

A Torsional Molecular Balance for Measuring Aliphatic CH- π Interactions

Authors:

William R. Carroll, Chen Zhao, Perry J. Pellechia, Mark D. Smith, Ken D. Shimizu

*Department of Chemistry and Biochemistry, University of South Carolina,
Columbia, South Carolina 29208 Fax: (803)7779521; Tel: (803)7776523
E-mail: shimizu@mail.chem.sc.edu*

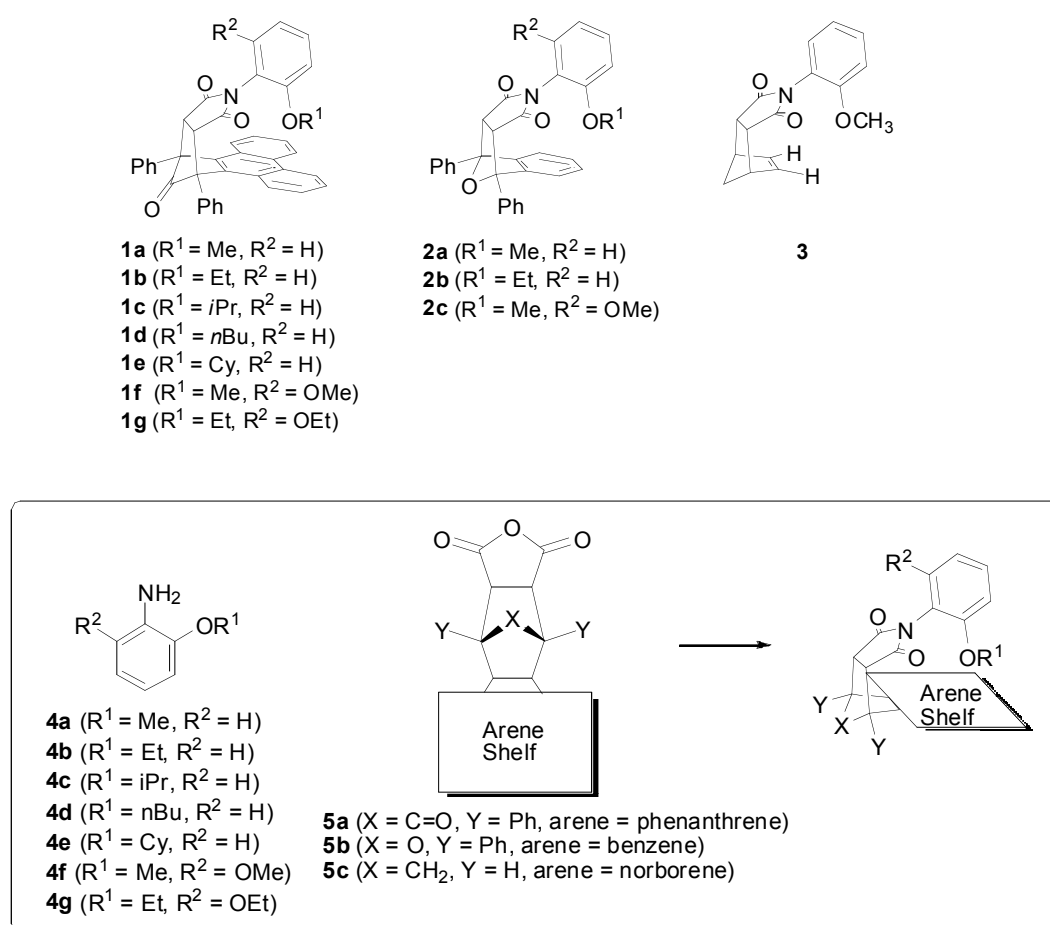
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General Experimental

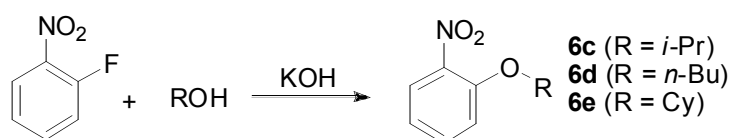
NMR spectra were recorded on Varian 300 MHz and 400 MHz spectrometers. Chemical shifts are reported in ppm (δ) referenced to TMS. All chemicals were purchased from commercial suppliers and used as received unless otherwise specified. Flash chromatography was carried out using silica gel from Sorbent Technologies (60 Å, 200-400 mesh). Thin layer chromatography (TLC) was performed using pre-coated TLC plates (Merck pre-coated 0.25 mm silica gel 60 F254 plates).

Synthesis:



Scheme 1. Overview of synthesis of balances **1a-1g**, **2a-2c** and **3** via Diels-Alder reaction between aniline **4** and anhydride **5**.

General procedure for formation of nitrophenylethers **6c-6e**



Compound **6c-6e** are known molecules. They are prepared via modified procedure from existing synthetic route:¹ to the mixture of potassium hydroxide or sodium hydride and alcohol, 1-fluoro-2-nitrobenzene was added dropwise while stirring under nitrogen. After reacted for 24 h, the solvent was removed under vacuum. The residue was then diluted with 30 mL ethyl acetate and washed with 50 mL water for 3 times. The ethyl acetate was then removed under reduced pressure to afford accordingly substituted nitrobenzene.

1-iso-Propoxy-2-nitrobenzene (6c): Potassium hydroxide (0.27 g, 4.8 mmol), 1-fluoro-2-nitrobenzene (0.33 g, 2.4 mmol) and *iso*-propanol (5.0 mL) were used as reactants. 0.40 g product was obtained as yellow solid, 94% yield. The spectra data were in agreement with reported.² ¹H NMR (400 MHz, CDCl₃) δ 7.77 (dd, J = 8.0 Hz, J = 1.4 Hz, 1 H), 7.47 (dt, J = 7.9 Hz, J = 1.4 Hz, 1 H), 7.07 (d, J = 8.4 Hz, 1 H), 6.97 (t, J = 7.8 Hz, 1 H), 4.65 (hp, J = 6.1 Hz, 1 H), 1.36 (d, J = 6.1 Hz, 6 H).

1-*n*-Butoxy-2-nitrobenzene (6d): Potassium hydroxide (0.23 g, 4.1 mmol), 1-fluoro-2-nitrobenzene (0.27 g, 1.9 mmol) and *n*-butanol (4.0 mL) were used as reactants. 0.33 g product was obtained as yellow oil, 90% yield. The spectra data were in agreement with reported.³ ¹H NMR (300 MHz CDCl₃) δ 7.82 (dd, J = 8.0 Hz, J = 1.9 Hz, 1 H), 7.51 (dt, J = 8.0 Hz, J = 1.9 Hz, 1 H), 7.07 (d, J = 8.0 Hz, 1 H), 7.00 (t, J = 8.0 Hz, 1 H), 4.11 (t, J = 6.5 Hz, 2 H), 1.83 (m, 2 H), 1.46-1.59 (m, 2 H), 0.97 (t, J = 7.5 Hz, 3 H).

1-Cyclohexyloxy-2-nitrobenzene (6e): Sodium hydride (0.04 g, 1.0 mmol), 1-fluoro-2-nitrobenzene (0.13 g, 0.94 mmol) and cyclohexanol (3.0 mL) were used as reactants. 0.19 g product was obtained as yellow oil, 92% yield. The spectra data were in agreement with reported.⁴ ¹H NMR (300 MHz CDCl₃) δ 7.75 (d, J = 7.5 Hz, 1 H), 7.47 (t, J = 7.5 Hz, 1 H), 7.08 (d, J = 7.5 Hz, 1 H), 6.96 (t, J = 7.5 Hz, 1 H), 4.44 (m, 1 H), 1.25-1.95 (m, 10 H).

General procedure for the formation of nitrophenylethers **6f**, **6g**



¹ Arca, V.; Paradisi, C.; Scorrano, G. *J. Org. Chem.* **1990**, *55*, 3617-3621.

² Wolin, R. L.; Stntillán, A., Jr.; Tang, L.; Huang, C.; Jiang, X.; Lovenberg, T. W. *Bioorg. Med. Chem.* **2004**, *12*, 4511-4532

³ Ueno, M.; Yonemoto, M.; Hashimoto, M.; Wheatley, A. E. H.; Naka, H.; Kondo, Y. *Chem. Comm.* **2007**, *22*, 2264-2266.

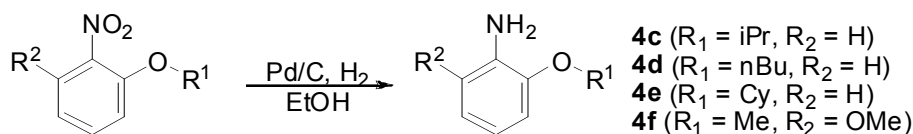
⁴ Haquette, P.; Dagorne, S.; Welter, R.; Jaouen, G. *J. Organomet. Chem.* **2003**, *628*, 240-247.

Compound **6f** and **6g** are both known substances.^{5,6} They are prepared via modified procedure from existing synthetic route of similar condensation reaction.⁷ For synthesis, iodoalkane was added dropwise to the mixture of potassium carbonate, 2-nitroresorcin and DMF while stirring under nitrogen. After stirred for 24 h, the reaction was poured into ice water mixture. The precipitate was then separated by filtration, washed with ice-cold water and dried under vacuum to give the product.

2, 6-Dimethoxynitrobenzene (6f): Iodomethane (0.19 g, 1.35 mmol), 2-nitroresorcin (0.10 g, 0.65 mmol), potassium carbonate (0.18 g, 1.29 mmol) were used as reactants. Product was obtained as 0.085 g white powder, 71% yield. ¹H NMR (300 MHz, CDCl₃) δ 7.24 (t, J = 8.5 Hz, 1 H), 6.57 (d, J = 8.5 Hz, 2 H), 3.81 (s, 6 H).

2, 6-diethoxynitrobenzene (6g): Ethyl iodine (1.12 g, 7.15 mmol), 2-nitroresorcin (0.50 g, 3.25 mmol) and potassium carbonate (0.89 g, 6.45 mmol) were used as reactant. Product was obtained as 0.57 g white powder, 83% yield. ¹H NMR (300 MHz, CDCl₃) δ 7.26 (dt, J = 7.8 Hz, J = 1.4 Hz, 1 H), 6.58 (d, J = 8.6 Hz, 2 H), 4.10 (q, J = 13.8 Hz, J = 7.0 Hz, 4 H), 1.38 (t, J = 6.8 Hz, 6 H).

General procedure for preparing anilines **4c-4f**



The synthetic routes of compounds **4c-4f** followed the general catalyzed hydrogenation method with Pd/C and H₂: the substituted nitrobenzene was dissolved in ethanol (40 mL) in a pressure vessel, and 20 mg of Pd/C (10% wt) was added. The vessel was pressurized at 40 psi with hydrogen gas and was stirred for 2 h. The resulting mixture was filtered through celite and the solvent was removed by rotary evaporation to afford the aniline product.

2-iso-Propoxyaniline (4c): compound **6c** (0.16 g, 0.89 mmol) was used as reactant. The product was obtained as brown liquid (0.13 g, 0.86 mmol, 97% yield). The spectra data were in agreement with reported.² ¹H NMR (300 MHz, CDCl₃) δ 6.90-6.70 (m, 4 H), 4.57 (hp, J = 6.1 Hz, 1 H), 3.80 (brs, 2 H), 1.38 (d, J = 6.1 Hz, 6 H).

⁵ McNulty, J.; Nair, J. J.; Capretta, A. *Tetrahedron Lett.*, **2009**, 50, 4087-4091.

⁶ Turner, E. E. *J. Chem. Soc., Trans.*, **1915**, 107, 469-474.

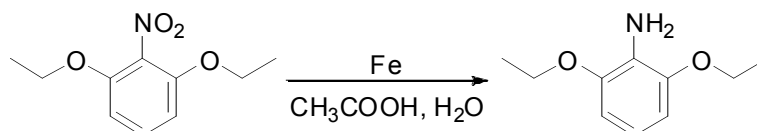
⁷ Xie, H.; Ng, D.; Savinov, S. N.; Dey, B.; Kwong, P. D.; Wyatt, R.; Smith, A. B.; Hendrickson, W. A. *J. Med. Chem.*, **2007**, 50, 4898-4908.

2-*n*-Butoxyaniline (4d): compound **6d** (0.33 g, 1.7 mmol) was used as reactant. Product was obtained as brown oil (0.28 g, 1.7 mmol, 98% yield). The compound is known and has been reported.⁸ ¹H NMR (300 MHz CDCl₃) δ 6.93-6.86 (m, 5 H), 4.07 (t, *J* = 6.4 Hz, 2 H), 1.91 (m, 2 H), 1.65 (m, 2 H), 1.12 (t, *J* = 7.4 Hz, 3 H).

2-Cyclohexyloxyaniline (4e): compound **6e** (0.27 g, 1.2 mmol) was used as reactant. Product was obtained as brown liquid (0.22 g, 1.1 mmol, 94% yield). The spectra data were in agreement with reported.⁴ ¹H NMR (300 MHz CDCl₃) δ 6.94-6.60 (m, 4 H), 4.27 (m, 1 H), 3.83 (brs, 2 H), 1.30-2.10 (m, 10 H).

2, 6-Dimethoxyaniline (4f): compound **6f** (0.39 g, 2.1 mmol) was used as reactant and was reacted for two days. Product was obtained as yellow solid (0.31 g, 2.0 mmol, 95% yield). The spectra data were in agreement with reported.⁹ ¹H NMR (300 MHz, CDCl₃) δ 6.69 (t, *J* = 8.1 Hz, 1 H), 6.53 (d, *J* = 8.1 Hz, 2 H), 3.85 (s, 6 H), 3.82 (s, 2 H).

Preparation of 2, 6-diethoxyaniline (4g)



Compound **4g** is a known molecule.¹⁰ The synthesis of **4g** follows the reduction of a similar nitrobenzene with different substituents.¹¹ To the mixture of compound **6g** (0.10 g, 0.55 mmol) and acetic acid (0.17 mL, 2.8 mmol) in water (5 mL), iron powder (0.31 g, 5.5 mmol) was added while stirring. The reaction was heated at reflux for 2 h and then neutralized by addition of saturated NaHCO₃ solution. The resulting suspension was extracted 3 times with 30 mL ethyl acetate. The organic layer was combined, and the solvent was removed by rotary evaporation to give compound **4g** (0.092 g, 0.51 mmol, 92% yield) as yellow oil. ¹H NMR (300 MHz, CDCl₃) δ 6.69 (m, 1 H), 6.54 (d, *J* = 6.5 Hz, 2 H), 4.06 (q, *J* = 13.9 Hz, *J* = 6.9 Hz, 4 H), 3.83 (brs, 2 H), 1.42 (t, *J* = 6.9 Hz, 6 H).

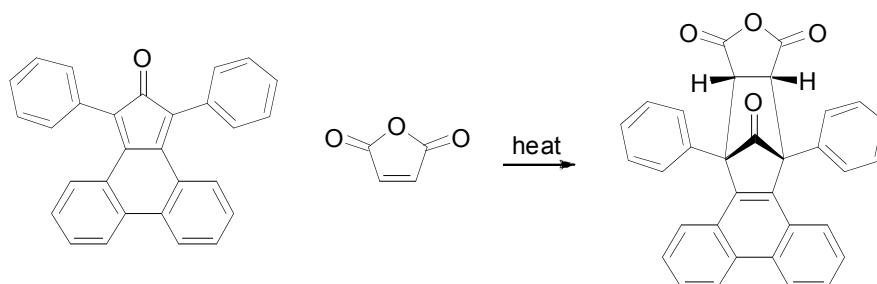
⁸ Tong, Y. F.; Zhang, P.; Chen, F.; Hao, L. H.; Wu, S.; Ye, F.; Tian, J. Y. *Chinese Chemical Letters*, **2010**, 21, 1415-1418.

⁹ Hoshino, Y.; Okuno, M.; Kawamura, E.; Honda, K.; Inoue, S. *Chem. Commun.*, **2009**, 2281-2283.

¹⁰ Tortolani, D. R.; Poss, M. A. *Org. Lett.*, **1999**, 1, 1261-1262.

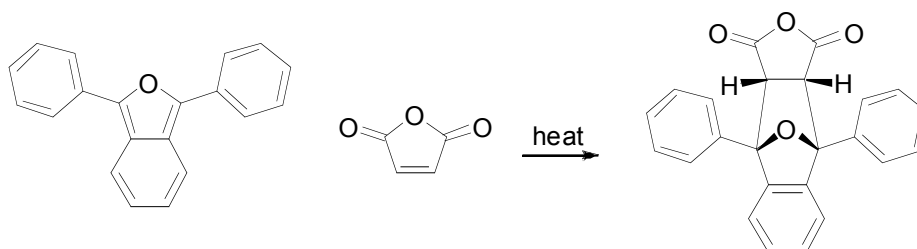
¹¹ Quideau, S.; Lyvinec, G.; Marguerit, M.; Bathany, K.; Ozanne-Beaudenon, A.; Buffeteau, T.; Cavagnat, D.; Chénédé, A. *Angew. Chem. Int. Ed.* **2009**, 48, 4605-4609.

Preparation of anhydride **5a**



Anhydride **5a** was synthesized as described in reference.¹² Phencyclone (0.50 g, 1.3 mmol) and maleic anhydride (0.12 g, 1.3 mmol) were mixed in 5 mL of toluene and were heated with a heating gun until the dark green color faded. After cooling, the precipitated product was separated by filtration and washed with cold diethyl ether to give anhydride **5a** (0.49 g, 1.0 mmol, 77% yield) as white solid. The crude product was used for next step without further purification. The spectra data were in agreement with reported. ¹H NMR (300 MHz, CDCl₃) δ 8.69 (d, J = 8.0 Hz, 2 H), 7.12-7.76 (m, 16 H), 4.75 (s, 2 H).

Preparation of anhydride **5b**



Anhydride **5b** is a known compound,¹³ and was synthesized via similar procedure as anhydride **5a**. For preparation, 1, 3-diphenylisobenzofuran (0.50 g, 1.9 mmol) and maleic anhydride (0.36 g, 3.7 mmol) were mixed in 5 mL of toluene, and the mixture was heated until the light yellow color faded. After cooling, the precipitated product was separated by filtration and washed with cold diethyl ether to obtain anhydride **5b** (0.57 g, 1.0 mmol, 84% yield) as white solid. ¹H NMR (300 MHz, CDCl₃) δ 7.94 (d, J = 6.8 Hz, 4 H), 6.94-7.70 (m, 10 H), 4.38 (s, 2 H).

General procedure for preparing molecular balances **1a-1g**, **2a-2c** and **3**

For the condensation reaction, the anhydride and aniline were dissolved in 5 mL of acetic acid, and the reaction mixture was heated at reflux for 24 h. The solvent was then removed by rotary evaporation. The residue was dissolved in 25 mL EtOAc, washed once with 50 mL saturated sodium bicarbonate, and twice with 50 mL water. The solvent of organic layer was then removed under vacuum to give the crude product.

¹² Yoshitake, Y.; Misaka, J.; Setoguchi, K.; Abe, M.; Kawaji, T.; Eto, M.; Harano, K. *J. Chem. Soc., Perkin Trans. 2*, **2002**, 9, 1611-1619.

¹³ Commercially available. Registration No.: 75925-22-3.

Balance 1a: Anhydride **5a** (0.50 g, 1.0 mmol) and anisidine **4a** (0.19 g, 1.5 mmol) were used as reactants, and 10 mL acetic acid was used as solvent. Purified by flash chromatography using silica gel (MeOH/CH₂Cl₂, v/v = 1/99). White solid, 0.54 g, 0.93 mmol, 93% yield. ¹H NMR (400 MHz, CDCl₃) δ 8.64-8.76 (m, 2 H major, 2 H minor), 8.42 (d, *J* = 6.7 Hz, 2 H minor), 8.38 (d, *J* = 6.8 Hz, 2 H major), 7.09-7.80 (m, 13 H major, 13 H minor), 7.04 (td, *J* = 8.1 Hz, *J* = 2.5 Hz, 2 H major), 6.96 (dd, *J* = 7.8 Hz, *J* = 1.7 Hz, 2 H minor), 6.82 (td, *J* = 7.5 Hz, *J* = 0.9 Hz, 2 H minor), 6.74 (d, *J* = 8.6 Hz, 1 H major), 6.44 (dd, *J* = 8.5 Hz, *J* = 1.0 Hz, 1 H minor), 6.28 (td, *J* = 7.7 Hz, *J* = 1.4 Hz, 1 H major), 4.64 (s, 2 H major), 4.62 (s, 2 H minor), 4.54 (dd, *J* = 7.8 Hz, *J* = 1.7 Hz, 1 H major), 3.71 (s, 3 H major), 2.16 (s, 3 H minor). ¹³C NMR (400 MHz, CDCl₃) δ 197.19, 173.15, 173.10, 154.22, 133.89, 133.80, 133.68, 133.57, 131.44, 131.11, 131.04, 130.89, 130.51, 130.44, 129.35, 129.28, 129.23, 128.61, 128.46, 128.41, 128.33, 128.30, 127.59, 127.18, 126.84, 126.59, 126.48, 126.32, 126.25, 125.90, 122.96, 122.76, 120.52, 120.07, 119.60, 111.73, 111.54, 63.58, 63.56, 55.72, 53.86, 45.33, 45.00, 29.72. HRMS (EI) calculated for C₄₀H₂₇NO₄: 585.1940; obs: 585.1939.

Balance 1b: Anhydride **5a** (0.37 g, 0.77 mmol) and phenetidine **4b** (0.11 g, 0.77 mmol) were used as reactants. Purified by flash chromatography using silica gel (MeOH/CH₂Cl₂, v/v = 1/99). White solid, 0.36 g, 0.59 mmol, 73% yield. ¹H NMR (400 MHz, CDCl₃) δ 8.3-8.4 (m, 2 H major, 2 H minor), 8.05 (dd, *J* = 7.9 Hz, *J* = 1.1 Hz, 2 H minor), 8.02 (dd, *J* = 6.6 Hz, *J* = 1.3 Hz, 2 H major), 6.4-7.4 (m, 15 H major, 16 H minor), 6.36 (dd, *J* = 8.4 Hz, *J* = 1.0 Hz, 1 H major), 6.06 (dd, *J* = 8.5 Hz, *J* = 1.0 Hz, 2 H minor), 5.90 (td, *J* = 7.7 Hz, *J* = 1.2 Hz, 1 H major), 4.26 (s, 2 H major), 4.22 (s, 2 H minor), 4.21 (dd, *J* = 7.8 Hz, *J* = 1.6 Hz, 1 H major), 3.58 (q, *J* = 7.0 Hz, 2 H major), 2.13 (q, *J* = 7.0 Hz, 2 H minor), 0.96 (t, *J* = 7.0 Hz, 3 H major), -0.21 (t, *J* = 7.0 Hz, 3 H minor). ¹³C NMR (400 MHz, CDCl₃) δ 197.21, 173.04, 153.59, 133.84, 133.58, 131.13, 130.91, 130.33, 129.52, 129.41, 129.37, 129.33, 129.23, 128.67, 128.62, 128.41, 128.30, 127.58, 127.18, 126.83, 126.60, 126.44, 126.34, 125.91, 122.98, 122.74, 120.37, 119.90, 119.75, 112.58, 64.14, 63.56, 61.80, 45.38, 44.93, 29.73, 14.72, 12.76. HRMS (EI) calculated for C₄₁H₂₉NO₄: 599.2097; obs: 599.2116.

Balance 1c: Anhydride **5a** (0.21 g, 0.43 mmol) and compound **4c** (0.13 g, 0.85 mmol) were used as reactants. Purified by flash chromatography using silica gel (EtOAc/Hexane, v/v = 1:5). Yellow crystal, 0.22 g, 0.36 mmol, 85% yield. ¹H NMR (400 MHz, CDCl₃) □ 8.71 (d, *J* = 8.3 Hz, 2 H), 8.37 (d, *J* = 7.8 Hz, 2 H), 6.81-7.91 (m, 15 H), 6.73 (d, *J* = 8.3 Hz, 1 H), 6.24 (t, *J* = 7.7 Hz, 1 H), 4.61 (s, 2 H), 4.55 (dd, *J* = 7.7 Hz, *J* = 1.0 Hz, 1 H), 4.42 (m, 1 H), 1.37 (d, *J* = 6.2 Hz, 6 H). ¹³C NMR (300 MHz, CDCl₃) □ 197.43, 173.19, 153.95, 134.09, 133.81, 131.36, 131.14, 130.54, 129.57, 129.44, 128.84, 128.62, 127.81, 127.38, 127.04, 126.59, 126.05, 123.19, 120.56, 120.15, 112.76, 68.48, 63.78, 45.17, 31.27, 19.40, 14.13. HRMS (EI) calculated for C₄₂H₃₁NO₄: 613.2253; observed: 613.2256.

Balance 1d: Anhydride **5a** (0.10 g, 0.21 mmol) and compound **4d** (0.068 g, 0.42 mmol) were used as reactants. Purified by flash chromatography using silica gel (MeOH/CH₂Cl₂, v/v = 1:99). Yellow crystal, 0.11 g, 0.17 mmol, 81% yield. ¹H NMR (300 MHz, CDCl₃) δ 8.70 (m, 2 H major, 2 H minor), 8.37 (m, 2 H major, 2 H minor), 7.71 (t, *J* = 7.6 Hz, 2 H major), 6.90-7.60 (m, 13 H major, 16 H minor), 6.79 (t, *J* = 8.0 Hz, 1 H minor), 6.73 (d, *J* = 8.6 Hz, 1 H major), 6.42 (d, *J* = 8.0 Hz, 1 H minor), 6.27 (t, *J* = 7.6 Hz, 1 H major), 4.62 (ds, 2 H major, 2 H minor), 4.60 (dd, *J* = 4.1 Hz, *J* = 1.3 Hz, 1 H major), 3.87 (t, *J* = 6.2 Hz, 2 H major, 2 H minor), 1.70 (m, 2 H major), 1.43 (m, 2 H major), 0.98 (t, *J* = 7.5 Hz, 3 H major), 0.34-0.80 (m, 7 H minor). ¹³C NMR (400 MHz, CDCl₃) δ 197.21, 172.97, 153.71, 133.84, 133.57, 131.12, 130.90, 130.32, 129.35, 129.21, 128.61, 128.40, 127.57, 127.16, 126.81, 126.34, 125.91, 122.97, 122.86, 122.83, 120.13, 119.89, 112.51, 105.00, 68.23, 63.54, 44.93, 31.03, 19.18, 13.91. HRMS (EI) calculated for C₄₃H₃₃NO₄: 627.2410; observed: 627.2416.

Balance 1e: Anhydride **5a** (0.27 g, 0.57 mmol) and compound **4e** (0.22 g, 1.14 mmol) were used as reactants. Purified by flash chromatography using silica gel (MeOH/CH₂Cl₂, v/v = 1:99). Yellow solid, 0.29 g, 0.44 mmol, 78% yield. ¹H NMR (400 MHz, CDCl₃) δ 8.71 (d, *J* = 8.5 Hz, 2 H), 8.38 (d, *J* = 7.8 Hz, 2 H), 7.72 (t, *J* = 7.8 Hz, 2 H), 6.94-7.60 (m, 13 H), 6.73 (d, *J* = 8.5 Hz, 1 H), 6.24 (t, *J* = 7.8 Hz, 1 H), 4.61 (s, 2 H), 4.58 (dd, *J* = 7.8 Hz, *J* = 1.4 Hz, 1 H), 4.15 (m, 1 H), 1.20-1.92 (m, 10 H). ¹³C NMR (400 MHz, CDCl₃) δ 197.25, 172.95, 152.64, 133.88, 133.58, 131.12, 130.91, 130.18, 129.36, 129.24, 128.60, 128.38, 127.81, 127.15, 126.81, 126.36, 125.94, 122.96, 120.58, 120.07, 133.62, 63.56, 44.88, 31.58, 25.49, 23.55. HRMS (EI) calculated for C₄₅H₃₅NO₄: 653.2566; observed: 653.2553.

Balance 1f: Anhydride **5a** (0.47 g, 0.99 mmol) and compound **4f** (0.30 g, 2.0 mmol) were used as reactants. Recrystallized from MeCN. White crystal, 0.35 g, 0.57 mmol, 58% yield. ¹H NMR (400 MHz, CDCl₃) δ 8.69 (d, *J* = 8.5 Hz, 2 H), 8.45 (d, *J* = 7.5 Hz, 2 H), 7.70 (t, *J* = 7.5 Hz, 2 H), 6.46-7.80 (m, 13 H), 6.42 (d, *J* = 8.5 Hz, 1 H), 6.05 (d, *J* = 8.5 Hz, 1 H), 4.66 (s, 2 H), 3.76 (s, 3 H), 2.17 (s, 3 H). ¹³C NMR (400 MHz, CDCl₃) δ 195.96, 173.06, 155.75, 155.16, 134.03, 133.78, 131.43, 130.56, 129.46, 129.27, 128.40, 128.25, 126.75, 126.66, 126.44, 126.29, 122.67, 103.97, 103.38, 63.60, 56.10, 54.15, 45.29. HRMS (EI) calculated for C₄₁H₂₉NO₅: 615.2046; observed: 615.2043.

Balance 1g: Anhydride **5a** (0.11 g, 0.22 mmol) and compound **4g** (0.08 g, 0.44 mmol) were used as reactants. Pale yellow solid, 0.12 g, 0.19 mmol, 88% yield. ¹H NMR (400 MHz, CDCl₃) δ 8.69 (d, *J* = 8.7 Hz, 2 H), 8.45 (d, *J* = 7.6 Hz, 2 H), 7.71 (t, *J* = 7.6 Hz, 2 H), 7.08-7.58 (m, 12 H), 7.01 (t, *J* = 8.5 Hz, 1 H), 6.37 (d, *J* = 8.3 Hz, 1 H), 6.04 (d, *J* = 8.3 Hz, 1 H), 4.63 (s, 2 H), 4.00 (q, *J* = 13.9 Hz, *J* = 6.95 Hz, 2 H), 2.56 (q, *J* = 13.9 Hz, *J* = 7.0 Hz, 2 H), 1.38 (t, *J* = 7.0 Hz, 3 H), 0.10 (t, *J* = 7.0 Hz, 3 H). ¹³C NMR (400 MHz, CDCl₃) δ 195.91, 173.08, 154.66, 154.32, 134.06, 133.86, 131.38, 131.03, 130.26, 129.56, 129.41, 129.11, 128.51, 128.37, 128.07,

126.91, 126.66, 126.38, 122.68, 109.36, 104.54, 104.31, 104.08, 103.83, 64.33, 63.59, 62.16, 45.39, 45.11, 14.88, 14.79. HRMS (EI) calculated for $C_{43}H_{33}NO_5$: 643.2359; observed: 643.2372.

Balance 2a: Anhydride **5b** (0.22 g, 0.59 mmol) and anisidine **4a** (0.11 g, 0.89 mmol) were used as reactants. Pale yellow solid, 0.23 g, 0.48 mmol, 82% yield. 1H NMR (400 MHz, $CDCl_3$) δ 8.08 (m, 4 H major, 4 H minor), 6.78-7.60 (m, 13 H major, 14 H minor), 5.68 (dd, $J = 7.7$ Hz, $J = 1.2$ Hz, 1 H major), 4.31 (s, 2 H major), 4.28 (s, 2 H minor), 3.76 (s, 3 H major), 3.48 (s, 3 H minor). ^{13}C NMR (400 MHz, $CDCl_3$) δ 173.17, 154.77, 144.34, 136.46, 128.82, 128.58, 128.37, 128.00, 127.66, 127.39, 127.02, 120.96, 119.80, 90.53, 55.87, 55.65, 54.80, 54.72, 54.68. HRMS (EI) calculated for $C_{31}H_{23}NO_4$: 473.1627; observed: 473.1613.

Balance 2b: Anhydride **5b** (0.050 g, 0.13 mmol) and phenetidine **4b** (0.023 g, 0.16 mmol) were used as reactants. Pale yellow solid, 0.053 g, 0.11 mmol, 84% yield. 1H NMR (300 MHz, $CDCl_3$) δ 8.08 (m, 4 H major, 4 H minor), 6.70-7.58 (m, 13 H major, 14 H minor), 5.69 (dd, $J = 7.8$ Hz, $J = 1.7$ Hz, 1 H major), 4.30 (s, 2 H major), 4.28 (s, 2 H minor), 4.00 (q, $J = 14.0$ Hz, $J = 7.0$ Hz, 2 H major), 3.91 (q, $J = 14.0$ Hz, $J = 7.0$ Hz, 2 H minor), 1.31 (t, $J = 7.0$ Hz, 3 H major), 1.12 (t, $J = 7.0$ Hz, 3 H minor). ^{13}C NMR (400 MHz, $CDCl_3$) δ 173.09, 154.12, 144.32, 136.50, 130.66, 128.62, 128.57, 128.46, 128.16, 128.12, 127.26, 127.18, 120.96, 120.44, 120.12, 112.83, 90.51, 64.16, 54.68, 14.65. HRMS (EI) calculated for $C_{32}H_{25}NO_4$: 487.1784; observed: 487.1778.

Balance 2c: Anhydride **5b** (0.11 g, 0.30 mmol) and aniline **4f** (0.07 g, 0.45 mmol) were used as reactants. Yellow solid, 0.11 g, 0.23 mmol, 75% yield. 1H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, $J = 7.5$ Hz, 4 H), 6.96-7.59 (m, 11 H), 6.47 (dd, $J = 39.1$ Hz, $J = 8.3$ Hz, 2 H), 4.33 (s, 2 H), 3.74 (s, 3 H), 3.43 (s, 3 H). ^{13}C NMR (400 MHz, $CDCl_3$) δ 172.77, 156.18, 155.58, 144.60, 136.91, 128.77, 128.26, 127.78, 127.38, 127.00, 126.53, 124.64, 123.09, 120.88, 104.32, 104.06, 103.86, 103.58, 90.15, 56.20, 55.99, 55.74, 55.49, 54.76, 54.68. HRMS (EI) calculated for $C_{32}H_{25}NO_5$: 503.1733; observed: 503.1717.

Balance 3: It is a known compound that has been reported.¹⁴ Anhydride **5c** (0.11 g, 0.68 mmol) and o-anisidine (0.10 g, 0.81 mmol, 0.09 mL) were used as reactants. The crude product was heated in oven (130 °C) for 16 h to give the product as white crystal (0.12 g, 0.45 mmol, 66% yield). 1H NMR (400 MHz, $CDCl_3$) δ 7.36 (dt, $J = 7.8$ Hz, $J = 1.4$ Hz, 1 H major, 1 H minor), 6.86-7.06 (m, 3 H major, 3 H minor), 6.28 (s, 2 H major), 6.21 (s, 2 H minor), 3.78 (ds, 3 H major, 3 H minor), 3.37-3.54 (m, 4 H major, 4 H minor), 1.54-1.82 (m, 2 H major, 2 H minor).

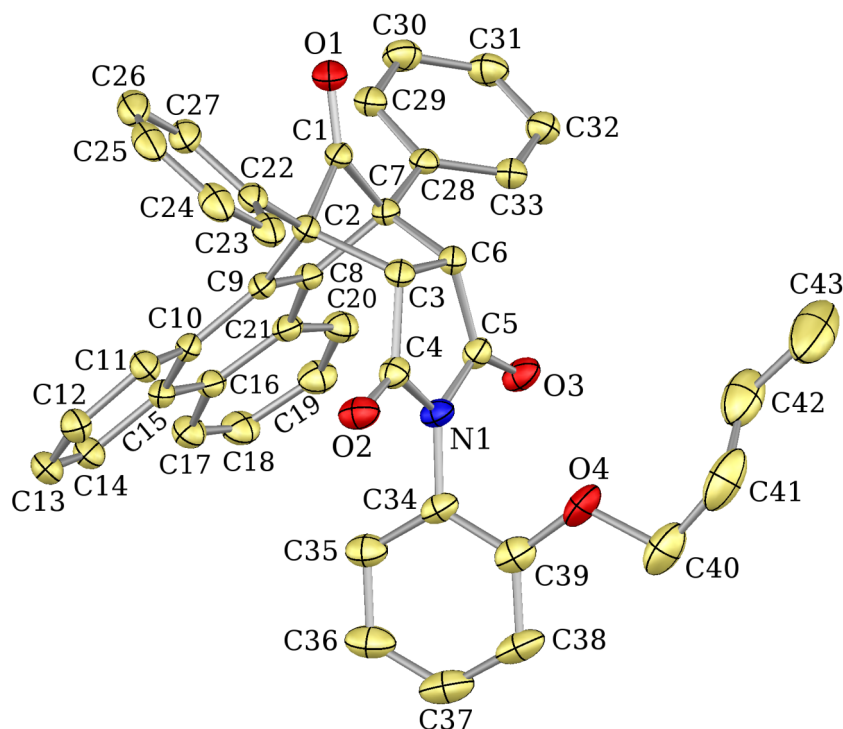
¹⁴ Bagmanov, B. T. *Russ. J. Org. Chem.*, **2007**, *43*, 1635-1641.

Crystal Structures

X-Ray Structure Determination of balance 1d ($C_{43}H_{33}NO_4$)

X-ray intensity data from a colorless plate like crystal were measured at 150(2) K using a Bruker SMART APEX diffractometer (Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å).¹ Raw area detector data frame processing was performed with the SAINT+ program.¹ Final unit cell parameters were determined by least-squares refinement of 2929 reflections from the data set. Direct methods structure solution, difference Fourier calculations and full-matrix least-squares refinement against F^2 were performed with SHELXTL.²

The compound crystallizes in the space group C2/c. The asymmetric unit consists of one $C_{43}H_{33}NO_4$ molecule and an acetonitrile molecule. The acetonitrile is disordered about a two-fold axis of rotation, and therefore only half is present per asymmetric unit. All non-hydrogen atoms were refined with anisotropic displacement parameters. Hydrogen atoms were placed in geometrically idealized positions and included as riding atoms. Large displacement parameters for atom C43 at the end of the butyl group, and for the disordered acetonitrile are because of mild positional disorder of these species.



(1) SMART Version 5.630, SAINT+ Version 6.45. Bruker Analytical X-ray Systems, Inc., Madison, Wisconsin, USA, 2003.

(2) Sheldrick, G. M. SHELXTL Version 6.14; Bruker Analytical X-ray Systems, Inc., Madison, Wisconsin, USA, 2000.

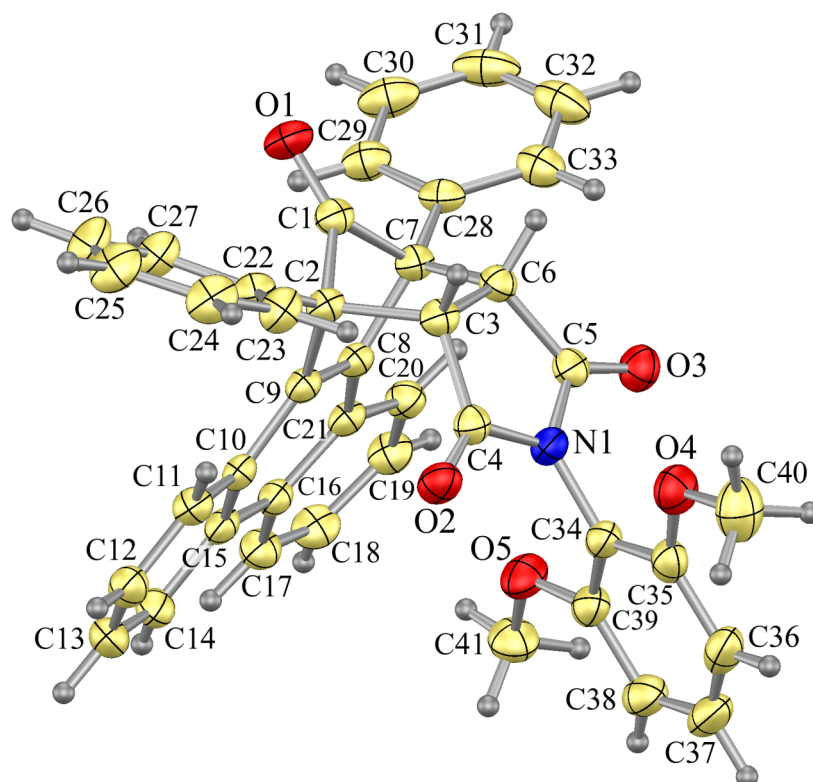
Table 1. Crystal data and structure refinement for balance **1d** ($\text{C}_{43}\text{H}_{33}\text{NO}_4 \cdot 0.5 \text{CH}_3\text{CN}$).

Identification code	cza29m	
Empirical formula	C ₄₄ H _{34.50} N _{1.50} O ₄	
Formula weight	648.23	
Temperature	150(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	C 2/c	
Unit cell dimensions	a = 34.5471(19) Å	$\alpha = 90^\circ$.
	b = 10.8695(6) Å	$\beta = 117.0930(10)^\circ$.
	c = 20.1542(11) Å	$\gamma = 90^\circ$.
Volume	6737.6(6) Å ³	
Z	8	
Density (calculated)	1.278 Mg/m ³	
Absorption coefficient	0.082 mm ⁻¹	
F(000)	2728	
Crystal size	0.12 x 0.10 x 0.08 mm ³	
Theta range for data collection	1.99 to 23.26°.	
Index ranges	-38 ≤ h ≤ 38, -12 ≤ k ≤ 12, -22 ≤ l ≤ 22	
Reflections collected	33988	
Independent reflections	4841 [R(int) = 0.0854]	
Completeness to theta = 23.26°	100.0 %	
Absorption correction	None	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	4841 / 0 / 462	
Goodness-of-fit on F ²	0.868	
Final R indices [I > 2σ(I)]	R1 = 0.0426, wR2 = 0.0728	
R indices (all data)	R1 = 0.0836, wR2 = 0.0851	
Largest diff. peak and hole	0.215 and -0.161 e.Å ⁻³	

X-Ray Structure Determination of balance 1f (C₄₁H₂₉NO₅)

X-ray intensity data from a light brown crystal were measured at 150(2) K using a Bruker SMART APEX diffractometer (Mo K α radiation, $\lambda = 0.71073$ Å).¹ Raw area detector data frame processing was performed with the SAINT+ program.¹ Final unit cell parameters were determined by least-squares refinement of 5287 reflections from the data set. Direct methods structure solution, difference Fourier calculations and full-matrix least-squares refinement against F² were performed with SHELXTL.²

The compound crystallizes in the space group P2₁/n as determined by the pattern of systematic absences in the intensity data. The asymmetric unit consists of one C₄₁H₂₉NO₅ molecule and one acetonitrile molecule of crystallization. All non-hydrogen atoms were refined with anisotropic displacement parameters. Hydrogen atoms were placed in geometrically idealized positions and included as riding atoms.



(1) SMART Version 5.630, SAINT+ Version 6.45. Bruker Analytical X-ray Systems, Inc., Madison, Wisconsin, USA, 2003.

(2) Sheldrick, G. M. SHELXTL Version 6.14; Bruker Analytical X-ray Systems, Inc., Madison, Wisconsin, USA, 2000.

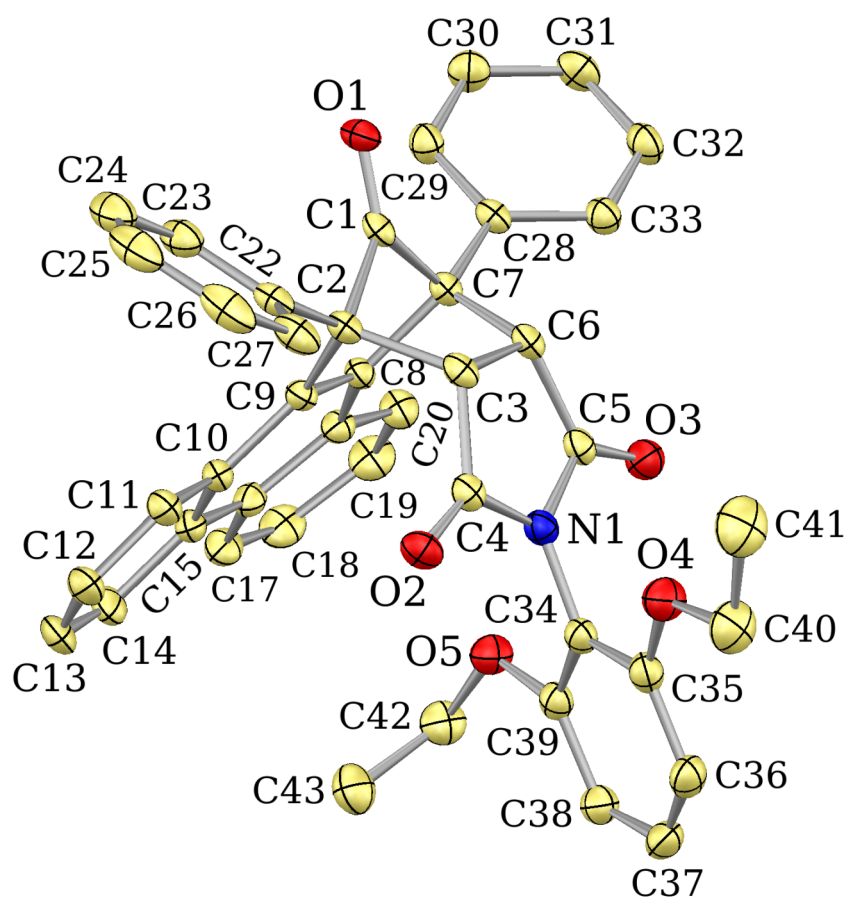
Table 2. Crystal data and structure refinement for balance **1f** (C₄₁H₂₉NO₅).

Identification code	cza39m
Empirical formula	C ₄₃ H ₃₂ N ₂ O ₅
Formula weight	656.71
Temperature	150(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P2 ₁ /n
Unit cell dimensions	a = 9.9283(5) Å α = 90°. b = 29.9924(15) Å β = 107.5400(10)° c = 11.1441(6) Å γ = 90°.
Volume	3164.1(3) Å ³
Z	4
Density (calculated)	1.379 Mg/m ³
Absorption coefficient	0.091 mm ⁻¹
F(000)	1376
Crystal size	0.24 x 0.22 x 0.18 mm ³
Theta range for data collection	2.03 to 25.03°.
Index ranges	-11 ≤ h ≤ 11, -35 ≤ k ≤ 35, -13 ≤ l ≤ 13
Reflections collected	46423
Independent reflections	5587 [R(int) = 0.0566]
Completeness to theta = 25.03°	100.0 %
Absorption correction	None
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	5587 / 0 / 454
Goodness-of-fit on F ²	1.000
Final R indices [I > 2σ(I)]	R1 = 0.0410, wR2 = 0.0991
R indices (all data)	R1 = 0.0567, wR2 = 0.1056
Largest diff. peak and hole	0.248 and -0.219 e.Å ⁻³

X-Ray Structure Determination of balance 1g (C₄₃H₃₃NO₅)

X-ray intensity data from a colorless crystal were measured at 150(2) K using a Bruker SMART APEX diffractometer (Mo K α radiation, λ = 0.71073 Å).¹ Raw area detector data frame processing was performed with the SAINT+ program.¹ Final unit cell parameters were determined by least-squares refinement of 8631 reflections from the data set. Direct methods structure solution, difference Fourier calculations and full-matrix least-squares refinement against F² were performed with SHELXTL.²

The compound crystallizes in the space group P2₁/n as determined by the pattern of systematic absences in the intensity data. The asymmetric unit consists of one C₄₃H₃₃NO₅ molecule and one acetonitrile molecule of crystallization. All non-hydrogen atoms were refined with anisotropic displacement parameters. Hydrogen atoms were placed in geometrically idealized positions and included as riding atoms.



(1) SMART Version 5.630, SAINT+ Version 6.45. Bruker Analytical X-ray Systems, Inc., Madison, Wisconsin, USA, 2003.

(2) Sheldrick, G. M. SHELXTL Version 6.14; Bruker Analytical X-ray Systems, Inc., Madison, Wisconsin, USA, 2000.

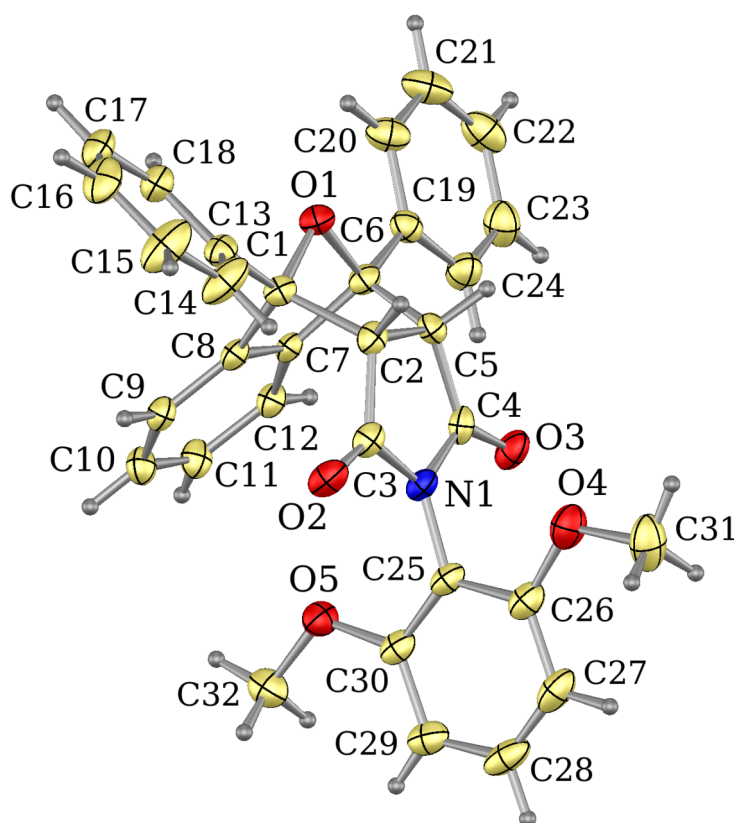
Table 3. Crystal data and structure refinement for balance **1g** (C₄₃H₃₃NO₅).

Identification code	cza125s
Empirical formula	C ₄₅ H ₃₆ N ₂ O ₅
Formula weight	684.76
Temperature	150(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P2 ₁ /n
Unit cell dimensions	a = 9.6496(6) Å α = 90°. b = 21.2791(13) Å β = 92.2550(10)°. c = 17.3549(11) Å γ = 90°.
Volume	3560.8(4) Å ³
Z	4
Density (calculated)	1.277 Mg/m ³
Absorption coefficient	0.083 mm ⁻¹
F(000)	1440
Crystal size	0.48 x 0.40 x 0.26 mm ³
Theta range for data collection	1.51 to 26.41°.
Index ranges	-12 ≤ h ≤ 12, -26 ≤ k ≤ 26, -21 ≤ l ≤ 21
Reflections collected	50276
Independent reflections	7296 [R(int) = 0.0377]
Completeness to theta = 26.41°	99.9 %
Absorption correction	None
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	7296 / 0 / 472
Goodness-of-fit on F ²	1.036
Final R indices [I > 2σ(I)]	R1 = 0.0443, wR2 = 0.1079
R indices (all data)	R1 = 0.0525, wR2 = 0.1138
Largest diff. peak and hole	0.305 and -0.222 e.Å ⁻³

X-Ray Structure Determination of balance 2c (C₃₂H₂₅NO₅)

X-ray intensity data from a thin colorless plate crystal were measured at 150(1) K on a Bruker SMART APEX diffractometer (Mo K α radiation, λ = 0.71073 Å).¹ Raw area detector data frame processing was performed with the SAINT+ program.¹ Final unit cell parameters were determined by least-squares refinement of 1918 reflections from the data set. Direct methods structure solution, difference Fourier calculations and full-matrix least-squares refinement against F² were performed with SHELXTL.²

The compound crystallizes in the triclinic crystal system. The space group P $\bar{1}$ was confirmed by the successful solution and refinement of the data. The asymmetric unit consists of one C₃₂H₂₅NO₅ molecule and half of an ethyl acetate molecule. The ethyl acetate is disordered across an inversion center, therefore only half is present per asymmetric unit. A model using two components with occupancies 30% and 20% was refined with the aid of 20 distance restraints. Atoms of each disorder component were given a common isotropic displacement parameter. All other non-hydrogen atoms were refined with anisotropic displacement parameters. Hydrogen atoms were placed in geometrically idealized positions and included as riding atoms.



(1) SMART Version 5.630, SAINT+ Version 6.45 and SADABS Version 2.10. Bruker Analytical X-ray Systems, Inc., Madison, Wisconsin, USA, 2003.

(2) Sheldrick, G. M. SHELXTL Version 6.14; Bruker Analytical X-ray Systems, Inc., Madison, Wisconsin, USA, 2000.

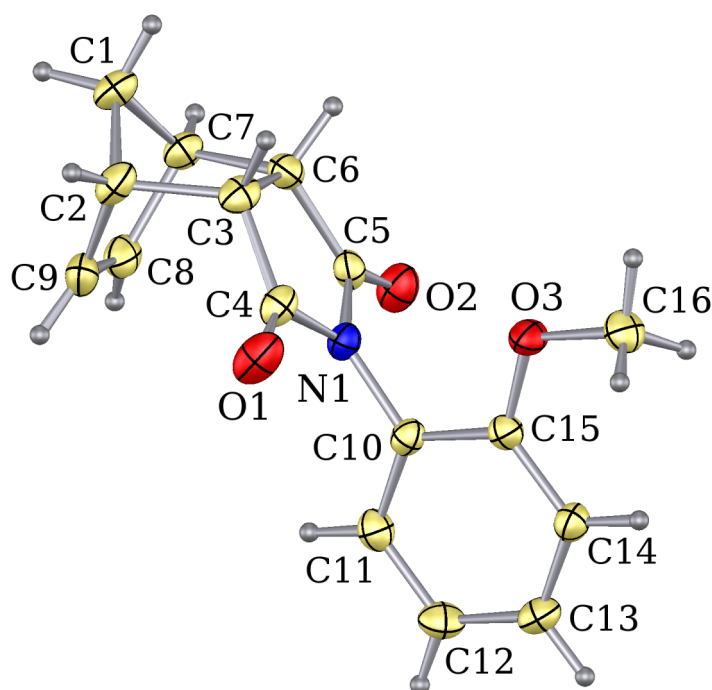
Table 4. Crystal data and structure refinement for balance **2c** (C₃₂H₂₅NO₅).

Identification code	cza137m	
Empirical formula	C ₃₄ H ₂₉ N O ₆	
Formula weight	547.58	
Temperature	150(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P $\bar{1}$	
Unit cell dimensions	a = 8.2930(6) Å	$\alpha = 81.447(2)^\circ$.
	b = 11.2021(9) Å	$\beta = 75.918(2)^\circ$.
	c = 16.2621(12) Å	$\gamma = 70.351(2)^\circ$.
Volume	1376.30(18) Å ³	
Z	2	
Density (calculated)	1.321 Mg/m ³	
Absorption coefficient	0.091 mm ⁻¹	
F(000)	576	
Crystal size	0.24 x 0.20 x 0.04 mm ³	
Theta range for data collection	1.94 to 24.11°.	
Index ranges	-9 ≤ h ≤ 9, -12 ≤ k ≤ 12, -18 ≤ l ≤ 18	
Reflections collected	14569	
Independent reflections	4373 [R(int) = 0.0728]	
Completeness to theta = 24.11°	100.0 %	
Absorption correction	None	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	4373 / 20 / 383	
Goodness-of-fit on F ²	0.863	
Final R indices [I > 2σ(I)]	R1 = 0.0477, wR2 = 0.0894	
R indices (all data)	R1 = 0.0909, wR2 = 0.1007	
Largest diff. peak and hole	0.391 and -0.429 e.Å ⁻³	

X-Ray Structure Determination of balance 3 (C₁₆H₁₅NO₃)

X-ray intensity data from a colorless block-like crystal were measured at 150(2) K using a Bruker SMART APEX diffractometer (Mo K α radiation, $\lambda = 0.71073$ Å).¹ Raw area detector data frame processing was performed with the SAINT+ program.¹ Final unit cell parameters were determined by least-squares refinement of 6028 reflections from the data set. Direct methods structure solution, difference Fourier calculations and full-matrix least-squares refinement against F² were performed with SHELXTL.²

The compound crystallizes in the orthorhombic system. The space group P2₁2₁2₁ was determined uniquely by examination of the pattern of systematic absences in the intensity data. The asymmetric unit consists of one molecule. All non-hydrogen atoms were refined with anisotropic displacement parameters. Hydrogen atoms were placed in geometrically idealized positions and included as riding atoms. Because of the absences of heavy atoms in the crystal, Friedel opposites were merged during the refinement and the absolute structure not determined.



(1) SMART Version 5.630, SAINT+ Version 6.45. Bruker Analytical X-ray Systems, Inc., Madison, Wisconsin, USA, 2003.

(2) Sheldrick, G. M. SHELXTL Version 6.14; Bruker Analytical X-ray Systems, Inc., Madison, Wisconsin, USA, 2000.

Table 5. Crystal data and structure refinement for balance **3** (C₁₆H₁₅NO₃).

Identification code	cza103m	
Empirical formula	C ₁₆ H ₁₅ N O ₃	
Formula weight	269.29	
Temperature	150(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P2 ₁ 2 ₁ 2 ₁	
Unit cell dimensions	a = 10.1874(5) Å	α = 90°.
	b = 10.7672(6) Å	β = 90°.
	c = 11.9335(6) Å	γ = 90°.
Volume	1308.98(12) Å ³	
Z	4	
Density (calculated)	1.366 Mg/m ³	
Absorption coefficient	0.095 mm ⁻³	
F(000)	568	
Crystal size	0.42 x 0.38 x 0.20 mm ³	
Theta range for data collection	2.55 to 27.54°.	
Index ranges	-13 ≤ h ≤ 13, -14 ≤ k ≤ 14, -15 ≤ l ≤ 15	
Reflections collected	23394	
Independent reflections	1733 [R(int) = 0.0380]	
Completeness to theta = 27.54°	100.0 %	
Absorption correction	None	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	1733 / 0 / 182	
Goodness-of-fit on F ²	1.059	
Final R indices [I > 2σ(I)]	R1 = 0.0325, wR2 = 0.0867	
R indices (all data)	R1 = 0.0337, wR2 = 0.0879	
Absolute structure parameter	opposites merged	
Largest diff. peak and hole	0.261 and -0.174 e.Å ⁻³	

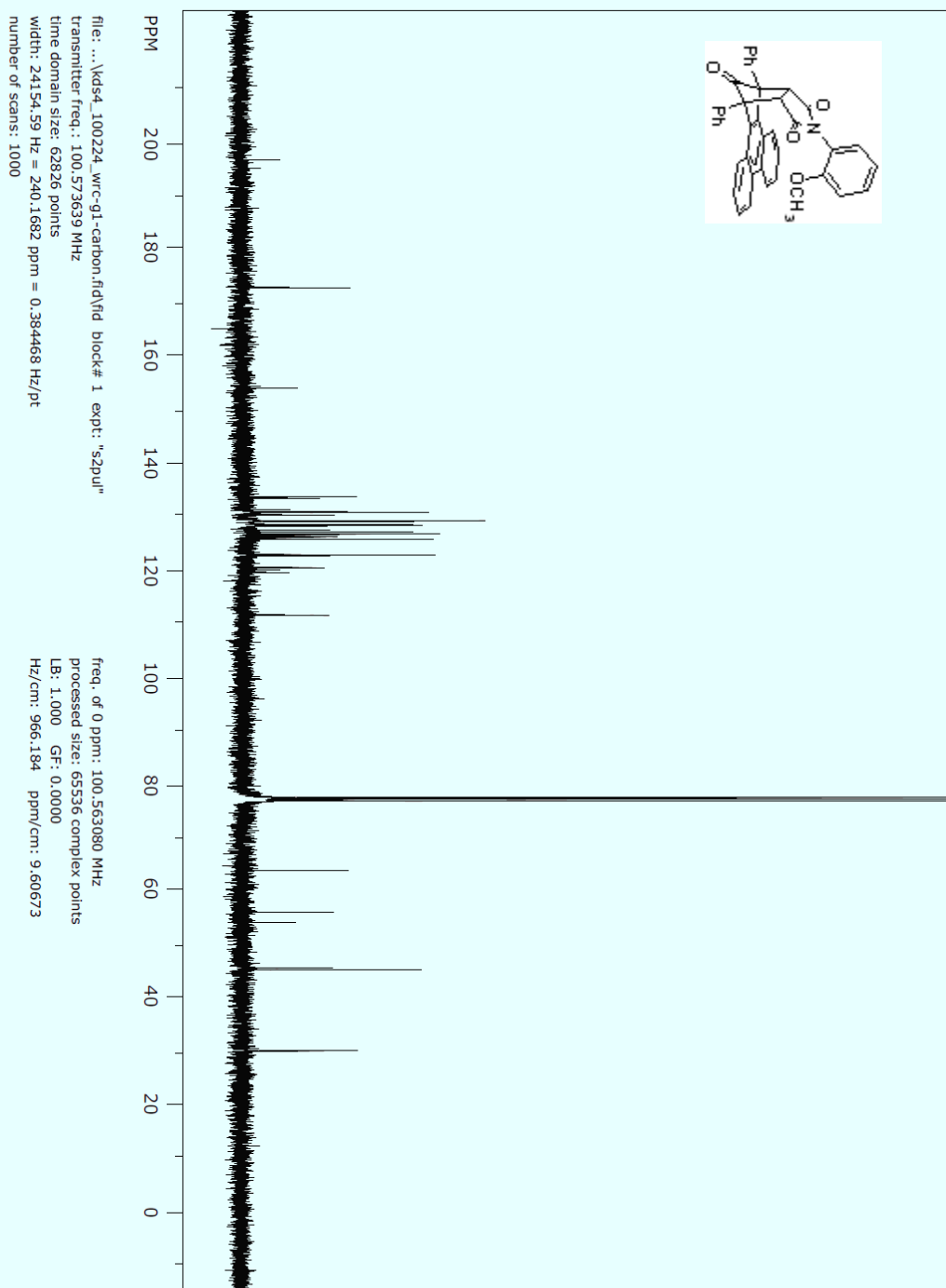
SpinWorks 3:

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time domain size: 38388 points
width: 6397.95 Hz = 15.9981 ppm = 0.16665 Hz/pt
number of scans: 16

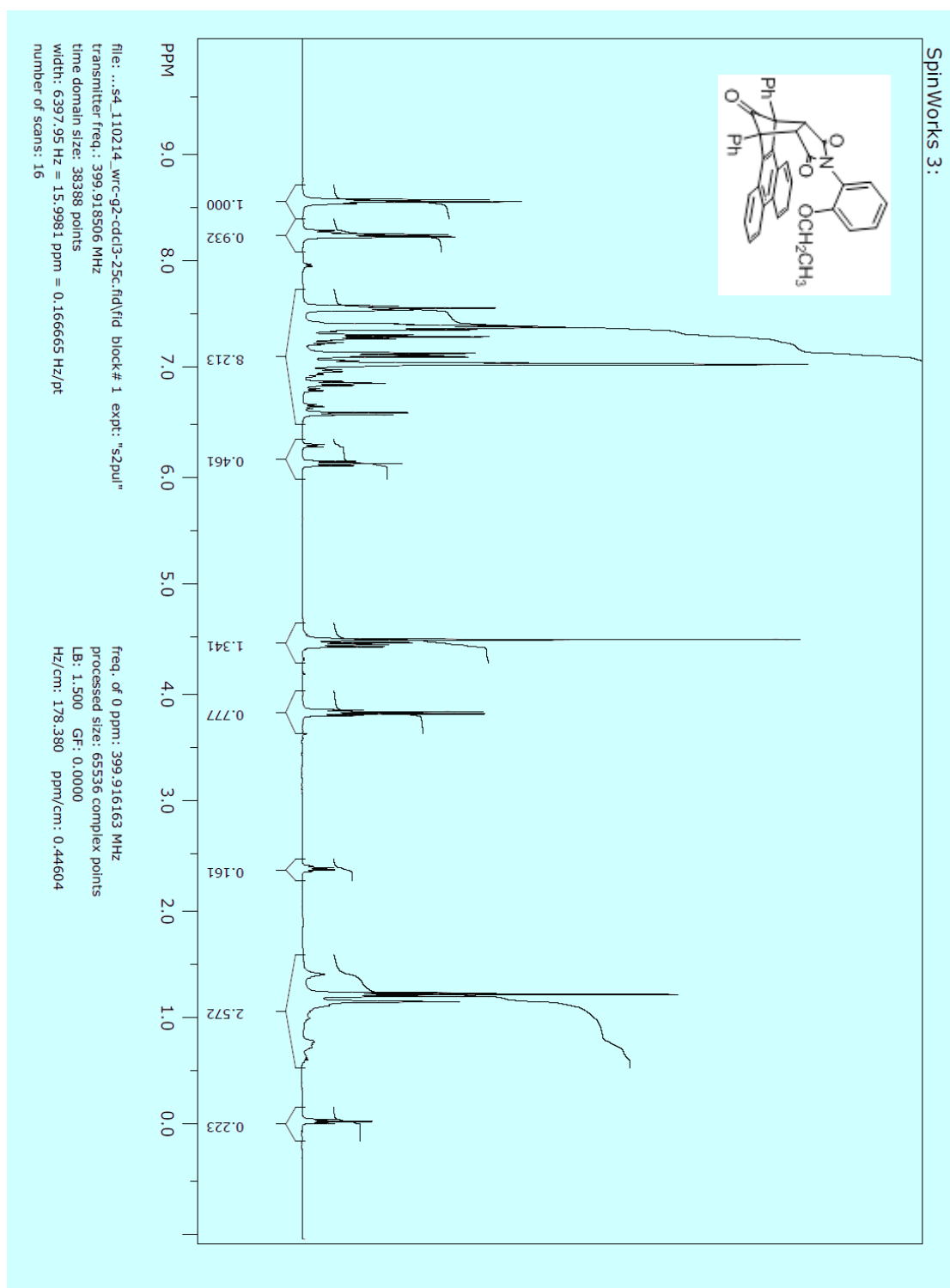
freq. of 0 ppm: 399.916107 MHz
processed size: 65536 complex points
LB: 0.500 GF: 0.0000
Hz/cm: 168.579 ppm/cm: 0.42153

S20

SpinWorks 3:

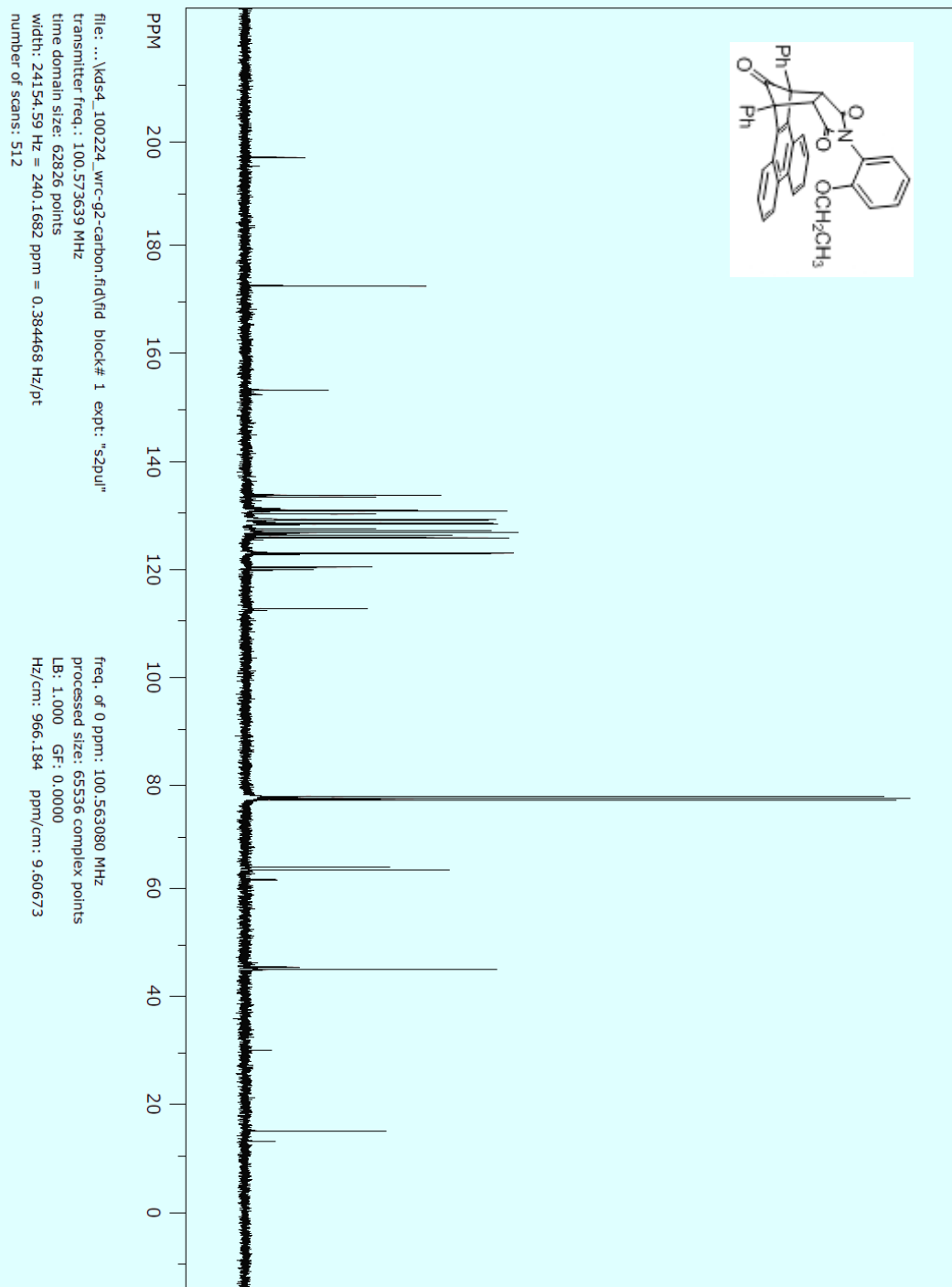
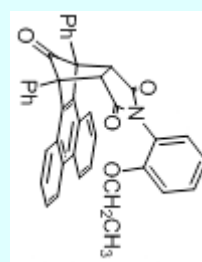


Spectrum 2: 400 MHz ¹³C NMR spectrum of balance **1a** in CDCl₃.



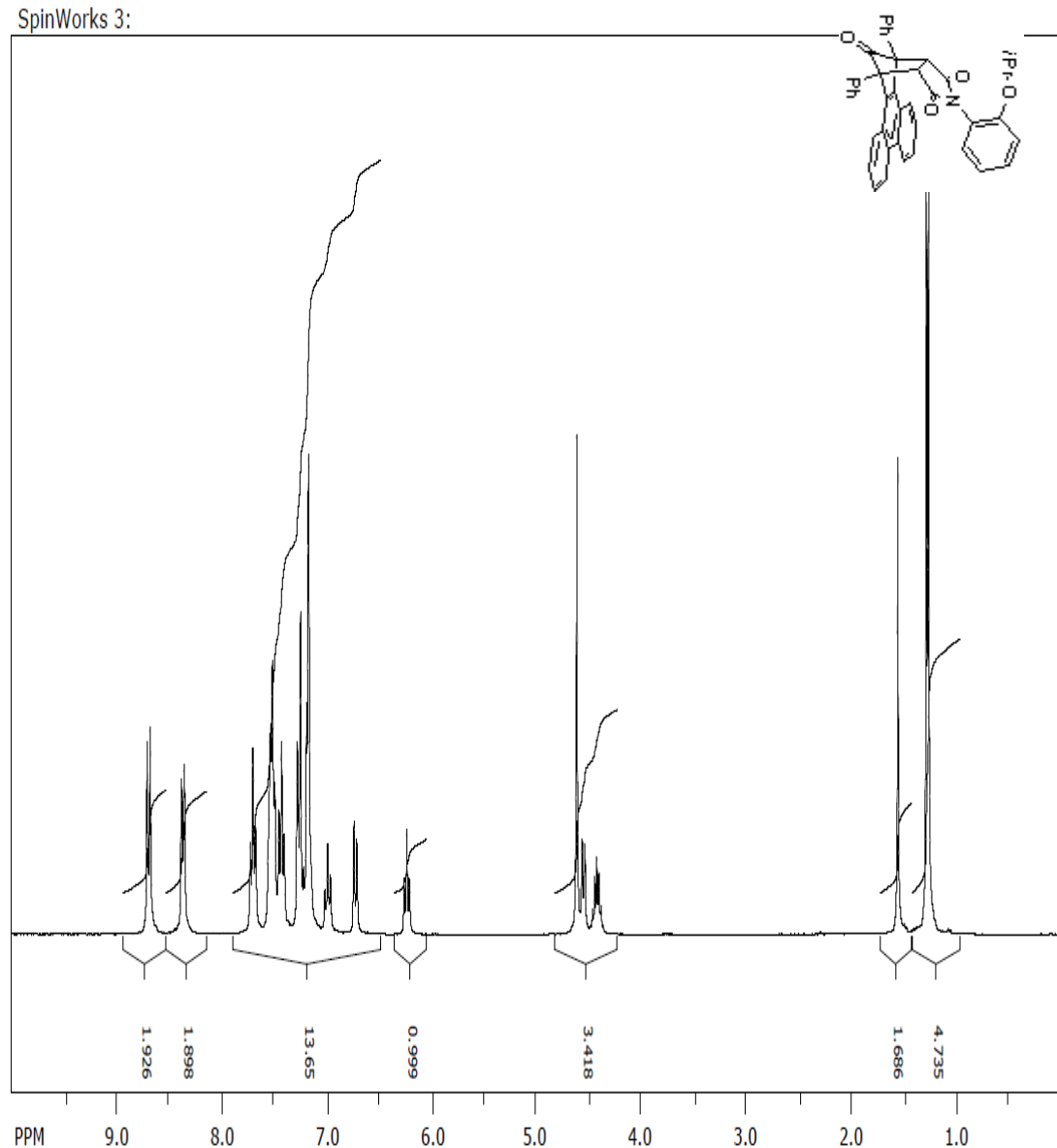
Spectrum 3: 400 MHz ^1H NMR spectrum of balance **1b** in CDCl_3

SpinWorks 3:



Spectrum 4: 400 MHz ^{13}C NMR spectrum of balance **1b** in CDCl_3

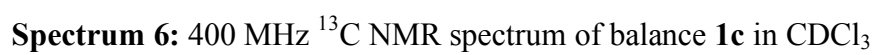
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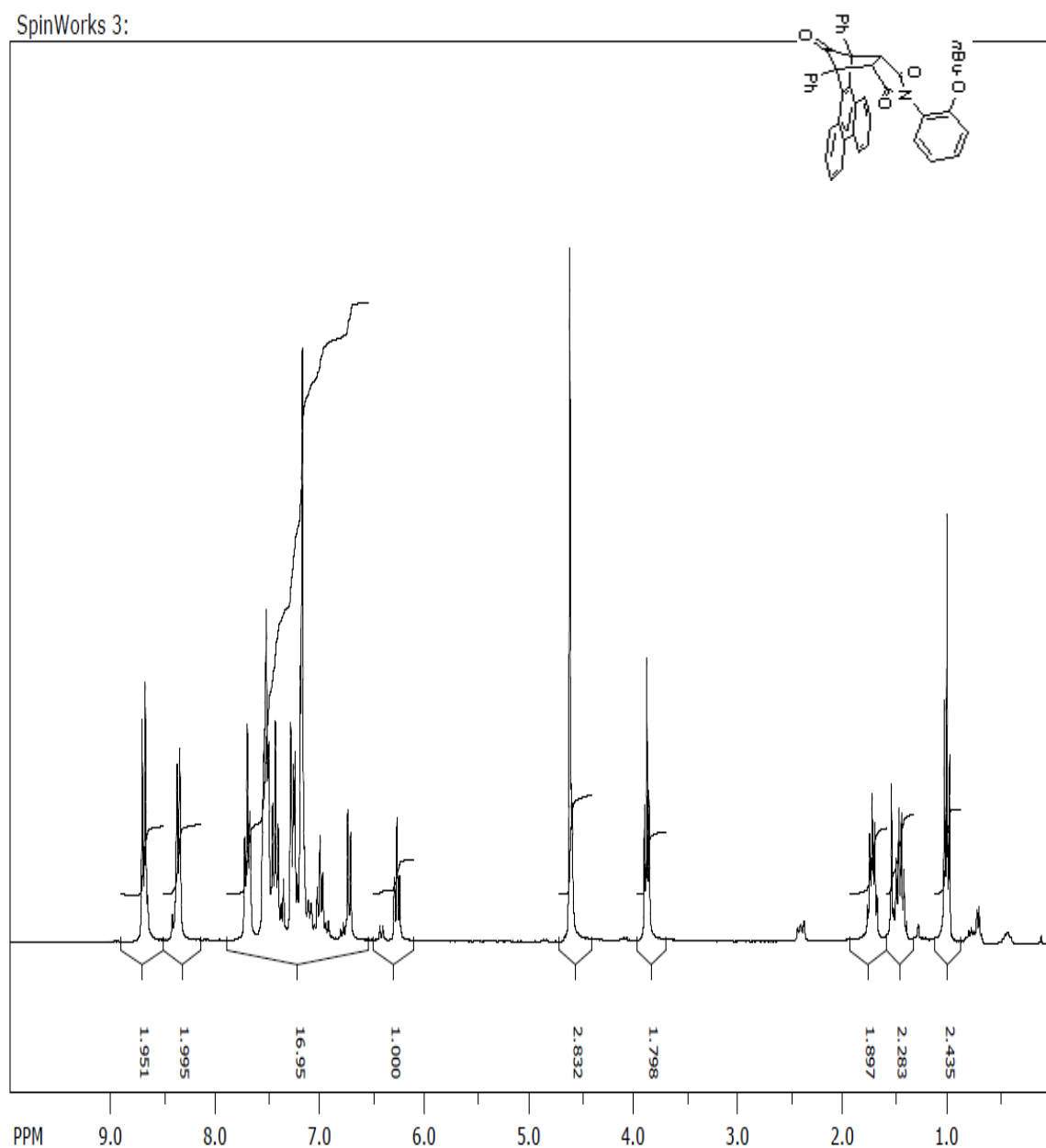
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 transmitter freq.: 300.106300 MHz
 time domain size: 19184 points
 width: 4803.07 Hz = 16.0046 ppm = 0.250369 Hz/pt
 number of scans: 16

freq. of 0 ppm: 300.104499 MHz
 processed size: 32768 complex points
 LB: 1.500 GF: 0.0000
 Hz/cm: 120.670 ppm/cm: 0.40209

Spectrum 5: 300 MHz ¹H NMR spectrum of balance **1c** in CDCl₃



SpinWorks 3:

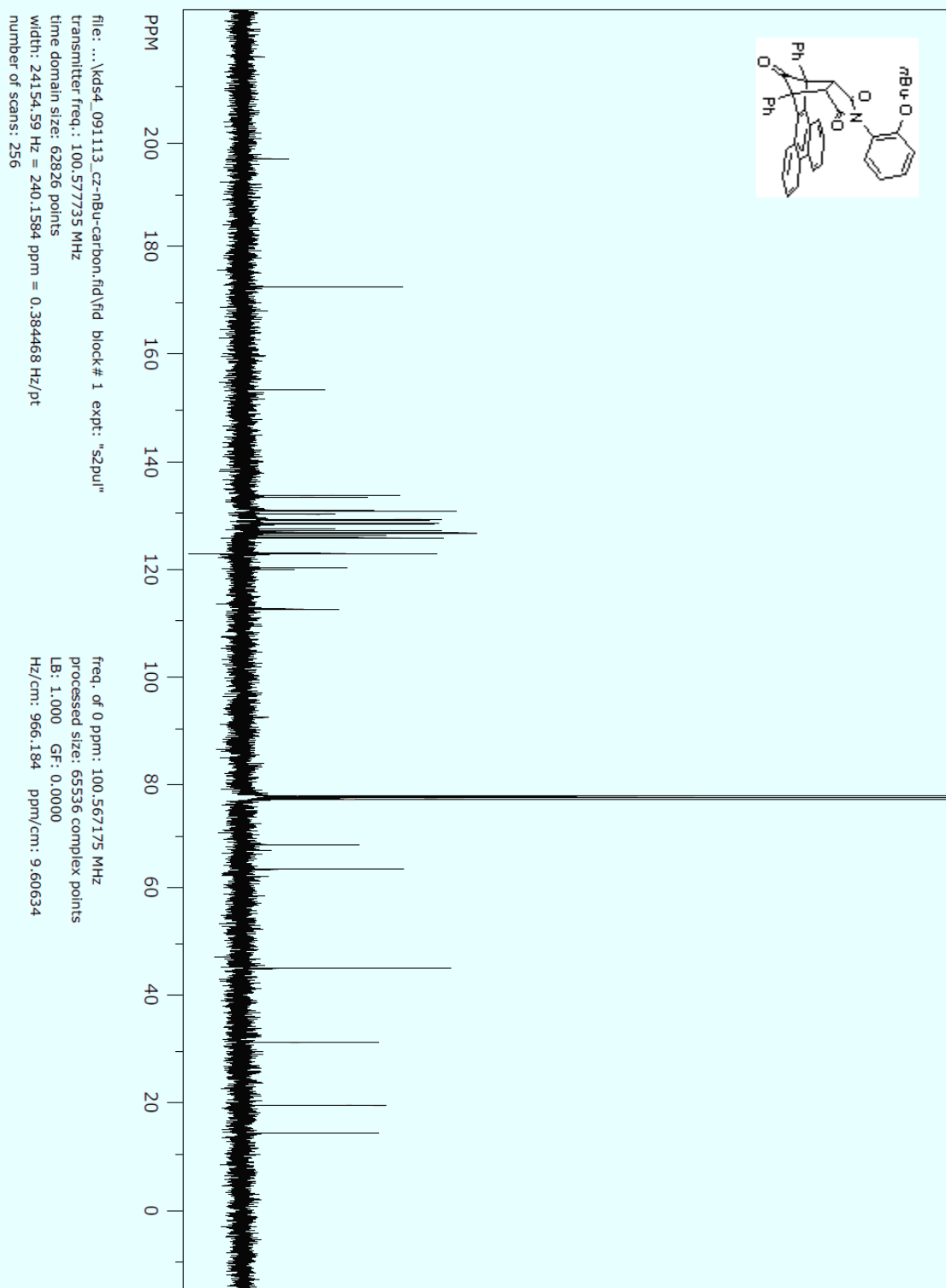


file: ...\\NMR\\kds3_100504_cz-a-OnBu.fid\\fid_block# 1 expt: "s2pul"
 transmitter freq.: 300.106300 MHz
 time domain size: 28804 points
 width: 4800.77 Hz = 15.9969 ppm = 0.166670 Hz/pt
 number of scans: 16

freq. of 0 ppm: 300.104499 MHz
 processed size: 32768 complex points
 LB: 1.500 GF: 0.0000
 Hz/cm: 120.121 ppm/cm: 0.40026

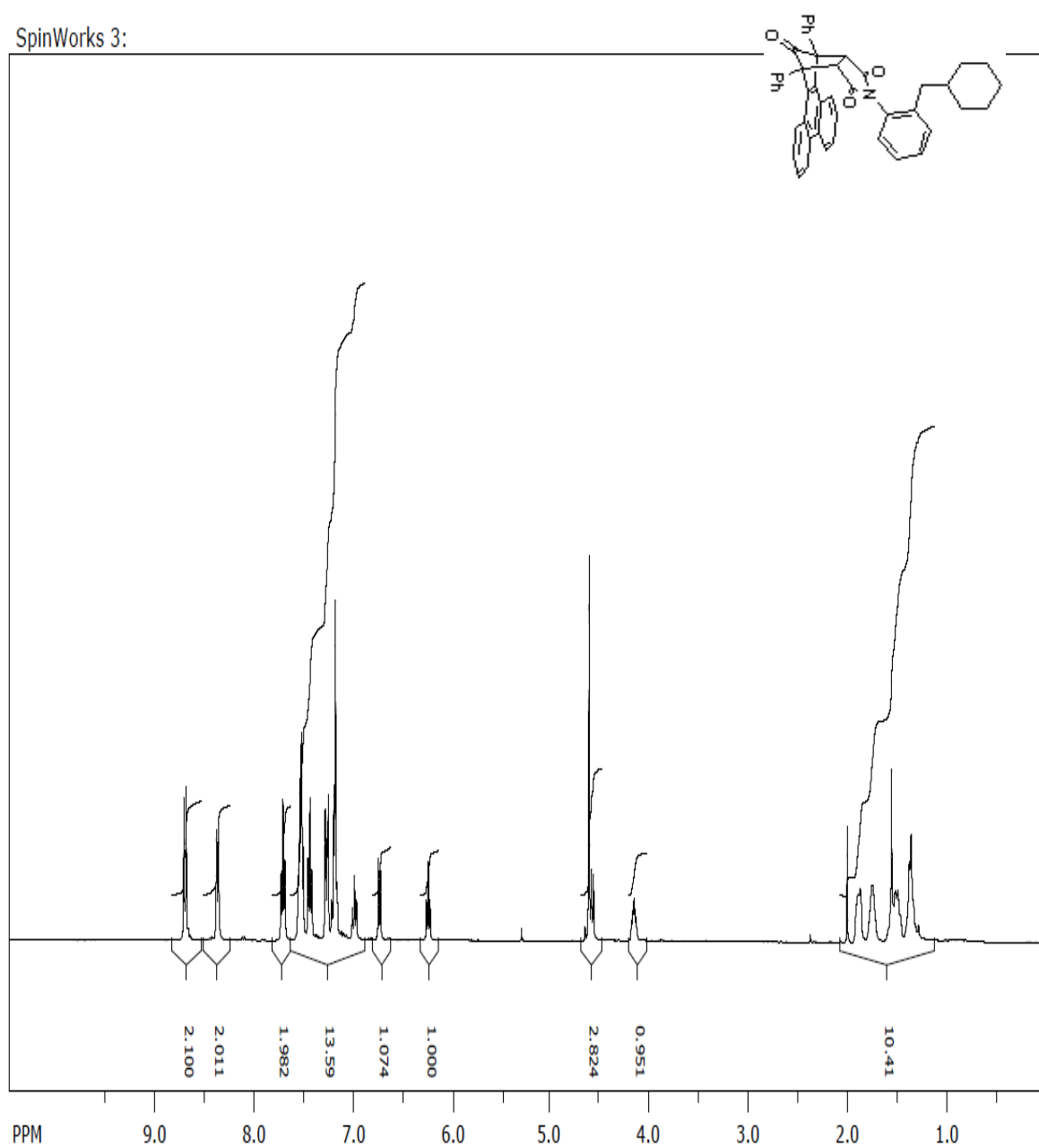
Spectrum 7: 300 MHz ^1H NMR spectrum of balance **1d** in CDCl_3 .

SpinWorks 3:



Spectrum 8: 400 MHz ^{13}C NMR spectrum of balance **1d** in CDCl₃.

SpinWorks 3:

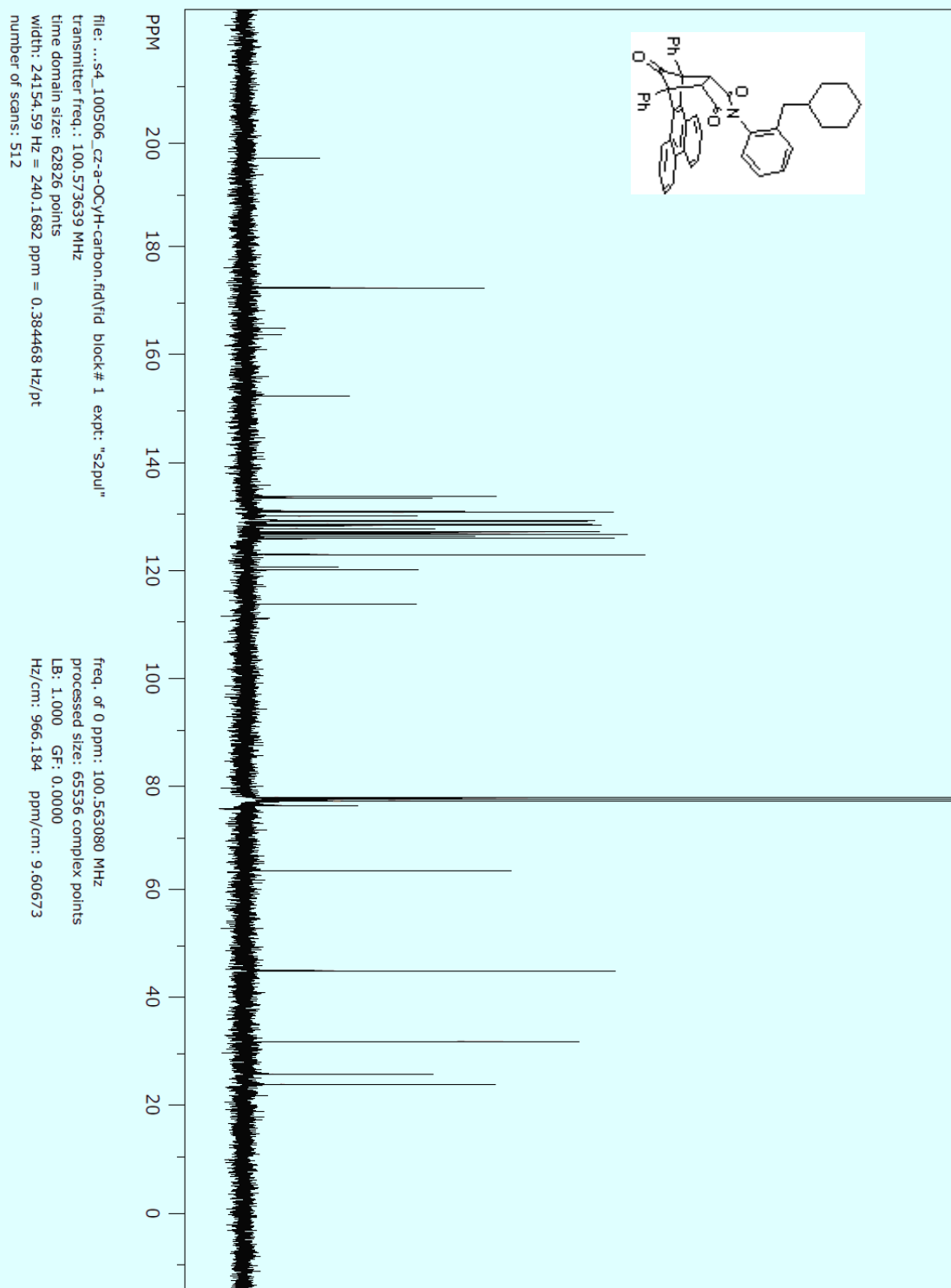


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 width: 6397.95 Hz = 15.9975 ppm = 0.166665 Hz/pt
 number of scans: 16

freq. of 0 ppm: 399.932393 MHz
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 LB: 1.500 GF: 0.0000
 Hz/cm: 167.926 ppm/cm: 0.41988

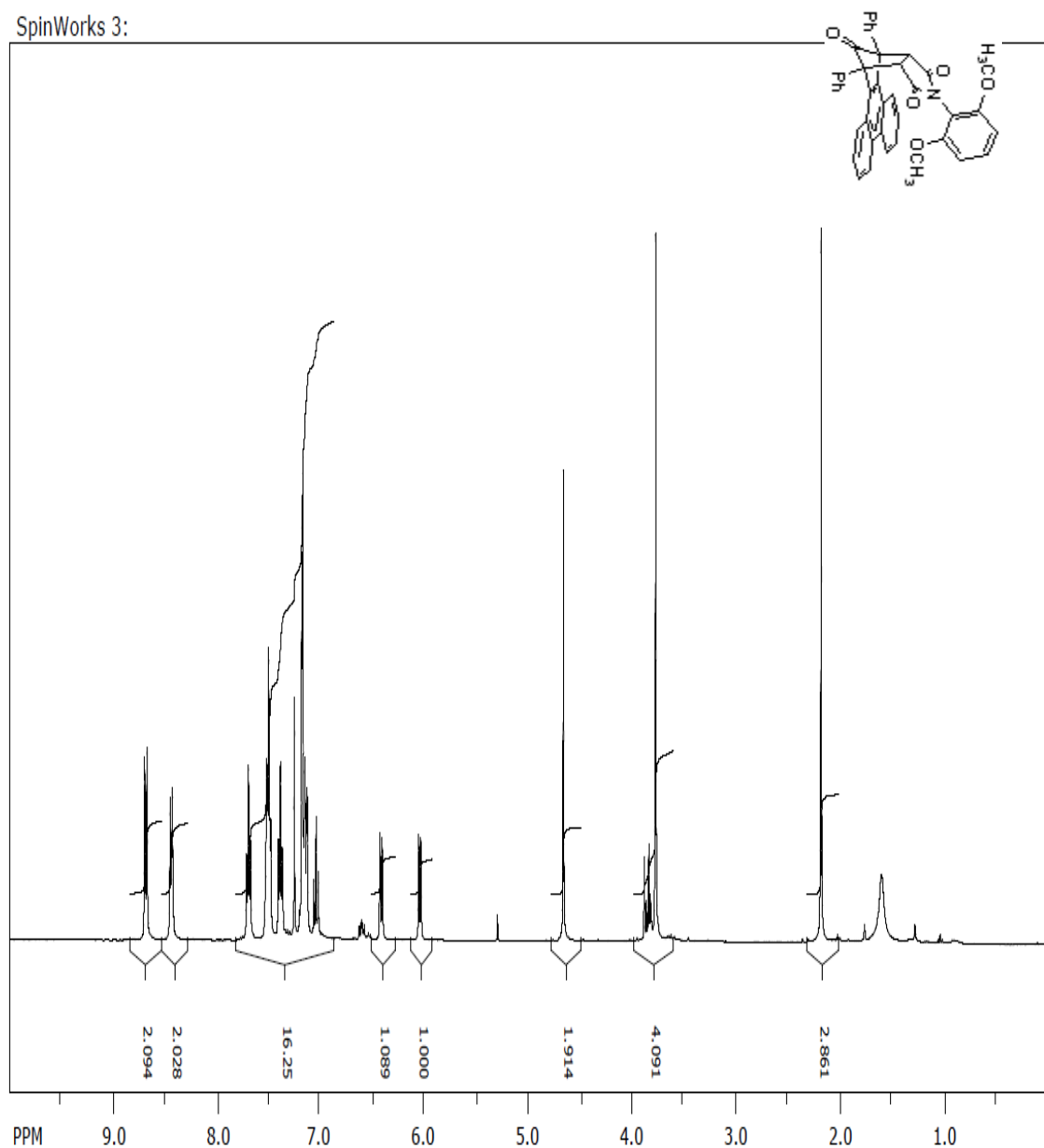
Spectrum 9: 400 MHz ¹H NMR spectrum of balance **1e** in CDCl₃.

SpinWorks 3:



Spectrum 10: 400 MHz ^{13}C NMR spectrum of balance **1e** in CDCl_3 .

SpinWorks 3:

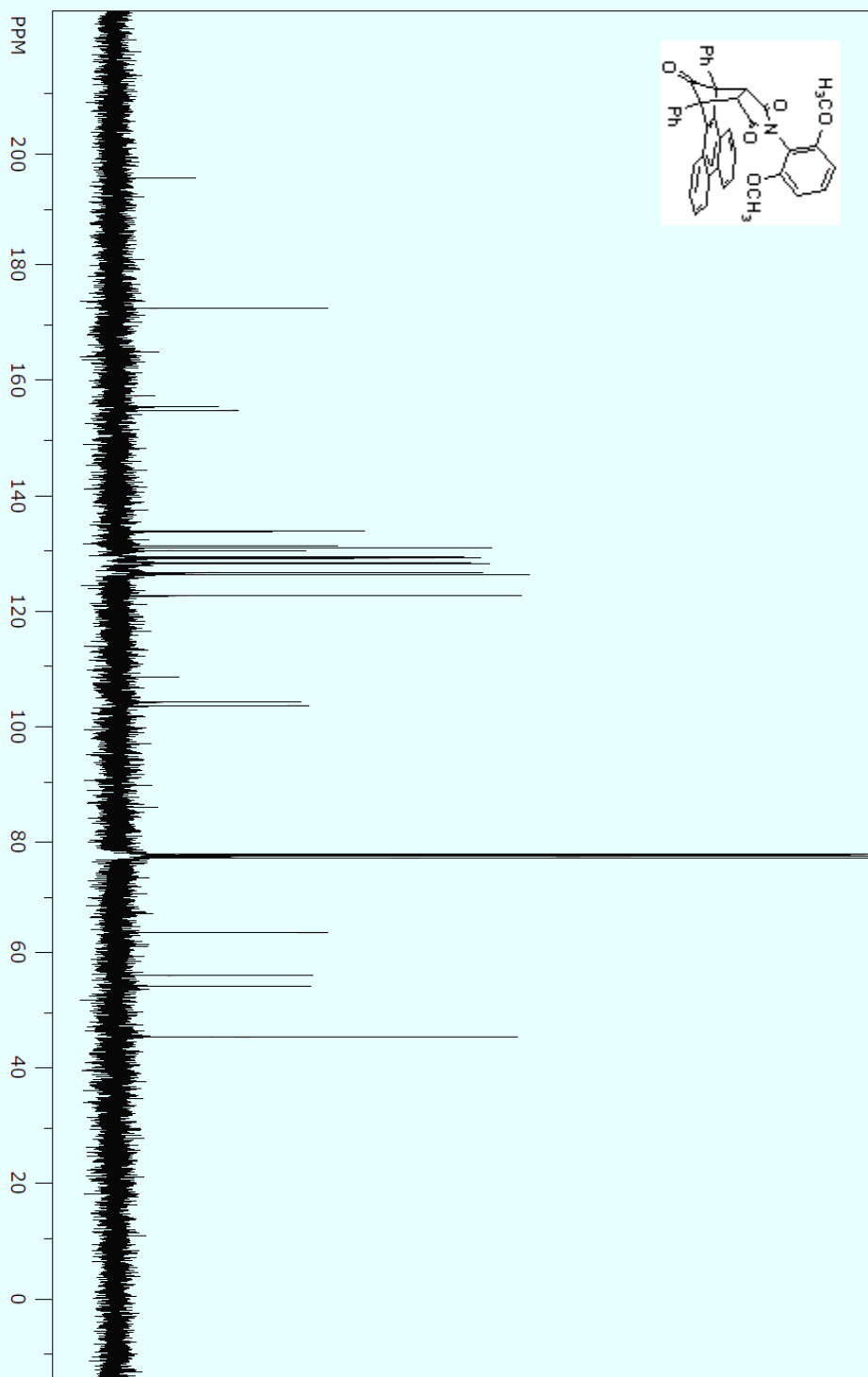
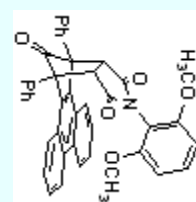


file: ...MR\kds4_100518_cz-a-35.2-p.fid\fid_block# 1 expt: "s2pul"
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 time domain size: 38388 points
 width: 6397.95 Hz = 15.9975 ppm = 0.166665 Hz/pt
 number of scans: 16

freq. of 0 ppm: 399.932393 MHz
 processed size: 65536 complex points
 LB: 1.500 GF: 0.0000
 Hz/cm: 160.738 ppm/cm: 0.40191

Spectrum 11: 400 MHz ¹H NMR spectrum of balance **1f** in CDCl₃.

SpinWorks 3:

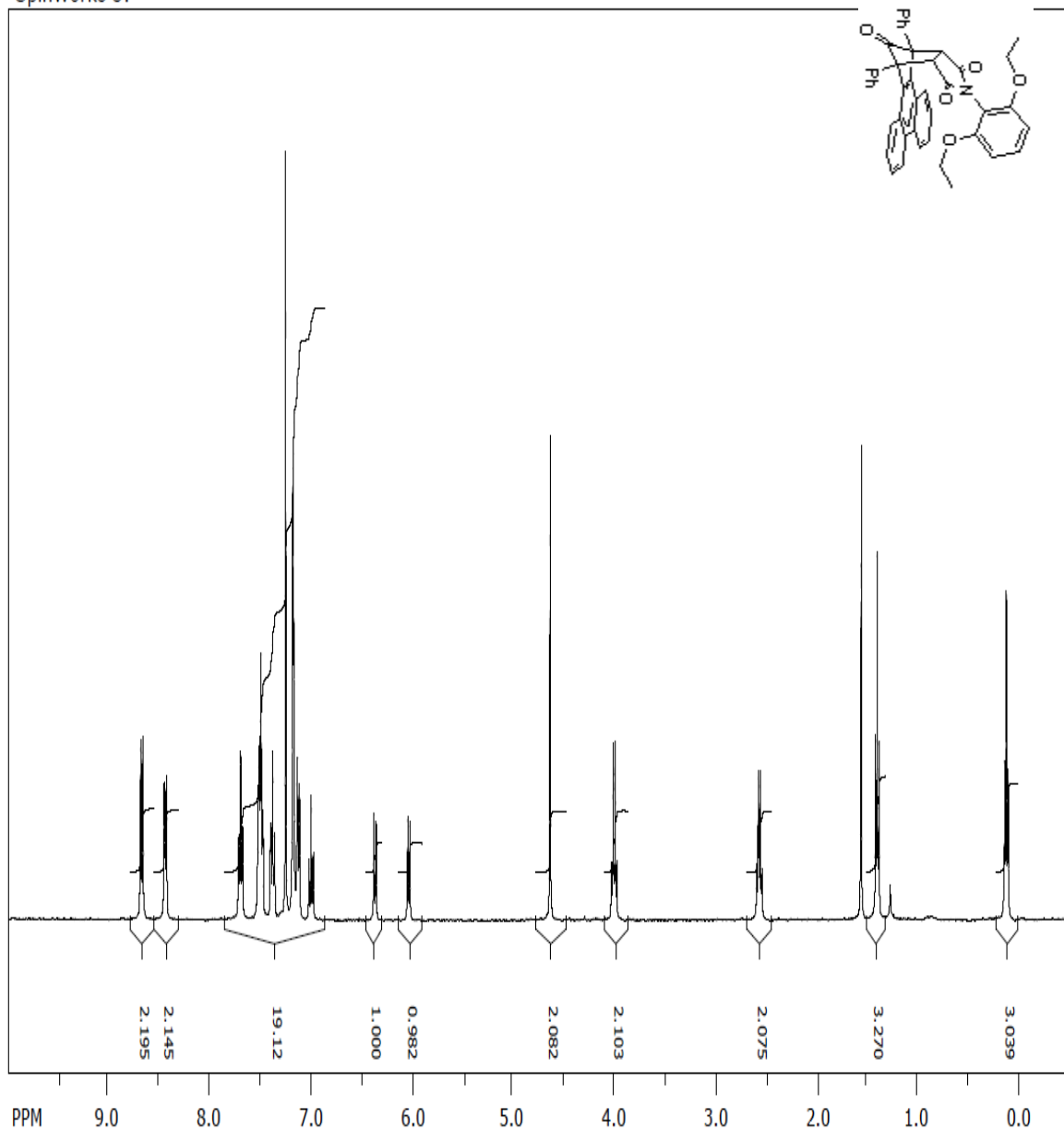


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 transmitter freq.: 100.573639 MHz
 time domain size: 62826 points
 width: 24154.59 Hz = 240.1682 ppm = 0.384468 Hz/pt
 number of scans: 512

freq. of 0 ppm: 100.563080 MHz
 processed size: 65536 complex points
 LB: 1.000 GF: 0.0000
 Hz/cm: 966.184 ppm/cm: 9.60673

Spectrum 12: 400 MHz ^{13}C NMR spectrum of balance **1f** in CDCl_3 .

SpinWorks 3:

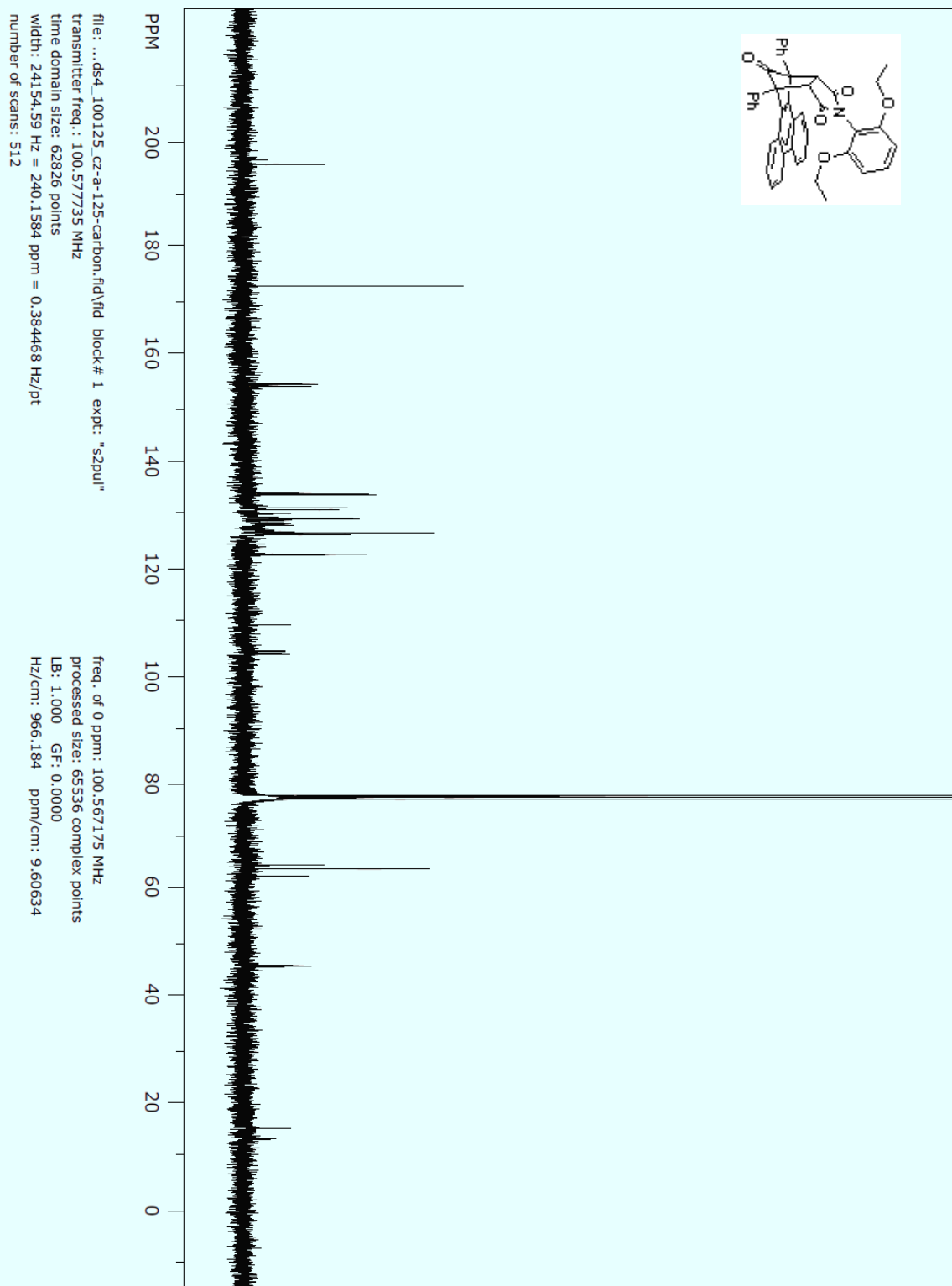


file: ...y\NMR\kds4_100120_cz-a-125.fid\fid block# 1 expt: "s2pul"
 transmitter freq.: 399.951078 MHz
 time domain size: 38388 points
 width: 6397.95 Hz = 15.9968 ppm = 0.166665 Hz/pt
 number of scans: 16

freq. of 0 ppm: 399.948678 MHz
 processed size: 65536 complex points
 LB: 1.500 GF: 0.0000
 Hz/cm: 168.579 ppm/cm: 0.42150

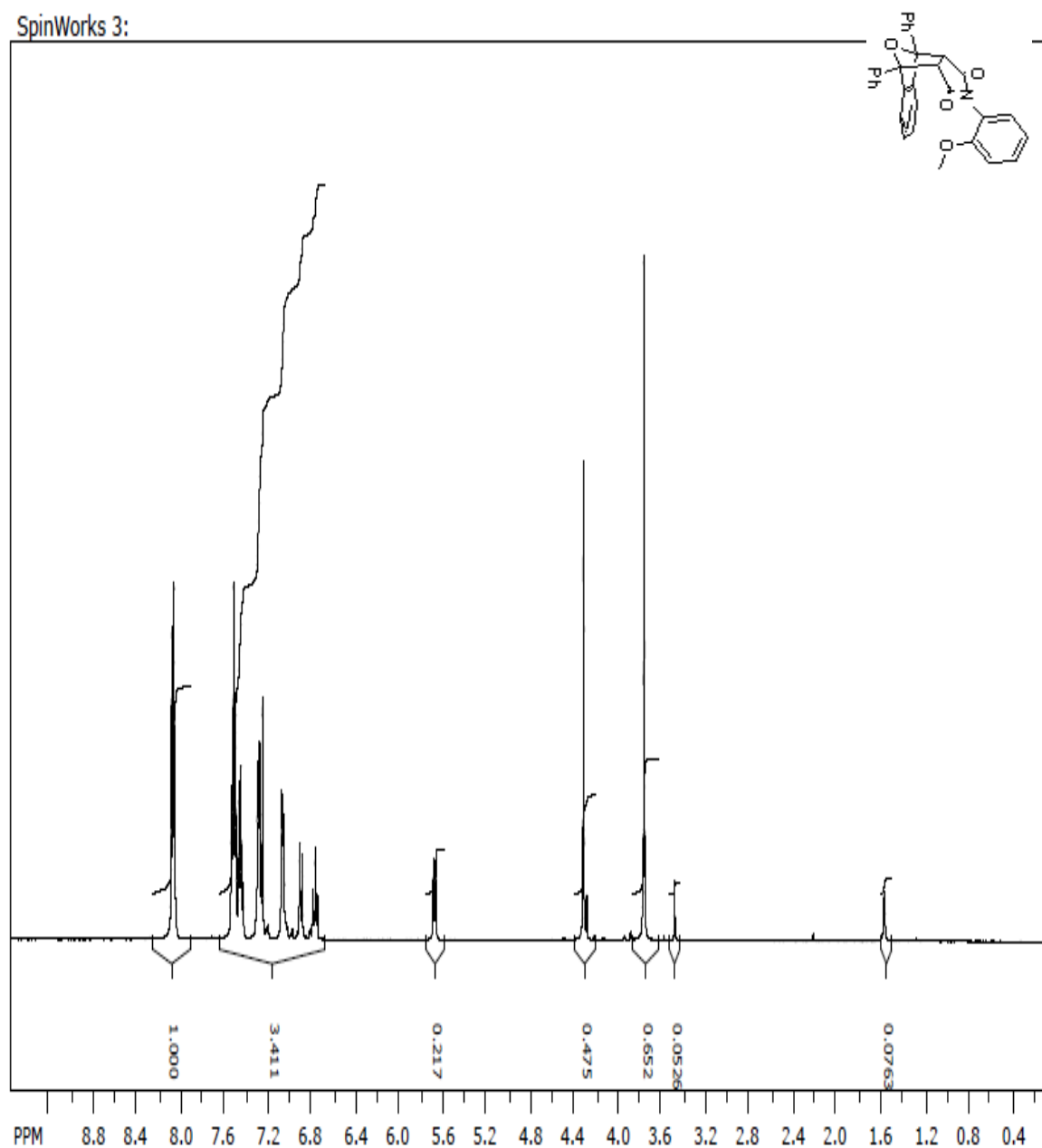
Spectrum 13: 400 MHz ¹H NMR spectrum of balance **1g** in CDCl₃.

SpinWorks 3:



Spectrum 14: 400 MHz ^{13}C NMR spectrum of balance **1g** in CDCl_3 .

SpinWorks 3:

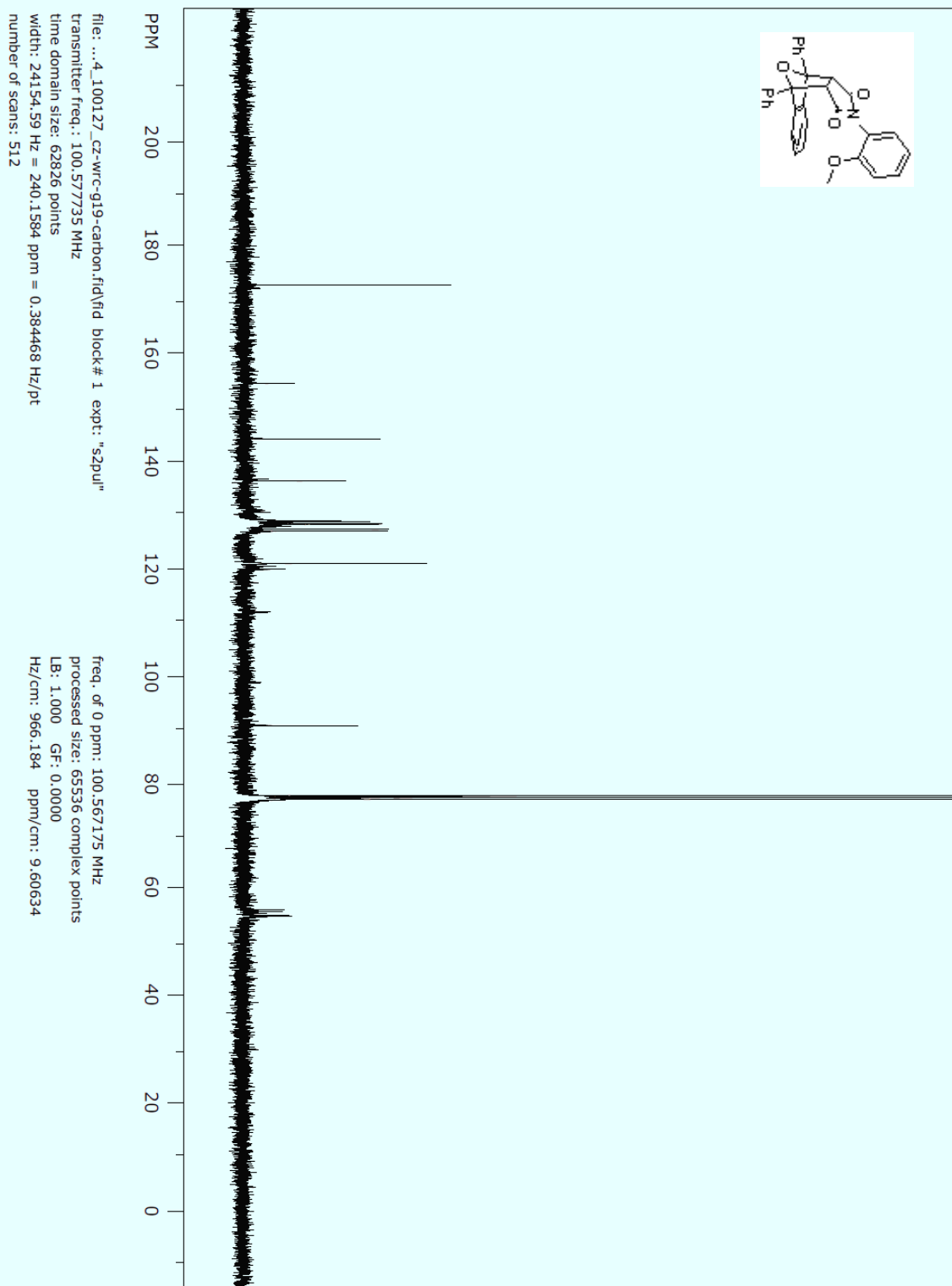
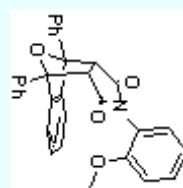


file: ...NMR\kds4_100127_cz-wrc-g19.fid\fid block# 1 expt: "s2pul"
 transmitter freq.: 399.951078 MHz
 time domain size: 38388 points
 width: 6397.95 Hz = 15.9968 ppm = 0.166665 Hz/pt
 number of scans: 16

freq. of 0 ppm: 399.940679 MHz
 processed size: 65536 complex points
 LB: 1.500 GF: 0.0000
 Hz/cm: 152.244 ppm/cm: 0.38066

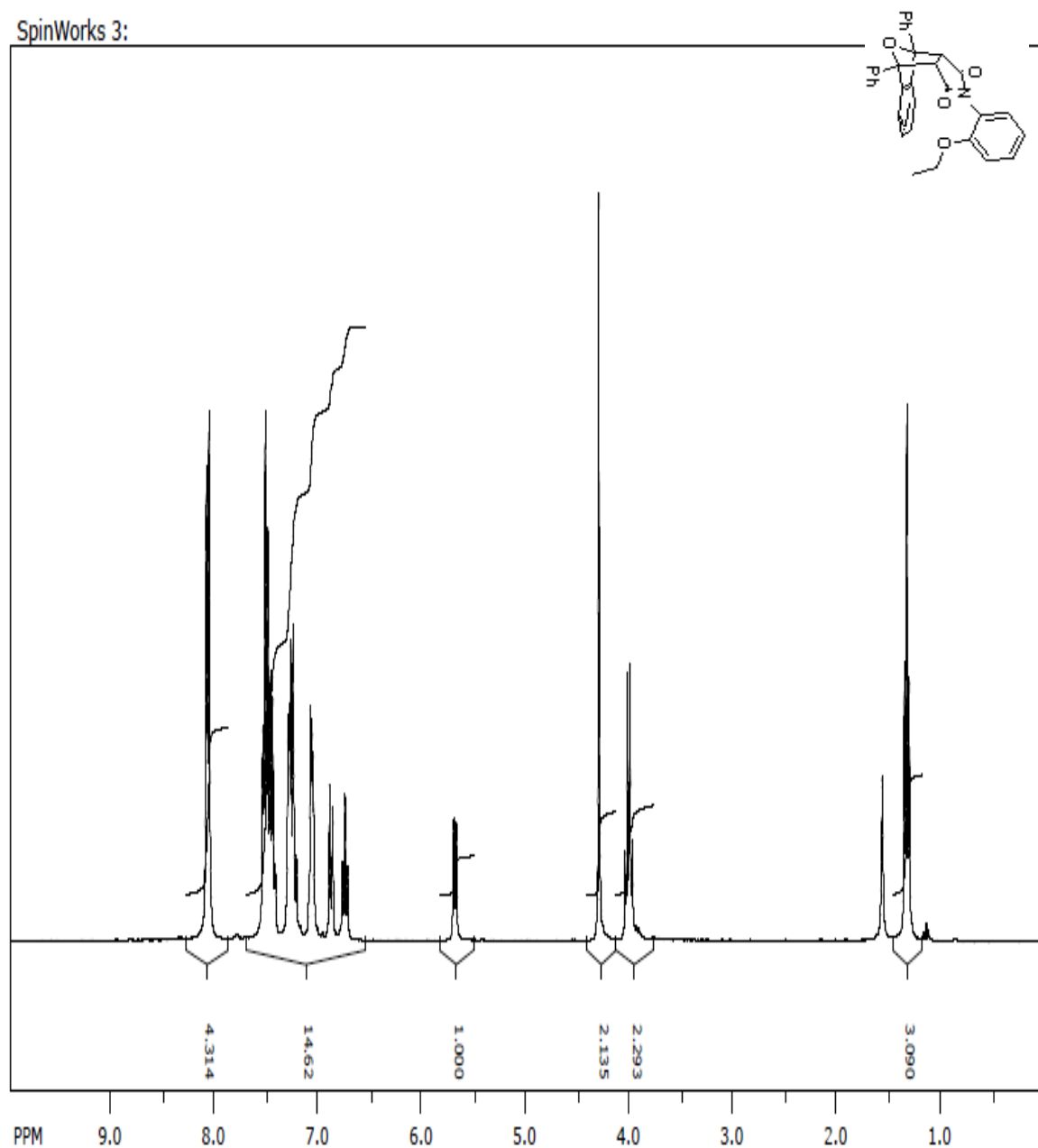
Spectrum 15: 400 MHz ^1H NMR spectrum of balance **2a** in CDCl_3 .

SpinWorks 3:



Spectrum 16: 400 MHz ^{13}C NMR spectrum of balance **2a** in CDCl_3 .

SpinWorks 3:

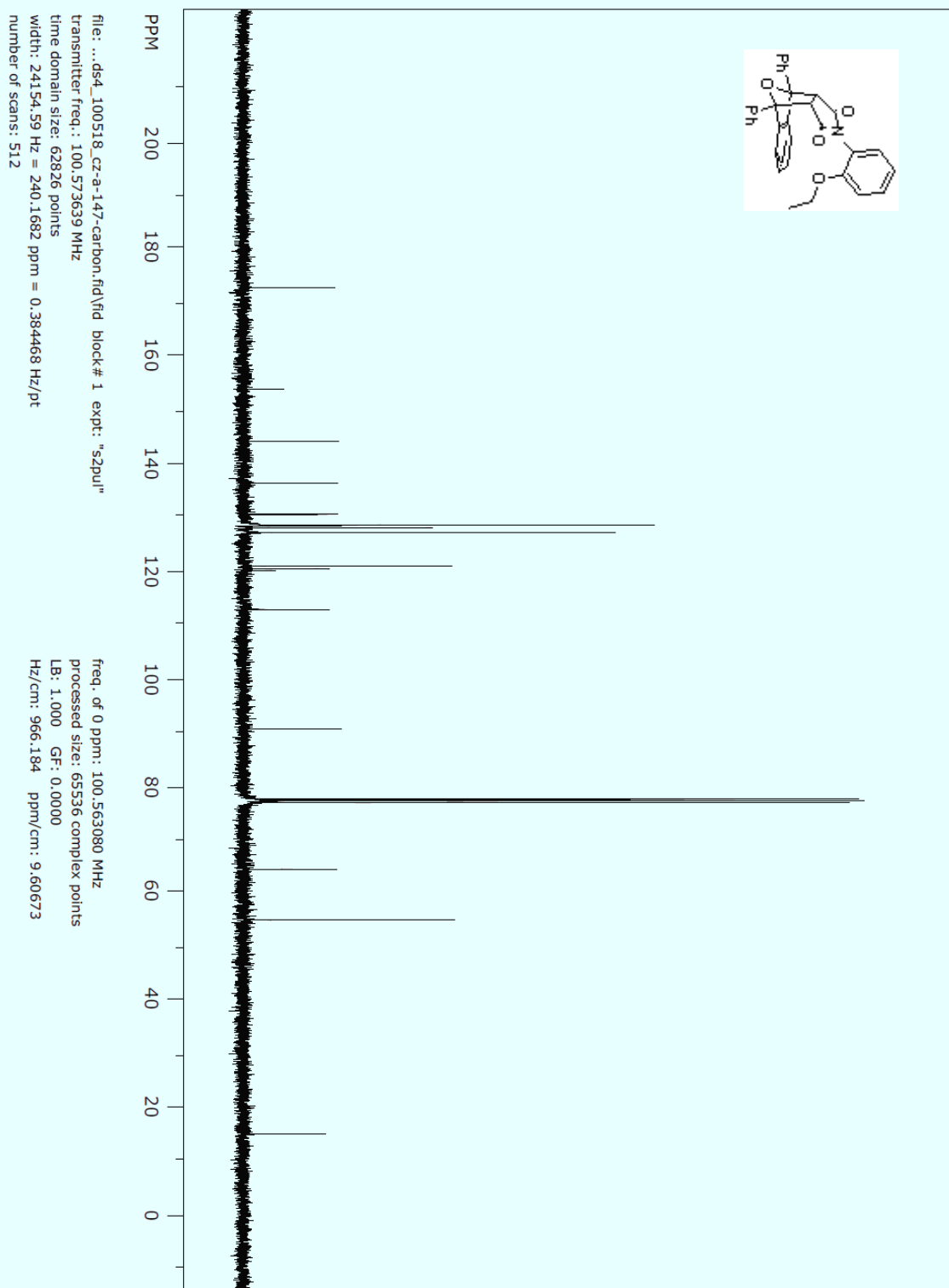


file: ...y\NMR\kds3_100504_cz-a-147.fid\fid block# 1 expt: "s2pul"
 transmitter freq.: 300.106300 MHz
 time domain size: 28804 points
 width: 4800.77 Hz = 15.9969 ppm = 0.166670 Hz/pt
 number of scans: 16

freq. of 0 ppm: 300.104499 MHz
 processed size: 32768 complex points
 LB: 1.500 GF: 0.0000
 Hz/cm: 120.121 ppm/cm: 0.40026

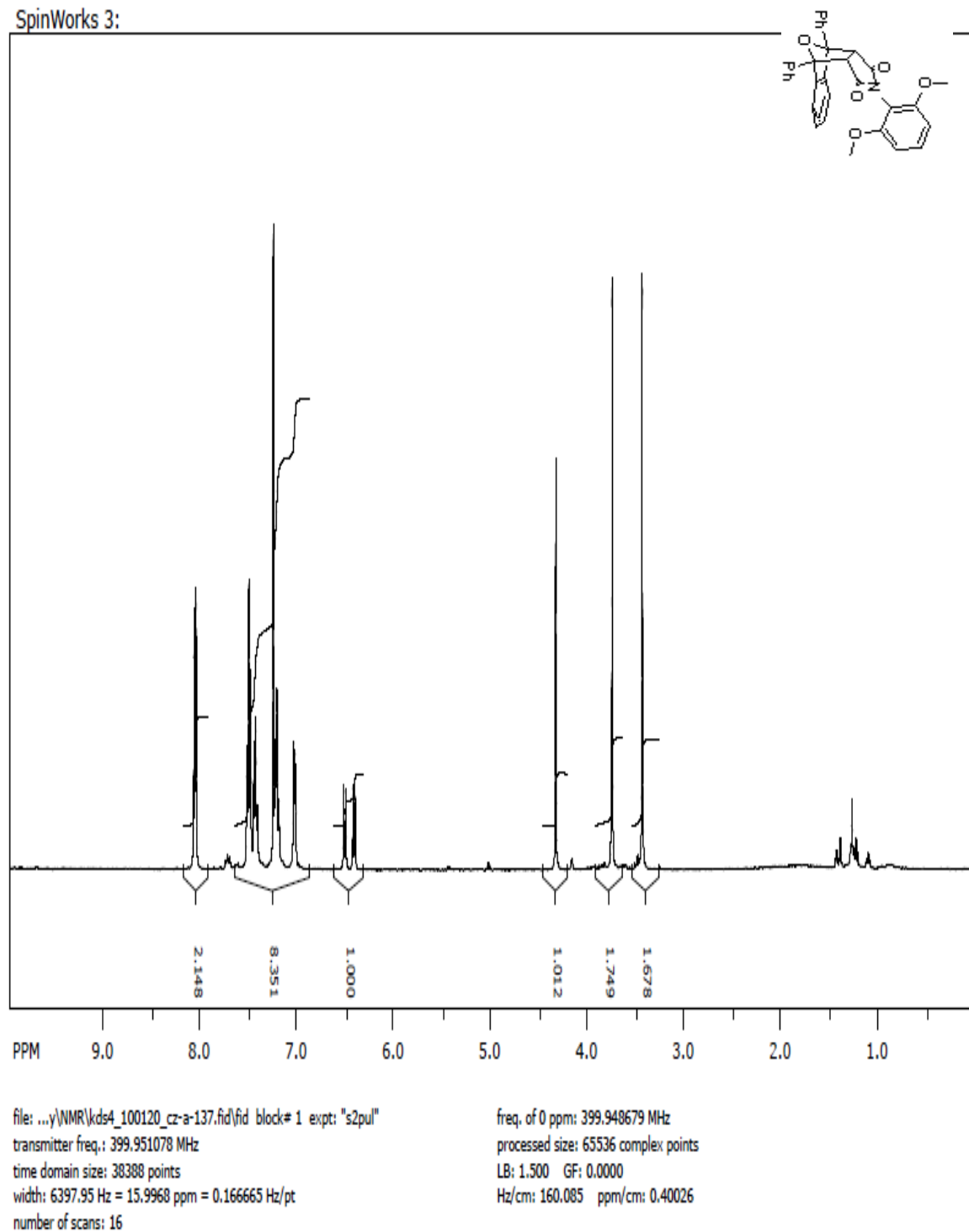
Spectrum 17: 400 MHz ^1H NMR spectrum of balance **2b** in CDCl_3 .

SpinWorks 3:



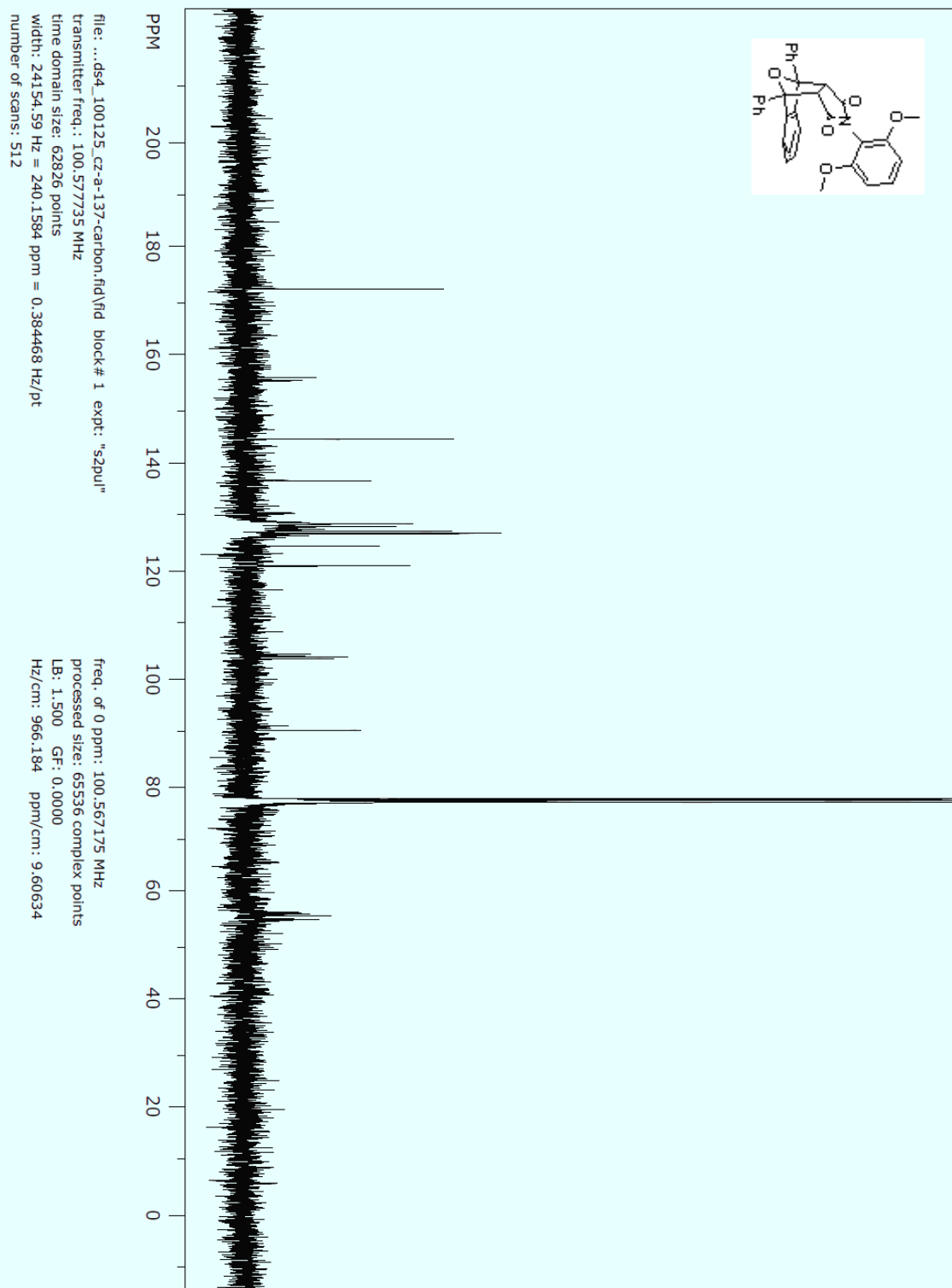
Spectrum 18: 400 MHz ^{13}C NMR spectrum of balance **2b** in CDCl_3 .

SpinWorks 3:



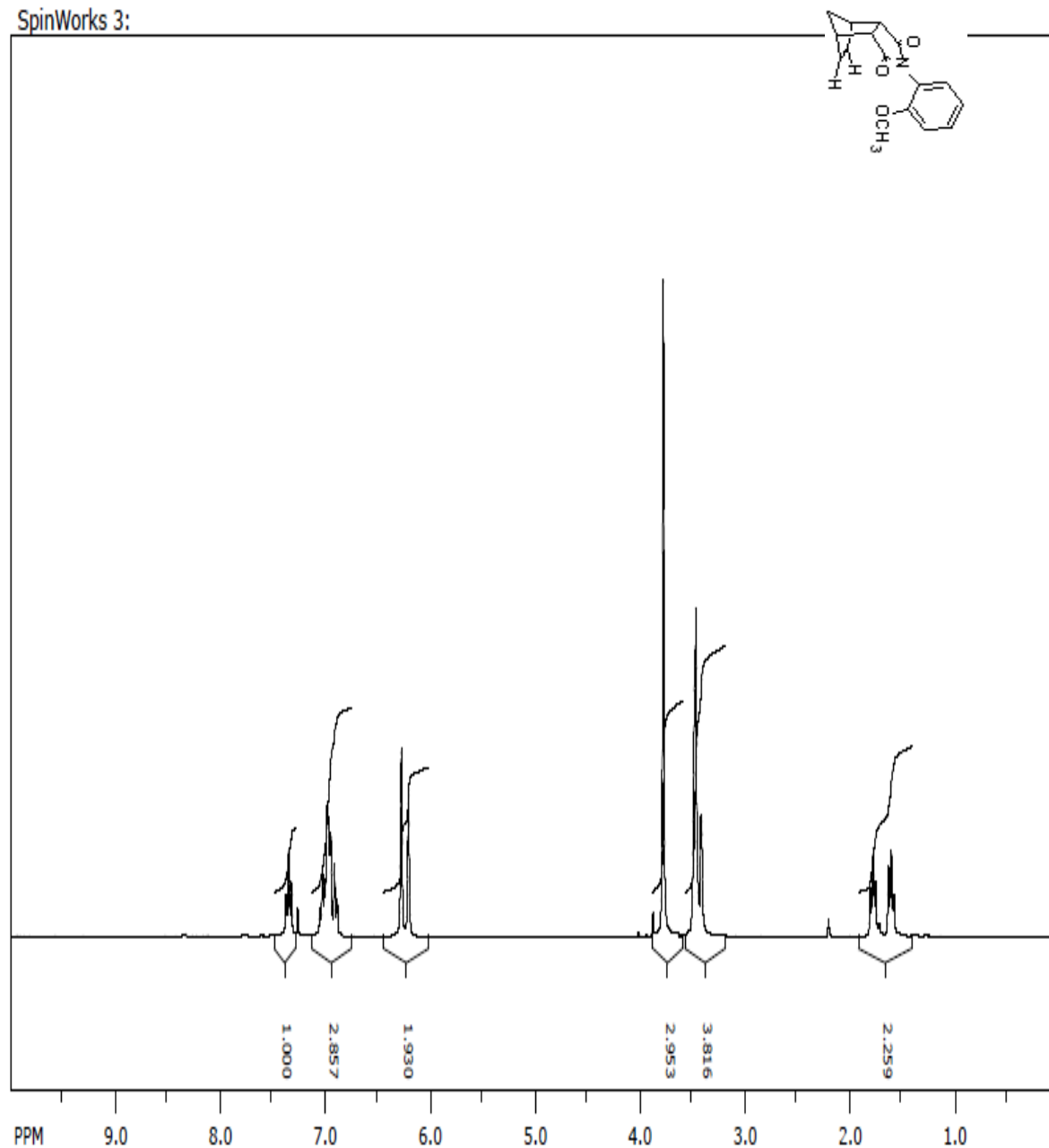
Spectrum 19: 400 MHz ¹H NMR spectrum of balance **2c** in CDCl₃.

SpinWorks 3:



Spectrum 20: 400 MHz ^{13}C NMR spectrum of balance **2c** in CDCl_3 .

SpinWorks 3:



file: ...3_100121_cz-a-111-highconc.fid\fid block# 1 expt: "s2pul"
transmitter freq.: 300.106300 MHz
time domain size: 28804 points
width: 4798.46 Hz = 15.9892 ppm = 0.166590 Hz/pt
number of scans: 16

freq. of 0 ppm: 300.104499 MHz
processed size: 32768 complex points
LB: 1.500 GF: 0.0000
Hz/cm: 120.064 ppm/cm: 0.40007

Spectrum 21: 300 MHz ^1H NMR spectrum of balance **3** in CDCl_3 .

Variable temperature ¹H NMR:

Thermodynamic Information:

Van't Hoft plot of the log of folded over unfolded versus the reciprocal of temperature are linear. Curvefits of these lines have slopes corresponding to $-\Delta H/R$ and y intercepts of $\Delta S/R$. The full spectra were acquired at 5 °C intervals and the area of the succinimide alpha singlets (balance **1a**, **1b**, **2a**, **2b** in acetone-d₃), the methyl singlets or the CH₂ quartet on the arm group (balance **1a**, **1b**, **2a**, **2b** in CDCl₃ because of the overlapped succinimide peaks), or the triplet for ethene protons (of balance **3a**) for folded and unfolded were obtained via spectral deconvolution using VNMRJ software fitspec command.

	balance 1a			balance 1b			
Temp	Unfolded	Folded	ln(F/U)	Unfolded	Folded	ln(F/U)	1/Temp
25	167.34	78.31	-0.75935	659.55	140.23	-1.54827	0.003356
30	310.15	144.32	-0.76502	637.06	134.26	-1.55709	0.003300
35	215.89	100.05	-0.76910	523.06	109.02	-1.56817	0.003247
40	216.3	100.75	-0.76402	565.21	117.62	-1.56974	0.003195
45	204.21	94.68	-0.76865	550.67	113.78	-1.57687	0.003145
50	236.82	109.41	-0.77220	540.52	111.55	-1.57806	0.003096
55	221.4	101.85	-0.77647	557.02	116.79	-1.56222	0.003049

Table 6. Spectral deconvolution integrations for variable temperature NMR of balance **1a** and **1b** in CDCl₃.

	balance 2a			balance 2b			
Temp	Unfolded	Folded	ln(F/U)	Unfolded	Folded	ln(F/U)	1/Temp
25	0.915	0.085	-2.37627	0.954	0.034	-3.33430	0.003356
30	0.911	0.089	-2.32591	0.970	0.030	-3.47610	0.003300
35	0.910	0.090	-2.31363	0.965	0.031	-3.43814	0.003247
40	0.907	0.093	-2.27754	0.958	0.037	-3.25393	0.003195
45	0.906	0.094	-2.26574	0.956	0.035	-3.30741	0.003145
50	0.906	0.094	-2.26574	0.956	0.033	-3.36625	0.003096
55	0.906	0.094	-2.26574	0.952	0.036	-3.27505	0.003049

Table 7. Spectral deconvolution integrations for variable temperature NMR of balance **2a** and **2b** in CDCl₃.

	balance 3a			
Temp	Unfolded	Folded	ln(F/U)	1/Temp
25	0.553	0.447	-0.212799	0.003356
30	0.559	0.441	-0.237105	0.003300
35	0.56	0.44	-0.241162	0.003247
40	0.561	0.439	-0.245221	0.003195
45	0.562	0.438	-0.249283	0.003145
50	0.565	0.435	-0.26148	0.003096
55	0.565	0.435	-0.26148	0.003049

Table 8. Spectral deconvolution integrations for variable temperature NMR of balance **3a** in CDCl₃.

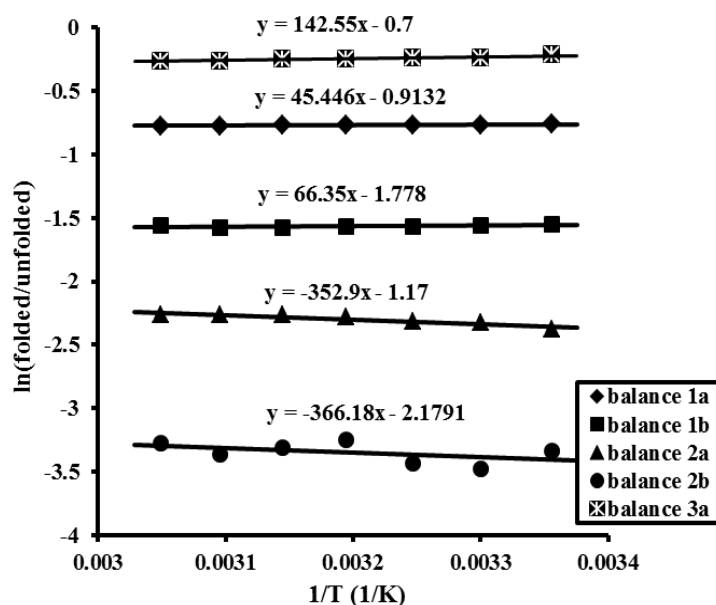


Figure 1: Van't Hoft plot of information in Table 6, Table 7, and Table 8.

	balance 1a			balance 1b			
Temp	Unfolded	Folded	ln(F/U)	Unfolded	Folded	ln(F/U)	1/Temp
25	134.14	105.58	-0.23942	187.69	71.39	-0.96663	0.003356
30	152.4	116.98	-0.26451	225.04	75.56	-1.09135	0.003300
35	108.08	81.19	-0.28608	192.84	70.09	-1.01208	0.003247
40	161.14	120.54	-0.29029	242.65	83.63	-1.06521	0.003195
45	136.47	104.9	-0.26310	200.59	70.13	-1.05091	0.003145
50	155.97	112.2	-0.32938	221.21	74.83	-1.08389	0.003096
55	192.98	135.22	-0.35568	220.86	73.17	-1.10474	0.003049

Table 9. Spectral deconvolution integrations for variable temperature NMR in acetone-d₆ of balance **1a** and **1b**.

	balance 2a			balance 2b			
Temp	Unfolded	Folded	ln(F/U)	Unfolded	Folded	ln(F/U)	1/Temp
25	179.05	33.55	-1.67463	165.37	11.00	-2.710	0.003356
30	172.07	32.80	-1.65747	174.31	11.82	-2.691	0.003300
35	169.91	32.44	-1.65588	184.98	12.33	-2.708	0.003247
40	190.93	37.11	-1.63802	209.67	14.87	-2.646	0.003195
45	205.85	40.46	-1.62683	147.61	10.35	-2.658	0.003145
50	183.72	36.22	-1.62380	156.60	11.16	-2.641	0.003096
55	188.30	37.54	-1.61263	153.25	11.18	-2.618	0.003049

Table 10. Spectral deconvolution integrations for variable temperature NMR in acetone-d6 of balance 2a and 2b.

	balance 3a			
Temp	Unfolded	Folded	ln(F/U)	1/Temp
25	0.54	0.46	-0.160343	0.003356
30	0.539	0.46	-0.158489	0.003300
35	0.545	0.456	-0.178293	0.003247
40	0.541	0.459	-0.164369	0.003195
45	0.543	0.456	-0.174617	0.003145
50	0.54	0.46	-0.160343	0.003096
55	0.54	0.46	-0.160343	0.003049

Table 8. Spectral deconvolution integrations for variable temperature NMR in acetone-d6 of balance 3a.

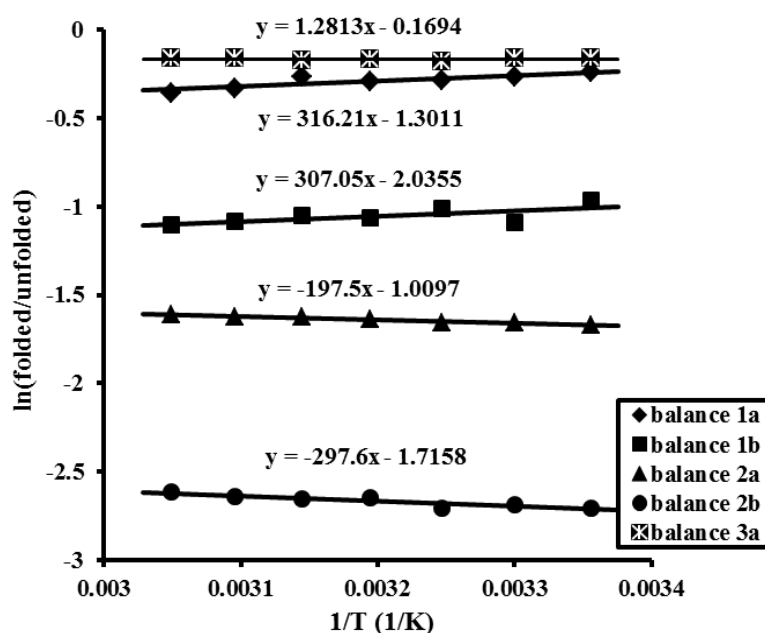


Figure 2: Van't Hoft plot of information in Table 6, Table 7, and Table 8. The errors for slopes and intercepts are measured by the regression add-in in

excel, and the calculation of entropy/enthalpy values is based on the following equations:

$$\Delta H = -\text{slope} \times R$$

$$\Delta S = y_{\text{int}} \times R$$

$$\Delta G = \Delta H - T\Delta S$$

The results are listed in Table 9:

balance	solvent	Slope	Intercept	ΔG (kcal/mol)	ΔH (kcal/mol)	ΔS (kcal/mol·K)	-T ΔS @25C (kcal/mol)
1a	CDCl ₃	45.5±10.3	-0.913±0.033	0.45±0.04	-0.09±0.02	-0.0018±6.6E-05	0.54±0.02
1b	CDCl ₃	116±14	-1.94±0.05	0.92±0.06	-0.23±0.03	-0.0039±9.3E-05	1.20±0.03
2a	CDCl ₃	-353±65	-1.17±0.21	1.4±0.3	0.70±0.13	-0.0023±0.0004	0.69±0.12
2b	CDCl ₃	-366±291	-2.18±0.93	2.0±1.1	0.73±0.58	-0.0043±0.0019	1.30±0.55
3a	CDCl ₃	-145±26	0.200±0.082	0.17±0.10	0.29±0.05	0.00040±0.00016	-0.12±0.05
1a	Acetone-d3	316±82	-1.30±0.26	0.14±0.32	-0.63±0.16	-0.0026±0.0005	0.77±0.16
1b	Acetone-d3	307±143	-2.04±0.46	0.60±0.56	-0.61±0.28	-0.0040±0.0009	1.20±0.27
2a	Acetone-d3	-198±14	-1.01±0.05	0.99±0.06	0.39±0.03	-0.0020±9.1E-05	0.60±0.03
2b	Acetone-d3	-298±58	-1.72±0.19	1.6±0.2	0.59±0.12	-0.0034±0.0004	1.02±0.11
3	Acetone-d3	1.28±32	-0.169±0.103	0.10±0.12	-0.003±0.064	-0.00034±0.0002	0.10±0.06

Table 9. Calculation of ΔG , ΔH , ΔS and T ΔS and their errors for balance **1a**, **1b**, **2a**, **2b**, and **3** by VT NMR experiment in CDCl₃ and acetone-d₆.