Electronic Supplementary Information for

(–)-(*S*)-Nakinadine B: First Asymmetric Synthesis

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1. Experimental

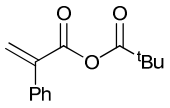
General Experimental Details

Reactions involving moisture-sensitive reagents were carried out under a nitrogen atmosphere using standard vacuum line techniques and glassware that was flame-dried and cooled under nitrogen before use. Solvents were dried according to the procedure outlined by Grubbs and co-workers.[1] Water was purified by an Elix® UV-10 system. BuLi was purchased from Sigma-Aldrich (as a 2.5 M solution in hexanes) and titrated against diphenylacetic acid before use. Thin layer chromatography was performed on aluminium plates coated with 60 F_{254} silica. Flash column chromatography was performed either on Kieselgel 60 silica on a glass column, or on a Biotage SP4 automated flash column chromatography platform.

Melting points were recorded on a Gallenkamp Hot Stage apparatus and are uncorrected. Optical rotations were recorded on a Perkin-Elmer 241 polarimeter with a water-jacketed 10 cm cell. Specific rotations are reported in 10^{-1} deg cm^2 g^{-1} and concentrations in g/100 mL. IR spectra were recorded on a Bruker Tensor 27 FT-IR spectrometer using an ATR module. Selected characteristic peaks are reported in cm^{-1}. UV spectra were recorded on a Perkin-Elmer Lambda 2 UV/Vis spectrometer in MeOH. NMR spectra were recorded on Bruker Avance spectrometers in the deuterated solvent stated. The field was locked by external referencing to the relevant deuteron resonance. Low-resolution mass spectra were recorded on either a VG MassLab 20-250 or a Micromass Platform 1 spectrometer. Accurate mass measurements were run on either a Bruker MicroTOF internally calibrated with polyalanine, or a Micromass GCT instrument fitted with a Scientific Glass Instruments BPX5 column (15 m × 0.25 mm) using amyl acetate as a lock mass.

Experimental Data

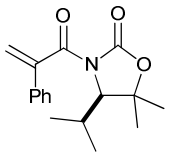
2-Phenylacrylic pivalic anhydride 2



Et_3N (1.88 mL, 13.5 mmol) and pivaloyl chloride (1.67 mL, 13.5 mmol) were added sequentially to a solution of atropic acid (2.00 g, 13.5 mmol) in THF (35 mL) at 0 °C. The resultant suspension was stirred at 0 °C for 1 h and then filtered. The filter cake was washed with THF (20 mL) and the filtrate was concentrated *in vacuo*. 30–40 °C Petrol (20 mL) was added to the residue, the resultant suspension was filtered, and the filtrate was concentrated *in vacuo* to give **2** as a yellow oil (2.78 g, 89%); δ_H (400 MHz, $CDCl_3$) 1.26 (9H, s, C*Me*$_3$), 6.09 (1H, d, *J* 1.0, C(3)*H*$_A$), 6.46 (1H, d, *J* 1.0, C(3)*H*$_B$), 7.36–7.46 (5H, m, *Ph*).

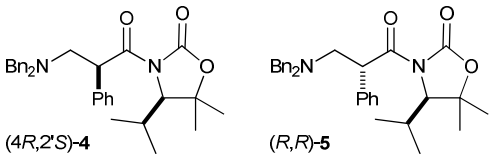
[1] A. B. Pangborn, M. A. Giardello, R. H. Grubbs, R. K. Rosen and F. J. Timmers, *Organometallics*, 1996, **15**, 1518.

(*R*)-*N*(3)-(2′-Phenylacryloyl)-4-isopropyl-5,5-dimethyloxazolidin-2-one 3



BuLi (2.50 M in hexanes, 5.28 mL, 13.2 mmol) was added dropwise via syringe to a stirred solution of **1** (1.89 g, 12.0 mmol) in THF (30 mL) at −78 °C. After stirring for 10 min, a solution of **2** (2.78 g, 12.0 mmol) in THF (10 mL) −78 °C was added dropwise via cannula. After a further 30 min, the cooling bath was removed and reaction mixture was left to warm to rt over 2 h, before the sequential addition of satd aq NH_4Cl (5 mL) and H_2O (10 mL). The layers were separated and the aqueous layer was extracted with EtOAc (2 × 20 mL). The combined organic extracts were washed with brine (10 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification via flash column chromatography (eluent 30–40 °C petrol/EtOAc, 4:1) gave **3** as a white solid (2.79 g, 72% from atropic acid, 81% from **1**);[2] mp 70–72 °C; {lit.[2] for enantiomer mp 73–74 °C}; $[\alpha]_D^{25}$ −68.0 (*c* 1.0 in $CHCl_3$); {lit.[2] for enantiomer $[\alpha]_D^{25}$ +70.8 (*c* 0.6 in $CHCl_3$)}; δ_H (400 MHz, $CDCl_3$) 1.00 (3H, d, *J* 6.8, CH*Me*$_A$), 1.15 (3H, d, *J* 6.8, CH*Me*$_B$), 1.39 (3H, s, C(5)*Me*$_A$), 1.52 (3H, s, C(5)*Me*$_B$), 2.20–2.27 (1H, m, C*H*Me$_2$), 4.25 (1H, d, *J* 3.1, C(4)*H*), 5.47 (1H, s, C(3′)*H*$_A$), 5.77 (1H, s, C(3′)*H*$_B$), 7.27–7.53 (5H, m, *Ph*).

(4*R*,2′*S*)-and (*R*,*R*)-*N*(3)-(2′-Phenyl-3′-*N*,*N*-dibenzylamino)propanoyl-4-isopropyl-5,5-dimethyloxazolidin-2-one (4*R*,2′*S*)-4 and (*R*,*R*)-5

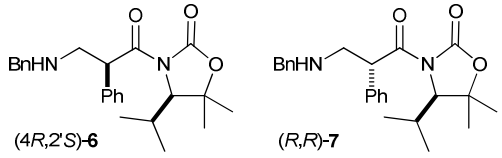


BuLi (2.30 M in hexanes, 37.3 mL, 85.9 mmol) was added dropwise via syringe to a stirred solution of dibenzylamine (17.4 mL, 90.4 mmol) in THF (250 mL) at −78 °C. After stirring for 30 min, a solution of **3** (13.0 g, 45.2 mmol) in THF (200 mL) at −78 °C was added dropwise via cannula and the resultant mixture was left to stir for a further 4 h at −78 °C, before the addition of 2-pyridone (13.0 g, 136 mmol) and the reaction mixture was left to warm to rt over 16 h. Et_2O (300 mL) was added and the resultant solution was washed sequentially with 10% aq citric acid (100 mL), satd aq $NaHCO_3$ (100 mL) and brine (100 mL), then dried ($MgSO_4$) and concentrated *in vacuo* to give an 87:13 mixture of **4** and **5**. Purification via flash column chromatography (gradient elution, 1% → 10% Et_2O in 30–40 °C petrol) gave **4** as a colourless oil (13.8 g,

[2] J. E. Beddow, S. G. Davies, K. B. Ling, P. M. Roberts, A. J. Russell, A. D. Smith and J. E. Thomson, *Org. Biomol. Chem.*, 2007, **5**, 2812.

63%, >99:1 dr);[3,4] $[\alpha]_D^{25}$ −5.1 (*c* 1.0 in $CHCl_3$); ν_{max} 1768 (C=O, exocyclic), 1697 (C=O, endocyclic); δ_H (400 MHz, $CDCl_3$) 0.96 (3H, s, C(5)*Me*$_A$), 1.08 (3H, d, *J* 6.9, CH*Me*$_A$), 1.16 (3H, d, *J* 6.9, CH*Me*$_B$), 1.46 (3H, s, C(5)*Me*$_B$), 2.14–2.26 (1H, m, C*H*Me$_2$), 2.87 (1H, dd, *J* 12.9, 6.1, C(3′)*H*$_A$), 3.43 (1H, dd, *J* 12.9, 8.3, C(3′)*H*$_B$), 3.72 (4H, app s, N(C*H*$_2$Ph)$_2$), 4.06 (1H, d, *J* 3.0, C(4)*H*), 5.59 (1H, dd, *J* 8.3, 6.1, C(2′)*H*), 7.22–7.36 (15H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 17.1 (CH*Me*$_B$), 21.2 (C(5)*Me*$_A$), 21.5 (CH*Me*$_A$), 28.1 (C(5)*Me*$_B$), 29.4 (*C*HMe$_2$), 46.9 (C(2′)), 57.0 (*C*(3′)), 58.2 (N(*C*H$_2$Ph)$_2$), 67.0 (*C*(4)), 82.7 (*C*(5)), 126.7, 127.3 (*p-Ph*), 128.0, 128.4, 128.6, 128.9 (*o*,*m-Ph*), 137.3, 138.9, 139.0, (*i-Ph*), 153.4 (*C*(2)), 173.2 (*C*(1′)); *m/z* (ESI^+) 485 ($[M+H]^+$, 100%); HRMS (ESI^+) $C_{31}H_{37}N_2O_3^+$ ($[M+H]^+$) requires 485.2799; found 485.2785. Further elution gave **5** as a colourless oil (1.99 g, 9%, >99:1 dr);[3,4] $[\alpha]_D^{25}$ +7.4 (*c* 2.0 in $CHCl_3$); ν_{max} 1768 (C=O, exocyclic), 1697 (C=O, endocyclic); δ_H (400 MHz, $CDCl_3$) 0.59 (3H, d, *J* 6.9, CH*Me*$_A$), 0.79 (3H, d, *J* 6.9, CH*Me*$_B$), 1.48 (3H, s, C(5)*Me*$_A$), 1.49 (3H, s, C(5)*Me*$_B$), 1.93–2.06 (1H, m, C*H*Me$_2$), 2.90 (1H, dd, *J* 13.1, 6.1, C(3′)*H*$_A$), 3.41 (1H, dd, *J* 13.1, 8.6, C(3′)*H*$_B$), 3.66 (4H, AB system, J_{AB} 13.6, N(C*H*$_2$Ph)$_2$), 4.26 (1H, d, *J* 3.0, C(4)*H*), 5.52 (1H, dd, *J* 8.6, 6.1, C(2′)*H*), 7.20–7.41 (15H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 16.3 (CH*Me*$_B$), 21.2 (C(5)*Me*$_A$), 21.3 (CH*Me*$_A$), 28.7 (C(5)*Me*$_B$), 29.7 (*C*HMe$_2$), 47.2 (C(2′)), 56.9 (*C*(3′)), 58.1 (N(*C*H$_2$Ph)$_2$), 65.8 (*C*(4)), 82.3 (*C*(5)), 126.8, 127.2 (*p-Ph*), 128.1, 128.3, 128.9 (*o*,*m-Ph*), 137.4, 139.0 (*i-Ph*), 153.1 (*C*(2)), 173.6 (*C*(1′)); *m/z* (ESI^+) 485 ($[M+H]^+$, 100%); HRMS (ESI^+) $C_{31}H_{37}N_2O_3^+$ ($[M+H]^+$) requires 485.2799; found 485.2785.

(4*R*,2′*S*)-and (*R*,*R*)-*N*(3)-(2′-Phenyl-3′-*N*-benzylamino)propanoyl-4-isopropyl-5,5-dimethyloxazolidin-2-one (4*R*,2′*S*)-6 and (*R*,*R*)-7



Method A. *Step 1.* BuLi (2.2 M in hexanes, 3.30 mL, 7.28 mmol) was added dropwise to a stirred solution of dibenzylamine (1.47 mL, 7.67 mmol) in THF (60 mL) at −78 °C under nitrogen. After stirring for 30 min, a solution of **3** (1.10 g, 3.83 mmol) in THF (50 mL) at −78 °C was added dropwise via cannula. The reaction mixture was stirred for 4 h at −78 °C, before the addition of 2-pyridone (1.09 g, 11.5 mmol). The resultant

[3] J. E. Beddow, S. G. Davies, K. B. Ling, P. M. Roberts, A. J. Russell, A. D. Smith and J. E. Thomson, *Org. Biomol. Chem.*, 2007, **5**, 2812.

[4] We have previously assigned **5** as being the major diastereoisomer resulting from this process by chemical correlation to 2-phenyl-3-aminopropanoic acid and comparison of specific rotation values. Unfortunately, further analysis of specific rotation data reported for the enantiomers of 2-phenyl-3-aminopropanoic acid revealed several discrepancies in the sign of the specific rotation, resulting in our initial configurational assignment being in error. Herein, the single crystal X-ray diffraction structure of **4**·HBF_4 unambiguously establishes the relative configuration within the major diastereoisomeric product **4**, and hence the absolute configuration of the synthetic nakinadine B (*S*)-**11**.

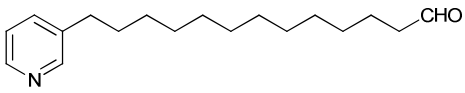
mixture was allowed to warm to rt over 16 h. Et_2O (50 mL) was added and the resultant solution was washed sequentially with 10% aq citric acid (30 mL), satd aq $NaHCO_3$ (30 mL) and brine (30 mL), then dried ($MgSO_4$) and concentrated *in vacuo* to give an 87:13 mixture of **4** and **5** (1.85 g).

Step 2. CAN (4.41 g, 8.05 mmol) was added to a solution of the 87:13 mixture of **4** and **5** (1.85 g, 3.83 mmol) in MeCN (50 mL) and H_2O (10 mL) at rt. The reaction mixture was stirred at rt for 16 h, before the addition of satd aq $NaHCO_3$ (40 mL). The resultant mixture was stirred vigorously for 20 min. The organic layer was decanted off and brine (40 mL) was added to the aqueous layer. The resultant solution was extracted with EtOAc (3 × 40 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo* to give an 87:13 mixture of **6** and **7**. Purification via flash column chromatography (eluent 30–40 °C petrol/Et_2O/Et_3N, 74:25:1) gave **6** as a colourless oil (1.10 g, 73% from **3**, >99:1 dr); $[\alpha]_D^{20}$ −89.8 (*c* 1.0 in $CHCl_3$); ν_{max} 1772 (C=O, exocyclic), 1697 (C=O, endocyclic); δ_H (400 MHz, $CDCl_3$) 1.00 (3H, d, *J* 6.9, CH*Me*$_A$), 1.03 (3H, s, C(5)*Me*$_A$), 1.10 (3H, d, *J* 6.9, CH*Me*$_B$), 1.45 (3H, s, C(5)*Me*$_B$), 1.57 (1H, br s, N*H*), 2.09–2.21 (1H, m, C*H*Me$_2$), 2.97 (1H, dd, *J* 11.9, 6.0, C(3′)*H*$_A$), 3.40 (1H, dd, *J* 11.9, 9.1, C(3′)*H*$_B$), 3.85 (2H, app s, NC*H*$_2$Ph), 4.08 (1H, d, *J* 3.3, C(4)*H*), 5.38 (1H, dd, *J* 9.1, 6.0, C(2′)*H*), 7.20–7.38 (10H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 17.1 (CH*Me*$_B$), 21.3 (C(5)*Me*$_A$), 21.6 (CH*Me*$_A$), 28.3 (C(5)*Me*$_B$), 29.5 (*C*HMe$_2$), 49.2 (*C*(2′)), 52.7 (*C*(3′)), 53.4 (N*C*H$_2$Ph), 67.0 (*C*(4)), 82.7 (*C*(5)), 126.8, 127.5 (*p-Ph*), 128.0, 128.3, 128.6, 128.6 (*o*,*m-Ph*), 136.9, 140.2 (*i-Ph*), 153.2 (*C*(2)), 173.7 (*C*(1′)); *m/z* (ESI$^+$) 395 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{24}H_{31}N_2O_3^+$ ([M+H]$^+$) requires 395.2329; found 395.2324. Further elution gave **7** as a pale yellow oil (0.14 g, 9% from **3**, >99:1 dr); $[\alpha]_D^{20}$ +20.2 (*c* 1.0 in $CHCl_3$); ν_{max} 1771 (C=O, exocyclic), 1698 (C=O, endocyclic); δ_H (400 MHz, $CDCl_3$) 0.63 (3H, d, *J* 6.9, CH*Me*$_A$), 0.83 (3H, d, *J* 6.9, CH*Me*$_B$), 1.42 (3H, s, C(5)*Me*$_A$), 1.46 (3H, s, C(5)*Me*$_B$), 1.76 (1H, br s, N*H*), 1.98–2.09 (1H, m, C*H*Me$_2$), 2.96 (1H, dd, *J* 11.9, 5.8 C(3′)*H*$_A$), 3.39 (1H, dd, *J* 11.9, 9.4, C(3′)*H*$_B$), 3.81 (2H, app s, NC*H*$_2$Ph), 4.24 (1H, d, *J* 2.8, C(4)*H*), 5.38 (1H, dd, *J* 9.4, 5.8, C(2′)*H*), 7.20–7.35 (8H, m, *Ph*), 7.43–7.48 (2H, m, *Ph*); δ_C (100 MHz, $CDCl_3$) 16.3 (CH*Me*$_A$), 21.3 (C(5)*Me*$_B$), 21.3 (CH*Me*$_B$), 28.8 (C(5)*Me*$_A$), 29.7 (*C*HMe$_2$), 49.2 (*C*(2′)), 52.2 (C(3′)), 53.6 (N*C*H$_2$Ph), 66.0 (*C*(4)), 82.6 (*C*(5)), 126.9, 127.5 (*p-Ph*), 128.0, 128.3, 128.5, 128.8, (*o*,*m-Ph*), 137.0, 140.0 (*i-Ph*), 153.2 (*C*(2)), 173.9 (*C*(1′)); *m/z* (ESI$^+$) 395 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{24}H_{31}N_2O_3^+$ ([M+H]$^+$) requires 395.2329; found 395.2317.

Method B. CAN (1.90 g, 3.47 mmol) was added to a solution of **4** (0.80 g, 1.65 mmol) in MeCN (25 mL) and H_2O (5 mL) at rt. The reaction mixture was stirred at rt for 16 h, before the addition of satd aq $NaHCO_3$ (20 mL). The resultant mixture was stirred vigorously for 20 min. The organic layer was decanted off and brine (20 mL) was added to the aqueous layer. The resultant solution was extracted with EtOAc (3 × 20 mL).

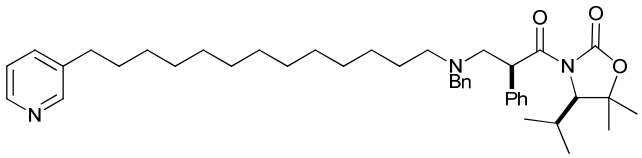
The combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo*. Purification via flash column chromatography (eluent 30–40 °C petrol/Et_2O/Et_3N, 74:25:1) gave **6** as a colourless oil (0.49 g, 76%, >99:1 dr).

13-(Pyridin-3′-yl)tridecanal 8



IBX (2.07 g, 7.39 mmol) was added to a solution of 13-(pyridin-3′-yl)tridecan-1-ol[5] (0.68 g, 2.46 mmol) in EtOAc (15 mL) at rt and the reaction mixture was stirred at 80 °C for 3 h, before being cooled to rt and filtered though Celite® (eluent EtOAc, ~30 mL) and the filtrate was concentrated *in vacuo* to give **8** as a yellow oil (0.67 g, 99%); δ_H (400 MHz, $CDCl_3$) 1.22–1.37 (16H, m, C(4)H_2–C(11)H_2), 1.56–1.68 (4H, m, C(3)H_2, C(12)H_2), 2.43 (2H, td, *J* 7.4, 1.9, C(2)H_2), 2.61 (2H, t, *J* 7.7, C(13)H_2), 7.19–7.24 (1H, m, C(5′)*H*), 7.48–7.53 (1H, m, C(4′)*H*), 8.41–8.47 (2H, m, C(2′)*H*, C(6′)*H*), 9.77 (1H, t, *J* 1.9, C(1)*H*).

(4*R*,2′*S*)-*N*(3)-{2′-Phenyl-3′-[*N*-benzyl-*N*-13″-(pyridin-3‴-yl)tridecylamino]propanoyl}-4-isopropyl-5,5-dimethyloxazolidin-2-one 9

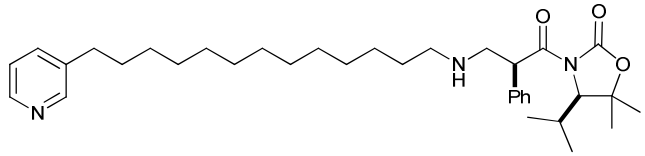


A solution of **6** (0.64 g, 1.62 mmol) in 1,2-dichloroethane (10 mL) was added to a stirred solution of **8** (0.67 g, 2.44 mmol) in 1,2-dichloroethane (10 mL) at rt. After 5 min, AcOH (0.1 mL) and $NaBH(OAc)_3$ (0.69 g, 3.23 mmol) were added and the resultant mixture was stirred at rt for 16 h, before the addition of satd aq $NaHCO_3$ (30 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo*. Purification via flash column chromatography (eluent 30–40 °C petrol/Et_2O/Et_3N, 59:40:1) gave **9** as a yellow oil (0.90 g, 85%, >99:1 dr); $[\alpha]_D^{20}$ −26.2 (*c* 1.0 in $CHCl_3$); ν_{max} 1774 (C=O, exocyclic), 1700 (C=O, endocyclic); δ_H (400 MHz, $CDCl_3$) 0.96 (3H, s, C(5)Me_A), 1.02 (3H, d, *J* 6.9, CHMe_A), 1.11 (3H, d, *J* 6.9, CHMe_B), 1.14–1.38 (18H, m, C(3″)H_2–C(11″)H_2), 1.39–1.51 (5H, m, C(12″)H_2, C(5)Me_B), 1.62 (2H, quintet, *J* 7.3, C(2″)H_2), 2.09–2.21 (1H, m, C*H*Me$_2$), 2.36–2.45 (1H, m, C(1″)H_A), 2.47–2.56 (1H, m, C(1″)H_B), 2.60 (2H, t, *J* 7.8, C(13″)H_2), 2.67 (1H, dd, *J* 12.8, 4.8, C(3′)H_A), 3.46 (1H, dd, *J* 12.8, 9.7, C(3′)H_B), 3.59 (1H, d, *J* 13.7,

[5] B. J. Shorey, V. Lee and J. E. Baldwin, *Tetrahedron*, 2007, **63**, 5587.

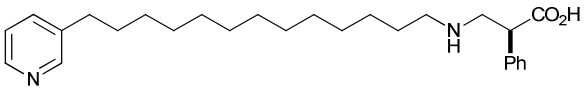
NC*H*$_A$H$_B$Ph), 3.77 (1H, d, *J* 13.7, NCH$_A$*H*$_B$Ph), 4.06 (1H, d, *J* 3.0, C(4)*H*), 5.52 (1H, dd, *J* 9.7, 4.8, C(2′)*H*), 7.16–7.34 (11H, m, C(5‴)*H*, *Ph*), 7.45–7.50 (1H, m, C(4‴)*H*), 8.40–8.48 (2H, m, C(2‴)*H*), C(6‴)*H*); δ_C (100 MHz, $CDCl_3$) 17.0 (CH*Me*$_A$), 21.2 (C(5)*Me*$_B$), 21.4 (CH*Me*$_B$), 26.7 (C(5)*Me*$_A$), 27.2 (*C*HMe$_2$), 29.1, 29.3, 29.5 (C(3″)-C(12″)), 31.1 (C(2″)), 32.9 (C(13″)), 47.0 (*C*(2′)), 53.8 (C(1″)), 58.0 (*C*(3′)), 58.7 (N*C*H$_2$Ph), 66.9 (*C*(4)), 82.5 (*C*(5)), 123.1 (*C*(5‴)), 126.6, 127.2 (*p-Ph*), 127.8, 128.4, 128.9 (*o*,*m-Ph*), 135.6 (*C*(4‴)), 137.4, 137.9, 139.4 (*i-Ph*, *C*(3‴)), 147.1 (*C*(6‴)), 149.9 (*C*(2‴)), 153.4 (*C*(2)), 173.5 (*C*(1′)); *m/z* (ESI$^+$) 654 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{42}H_{60}N_3O_3^+$ ([M+H]$^+$) requires 654.4629; found 654.4625.

(4*R*,2′*S*)-*N*(3)-{2′-Phenyl-3′-[*N*-13″-(pyridin-3‴-yl)tridecylamino]propanoyl}-4-isopropyl-5,5-dimethyloxazolidin-2-one 10



CAN (705 mg, 1.29 mmol) was added to a solution of **9** (400 mg, 0.61 mmol) in MeCN (10 mL) and H_2O (2 mL) at rt. The reaction mixture was stirred for 16 h, before the addition of satd aq $NaHCO_3$ (10 mL). The reaction mixture was stirred vigorously for 20 min. The organic layer was decanted off and brine (10 mL) was added to the aqueous layer. The resultant solution was extracted with EtOAc (3 × 20 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo*. Purification via flash column chromatography (eluent $CHCl_3$/NH_4OH, 99:1) gave **10** as a colourless oil (245 mg, 71%, >99:1 dr); $[\alpha]_D^{20}$ −57.3 (*c* 1.0 in $CHCl_3$); ν_{max} 1774 (C=O, exocyclic), 1700 (C=O, endocyclic); δ_H (500 MHz, $CDCl_3$) 0.99 (3H, d, *J* 6.9, CH*Me*$_A$), 1.01 (3H, s, C(5)*Me*$_A$), 1.08 (3H, d, *J* 6.9, CH*Me*$_B$), 1.17–1.36 (18H, m, C(3″)*H*$_2$–C(11″)*H*$_2$), 1.38–1.48 (5H, m, C(12″)*H*$_2$, C(5)*Me*$_B$), 1.61 (2H, quintet, *J* 7.4, C(2″)*H*$_2$), 2.09–2.19 (1H, m, C*H*Me$_2$), 2.55–2.71 (4H, m, C(1″)*H*$_2$), C(13″)*H*$_2$), 2.93 (1H, dd, *J* 12.1, 6.0, C(3′)*H*$_A$), 3.36 (1H, dd, *J* 12.1, 9.1, C(3′)*H*$_B$), 4.07 (1H, d, *J* 3.15, C(4)*H*), 5.33 (1H, dd, *J* 9.1, 6.0, C(2′)*H*), 7.16–7.37 (6H, m, C(5‴)*H*, *Ph*), 7.46–7.50 (1H, m, C(4‴)*H*), 8.41–8.46 (2H, m, C(2‴)*H*), C(6‴)*H*); δ_C (125 MHz, $CDCl_3$) 17.0 (CH*Me*$_A$), 21.2 (C(5)*Me*$_B$), 21.6 (CH*Me*$_B$), 28.3 (C(5)*Me*$_A$), 29.4 (*C*HMe$_2$), 29.1, 29.5, 29.6, 30.1 (C(3″)-C(12″)), 31.1 (C(2″)), 33.0 (C(13″)), 49.1 (*C*(2′)), 49.4 (C(1″)), 53.3 (C(3′)), 66.9 (*C*(4)), 82.6 (*C*(5)), 123.2 (*C*(5‴)), 127.5 (*p-Ph*), 128.6 (*o*,*m-Ph*), 135.7 (*C*(4‴)), 137.0, 138.0 (*C*(3‴), *i-Ph*), 147.1 (*C*(6‴)), 150.0 (*C*(2‴)), 153.1 (*C*(2)), 173.8 (*C*(1′)); *m/z* (ESI$^+$) 564 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{35}H_{54}N_3O_3^+$ ([M+H]$^+$) requires 564.4160; found 564.4154.

(*S*)-3-[*N*-13′-(Pyridin-3″-yl)tridecylamino]propanoic acid [(−)-(*S*)-Nakinadine B] 11



Step 1. $NaHCO_3$ (53 mg, 0.64 mmol) and Boc_2O (0.11 mL, 0.48 mmol) were added sequentially to a stirred solution of **10** (180 mg, 0.32 mmol) in EtOH (5 mL) at 0 °C, and the reaction mixture was left to warm to rt over 16 h, before being concentrated *in vacuo*. The residue was dissolved in EtOAc (15 mL) and the resultant solution was washed with satd aq $NaHCO_3$ (2 × 15 mL) and brine (2 × 15 mL), dried (Na_2SO_4) and concentrated *in vacuo* to give *N*-Boc-**10** as a yellow oil (180 mg, 85%).

Step 2. H_2O_2 (30% aq, 0.81 mL) and LiOH (69 mg, 1.63 mmol) were sequentially added to *N*-Boc-**10** (180 mg, 0.27 mmol) in THF (2.5 mL) at 0 °C and the reaction mixture was left to warm to rt over 16 h, before the addition of satd aq Na_2SO_3 (10 mL). EtOAc (10 mL) was added and the phases were separated. The aqueous layer was extracted with EtOAc (3 × 10 mL) and the combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo*. The residue was dissolved in HCl (2.0 M in Et_2O, 3 mL) and left to stir for 30 min at rt before concentrated *in vacuo* to give a 50:50 mixture of **1** and (*S*)-**11**•HCl. Purification via ion exchange chromatography on Dowex 50WX8 (100-200 mesh, eluent H_2O) gave **1** as white needles (37 mg, 73% from **10**); mp 86–88 °C; {lit.[6] mp 87 °C}; $[\alpha]_D^{20}$ −21.0 (*c* 1.0 in $CHCl_3$); {lit.[6] $[\alpha]_D^{23}$ −24.2 (*c* 1.0 in $CHCl_3$)}. Further elution (eluent 35% aq NH_4OH), followed by filtration of the precipitate formed after 24 h gave (*S*)-**11** as a white solid (74 mg, 55% from **10**, >99% ee);[7] mp 121–122 °C; $[\alpha]_D^{20}$ −6.3 (*c* 1.0 in $CHCl_3$); ν_{max} 3030, 2921, 2851, 1653, 1560; λ_{max} (MeOH) 258 (3900), 263 (4400), 269 (3200); δ_H (400 MHz, 9mM, $CDCl_3$) 1.16–1.38 (18H, m, C(3′)H_2–C(11′)H_2), 1.56–1.74 (4H, m, C(2′)H_2, C(12′)H_2), 2.56–2.64 (2H, m, C(13′)H_2), 2.81–3.09 (3H, m, C(3)H_A, C(1′)H_2), 3.35–3.47 (1H, m, C(3)H_B), 4.04 (1H, dd, *J* 12.0, 3.9 C(2)*H*), 7.18–7.21 (1H, m, C(5″)*H*), 7.21–7.26 (1H, m, *p-Ph*), 7.28–7.33 (2H, m, *m-Ph*), 7.36–7.40 (2H, m, *o-Ph*), 7.49 (1H, app dt, *J* 7.8, 2.2, C(4″)*H*), 8.41–8.47 (2H, m, C(2″)*H*, C(6″)*H*); δ_H (700 MHz, 127 mM, $CDCl_3$) 1.10–1.44 (18H, m, C(3′)H_2–C(11′)H_2), 1.59–1.65 (2H, m, C(12′)H_2), 1.65–1.77 (2H, m, C(2′)H_2), 2.60 (2H, t, *J* 7.8, C(13′)H_2), 2.80–2.86 (1H, m, C(3)H_A), 2.94–3.01 (1H, m, C(1′)H_A), 3.04–3.14 (1H, m, C(1′)H_B), 3.44–3.52 (1H, m, C(3)H_B), 4.07 (1H, dd, *J* 11.9, 3.4 C(2)*H*), 7.20 (1H, app dd, *J* 7.8, 4.9, C(5″)*H*), 7.21–7.24 (1H, m, *p-Ph*), 7.27–7.31 (2H, m, *m-Ph*), 7.40 (2H, app d, *J* 7.3, *o-Ph*), 7.47–7.50 (1H, m, C(4″)*H*), 8.40–8.47 (2H, m, C(2″)*H*), C(6″)*H*), 10.1 (1H, br s, N*H*); δ_C (175 MHz, 127 mM, $CDCl_3$) 25.2

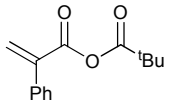
[6] S. D. Bull, S. G. Davies, S. Jones and H. J. Sanganee, *J. Chem. Soc., Perkin Trans. 1*, 1999, **4**, 387.

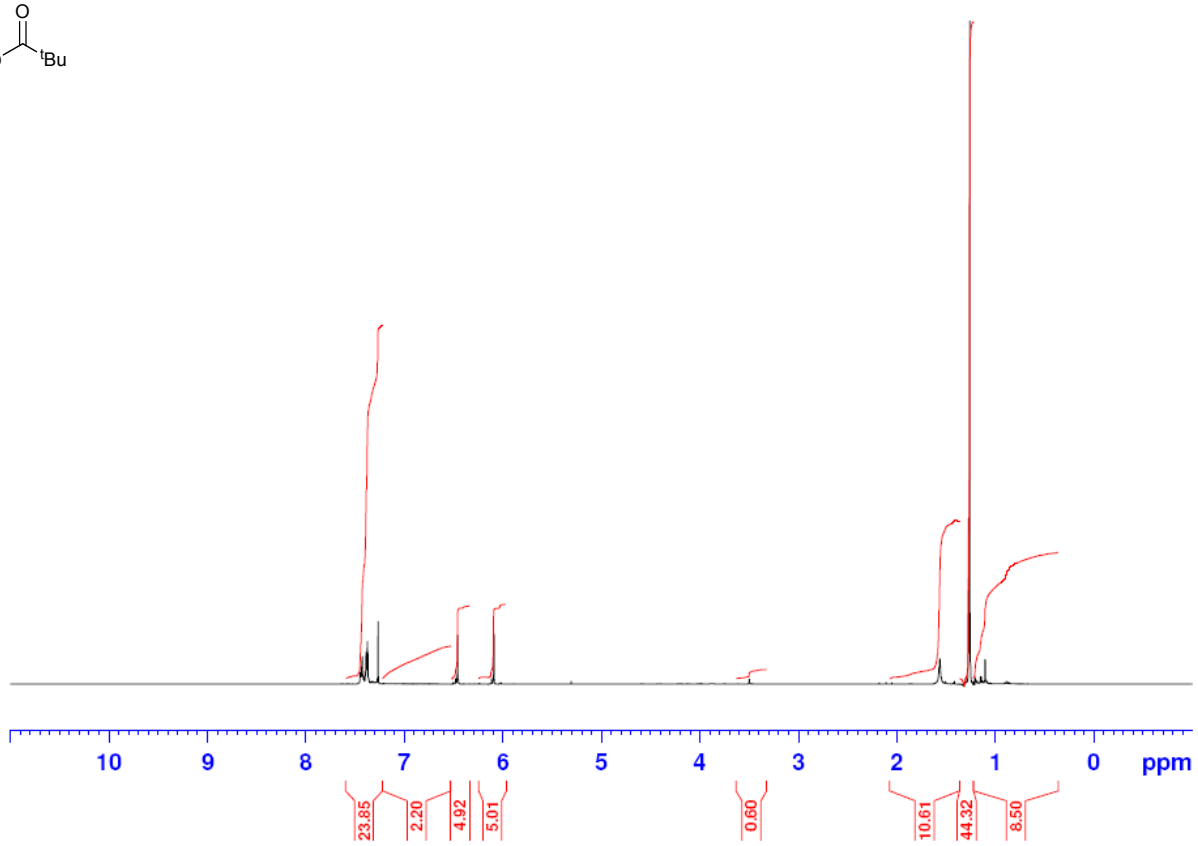
[7] The enantiomeric purity of (*S*)-**11** was determined by conversion to the corresponding methyl ester upon treatment with $SOCl_2$ in MeOH, and subsequent ^{1}H NMR spectroscopic analysis of the corresponding Mosher's amides; see: J. A. Dale, D. L. Dull and H. S. Mosher, *J. Org. Chem.*, 1969, **34**, 2543. This confirms that neither the hydrolysis of **10** nor the esterification of (*S*)-**11** are accompanied by racemisation.

(*C*(12′)), 26.9, 29.07, 29.09, 29.34, 29.36, 29.46, 29.47, 29.50, 29.53, (*C*(3′)-*C*(11′)), 31.1 (*C*(2′)), 33.0 (*C*(13′)), 47.6 (*C*(1′)), 51.0 (*C*(3)), 52.2 (*C*(2)), 123.1 (*C*(5″)), 127.1 (*p-Ph*), 128.1 (*m-Ph*), 128.8 (*o-Ph*), 135.7 (*C*(4″)), 137.9 (*C*(3″)), 139.0 (*i-Ph*), 147.1 (*C*(6″)), 149.9 (*C*(2″)), 176.2 (*C*(1)); *m/z* (ESI^+) 425 ($[M+H]^+$, 100%); HRMS (ESI^+) $C_{27}H_{41}N_2O_2^+$ ($[M+H]^+$) requires 425.3163; found 425.3165.

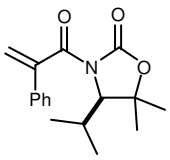
2. Copies of ^{1}H and ^{13}C NMR Spectra

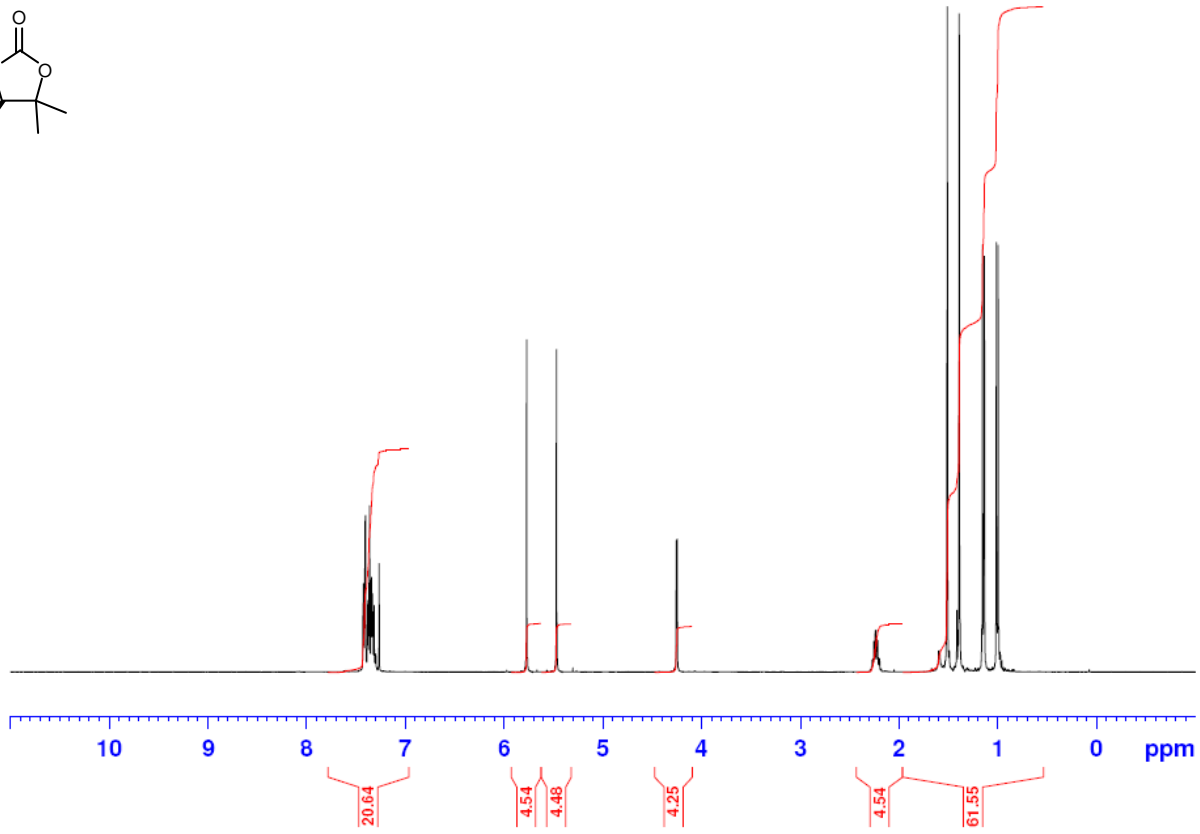
2-Phenylacrylic pivalic anhydride 2 (400 MHz ^{1}H, $CDCl_3$)





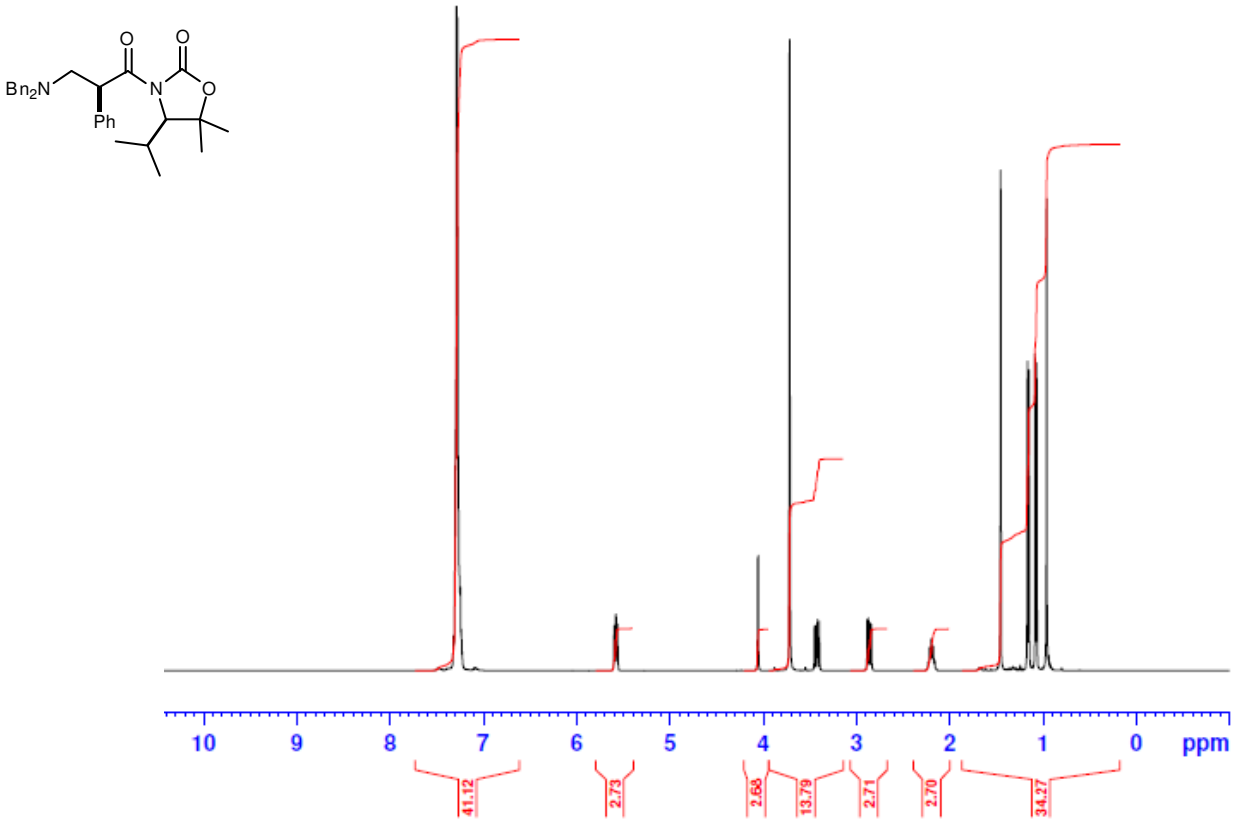
(*R*)-*N*(3)-(2′-Phenylacryloyl)-4-isopropyl-5,5-dimethyloxazolidin-2-one 3 (400 MHz ^{1}H, $CDCl_3$)





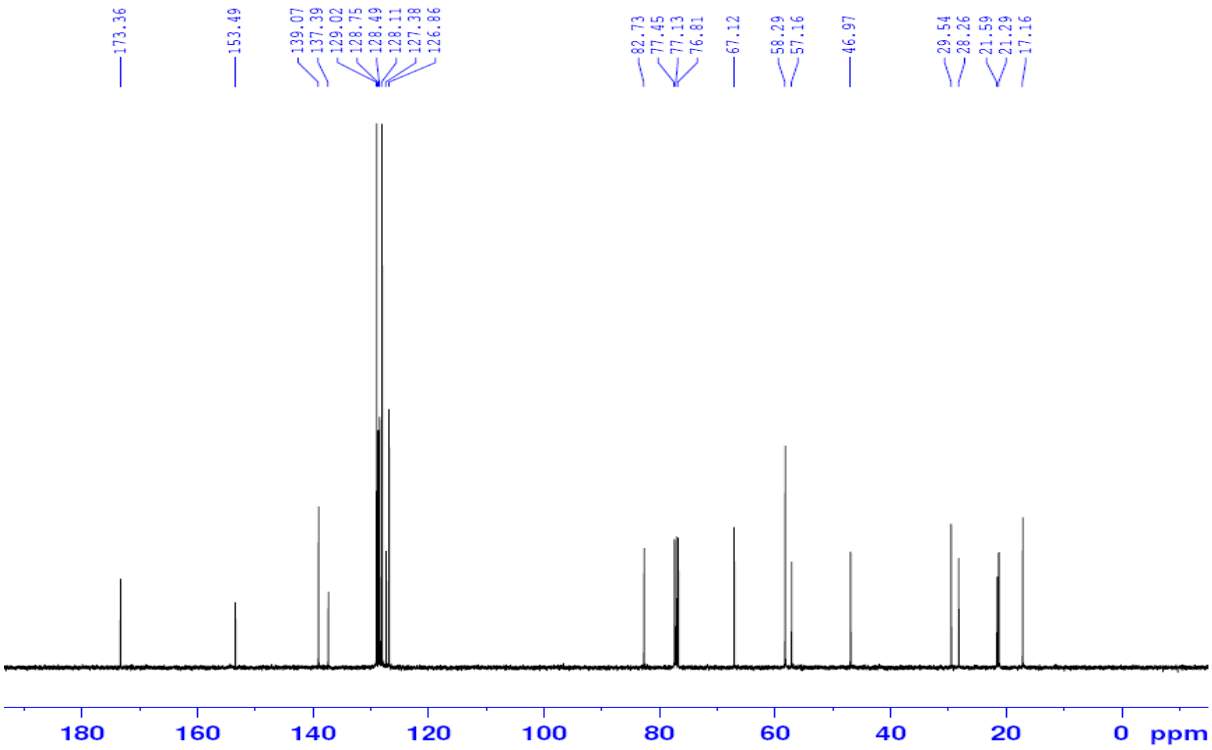
(4*R*,2′*S*)-*N*(3)-(2′-Phenyl-3′-*N*,*N*-dibenzylamino)propanoyl-4-isopropyl-5,5-dimethyloxazolidin-2-one 4

(400 MHz ^{1}H, $CDCl_3$)



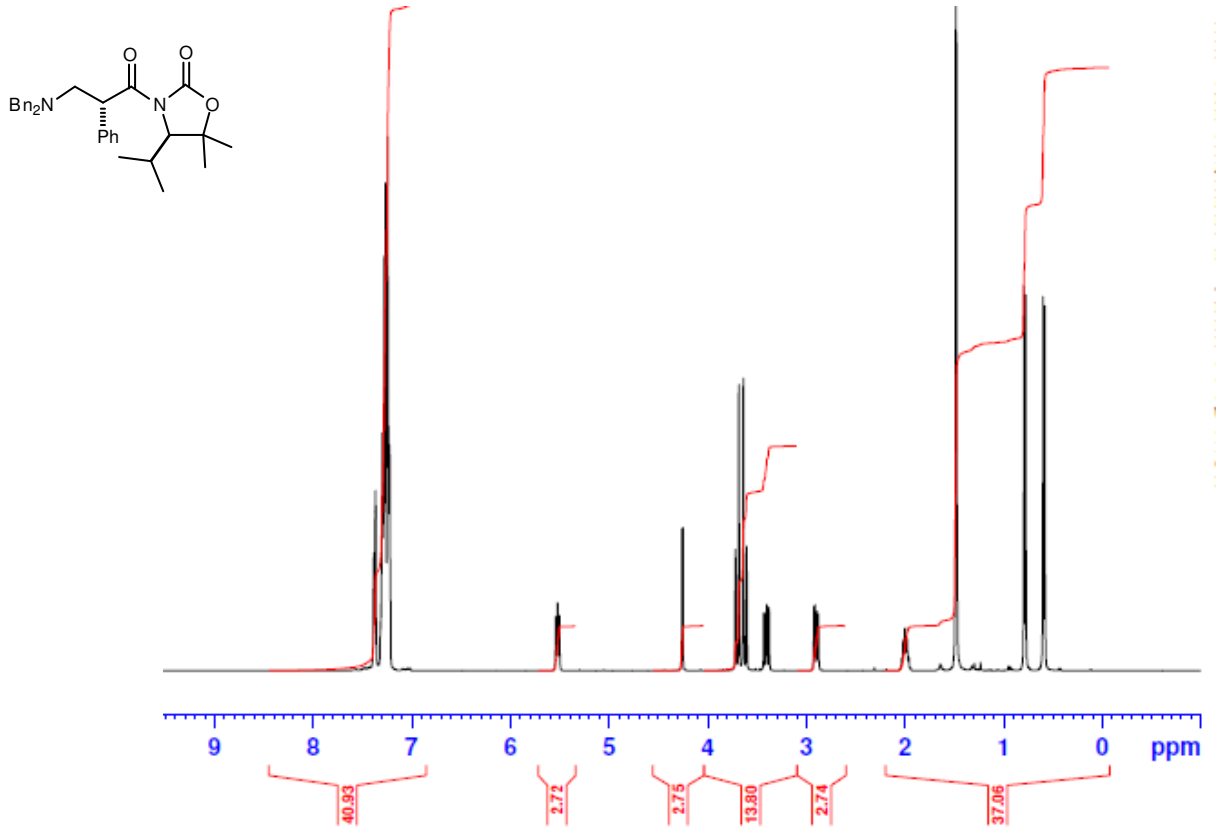
(4*R*,2′*S*)-*N*(3)-(2′-Phenyl-3′-*N*,*N*-dibenzylamino)propanoyl-4-isopropyl-5,5-dimethyloxazolidin-2-one 4

(100 MHz ^{13}C, $CDCl_3$)



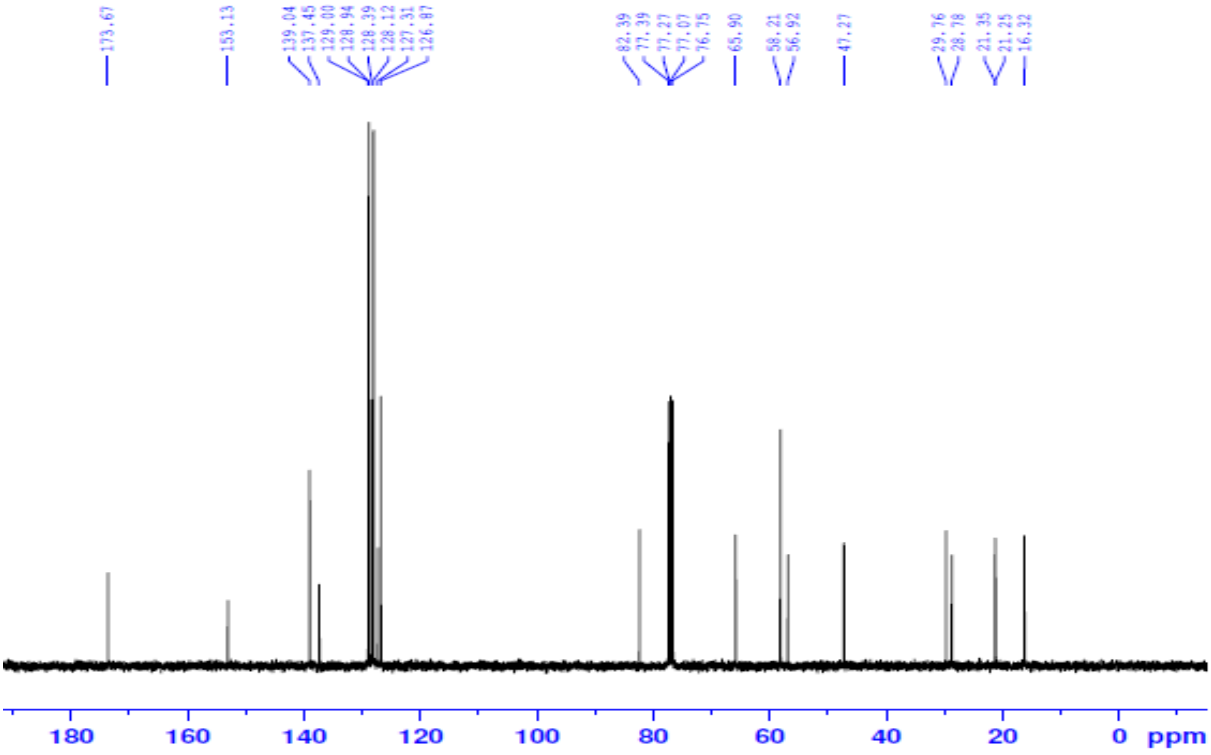
(*R*,*R*)-*N*(3)-(2′-Phenyl-3′-*N*,*N*-dibenzylamino)propanoyl-4-isopropyl-5,5-dimethyloxazolidin-2-one 5

(400 MHz ^{1}H, $CDCl_3$)



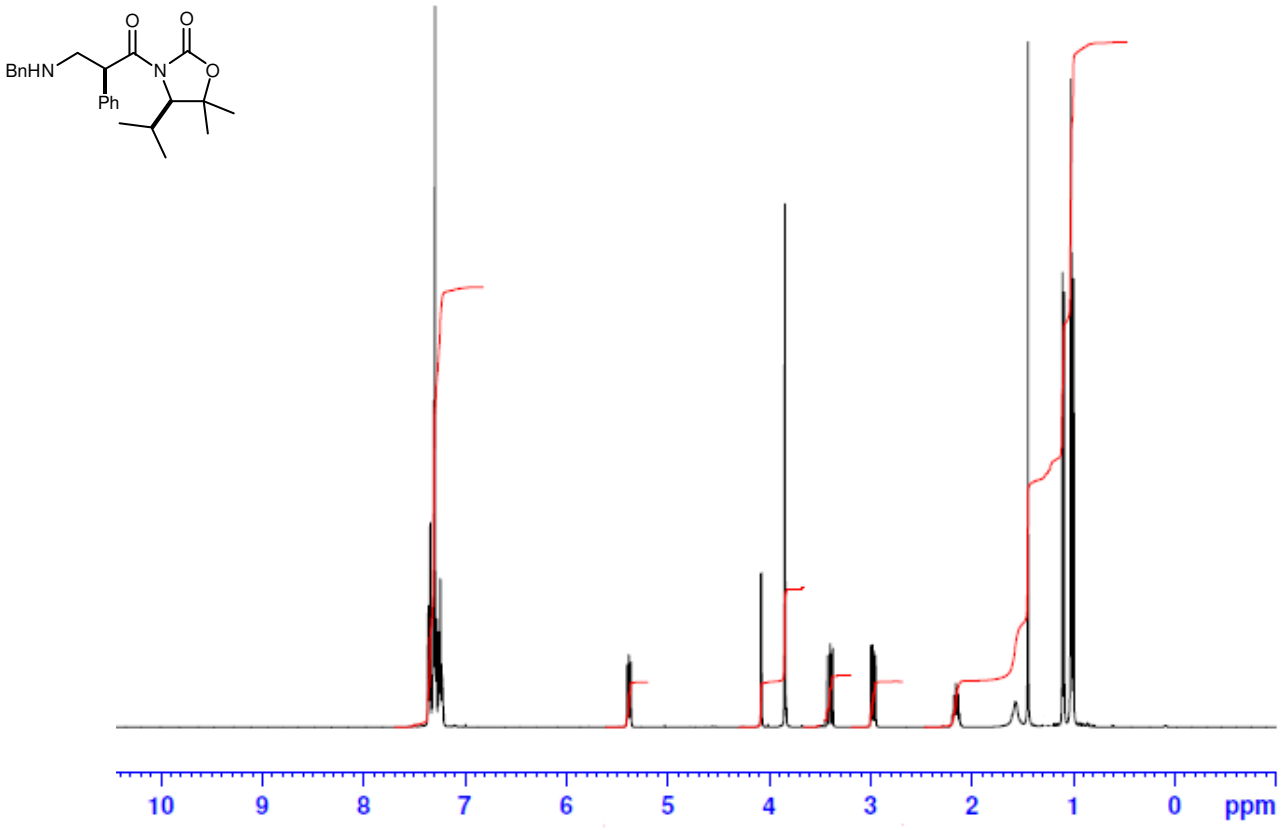
(*R*,*R*)-*N*(3)-(2′-Phenyl-3′-*N*,*N*-dibenzylamino)propanoyl-4-isopropyl-5,5-dimethyloxazolidin-2-one 5

(100 MHz ^{13}C, $CDCl_3$)



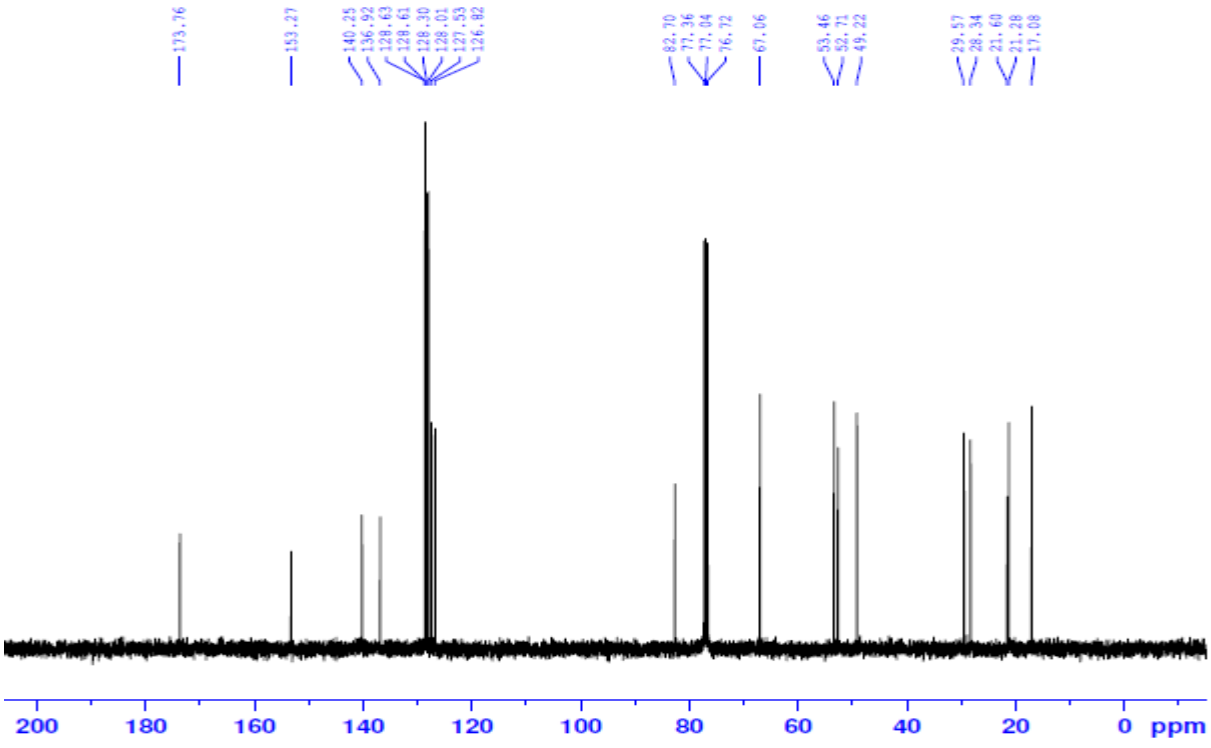
(4*R*,2′*S*)-*N*(3)-(2′-Phenyl-3′-*N*-benzylamino)propanoyl-4-isopropyl-5,5-dimethyloxazolidin-2-one 6

(400 MHz ^{1}H, $CDCl_3$)



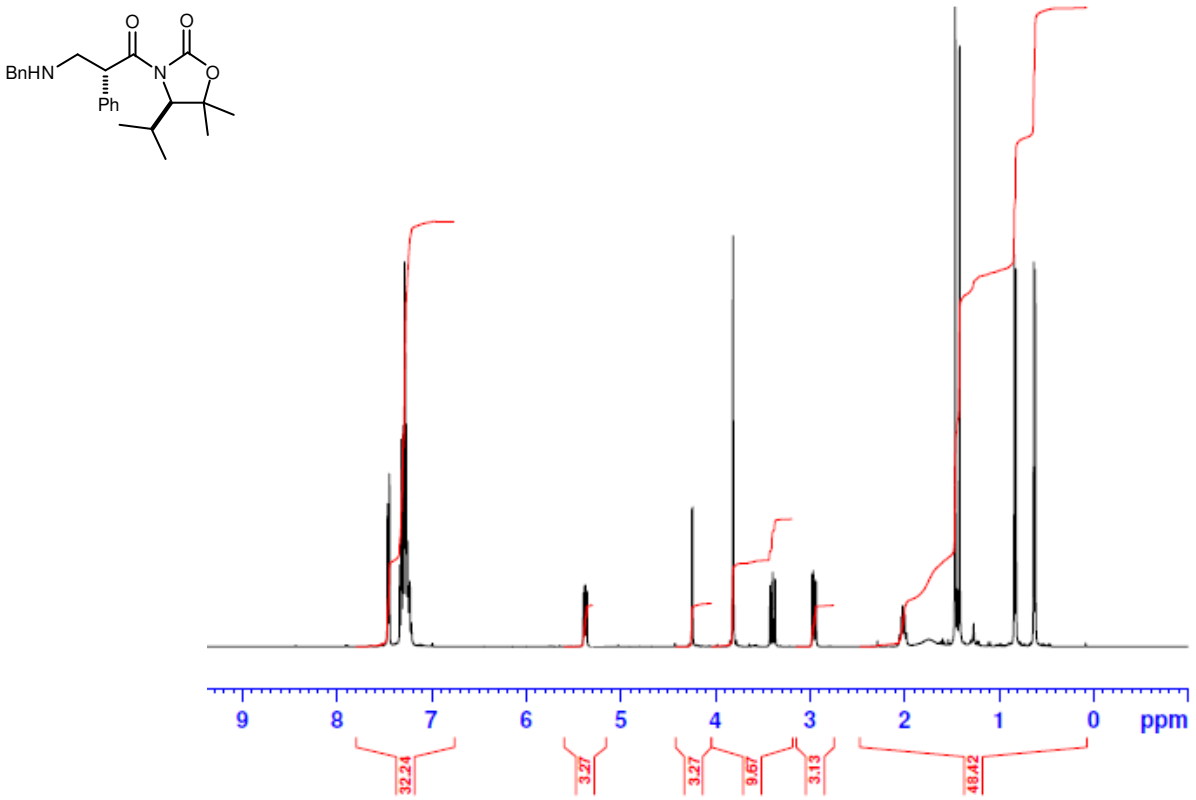
(4*R*,2′*S*)-*N*(3)-(2′-Phenyl-3′-*N*-benzylamino)propanoyl-4-isopropyl-5,5-dimethyloxazolidin-2-one 6

(100 MHz ^{13}C, $CDCl_3$)



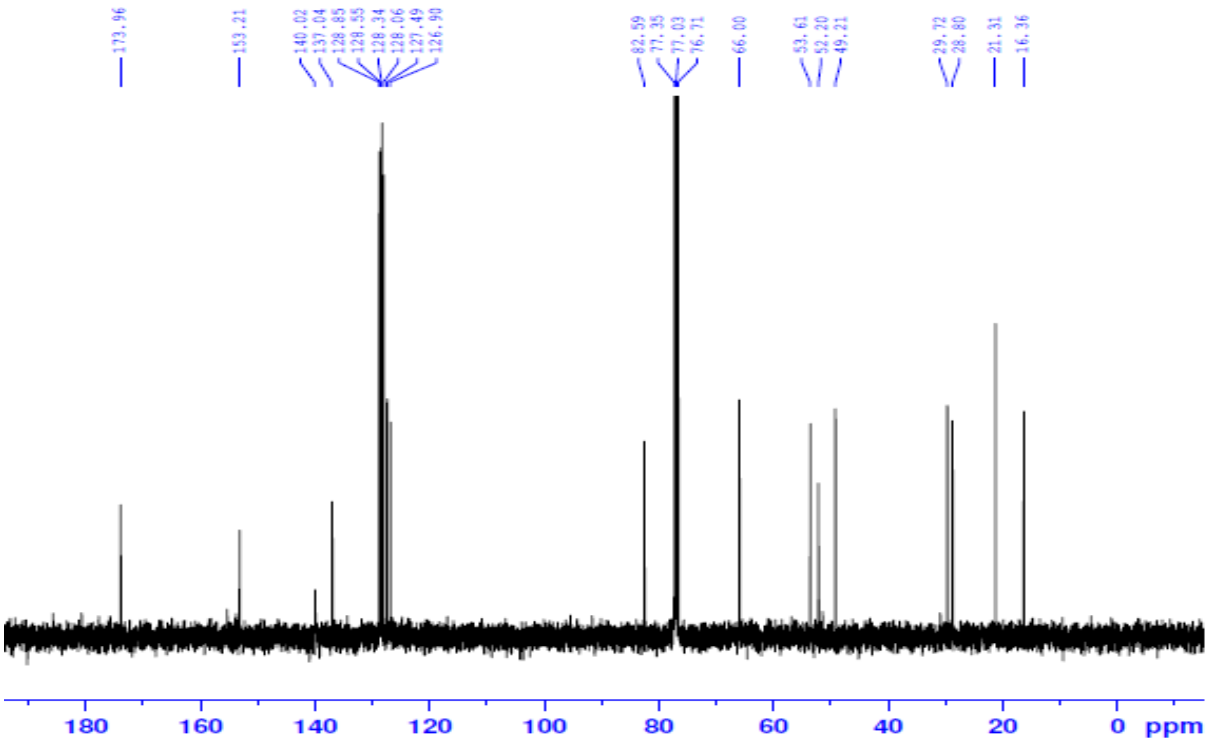
(*R*,*R*)-*N*(3)-(2′-Phenyl-3′-*N*-benzylamino)propanoyl-4-isopropyl-5,5-dimethyloxazolidin-2-one 7

(400 MHz ^{1}H, $CDCl_3$)

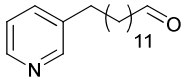


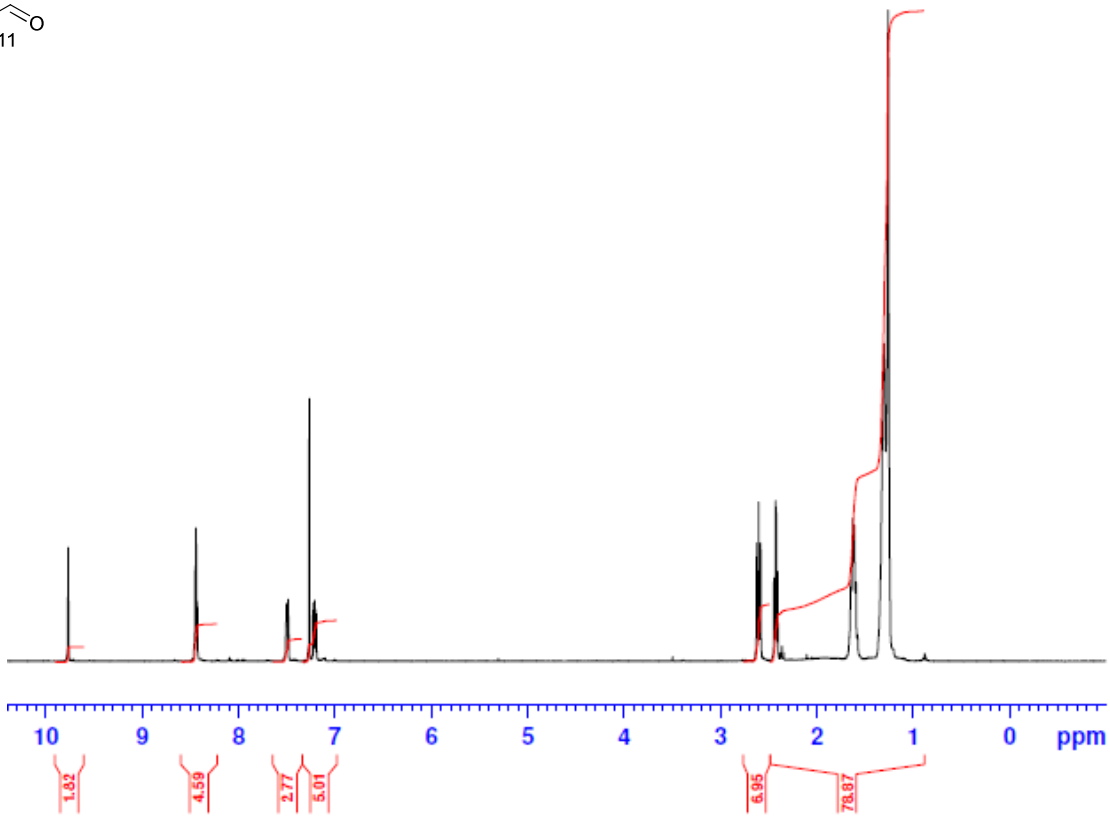
(*R*,*R*)-*N*(3)-(2′-Phenyl-3′-*N*-benzylamino)propanoyl-4-isopropyl-5,5-dimethyloxazolidin-2-one 7

(100 MHz ^{13}C, $CDCl_3$)

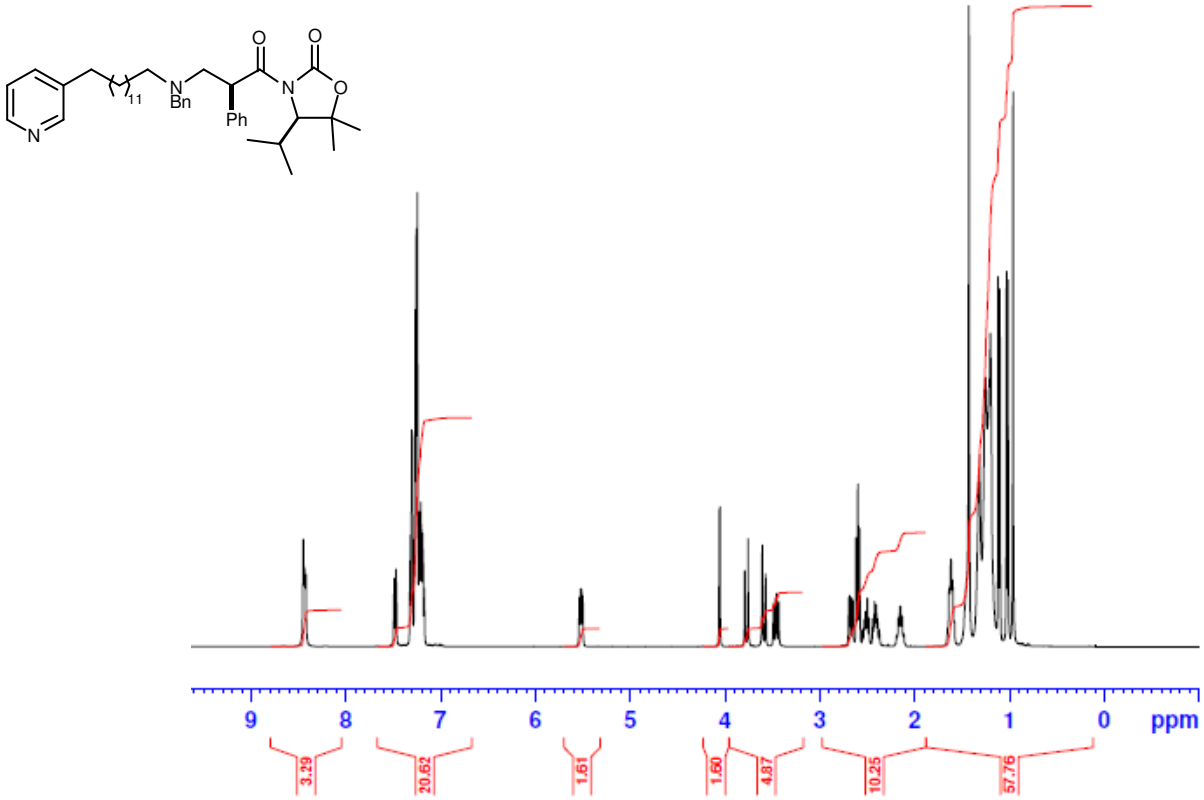


13-(Pyridin-3′-yl)tridecanal 8

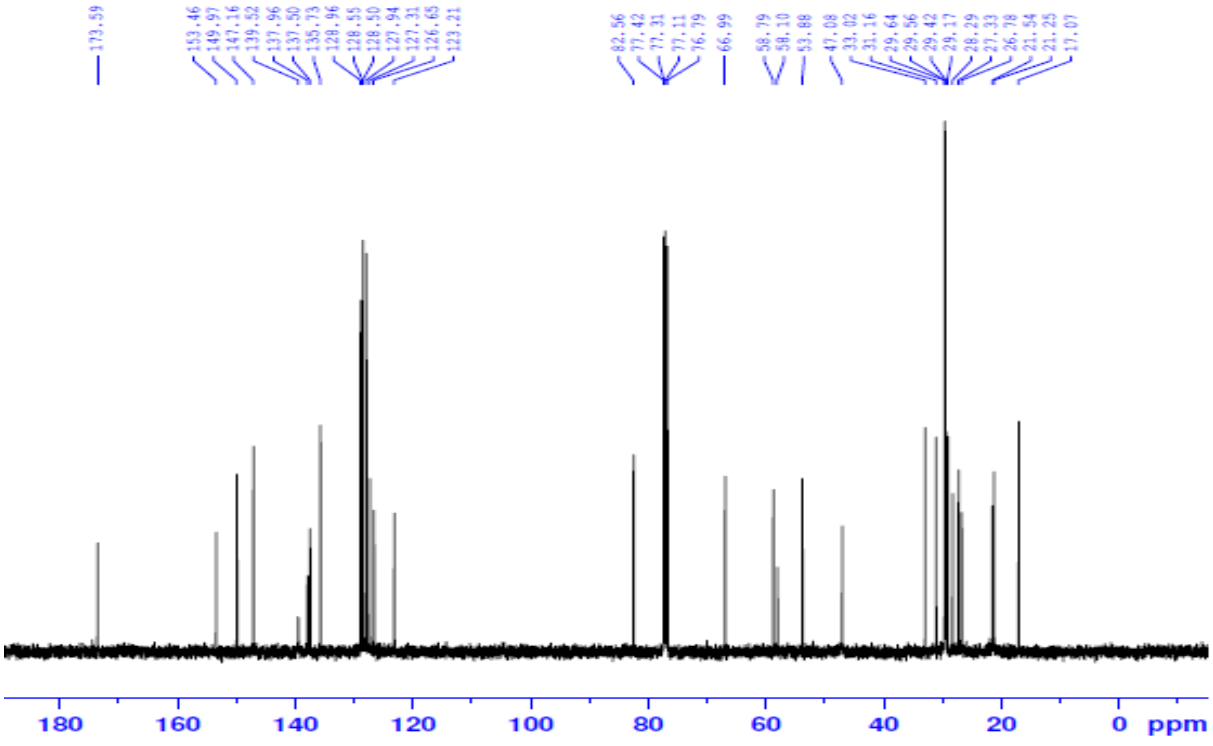




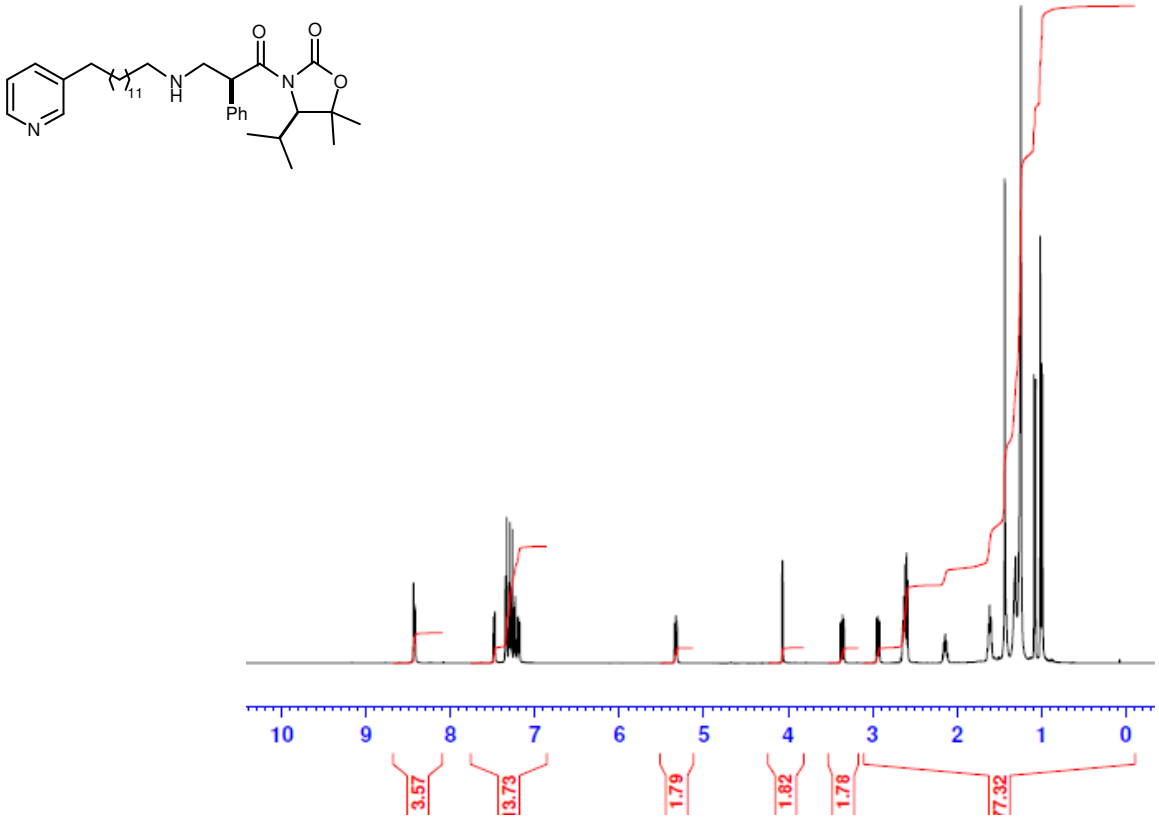
(4*R*,2′*S*)-*N*(3)-{2′-Phenyl-3′-[*N*-benzyl-*N*-13′′-(pyridine-3′′′-yl)tridecylamino]propanoyl}-4-isopropyl-5,5-dimethyloxazolidin-2-one 9 (400 MHz ^{1}H, $CDCl_3$)



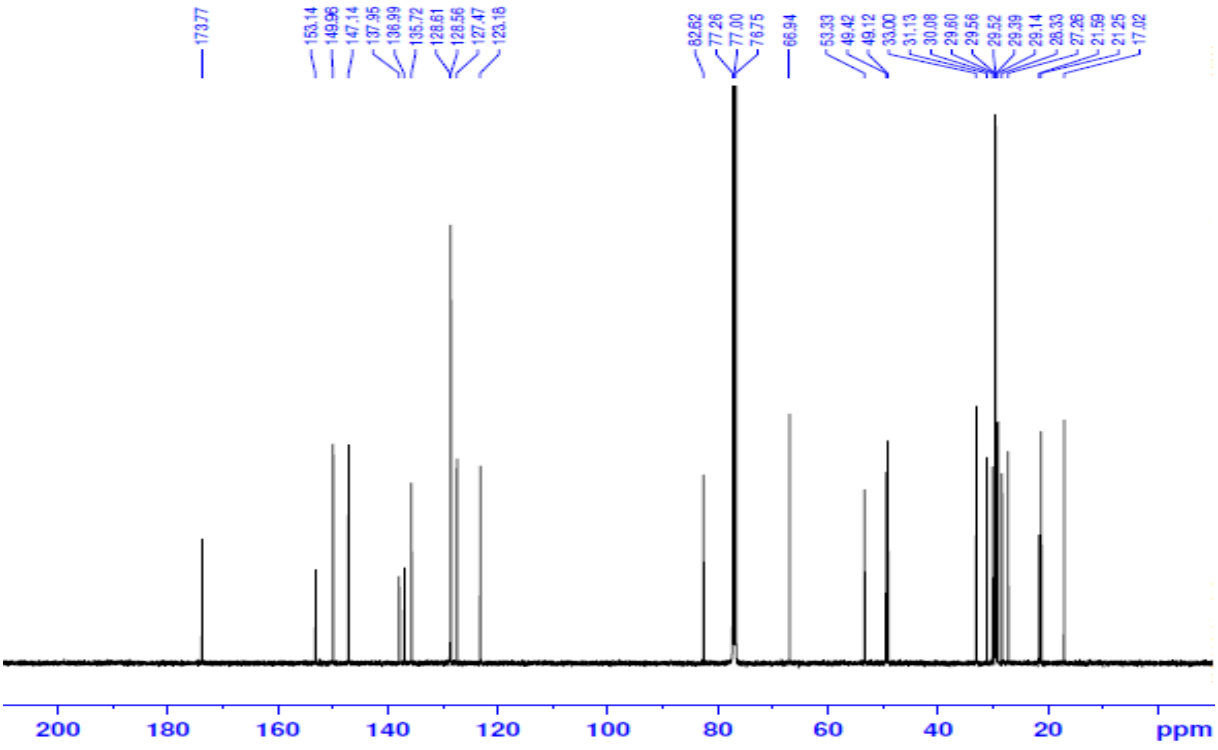
(4*R*,2′*S*)-*N*(3)-{2′-Phenyl-3′-[*N*-benzyl-*N*-13′′-(pyridine-3′′′-yl)tridecylamino]propanoyl}-4-isopropyl-5,5-dimethyloxazolidin-2-one 9 (100 MHz ^{13}C, $CDCl_3$)



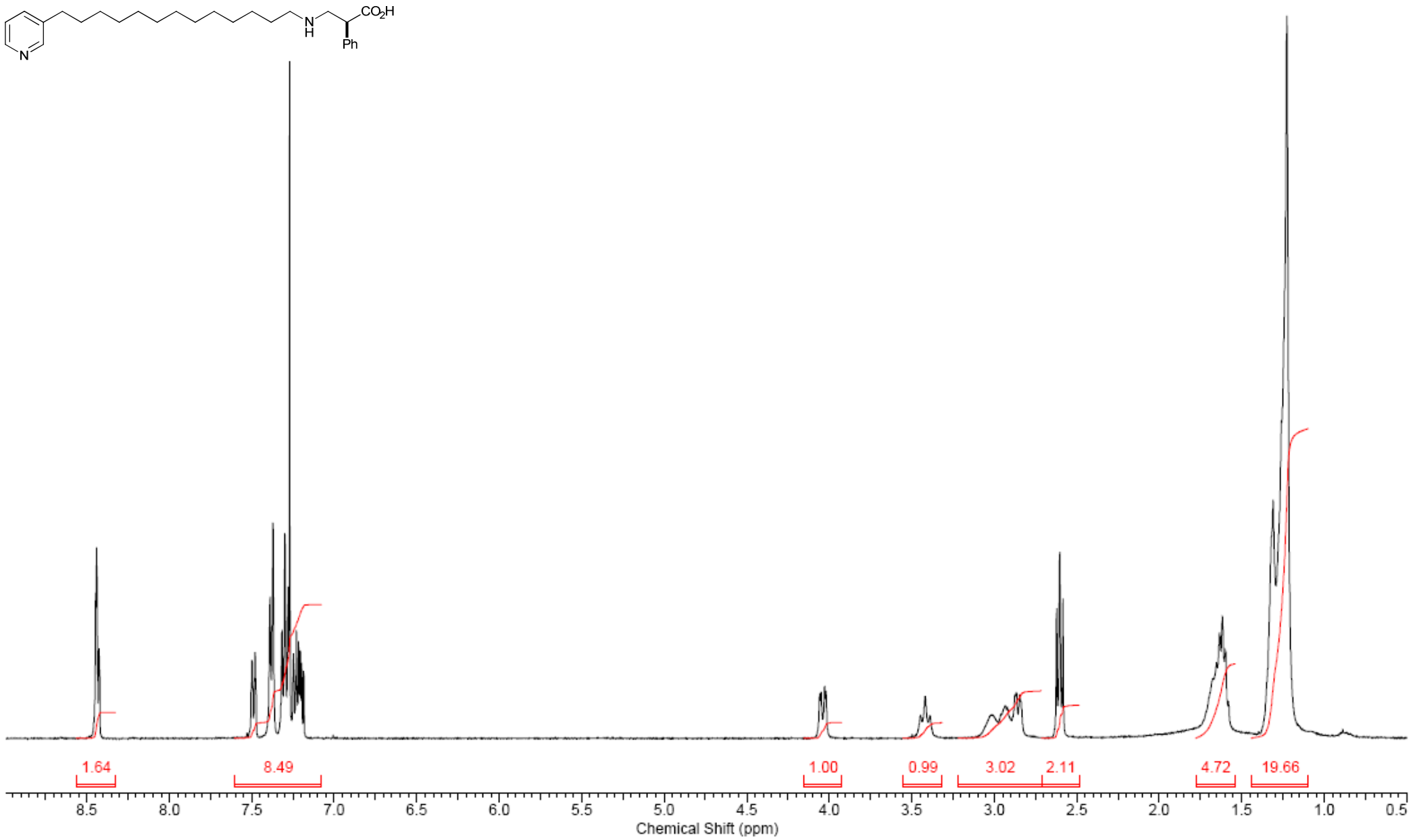
(4*R*,2′*S*)-*N*(3)-{2′-Phenyl-3′-[*N*-13′′-(pyridine-3′′′-yl)tridecylamino]propanoyl}-4-isopropyl-5,5-dimethyloxazolidin-2-one 10 (500 MHz ^{1}H, $CDCl_3$)



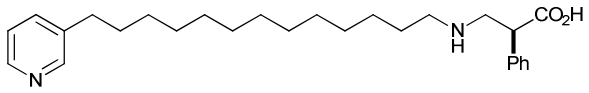
(4*R*,2′*S*)-*N*(3)-{2′-Phenyl-3′-[*N*-13′′-(pyridine-3′′′-yl)tridecylamino]propanoyl}-4-isopropyl-5,5-dimethyloxazolidin-2-one 10 (125 MHz ^{13}C, $CDCl_3$)



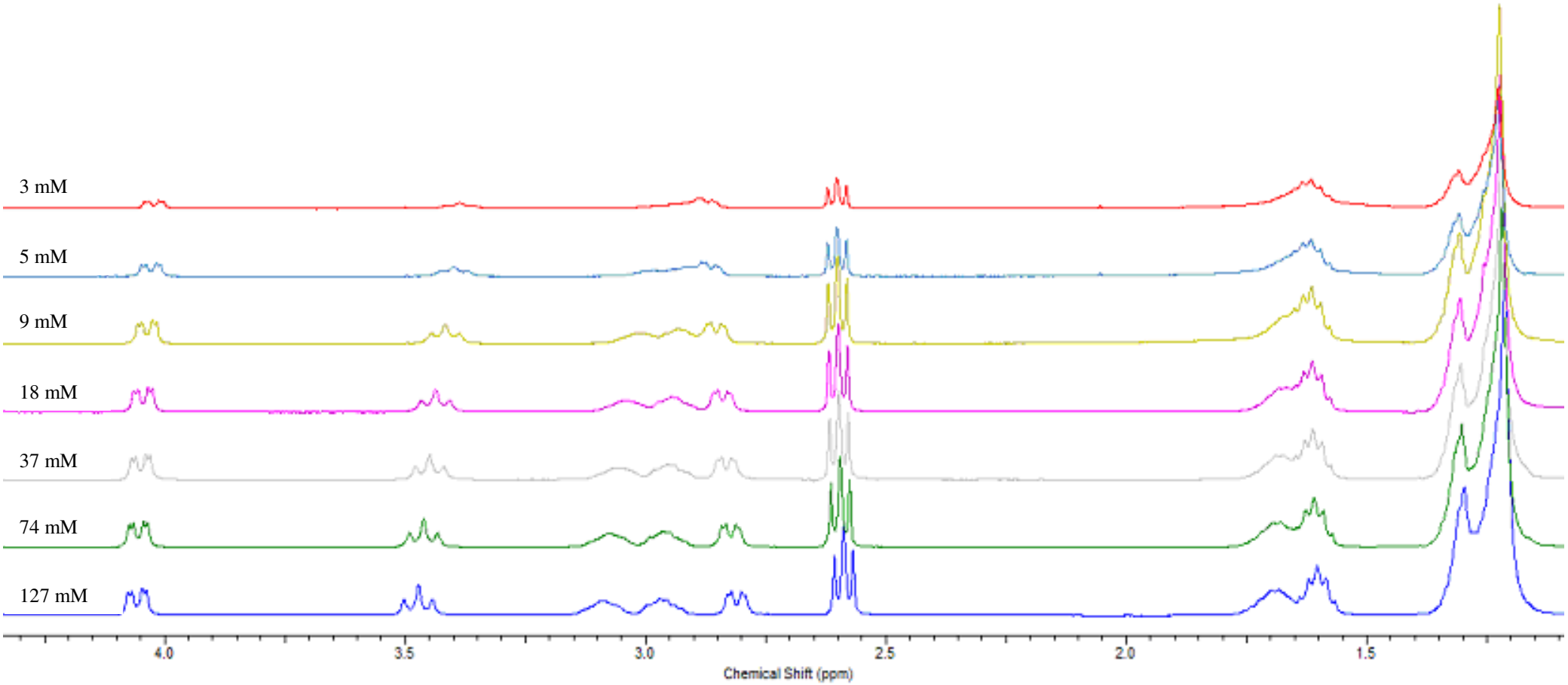
(*S*)-3-[*N*-13′-(Pyridin-3′′-yl)tridecylamino]propanoic acid [(–)-(*S*)-nakinadine B] 11 (400 MHz ^{1}H, 9 mM, $CDCl_3$)



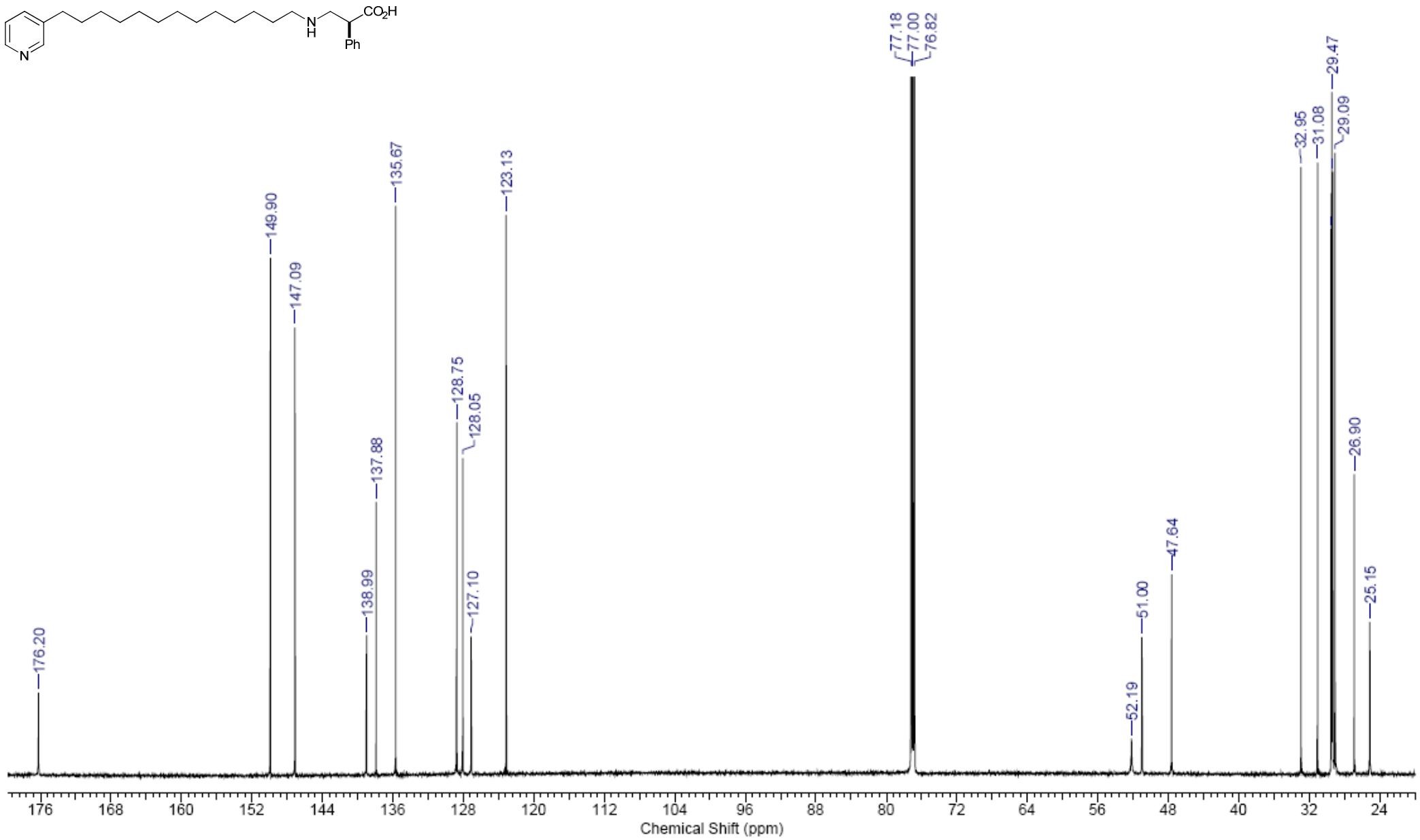
(*S*)-3-[*N*-13′-(Pyridin-3′′-yl)tridecylamino]propanoic acid [(–)-(*S*)-nakinadine B] 11 (700 MHz ^{1}H, 127 mM, $CDCl_3$)



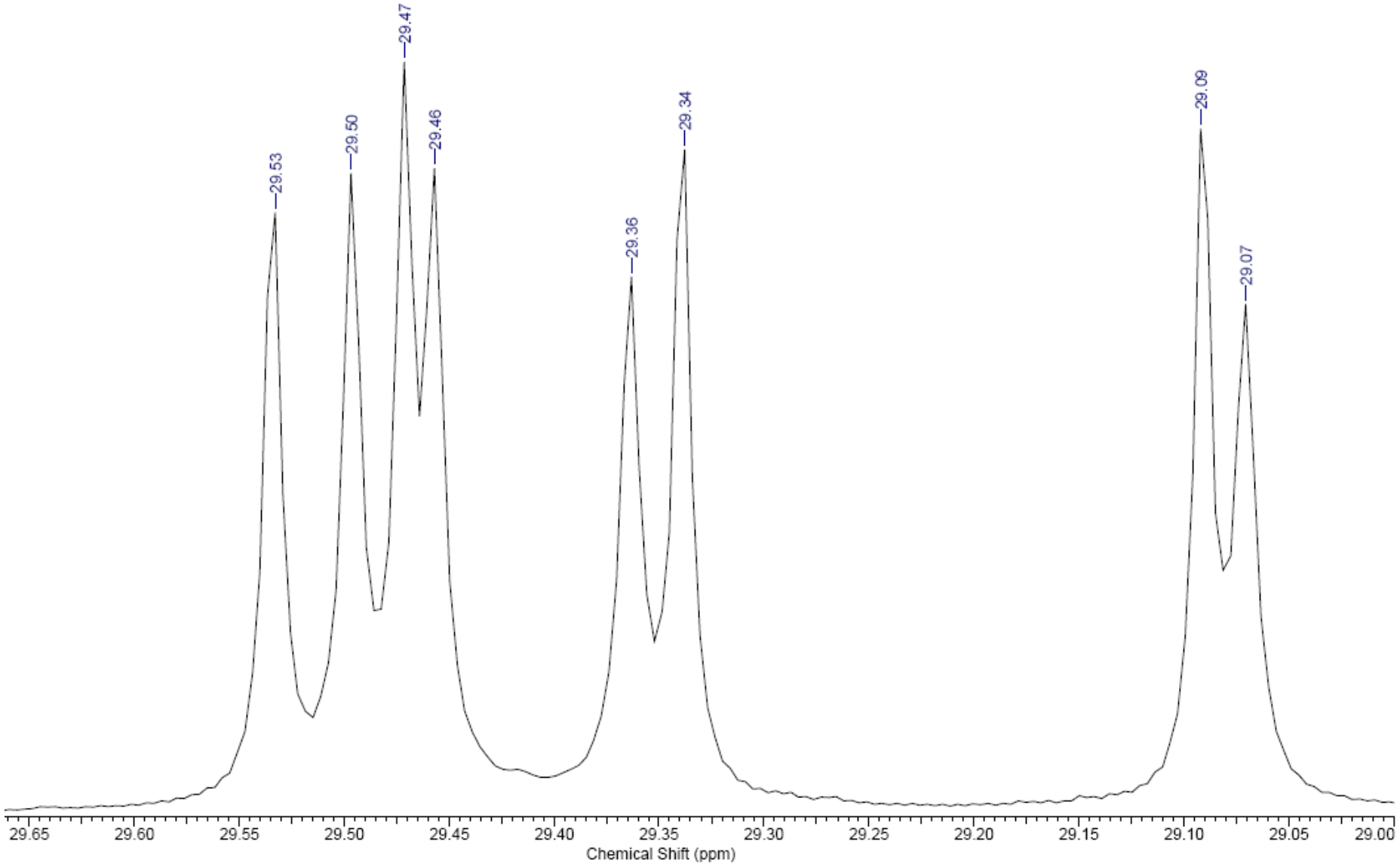
Dilution study for (*S*)-3-[*N*-13′-(pyridin-3′′-yl)tridecylamino]propanoic acid [(−)-(*S*)-nakinadine B] 11 (400 MHz ^{1}H, $CDCl_3$)



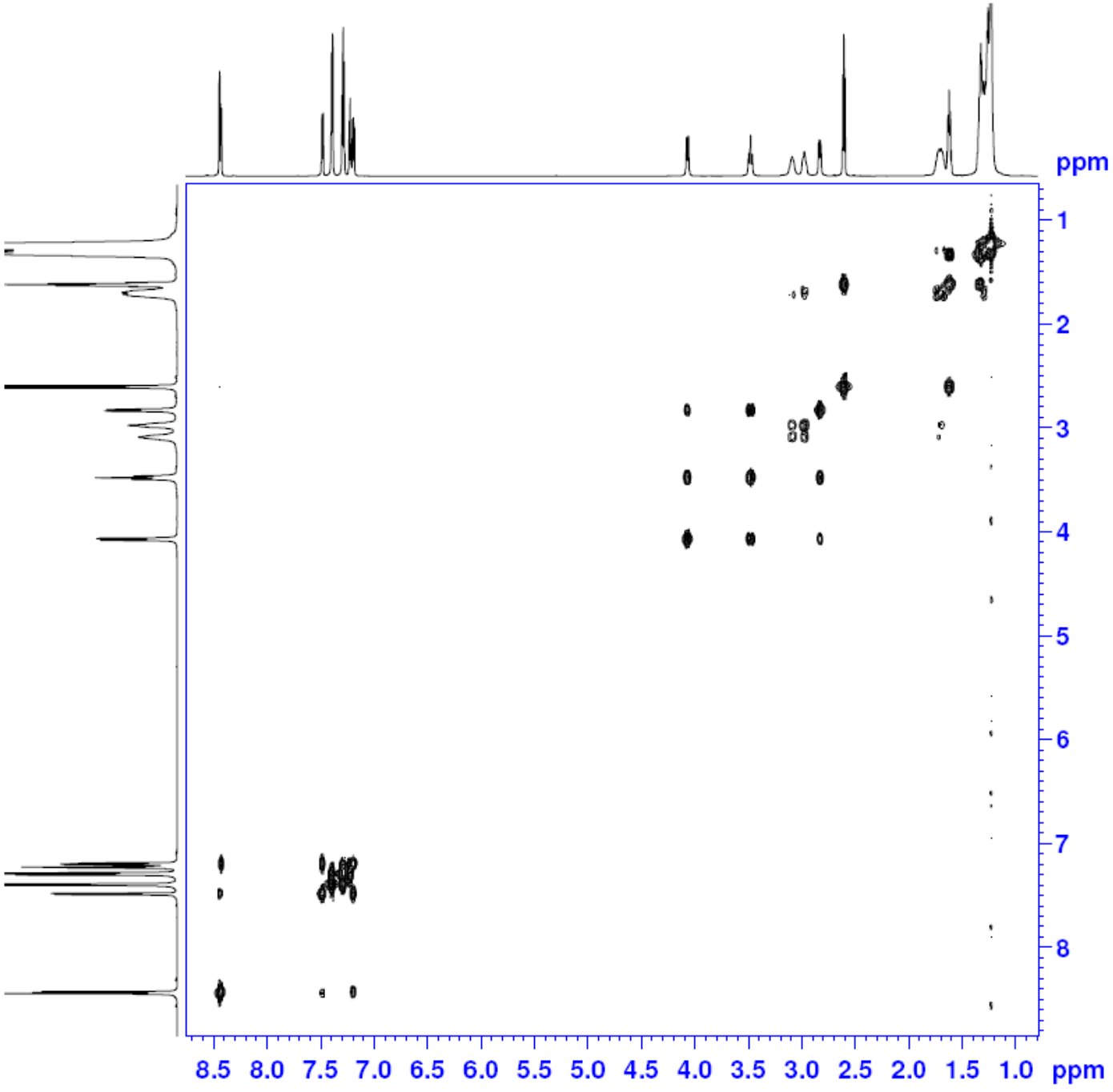
(*S*)-3-[*N*-13′-(Pyridin-3′′-yl)tridecylamino]propanoic acid [(–)-(*S*)-nakinadine B] 11 (175 MHz ^{13}C, 127 mM, $CDCl_3$)



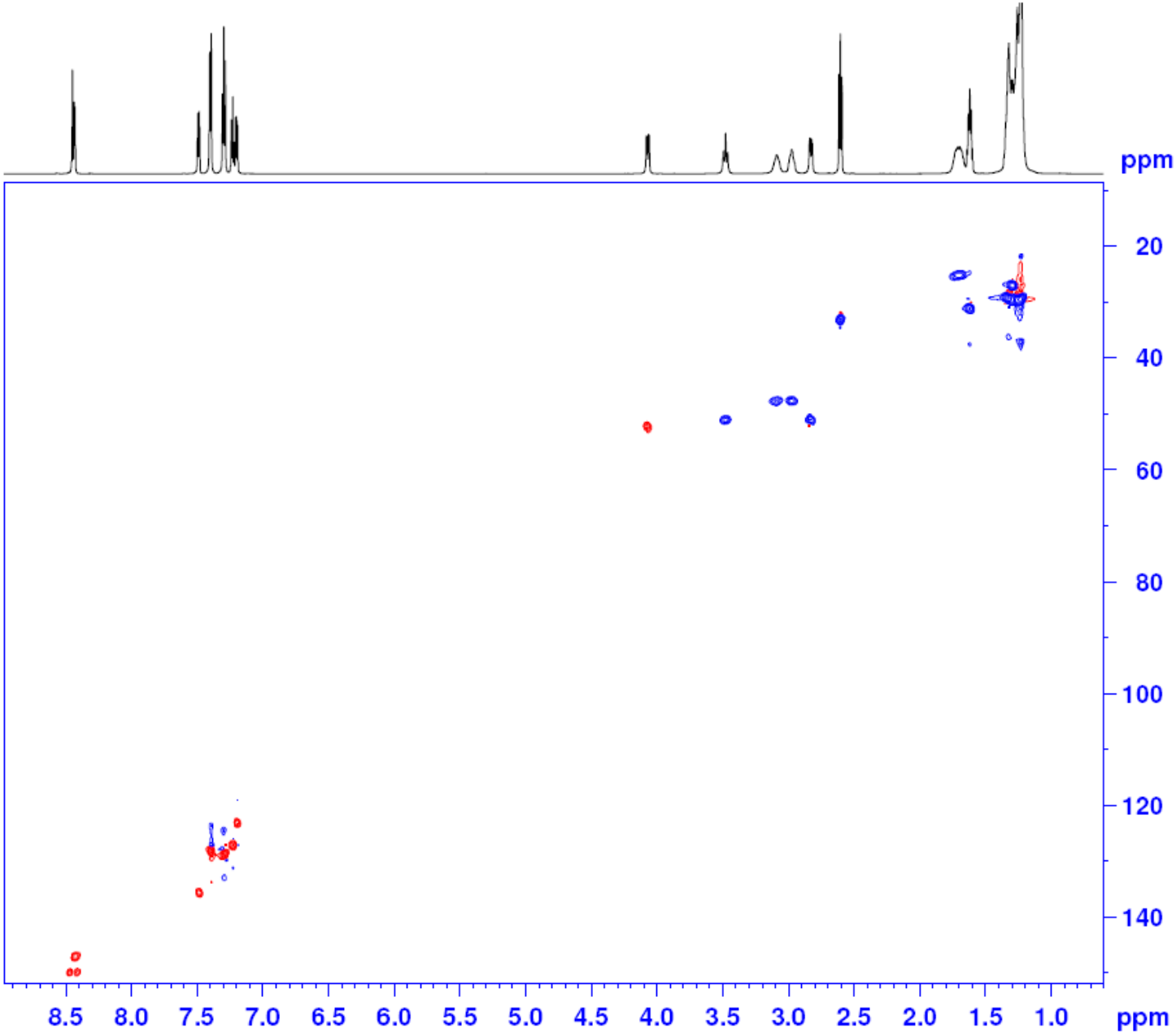
Expansion of ^{13}C NMR spectrum (δ_C 29.05-29.70 ppm) for (*S*)-3-[*N*-13′-(pyridin-3′′-yl)tridecylamino]propanoic acid [(−)-(*S*)-nakinadine B] 11 (175 MHz , 127 mM, $CDCl_3$)



^{1}H-^{1}H NMR COSY Spectrum of (*S*)-3-[*N*-13′-(pyridin-3′′-yl)tridecylamino]propanoic acid [(−)-(*S*)-nakinadine B] 11 (700 MHz, 127 mM, $CDCl_3$)



^{1}H-^{13}C NMR HSQC Spectrum of (*S*)-3-[*N*-13′-(pyridin-3″-yl)tridecylamino]propanoic acid [(–)-(*S*)-nakinadine B] 11 (700 MHz, 127 mM, $CDCl_3$)



^{1}H-^{13}C NMR HMBC Spectrum of (*S*)-3-[*N*-13′-(pyridin-3′′-yl)tridecylamino]propanoic acid [(−)-(*S*)-nakinadine B] 11 (700 MHz, 127 mM, $CDCl_3$)