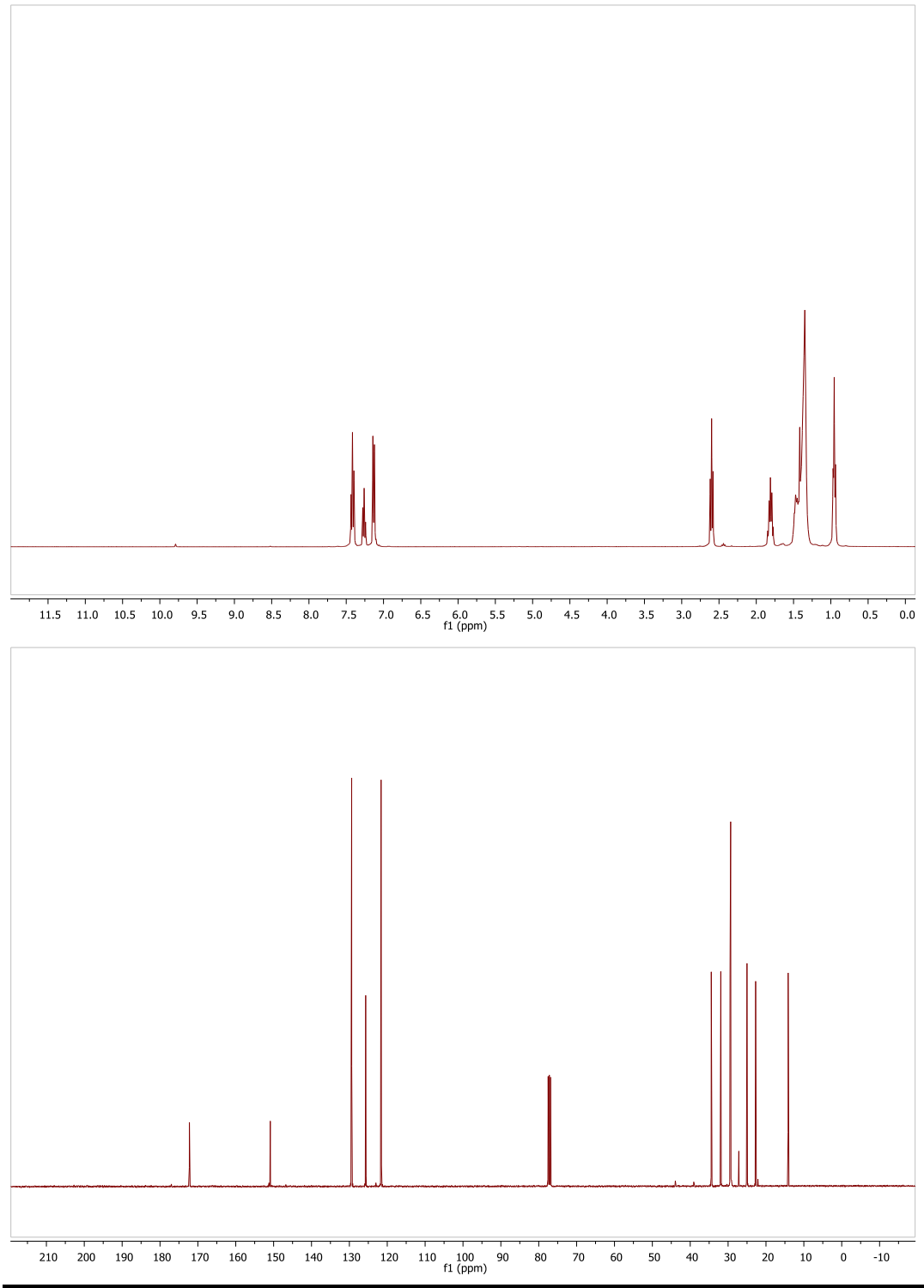
¹H NMR (400 MHz, CDCl₃) δ = 7.42 (t, *J* = 7.8 Hz, 2H), 7.27 (t, *J* = 7.2 Hz, 1H), 7.13 (d, *J* = 8.3 Hz, 2H), 2.60 (t, *J* = 7.5 Hz, 2H), 1.86 – 1.76 (m, 2H), 1.53 – 1.26 (m, 12H), 0.95 (t, *J* = 6.5 Hz, 3H). .

¹³C NMR (101 MHz, CDCl₃) δ = 172.22 , 129.32 , 125.74 , 121.59 , 34.40 , 31.89 , 29.29 , 27.16 , 24.97 , 22.69 , 14.10.

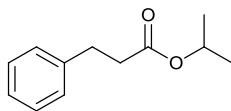
IR (thin film) ν 2927, 2858, 1751, 1631, 1595, 1483, 1462, 1365, 1200, 1151, 1111, 1018 cm⁻¹.

HRMS (ESI-negative mode) *m/z*: calcd for C₁₆H₂₄O₂ [M-1], 247.1698; found 247.1695.

6 S. Montiel-Smith, S. Meza-Reyes, O. Vinas-Bravo, M. A. Fernandez-Herrera, R. Martinez-Pascual, J. Sandoval-Ramirez, A. Fuente, M. Reyes and J. A. Ruiz, *ARKIVOC*, 2005, 127.



2-propyl 3-phenylpropanoate⁷ (Scheme 2)



The compound was prepared according to general procedure D using 2 mol% TEMPO and 10 mol% 2-methyl-6-nitro-benzoic acid.

The compound was purified by flash chromatography (7% EtOAc/Hexane) to give the product as an oil (93mg, 51 %).

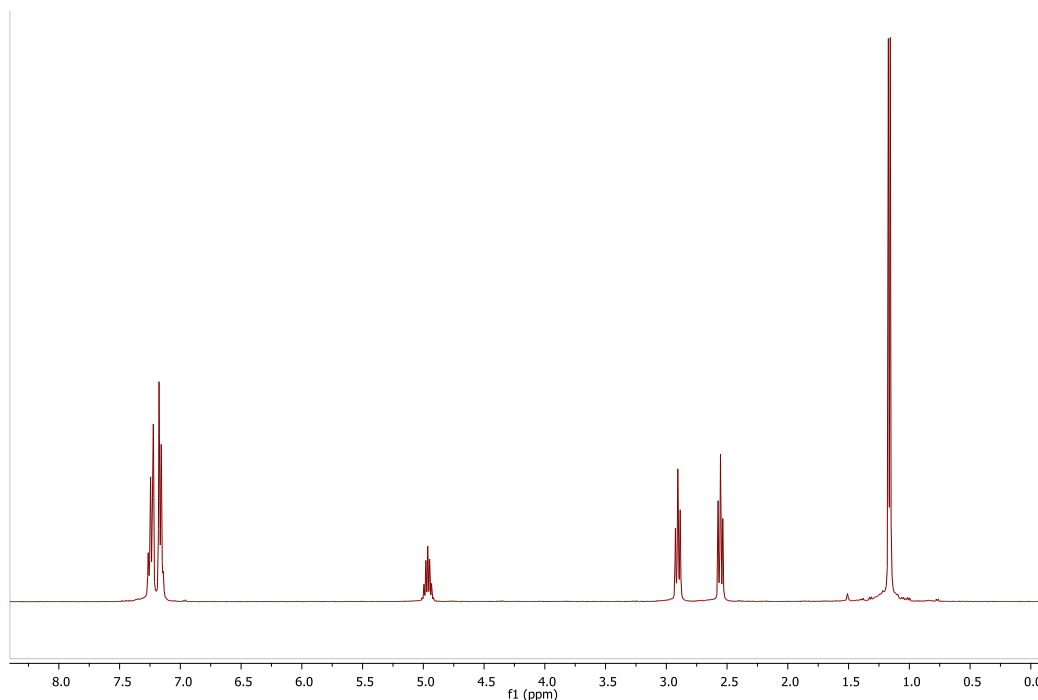
R_f=0.5 (10% EtOAc/Hexane).

¹H NMR (400 MHz, CDCl₃) δ = 7.34 – 7.07 (m, 5H), 5.02 – 4.90 (m, 1H), 2.91 (t, J = 7.8 Hz, 2H), 2.55 (t, J = 7.8 Hz, 2H), 1.16 (d, J = 6.2 Hz, 6H).

¹³C NMR (101 MHz, CDCl₃) δ = 172.57, 140.70, 128.39, 126.36, 100.60, 67.63, 36.26, 31.06, 21.92.

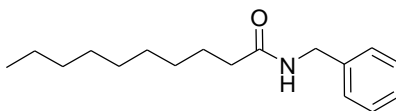
IR (thin film) ν 3022, 2983, 1720, 1637, 1498, 1452, 1357, 1217, 1107 cm⁻¹.

HRMS (ESI) m/z : calcd for C₁₂H₁₆O₂, [M+1], 192.1150; found 192.1157



⁷ N. Coskun and M. Er, *Tetrahedron*, 2003, **59**, 3481.

N-benzyldecanamide⁸ (Table 1, entry 4,5)



Made according to General Procedure B but using only 1 equiv of benzylamine. Under these conditions the product was isolated as a solid (199.7 mg, 75% yield) after column chromatography(40% EtOAc/Hexane). When the experiment was made using 4 equiv of benzylamine were used the yield was (84%, 219 mg).

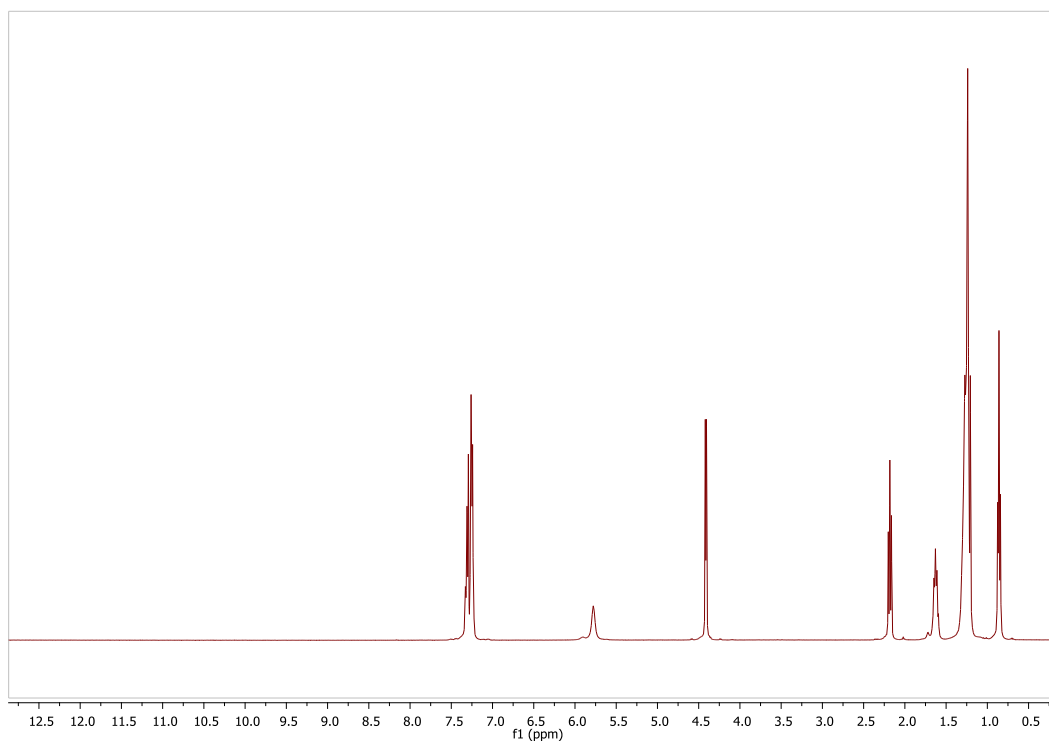
R_f = 0.19 (20% EtOAc/Hexane).

¹H NMR (400 MHz, CDCl₃) δ = 7.35 – 7.28 (m, 2H), 7.25 (dd, J = 5.5, 1.9 Hz, 3H), 5.78 (s, 1H), 4.41 (d, J = 5.6 Hz, 2H), 2.18 (t, J = 7.6 Hz, 2H), 1.68 – 1.58 (m, 2H), 1.33 – 1.22 (m, J = 13.7 Hz, 12H), 0.86 (t, J = 6.7 Hz, 3H).⁹

¹³C NMR (101 MHz, CDCl₃) δ = 173.18, 138.65, 128.87, 128.00, 127.67, 43.80, 36.93, 32.05, 29.59, 29.49, 29.47, 29.40, 27.78, 25.95, 22.81, 14.29.

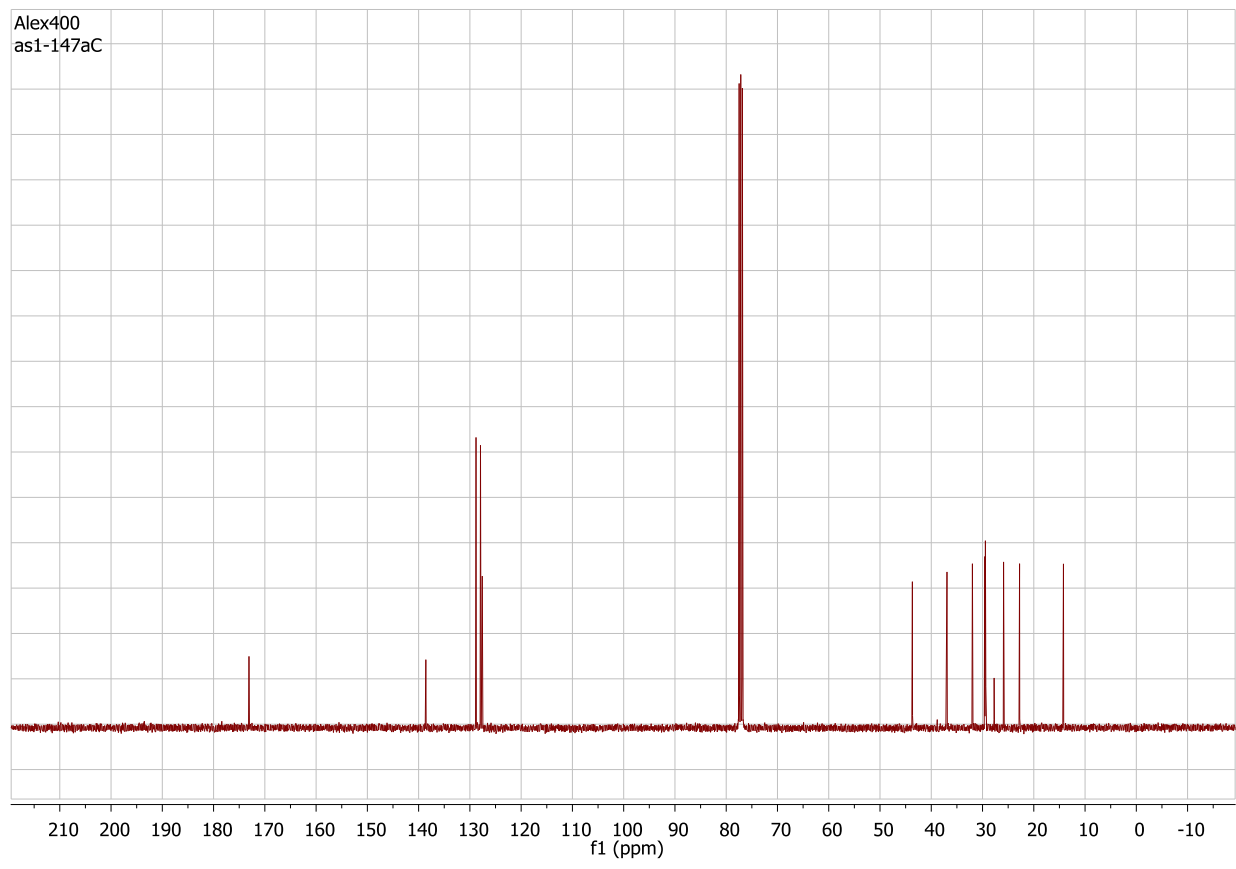
IR (thin film) ν 3001, 2927, 2858, 1664, 1510, 1460, 1217 cm⁻¹.

HRMS (ESI) *m/z*: calcd for C₁₇H₂₇NO [M+1], 262.2171; found 262.2145.

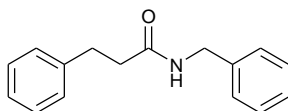


⁸ L. Perreux, A. Loupy and F. Volatron, *Tetrahedron*, 2002, **58**, 2155.

⁹ Mixture of Rotamers



N-Benzyl-3-phenylpropionamide¹⁰ (Table 1, entry 6)



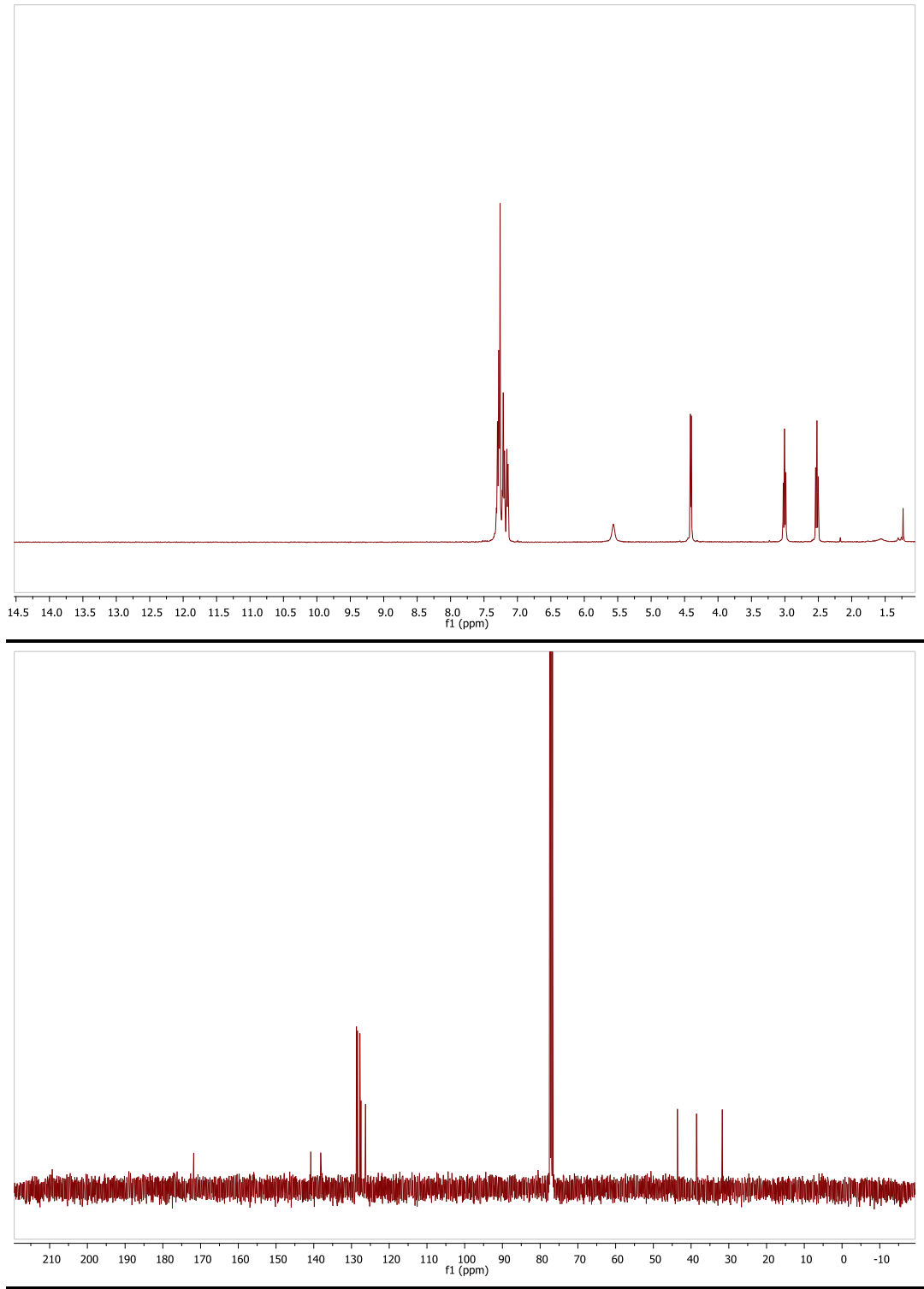
Made according to General Procedure B but using only 1 equiv of benzylamine. Under these conditions the product was isolated as a solid (131.7 mg, 55% yield) after column chromatography (40% EtOAc/Hexane).

R_f =0.42 (40% EtOAc/Hexane).

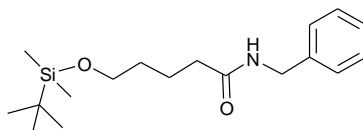
¹H NMR (400 MHz, CDCl₃) δ = 7.33 – 7.26 (m, 5H), 7.21 (t, J =6.3, 3H), 7.15 (d, J =7.1, 2H), 5.56 (s, 1H), 4.41 (d, J =5.7, 2H), 3.00 (t, J =7.6, 2H), 2.52 (t, J =7.6, 2H).⁹

¹³C NMR (101 MHz, CDCl₃) δ = 172.21, 140.92, 138.29, 128.82, 128.71, 128.55, 127.91, 127.62, 126.42, 43.76, 38.69, 31.83.

¹⁰ S. Kuwano, S. Harada, R. Oriez and K.-I Yamada, *Chem. Commun.*, 2012, **48**, 145–147



N-benzyl-5-(tert-butyldimethylsilyloxy)pentanamide (Table 1, entry 7)



The compound was prepared according to general procedure C and purified by flash chromatography (40% EtOAc/Hexane) to give the product as off-white solid (306.4 mg, 95%).

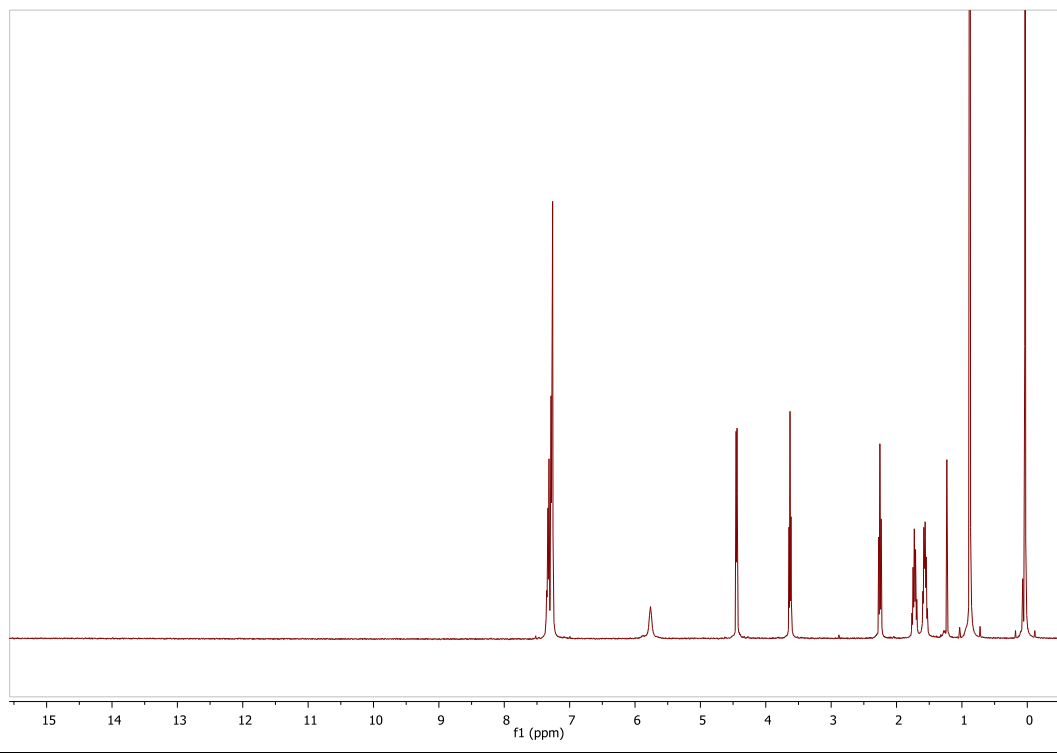
R_f=0.51 (40% EtOAc/Hexane)

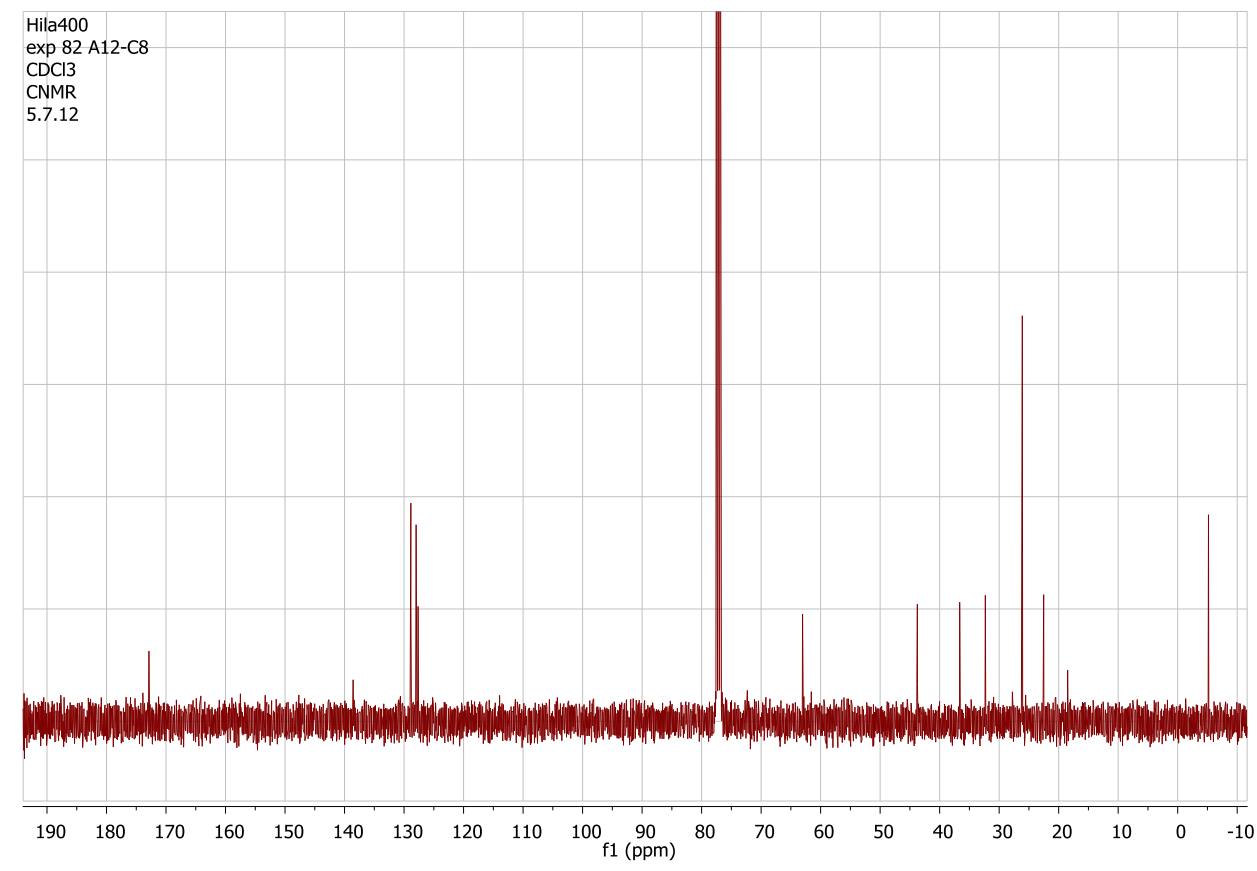
¹H NMR (400 MHz, CDCl₃) δ = 7.37 – 7.26 (m, 5H), 5.76 (s, 1H), 4.45 (d, J =5.6, 2H), 3.63 (t, J =6.2, 2H), 2.25 (t, J =7.5, 2H), 1.78 – 1.67 (m, J =15.3, 7.5, 2H), 1.61 – 1.54 (m, J =14.5, 6.5, 2H), 0.88 (s, 9H), 0.03 (s, 6H).⁹

¹³C NMR (101 MHz, CDCl₃) δ = 172.87, 138.56, 128.86, 127.97, 127.64, 77.16, 63.04, 43.75, 36.63, 32.32, 26.11, 22.52, 18.49, -5.17.

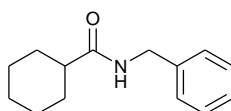
IR (thin film) ν 3446, 3002, 2954, 2931, 2857, 1664, 1513, 1463, 1255, 1097, 836, 767 cm⁻¹.

HRMS (ESI) m/z : calcd for C₁₈H₃₁NO₃Si [M+1], 322.2202; found 322.2232





N-Benzylcyclohexanecarboxamide¹¹ (Table 1, entry 8)



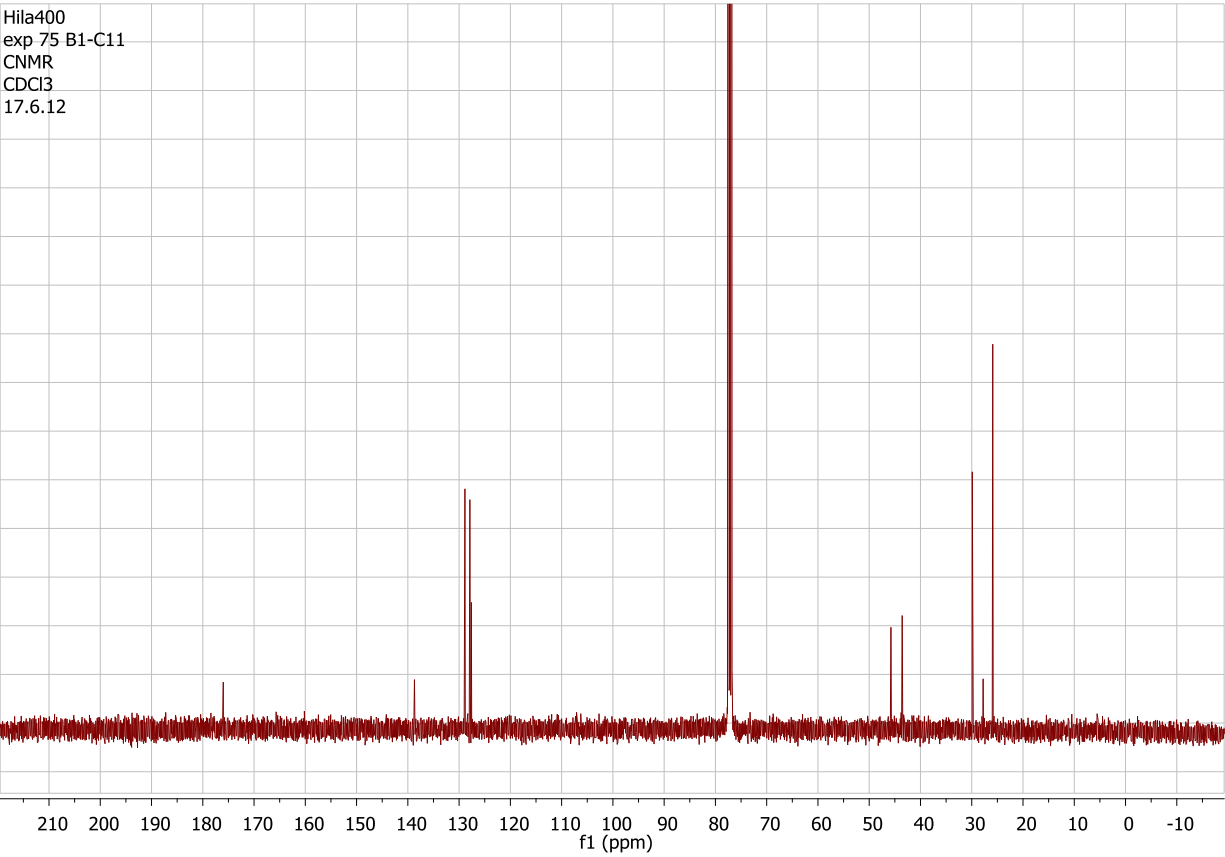
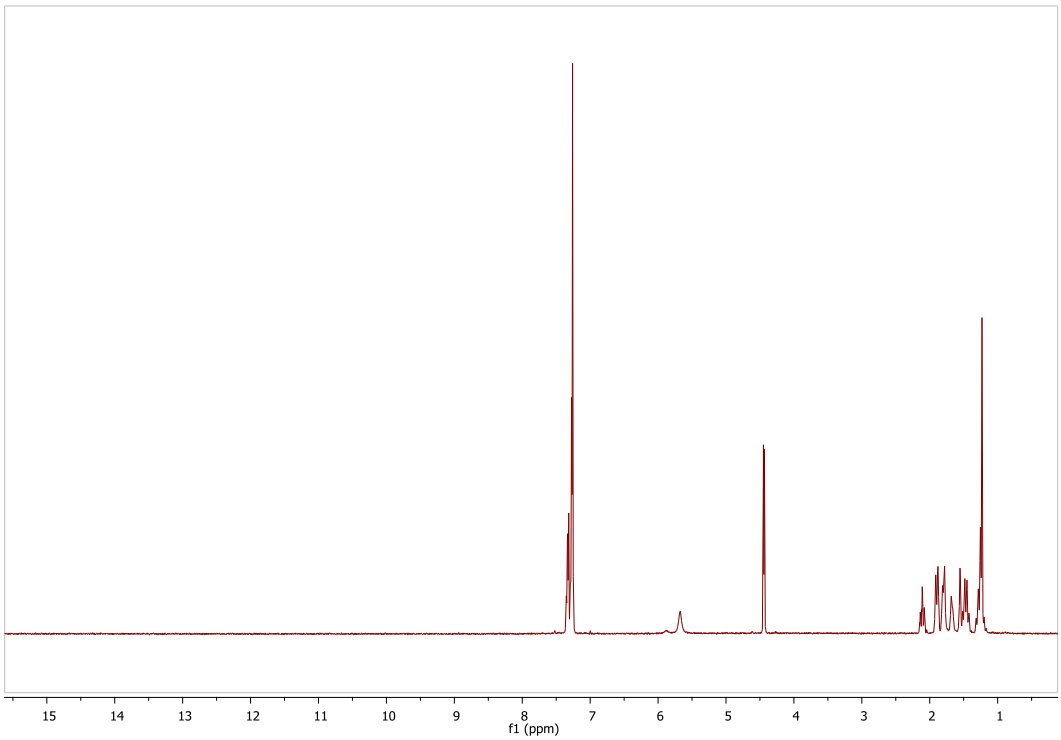
Made according to General Procedure B but using only 1 equiv of benzylamine. Under these conditions the product was isolated as an oil (153.9 mg, 71% yield) after column chromatography (30% EtOAc/Hexane).

R_f=0.59 (40% EtOAc/Hexane).

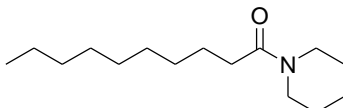
¹H NMR (400 MHz, CDCl₃) δ = 7.37 – 7.24 (m, 5H), 5.68 (s, 1H), 4.44 (d, J =5.6, 2H), 2.11 (tt, J =11.5, 3.3, 1H), 1.90 (d, J =13.0, 1H), 1.85 – 1.76 (m, 1H), 1.68 (d, J =8.1, 1H), 1.53 – 1.41 (m, 1H), 1.35 – 1.14 (m, 4H).⁹

¹³C NMR (101 MHz, CDCl₃) δ = 176.00, 138.80, 128.86, 127.90, 127.61, 45.76, 43.57, 29.90, 27.78, 25.90 .

¹¹ K. Ishihara, S. Ohara, and H. Yamamoto. *J. Org. Chem.*, 1996, **61**, 4196



1-(piperidin-1-yl)-decan-1-one¹² (Table 1, entry 9)

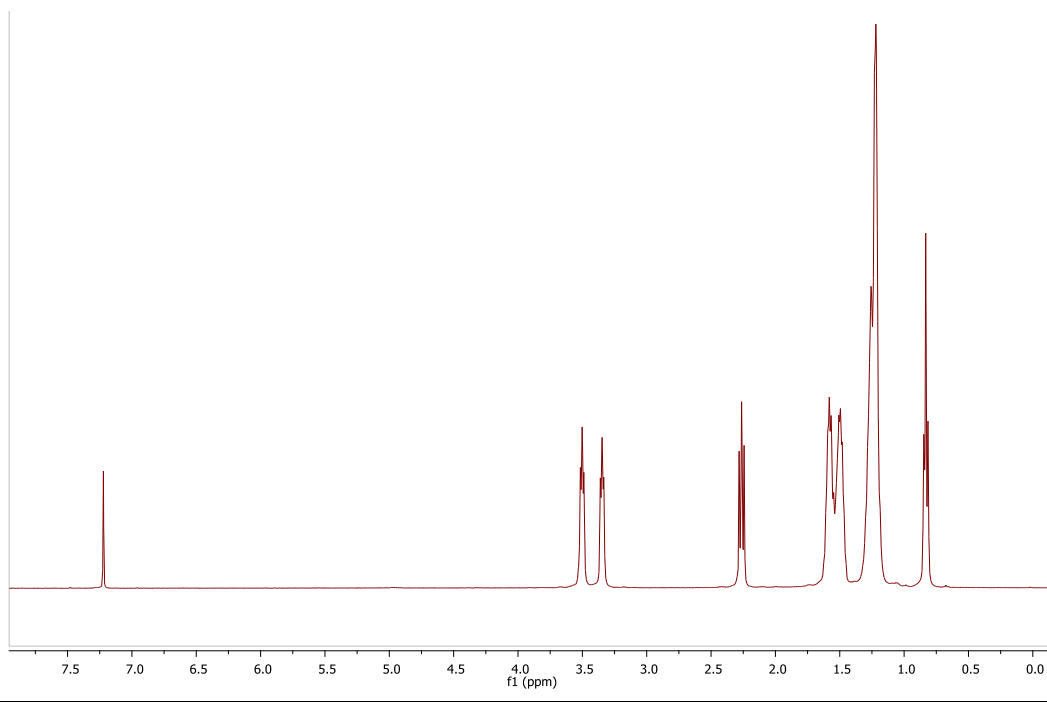


The compound was prepared according to general procedure B and purified by flash chromatography (40% EtOAc/Hexane) to give the product as a solid (180 mg, 75%).

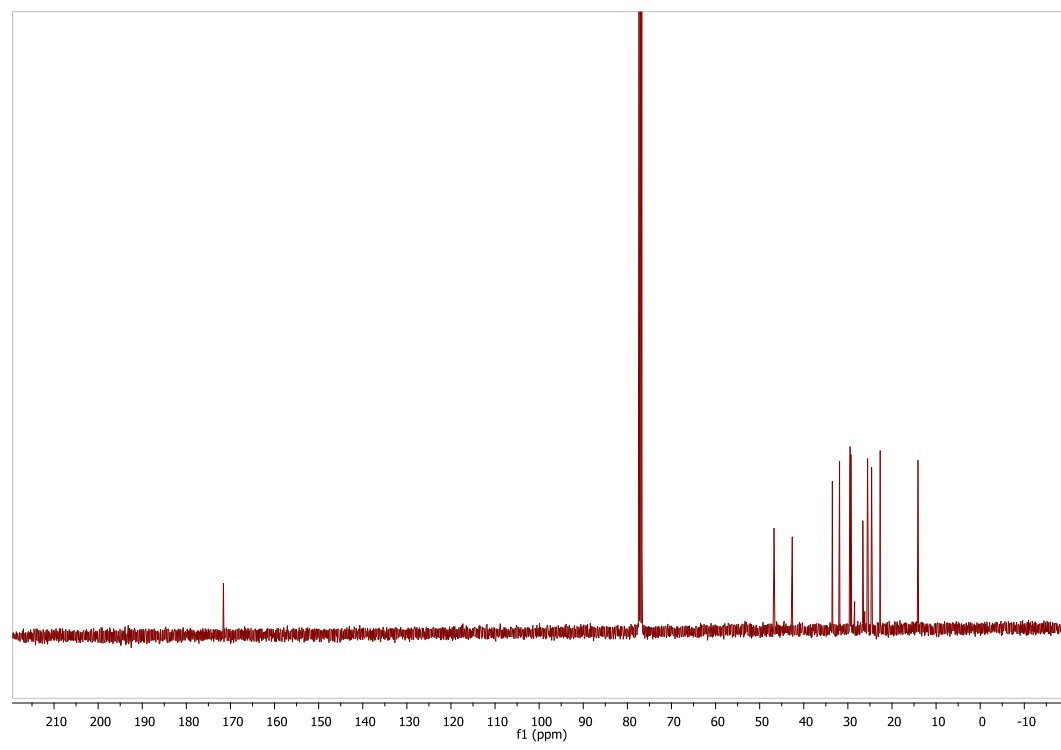
R_f = 0.55 (40% EtOAc/Hexane).

¹H NMR (400 MHz, CDCl₃) δ = 3.51 (t, J = 5.4 Hz, 2H), 3.35 (t, J = 5.5 Hz, 2H), 2.26 (t, J = 7.7 Hz, 2H), 1.65 – 1.43 (m, 8H), 1.34 – 1.15 (m, 12H), 0.83 (t, J = 6.0 Hz, 3H).

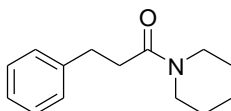
¹³C NMR (101 MHz, CDCl₃) δ = 171.71, 171.71, 77.48, 77.16, 77.16, 76.84, 46.87, 42.73, 33.64, 32.01, 29.69, 29.61, 29.59, 29.41, 28.59, 26.73, 25.73, 25.65, 24.74, 22.79, 14.22.



12 H. Huang, C. M. Morgan, R. N. Asolkar, M. E. Koivunen and P. G. Marrone, *J. Agric. Food Chem.*, 2010, **58**, 9994. The compound is also commercially available.



1-(3-phenylpropanoyl) piperidine¹³ (Table 1, entry 10)



The compound was prepared according to general procedure B and purified by flash chromatography (40% EtOAc/Hexane) to give the product as an oil (155 mg, 71%).

R_f=0.34 (40% EtOAc/Hexane).

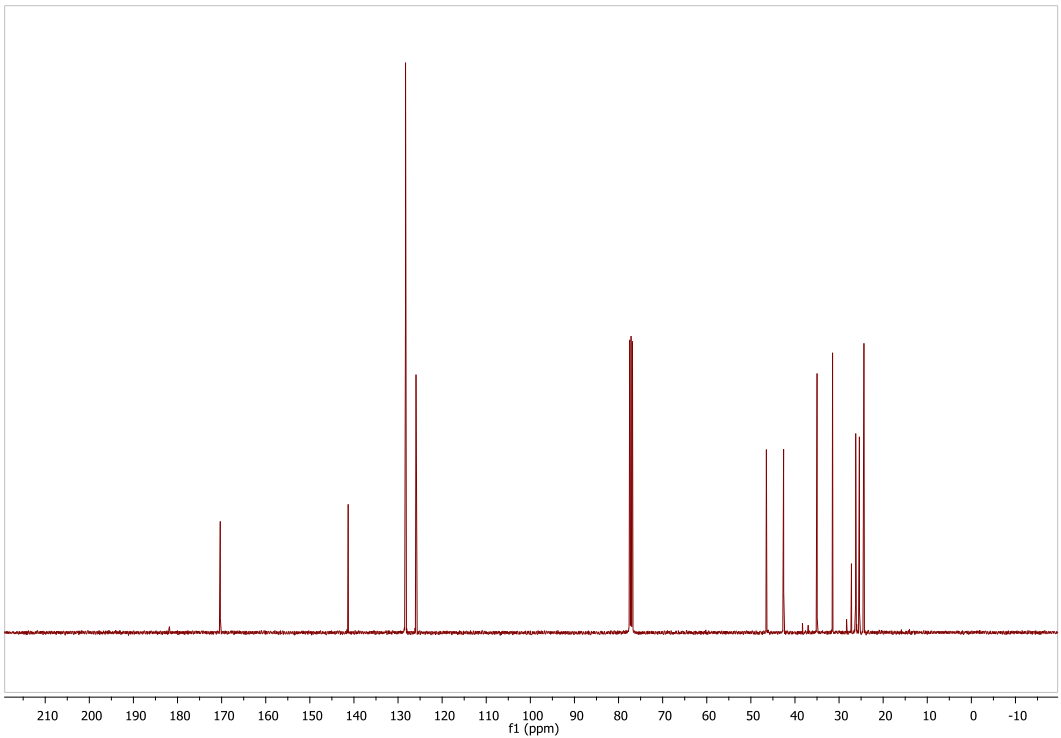
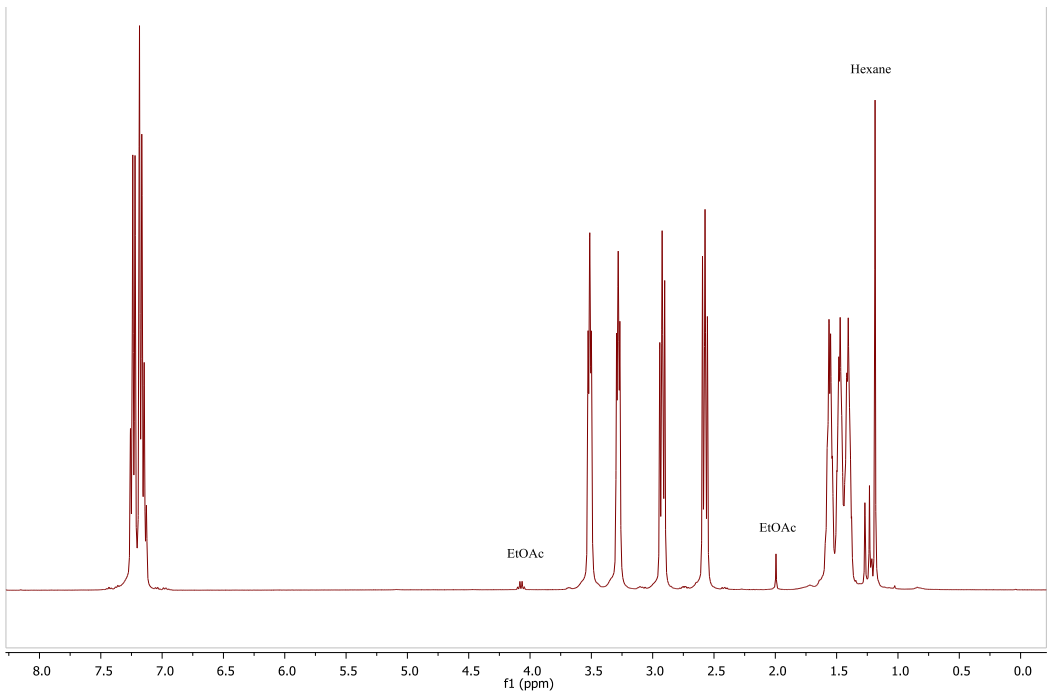
¹H NMR (400 MHz, CDCl₃) δ = 7.41 – 7.13 (m, 5H), 3.56 (t, J = 5.2 Hz, 2H), 3.33 (t, J = 5.4 Hz, 2H), 2.97 (t, J = 8.3 Hz, 2H), 2.62 (t, J = 7.6 Hz, 2H), 1.70 – 1.39 (m, 6H).

¹³C NMR (101 MHz, CDCl₃) δ = 170.49, 141.49, 128.49, 126.11, 46.66, 42.76, 35.17, 31.66, 26.41, 25.57, 24.54.

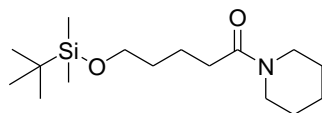
IR (thin film) ν 2999, 2941, 2862, 1626, 1450, 1362, 1244, 1132, 1016 cm⁻¹.

HRMS (ESI) m/z : calcd for C₁₄H₁₉NO, [M+1], 218.1545; found 218.1559

¹³ This compound has been described previously, but sufficient characterization data including HRMS data have not been published.



5-((tert-butyldimethylsilyl)oxy)-1-(piperidin-1-yl) pentan-1-one (Table 1, entry 11)



The compound was prepared according to general procedure B and purified by flash chromatography (20% EtOAc/Hexane) to give the product as an oil (240 mg, 80 %).

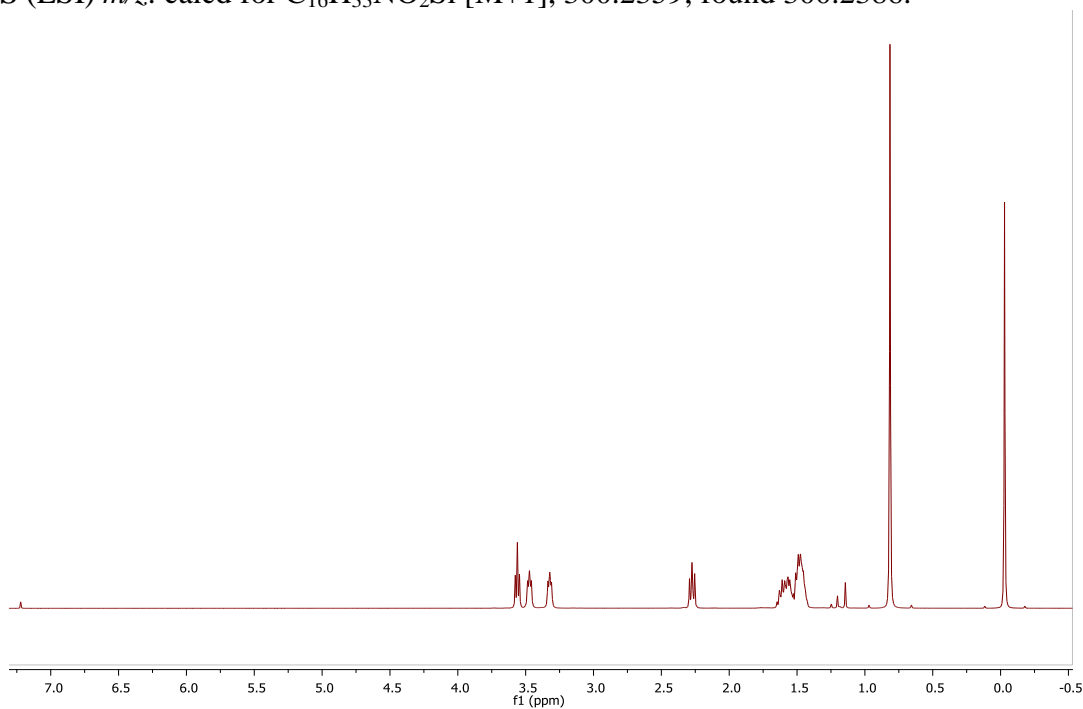
R_f=0.44 (40% EtOAc/Hexane).

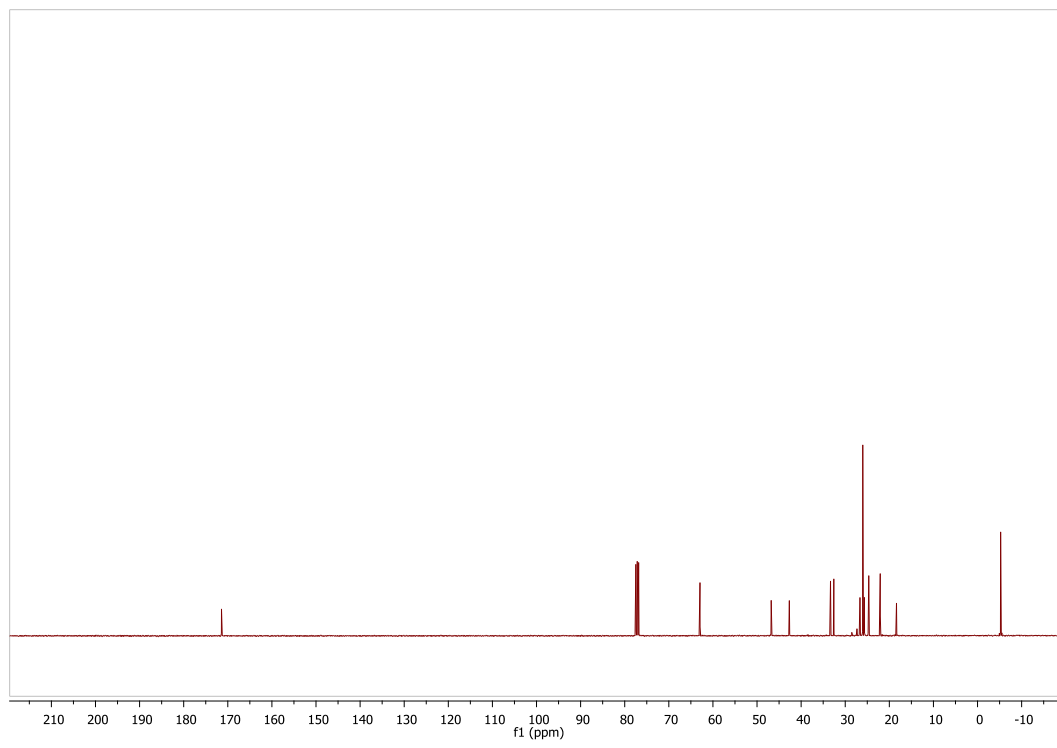
¹H NMR (400 MHz, CDCl₃) δ = 3.60 (t, J = 6.2 Hz, 2H), 3.50 (t, J = 5.3 Hz, 2H), 3.36 (t, J = 5.5 Hz, 2H), 2.31 (t, J = 7.4 Hz, 2H), 1.71 – 1.44 (m, 10H), 0.85 (s, 9H), 0.01 (s, 6H).

¹³C NMR (101 MHz, CDCl₃) δ = 171.43, 62.93, 46.79, 42.81, 33.43, 32.59, 26.78, 26.10, 24.81, 22.06, 18.38, -5.24.

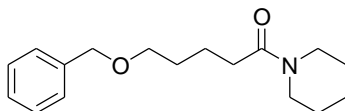
IR (thin film) ν 2995, 2937, 2860, 1624, 1457, 1396, 1359, 1251, 1178, 1099, 1014 cm⁻¹.

HRMS (ESI) m/z : calcd for C₁₆H₃₃NO₂Si [M+1], 300.2359; found 300.2386.





1-[5-(benzyloxy)pentanoyl]piperidine (Table 1, entry 12)



The compound was prepared according to general procedure B but starting from 200 mg (1.14 mmole) of aldehyde. The product was purified by flash chromatography (40% EtOAc/Hexane) to give the product as an oil (226 mg, 72 %).

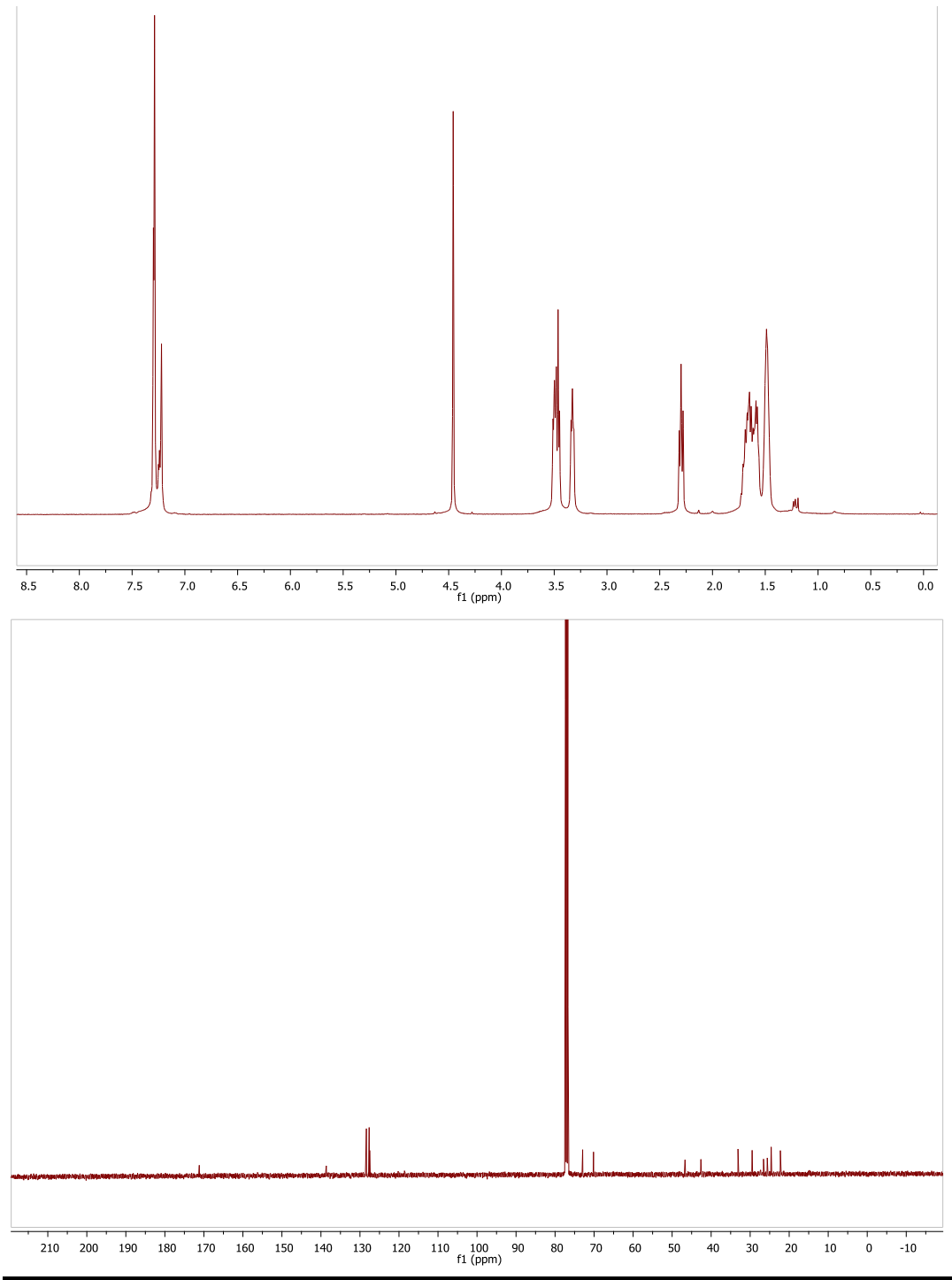
R_f=0.16 (40% EtOAc/Hexane).

¹H NMR (400 MHz, CDCl₃) δ = 7.33 (m, 5H), 4.50 (s, 2H), 3.57 – 3.35 (m, 4H), 3.37 (t, *J* = 5.1 Hz, 2H), 2.34 (t, *J* = 7.2 Hz, 2H), 1.82 – 1.59 (m, 6H), 1.52 (br, 4H).

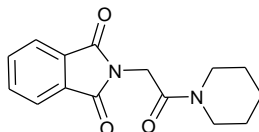
¹³C NMR (101 MHz, CDCl₃) δ = 171.18, 138.62, 128.35, 127.64, 127.50, 72.92, 70.14, 46.69, 42.62, 33.12, 29.49, 26.58, 25.61, 24.61, 22.26.

IR (thin film) ν 3014, 2943, 2866, 1624, 1446, 1362, 1250, 1217, 1095, 1020 cm⁻¹.

HRMS (ESI) *m/z*: calcd for C₁₇H₂₅NO₂, [M+1], 276.1964; found 276.1971



2-(2-oxo-2-piperidin-1-ylethyl)-1*H*-isoindole-1,3(2*H*)-dione^[14] (Table 1, entry 13)



Made according to General Procedure B but using only 1 equiv of piperidine. Under these conditions the product was isolated as a solid (150 mg, 55% yield) after column chromatography. When the experiment was made using 3.2 equiv of piperidine were used the yield was 32%.

The compound was purified by flash chromatography (40% EtOAc/Hexane) to give the product as a solid (149 mg, 55%).

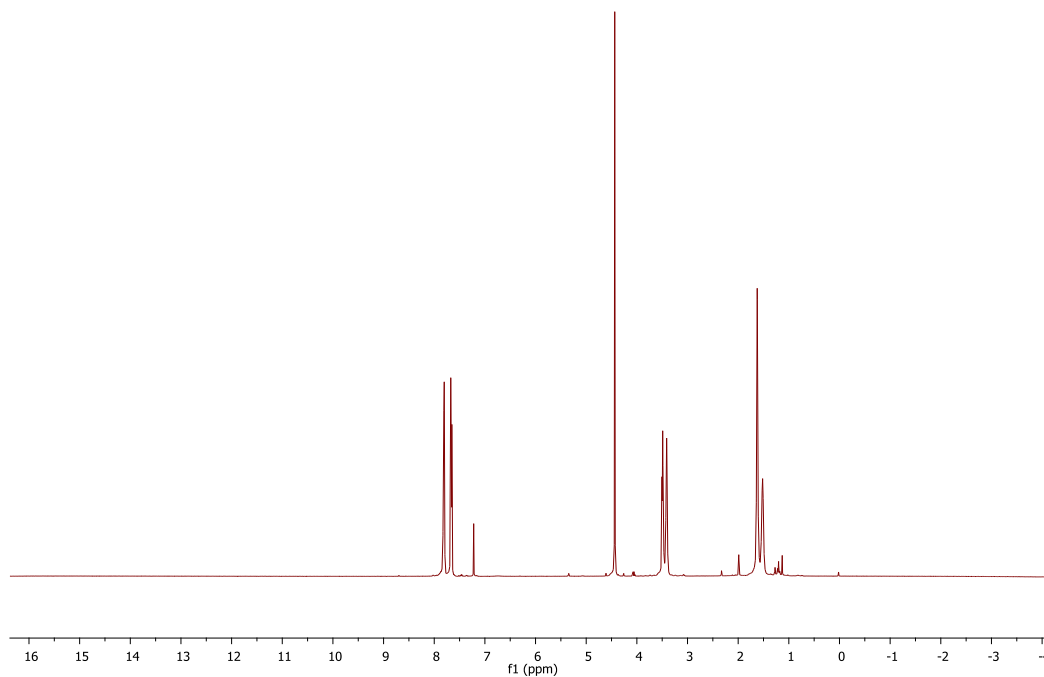
R_f = 0.5 (40% EtOAc/Hexane).

¹H NMR (400 MHz, CDCl₃) δ = 7.85 (dd, J = 5.4, 3.0 Hz, 2H), 7.70 (dd, J = 5.4, 3.1 Hz, 2H), 4.48 (s, 2H), 3.56 – 3.50 (t, J = 5.3 Hz, 2H), 3.45 (s, 2H), 1.66 (s, 4H), 1.56 (s, 2H).

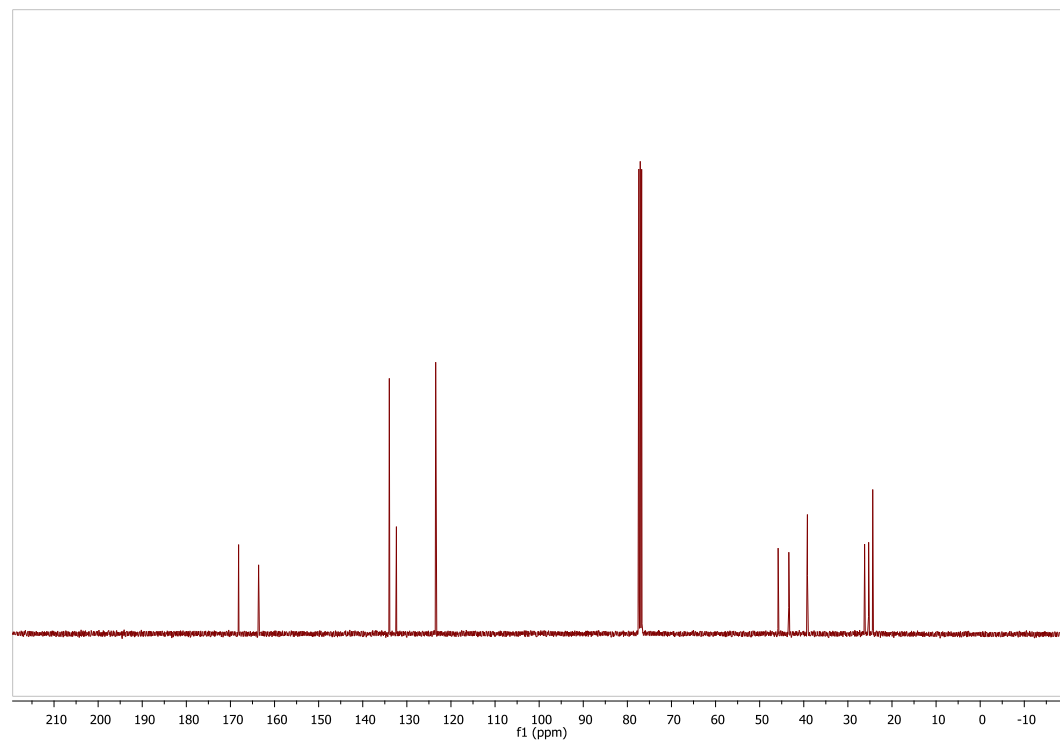
¹³C NMR (101 MHz, CDCl₃) δ = 168.15 , 163.61 , 133.98 , 132.27 , 123.52 , 45.81 , 43.39 , 39.17 , 26.21 , 25.29 , 24.44 .

IR (thin film) ν 3039, 3001, 2943, 2864, 1774, 1718, 1657, 1456, 1431, 1396, 1327, 1238, 1188, 1113, 1080, 1018 cm⁻¹.

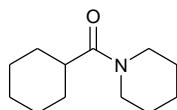
HRMS (ESI) m/z : calcd for C₁₅H₁₆N₂O₃ [M+1], 273.1239; found 273.1244



14 R. Lantsch and D. Arlt, *Synthesis*, 1975, 675.



1-(cyclohexylcarbonyl)piperidine¹⁵ (Table 1, entry 14)



The compound was prepared according to general procedure C and purified by flash chromatography (40% EtOAc/Hexane) to give the product as an oil (169 mg, 87%).

R_f=0.52 (40% EtOAc/Hexane).

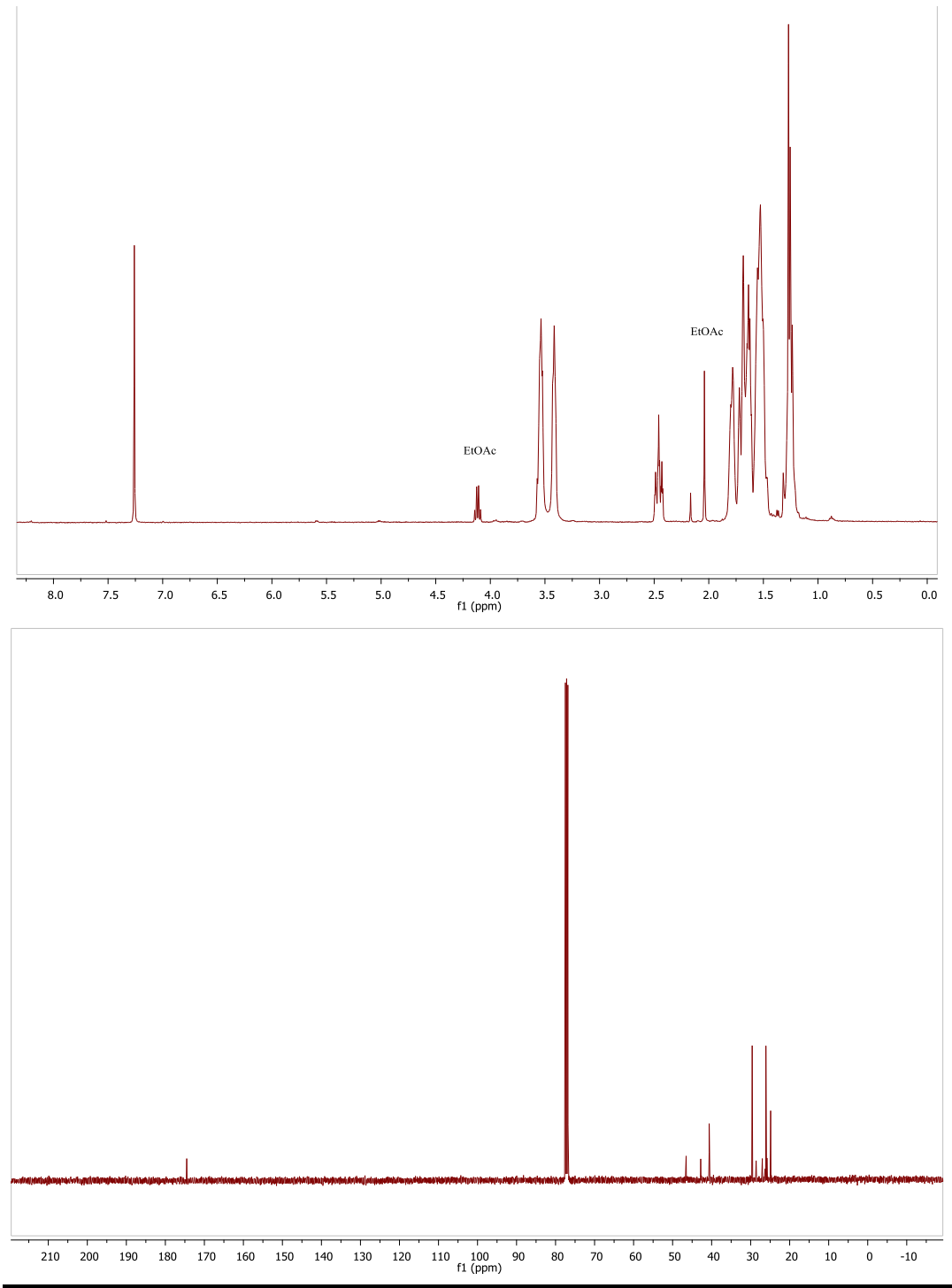
¹H NMR (400 MHz, CDCl₃) δ = 3.55 (t, J = 5.1 Hz, 2H), 3.42 (t, J = 4.9 Hz, 2H), 2.46 (t, J = 11.6 Hz, 1H), 1.86 – 1.44 (m, 12H), 1.32 – 1.19 (m, 4H).

¹³C NMR (101 MHz, CDCl₃) δ = 174.40, 46.41, 42.68, 40.50, 29.48, 28.47, 26.89, 26.18, 25.97, 25.93, 25.68, 24.75.

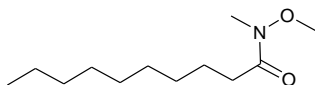
IR (thin film) ν 2996, 2935, 2858, 1618, 1446, 1358, 1254, 1215, 1128, 1012 cm⁻¹.

HRMS (ESI) m/z : calcd for C₁₂H₂₁NO [M+1], 196.3012; found 196.1717

¹⁵ K. Matsumoto, S. Hashimoto and S. Otani, *Angew. Chem. Int. Ed.*, 1986, **98**, 565.



N-methoxy-N-methyldecanamide (Table 1, entry 15)



The compound was prepared according to general procedure C and purified by flash chromatography (40% EtOAc/Hexane) to give the product as yellow oil (194.5 mg, 90%).

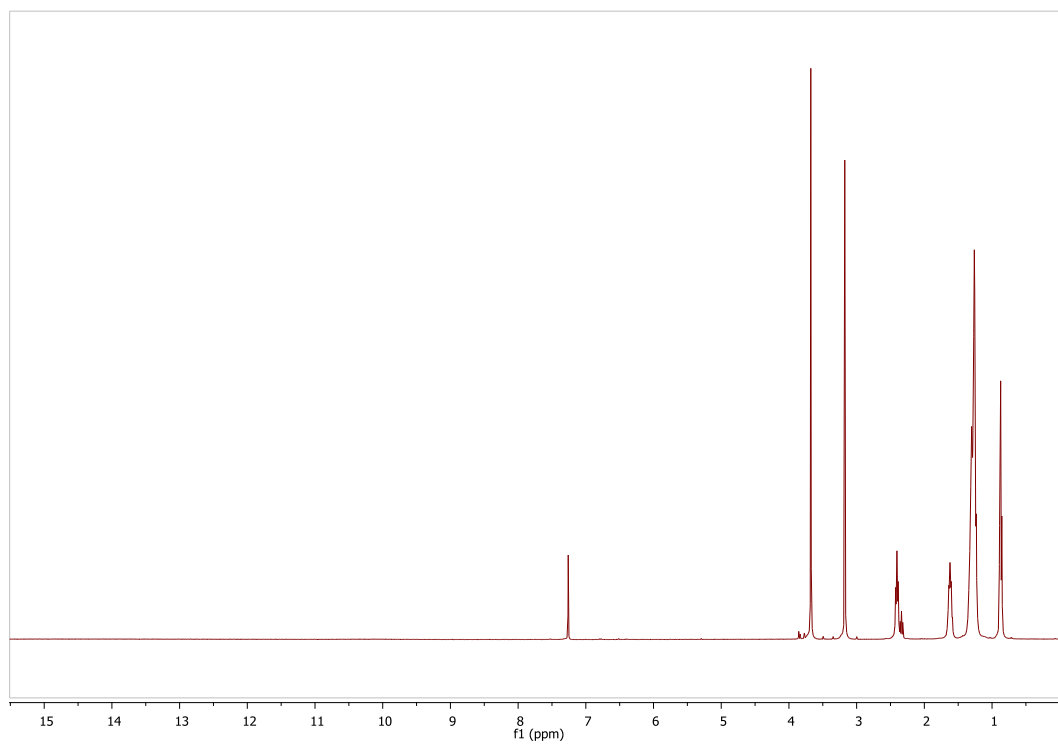
R_f =0.7 (40% EtOAc/Hexane).

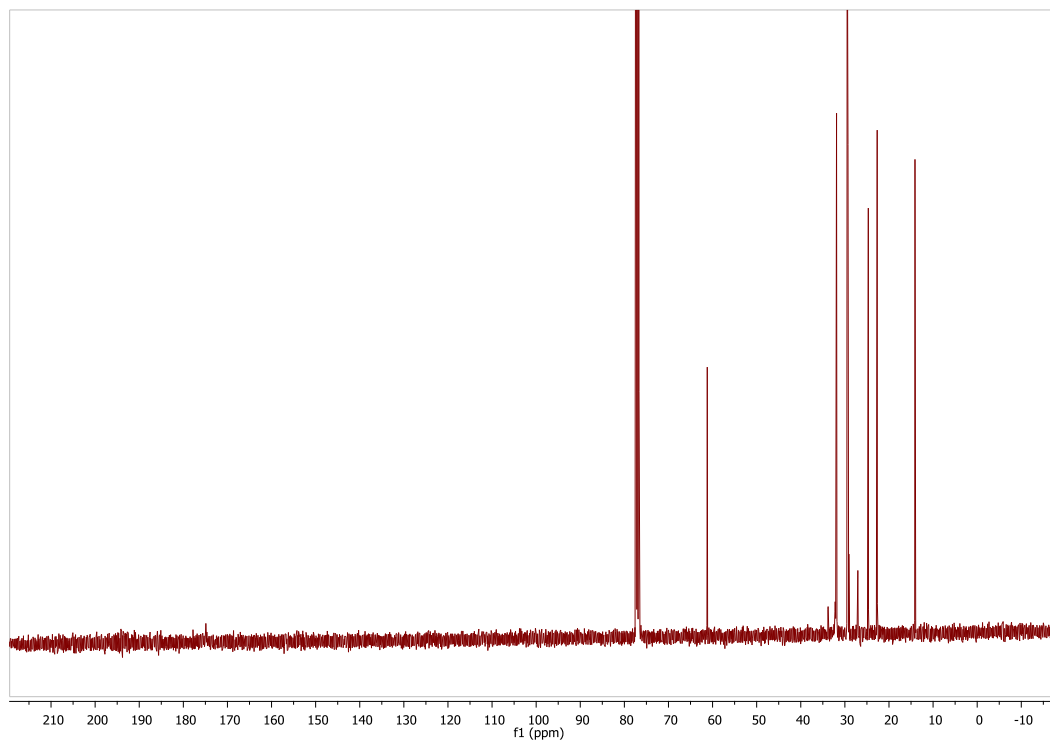
^1H NMR (400 MHz, CDCl_3) δ = 3.68 (s, 3H), 3.18 (s, 3H), 2.40 (t, J =7.5, 2H), 1.70 – 1.55 (m, J =14.3, 7.1, 2H), 1.37 – 1.24 (m, J =16.0, 12H), 0.87 (t, J =6.7, 3H).⁹

^{13}C NMR (101 MHz, CDCl_3) δ = 175.02, 77.16, 61.33, 33.95, 32.02, 29.61, 29.57, 29.54, 29.43, 29.39, 27.19, 24.90, 24.81, 22.80, 14.23.

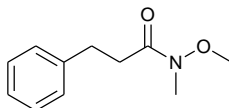
IR (thin film) ν 3004, 2956, 2929, 2856, 1708, 1646, 1463, 1419, 1386, 1178, 1000, 765 cm^{-1} .

HRMS (ESI) m/z : calcd for $\text{C}_{12}\text{H}_{25}\text{NO}_3$ [$\text{M}+1$], 216.1964; found 216.1960





Benzenepropanamide¹⁶ (Table 1, entry 16)



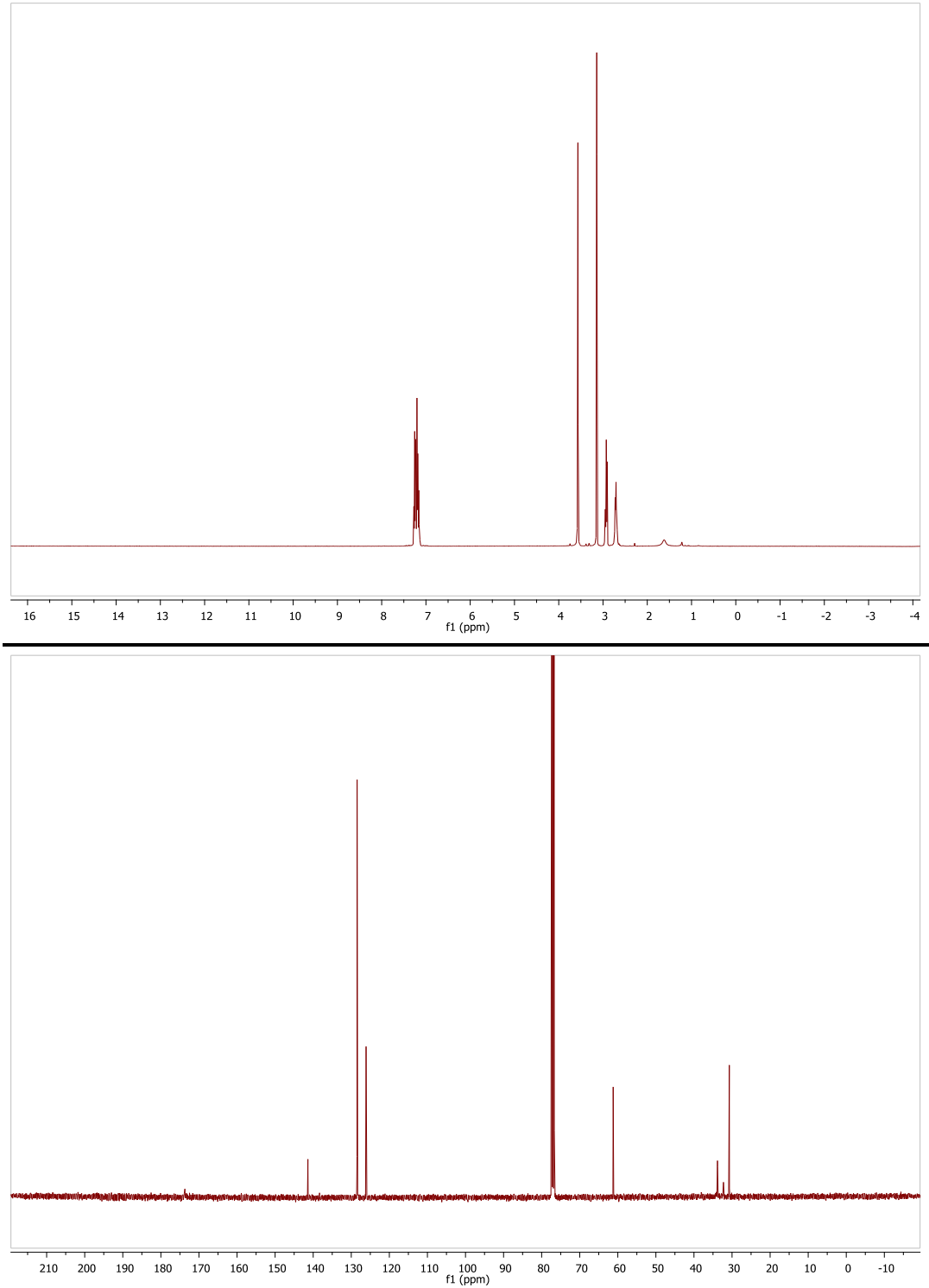
The compound was prepared according to general procedure C and purified by flash chromatography (20% EtOAc/Hexane) to give the product as colorless oil (155 mg, 80.2%).

R_f=0.51 (20% EtOAc/Hexane)

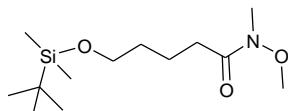
¹H NMR (400 MHz, CDCl₃) δ = 7.34 – 7.19 (m, 5H), 3.62 (s, 3H), 3.20 (s, 3H), 3.02 – 2.94 (m, 2H), 2.76 (t, *J*=7.7, 2H).⁹

¹³C NMR (101 MHz, CDCl₃) δ = 173.82, 141.51, 128.59, 128.58, 126.23, 61.34, 33.95, 32.38, 30.84.

16 P.-C. Chiang, Y. Kim and J. W. Bode. *Chem. Commun.*, 2009, 4566



5-(tert-butyldimethylsilyloxy)-N-methoxy-N-methylpentanamide (Table 1, entry 17)



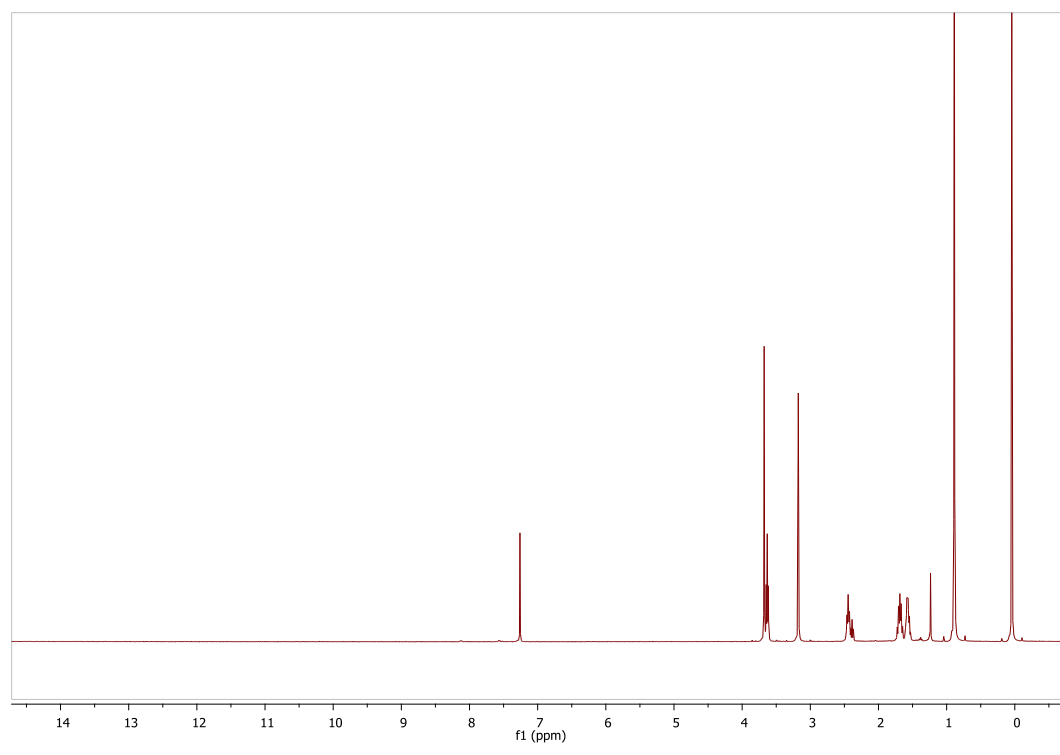
The compound was prepared according to general procedure C but starting from 156mg (0.72 mmole) of aldehyde. The product was purified by flash chromatography (20% EtOAc/Hexane) to give the product as an oil (142.4 mg, 71 %).

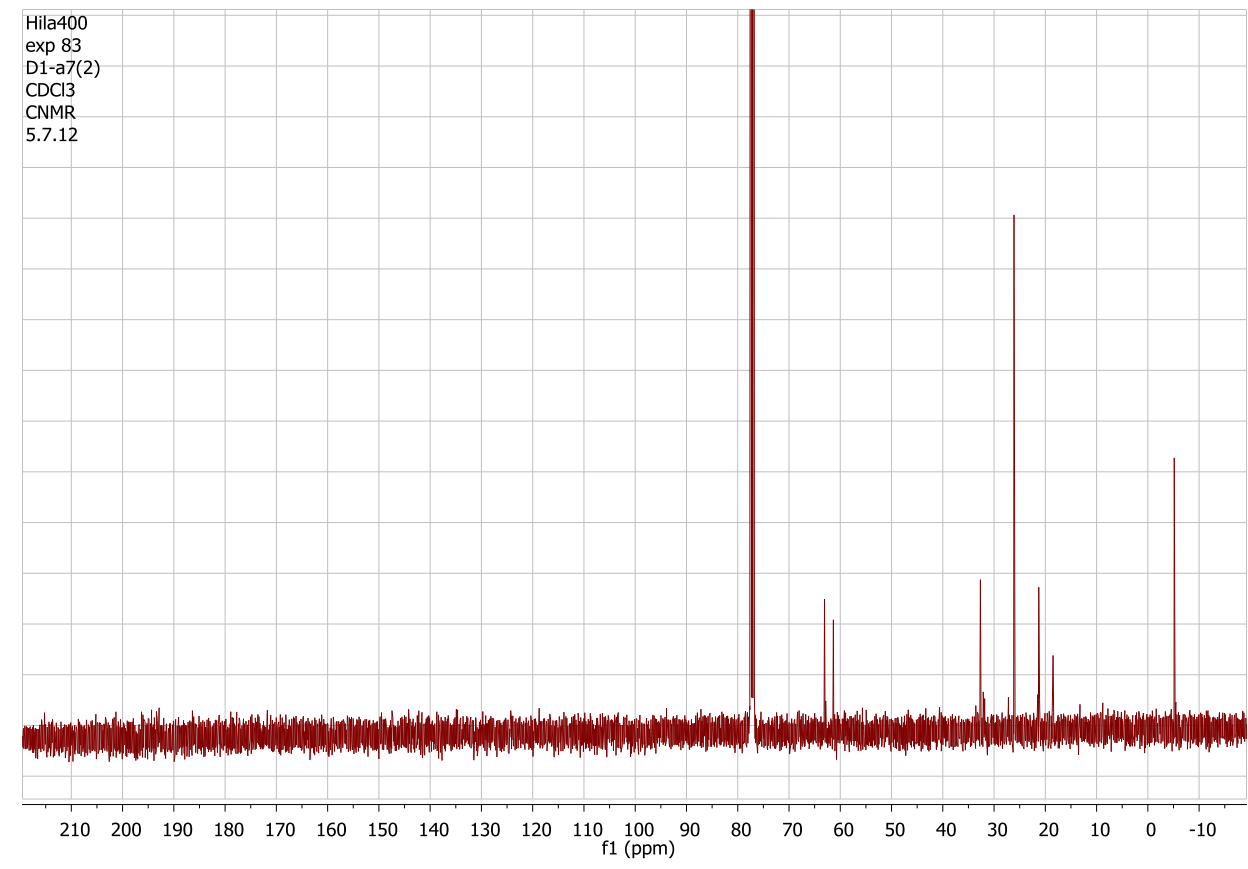
R_f=0.63 (40% EtOAc/Hexane)

¹H NMR (400 MHz, CDCl₃) δ = 3.68 (s, 3H), 3.63 (t, *J*=6.3, 2H), 3.18 (s, 3H), 2.42 (t, *J*=23.0, 2H), 1.73 – 1.64 (m, 2H), 1.60 – 1.52 (m, 2H), 0.89 (s, 9H), 0.04 (s, 6H).⁹

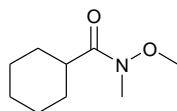
¹³C NMR (101 MHz, CDCl₃) δ= 77.16, 63.07, 62.87, 61.34, 33.64, 32.66, 32.17, 31.85, 27.19, 26.11, 21.50, 21.28, 18.45, -5.08.

HRMS (ESI) *m/z*: calcd for C₁₃H₂₉NO₃Si [M+1], 276.1927; found 276.1993





N-methoxy-N-methylcyclohexanecarboxamide¹⁷ (Table 1, entry 18)



The compound was prepared according to general procedure C and purified by flash chromatography (20% EtOAc/Hexane) to give the product as an orange oil (123 mg, 72%).

R_f =0.65 (20% EtOAc/Hexane)

¹H NMR (400 MHz, CDCl₃) δ = 3.64 (s, 2H), 3.11 (s, 2H), 2.62 (s, 1H), 1.79 – 1.61 (m, J =29.4, 14.9, 4H), 1.41 (q, J =23.4, 11.5, 2H), 1.30 – 1.13 (m, 3H).⁹

¹³C NMR (101 MHz, CDCl₃) δ = 177.74, 77.16, 61.48, 39.96, 32.25, 29.02, 27.17, 27.11, 25.81, 25.77.

¹⁷ T. Niu, W. Zhang, D. Huang, C. Xu, H. Wang and Yulai Hu. *Org. Lett.*, 2009, **11**,

