A Direct, Palladium Catalyzed, Multicomponent Synthesis of β-Lactams from Imines, Acid Chloride and Carbon Monoxide

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General Procedures

Unless otherwise noted, all manipulations were performed under an inert atmosphere in a vacuum atmosphere 553-2 dry box or by using standard Schlenk or vacuum line techniques.

Tris(dibenzylideneacetone)dipalladium·chloroform adduct was obtained from Strem Chemical Co. (Catalog No.46-3010) and was used without further purification. Carbon monoxide (99.99%) was purchased from Matheson and used as received. Imines,[1] (benzoyl-benzyl-amino)-phenylacetic acid[2] and Münchnone **2a**[3] were prepared using literature procedures. All other reagents were purchased from Aldrich® and used as received. Tetrahydrofuran (THF) was distilled from sodium/benzophenone ketyl under nitrogen. Acetonitrile and methylene chloride were distilled from CaH_2 under nitrogen. Deuterated solvents were dried as their protonoted analogues, but were transferred under vacuum from the drying agent, and stored over 3˜ molecular sieves.

^1H and ^{13}C NMR spectra were recorded on Varian 300 and Varian 400 Spectrometers. Infrared spectra were recorded on a Nicolet Avatar 320 FT-IR. Elemental analyses were performed at Guelph Analytical Facilities.

General Procedure for Catalytic Formation of β-Lactams

Imine (1.2 mmol) and acid chloride (0.54 mmol) were dissolved in 10 mL of CH_3CN/THF (1:1) and stirred for 15 min in a 50 mL reaction bomb. To this solution was added (4S)-4-phenyl-(2-pyridinyl)-2-oxazoline (3.3 mg, 2.7 mol%), $Pd_2(dba)_3.CHCl_3$ (7.7 mg, 1.4 mol%), and diisopropylethylamine (77 mg, 0.59 mmol). The solution was degassed once and pressurized with CO (1 atm). The reaction mixture was stirred at 55 °C for 96 hours. The β-

lactam product was isolated by chromatography on Silica Gel 60 using hexanes/ethyl acetate as eluent.

N-Benzyl-N-(1-benzyl-2-oxo-3,4-diphenyl-azetidin-3-yl)-benzamide (1a)

Yield: 58% isolated, white solid
^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.52 (d, 2H, 8Hz), δ 7.40-7.35 (3H, m), δ 7.28-7.67 (18H, m), δ 6.65 (d, 2H, 8Hz), δ 5.53(s, 1H), δ 4.98 (d, 1H, 15Hz), δ 4.92 (d, 1H, 17 Hz), δ4.84 (d, 1H, 17Hz), δ 3.84 (d, 1H, 15Hz).
^{13}C NMR (101 MHz, $CDCl_3$): δ174.0, δ 165.6, δ 138.3, δ 137.0, δ 135.6, δ 135.1, δ 134.3, δ 134.3, δ 130.0, δ 129.9, δ 129.6, δ 129.2, δ 128.1, δ 128.4, δ 128.3, δ 128.2, δ 128.1, δ 126.8, δ 126.8, δ 126.7, δ 81.2, δ 66.3, δ 52.3, δ 44.4
IR (KBr): ν_{CO}: 1753 cm^{-1}, 1639 cm^{-1}
Elemental analysis calcd. for $C_{36}H_{30}N_2O_2$: C, 82.73; H, 5.79; N, 5.36; found: C, 82.57; H, 6.13; N, 5.32

N-Benzyl-N-(1-benzyl-2-oxo-3,4-di-p-tolyl-azetidin-3-yl)-benzamide (1b)

Yield: 61% isolated, white solid
^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.38 (d, 2H, 8Hz), δ 7.36-7.01 (17H, m), δ 6.98 (d, 2H, 8Hz), δ 6.63 (d, 2H, 8Hz), δ 5.44(s, 1H), δ 4.90 (d, 1H, 15Hz), δ 4.86 (d, 1H, 17 Hz), δ4.72 (d, 1H, 17Hz), δ 3.88(d, 1H, 15Hz), δ 2.27(s, 3H), δ 2.23 (s, 3H)
^{13}C NMR (400 MHz, $CDCl_3$): δ 173.8, δ 165.8, δ 138.6, δ 138.0, δ 137.9, δ 137.1, δ 135.2, δ 132.5, δ 131.2, δ 129.8, δ 129.7, δ 129.5, δ 129.2, δ 129.1, δ 128.8, δ 128.8, δ 128.3, δ 128.2, δ 128.2, δ 128.1, δ 126.7, δ 126.6, δ 80.7, δ 66.2, δ 52.1, δ 44.2, δ 21.5, δ 21.4.
IR (KBr): ν_{CO}: 1751 cm^{-1}, 1638 cm^{-1}
Elemental analysis calcd. for $C_{38}H_{34}N_2O_2$: C, 82.88; H, 6.22; N, 5.09; found: C, 82.57; H, 6.54; N, 5.11

N-Benzyl-N-[1-benzyl-2,3-bis-(4-methylsulfanyl-phenyl)-4-oxo-azetidin-3-yl]-benzamide (1c)

Yield: 56% isolated, white solid
^{1}H-NMR (400 MHz, CD_3CN): δ 7.44-7.33 (m, 6H), δ 7.28-7.15 (m, 8H), δ 7.11-7.00 (m, 7H), δ 6.80 (d, 2H, 8Hz), δ 5.47(s, 1H), δ 4.82(d, 1H, 15Hz), δ 4.82 (d, 1H, 17 Hz), δ 4.71(d, 1H, 17Hz), δ 3.97(d, 1H, 15Hz), δ 2.44(s, 3H), δ 2.41(s, 3H)
^{13}C NMR (300 MHz, CD_3CN): δ173.6, δ 165.4, δ 139.2, δ 138.9, δ 138.6, δ 137.2, δ 135.6, δ 131.9, δ 131.2, δ 130.2, δ 129.7, δ 129.1, δ 129.0, δ 128.4, δ 128.2, δ 128.1, δ 126.8, δ 126.6, δ 126.6, δ 125.2, δ 125.2, δ 80.8, δ 66.6, δ 51.6, δ 44.5, δ 14.5, δ 14.5.
IR (KBr): ν_{CO}: 1752 cm^{-1}, 1638 cm^{-1}

Elemental analysis calcd. for $C_{38}H_{34}N_2O_2S_2$: C, 74.23; H, 5.57; N, 4.56; found: C, 74.22; H, 5.20; N, 4.49

N-Benzyl-N-[1-benzyl-2-oxo-3,4-bis-(4-trifluoromethyl-phenyl)-azetidin-3-yl]-benzamide (1d)

Yield: 32% isolated, white solid
^{1}H-NMR (400 MHz, CD_3CN): δ 7.55 (d, 2H, 8Hz), δ 7.48-7.32 (m, 12H), δ 7.24 (d, 2H, 8Hz), δ 7.05(m, 5H), δ 6.81 (d, 2H, 8Hz), δ 5.59 (s, 1H), δ 4.90(d, 1H, 15Hz), δ 4.87 (d, 1H, 17 Hz), δ 4.83(d, 1H, 17Hz), δ 4.06 (d, 1H, 15Hz)
^{13}C NMR (300 MHz, CD_3CN): δ173.8, δ 164.8, δ 139.7, δ 139.1, δ 137.9, δ 136.7, δ 135.2, δ 130.4, δ 130.2, δ 130.1, δ 129.9, δ 129.8, δ 129.5, δ 129.3, δ 129.1, δ 129.1, δ 128.6, δ 128.2, δ 126.9, δ 126.9, δ 126.3, δ 126.1, δ 124.8, δ 124.8, δ 124.7, δ 122.5 δ 81.0, δ 66.3, 51.9, δ 45.0
IR (KBr): ν_{CO}: 1759 cm^{-1}, 1643 cm^{-1}
Elemental analysis calcd. for $C_{38}H_{28}F_6N_2O_2$: C, 69.30; H, 4.28; N, 4.25; found: C, 69.25; H, 3.93; N, 4.05

N-Benzyl-N-(1-benzyl-2-oxo-3,4-di-p-tolyl-azetidin-3-yl)-isobutyramide (1e)

Yield: 45% isolated, white solid
^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.31 (d, 2H, 8Hz), δ 7.31-6.98 (10H, m), δ 6.97 (d, 2H, 8Hz), δ 6.88 (d, 2H, 8Hz), δ 6.56 (d, 2H, 8Hz), δ 5.40(s, 1H), δ 5.07 (d, 1H, 18Hz), δ 4.85 (d, 1H, 15 Hz), δ 4.54 (d, 1H, 18Hz), δ 3.69 (d, 1H, 15Hz), δ 2.48(m, 1H), δ 2.26(s, 3H), δ 2.21(s, 3H), δ 0.97(d, 3H), δ 0.91(s, 3H)
^{13}C NMR (400 MHz, $CDCl_3$): δ179.5, δ 165.5, δ 138.8, δ 137.9, δ 137.7, δ 135.3, δ 133.0, δ 131.3, δ 129.4, δ 129.2, δ 129.0, δ 128.9, δ 128.8, δ 128.1, δ 127.0, δ 125.6, δ 80.4, δ 66.1, δ 49.8, δ 44.0, δ 43.4, δ 31.7, δ 21.4, δ 21.3, δ 19.5, δ 19.4
IR (KBr): ν_{CO}: 1755 cm^{-1}, 1652 cm^{-1}
Elemental analysis calcd. for $C_{35}H_{36}N_2O_2$: C, 81.36; H, 7.02; N, 5.42; found: C, 81.58; H, 6.73; N, 5.26

N-(4-Methoxy-benzyl)-N-[1-(4-methoxy-benzyl)-2-oxo-3,4-diphenyl-azetidin-3-yl]-benzamide (1f)

Yield: 65% isolated, white solid
^{1}H-NMR (400 MHz, CD_3CN): δ 7.42 (d, 2H, 8Hz), δ 7.35-7.09 (15H, m), δ 6.94 (d, 2H, 8Hz), δ 6.62 (d, 2H, 8Hz), δ 6.56 (d, 2H, 8Hz), δ 5.48(s, 1H), δ 4.80 (d, 1H, 15Hz), δ 4.76 (d, 1H, 17 Hz), δ 4.66 (d, 1H, 17Hz), δ 3.91(d, 1H, 15Hz), δ 3.81(s, 3H), δ 3.70(s, 3H)
^{13}C NMR (400 MHz, CD_3CN): δ173.5, δ 165.5, δ 159.6, δ 158.5, δ 137.5, δ 135.9, δ 135.7, δ 134.8, δ 130.5, δ 130.4, δ 129.7, δ 129.6, δ 129.5, δ 128.4, δ 128.2, δ 128.1, δ 128.0, δ 127.9, δ 127.6, δ 126.6, δ 114.3, δ 113.5, δ 81.3, δ 66.7, δ 55.2, δ 55.0, δ 51.1, δ 43.9.
IR (KBr): ν_{CO}: 1754 cm^{-1}, 1640 cm^{-1}

Elemental analysis calcd. for $C_{38}H_{34}N_2O_4$: C, 78.33; H, 5.88; N, 4.81; found: C, 78.14; H, 6.14; N, 4.81

N-Furan-2-ylmethyl-N-(1-furan-2-ylmethyl-2-oxo-3,4-diphenyl-azetidin-3-yl)-benzamide (1g)

Yield: 66% isolated, white solid
^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.40-6.95 (m, 17H), δ 6.31 (m, 1H), δ 6.16 (m, 1H), δ 5.93 (m, 1H), δ 5.60 (m, 1H), δ 5.46(s, 1H), δ 4.90 (d, 1H, 15Hz), δ 4.89 (d, 1H, 17 Hz), δ 4.80 (d, 1H, 17Hz), δ 4.01(d, 1H, 15Hz)
^{13}C NMR (300 MHz, CD_3CN): δ173.6, δ 165.9, δ 151.2, δ 149.1, δ 143.2, δ 141.7, δ 137.1, δ 135.0, δ 134.8, δ 130.0, δ 129.4, δ 129.3, δ 128.6, δ 128.3, δ 128.1, δ 128.1, δ 127.8, δ 127.0, δ 126.8, δ 117.6, δ 110.8, δ 110.4, δ 109.3, δ 107.9, δ 81.6, δ 67.5, δ 45.5, δ 37.5
IR (KBr): ν_{CO}: 1758cm^{-1}, 1644cm^{-1}
Elemental analysis calcd. for $C_{32}H_{26}N_2O_4$: C, 76.48; H, 5.21; N, 5.57 ; found: C, 76.83; H, 5.59; N, 5.60

N-(2-Oxo-3,4-diphenyl-1-thiophen-2-ylmethyl-azetidin-3-yl)-N-thiophen-2-ylmethyl-benzamide (1h)

Yield: 62% isolated, white solid
^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.47-7.03 (m, 15H), δ 6.94 (m, 1H), δ 6.88 (m, 1H), δ 6.81 (m, 1H), δ 6.51 (m, 2H), δ 6.08 (m, 1H), δ 5.48(s, 1H), δ 5.15 (d, 1H, 17Hz), δ 5.13 (d, 1H, 15 Hz), δ 5.00 (d, 1H, 17Hz), δ 4.11(d, 1H, 15Hz)
^{13}C NMR (300 MHz, $CDCl_3$) : δ 173.8, δ 165.9, δ 141.1, δ 136.9, δ 136.9, δ 135.2, δ 134.2, δ 130.2, δ 130.0, δ 129.4, δ 128.6, δ 128.4, δ 128.3, δ 128.1, δ 128.1, δ 127.9, δ 127.4, δ 127.1, δ 126.5, δ 126.3, δ 125.0, δ 81.3, δ 66.3, δ 47.7, δ 38.7
IR (KBr): ν_{CO}: 1754 cm^{-1}, 1641 cm^{-1}
Elemental analysis calcd. for $C_{32}H_{26}N_2O_2S_2$: C, 71.88; H, 4.90; N, 5.24 ; found: C, 71.76; H, 5.10; N, 5.28

N-(4-Methoxy-phenyl)-N-[1-(4-methoxy-phenyl)-2-oxo-3,4-di-p-tolyl-azetidin-3-yl]-benzamide (1i)

Yield: 27% isolated, white solid
^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.36-7.30 (8H, m), δ 7.24 (d, 2H, 9Hz), δ 7.23-7.11 (m, 3H, 8Hz), δ 6.97 (d, 2H, 8Hz), δ 6.86 (d, 2H, 9Hz), δ 6.79 (d, 2H, 8Hz), δ 6.60-6.50(m, 2H) 6.17(s, 1H), δ 3.73(s, 3H), δ 3.66(s, 3H), δ 2.25(s, 3H), δ 2.21(s, 3H)
^{13}C NMR (400 MHz, $CDCl_3$): δ 172.7, δ 162.7, δ 159.0, δ 156.4, δ 137.9, δ 137.8, δ 137.0, δ 133.1, δ 132.4, δ 131.9, δ 131.9, δ 131.0, δ 130.2, δ 129.6, 129.1, δ 129.0, δ 128.6, δ 128.5, δ 128.4, δ 127.9, 119.5, δ 114.5, δ 113.5, δ 81.6, δ 67.4, δ 55.7, δ 55.3, δ 21.5, δ 21.4
IR (KBr): ν_{CO}: 1751cm^{-1}, 1650 cm^{-1}

Elemental analysis calcd.: C, 78.33; H, 5.88; N, 4.81 ; found: C, 78.18; H, 5.88; N, 4.51

N-Hexyl-N-(1-hexyl-2-oxo-3,4-diphenyl-azetidin-3-yl)-benzamide (1j)

Yield: 55% isolated, oil
^{1}H-NMR (400 MHz, CD_3CN): δ 7.48-7.42 (m, 7H), δ 7.34-7.31 (m, 2H), δ 7.17-7.12(m, 6H), δ 5.56 (s, 1H), δ 3.68-3.50 (m,2H), δ 3.50-3.35 (m, 1H), δ 2.95-2.84 (m, 1H), δ 1.58-0.68 (m, 22H)
^{13}C NMR (300 MHz, CD_3CN): δ 173.1, δ 166.1 , δ 138.0, δ 136.5, δ 135.2, δ 129.7, δ 129.5, δ 129.4, δ 128.7, δ 128.1, δ 128.0, δ 127.9, δ 127.8, δ 126.8, δ 81.2, δ 67.0, δ 48.9, δ 40.1, δ 31.2, δ 30.8, δ 29.9, δ 27.0, δ 26.7, δ 26.0, δ 22.6, δ 22.1, δ13.6, δ 13.4.
IR (KBr): ν_{CO}: 1754 cm^{-1}, 1639 cm^{-1}
Elemental analysis calcd. for $C_{34}H_{42}N_2O_2$: C, 79.96; H, 8.29; N, 5.49; found: C, 79.69; H, 8.63; N, 5.44

N-Ethyl-N-(1-ethyl-2-oxo-3,4-diphenyl-azetidin-3-yl)-benzamide (1k)

Yield: 56% isolated, white solid
^{1}H-NMR (300 MHz, CD_3CN): δ 7.54-7.43 (m, 6H), δ 7.36-7.20 (m,3H), δ 7.19-7.13 (m, 6H), δ 5.60 (s, 1H), δ 3.69 (m, 1H), δ 3.66 (m, 1H), δ 3.56 (m, 1H), δ 3.02 (m, 1H), δ 1.19(t, 3H, 7Hz), δ 0.71 (t, 3H, 7Hz)
^{13}C NMR (300 MHz, CD_3CN): δ173.1, δ 165.9, δ 138.0, δ 136.6, δ 135.4, δ 130.0, δ 129.4, δ 129.4, δ 129.0, δ 128.7, δ 128.1, δ 128.0, δ 127.7, δ 126.8, δ 80.9, δ 66.6, δ 43.4, δ 35.5, δ 15.4, δ 12.0
IR (KBr): ν_{CO}: 1753 cm^{-1}, 1639 cm^{-1}
Elemental analysis calcd. for $C_{26}H_{26}N_2O_2$: C, 78.36; H, 6.58; N, 7.03; found: C, 78.89; H, 6.33; N, 7.10
HRMS calcd.: 399.2073; found; 399.2073

***N*-Benzyl-*N*-(1-ethyl-2-oxo-3,4-di-p-tolyl-azetidin-3-yl)-4-methyl-benzamide (1l)**

Yield: 65%, white solid
^{1}H NMR (30 MHz, $CDCl_3$): δ 7.37 (d, 2H, 8.20 Hz), 7.31 (m, 2H), 7.26-7.22 (m, 2H), 7.22-7.14 (m, 4H), 7.06 (d, 2h, 8.20 Hz), 6.96-6.88(m, 4H), 5.26 (s, 1H), 5.01 (d, 1H, 14.70 Hz), 3.81 (d, 1H, 14.70 Hz), 3.81 (d, 1H, 14.70 Hz), 3.81-3.45 (m, 2H), 2.37 (s, 3H), 2.25 (s, 3H), 2.23 (s, 3H), 0.67 (t, 3H).
^{13}C NMR (75.5 MHz, CD_3CN): δ 173.7, 166.6, 139.9, 137.8, 137.6, 135.4, 134.7, 133.3, 131.3, 129.5, 129.3, 129.0, 128.8, 128.7, 128.9, 128.1, 126.9, 81.2, 66.3, 44.4, 43.9, 21.9, 21.7, 21.6, 16.3.
IR (CH_2Cl_2): ν_{CO}: 1750 cm^{-1}, 1633 cm^{-1}
HRMS. Calculated for $C_{34}H_{34}N_2O_2$: 502.26203; found 502.22256 + $[K]^+$.

_N_-Benzyl-_N_-(1-benzyl-2-furan-2-yl-4-oxo-3-phenyl-azetidi_N_-3-yl)-benzamide (1m)

Yield: 49%, white solid.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.56 (d, 2H, 7.90 Hz); 7.42-7.32 (m, 4H), 7.26-7.12 (m, 11H), 7.12-7.00 (m, 4H), 6.75 (d, 2H, 7.91Hz), 7.04-6.96 (m, 2H), 6.33(m, 1H), 6.24 (m, 1H), 5.54 (s, 1H), 4.96-4.72 (m, 3H), 3.97 (d, 2H, 14.66 Hz)

^{13}C NMR (75.5 MHz, $CDCl_3$): δ 173.8, 165.0, 148.3, 142.9, 142.7, 138.3, 136.6, 135.4, 135.0, 129.9, 129.1, 128.9, 128.3, 128.1, 126.7, 111.8, 111.6, 110.9, 110.7, 80.4, 61.0, 52.2, 45.3.

IR (CH_2Cl_2): ν_{CO}: 1759 cm^{-1}, 1640 cm^{-1}

Calculated for $C_{34}H_{28}N_2O_3$: 512.20999; found 512.20999 + [H^+]

_N_-Ethyl-_N_-(2-oxo-1-p-tolyl-1,4,5,9b-tetrahydro-2H-azeto[2,1-a]isoquinolin-1-yl)-benzamide (1n)

Yield: 48%, white solid

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.73 (d, 1H,7.62 Hz), 7.62-7.54 (m, 2H), 7.52-7.43 (m, 3H), 7.10-6.87 (m, 7H), 5.40 (s, 1H), 4.25 (m, 1H), 3.68 (q, 2H, 7.33 Hz), 3.20 (2H, 2H, 7.33 Hz), 3.20 (m, 2H), 2.80 (m, 1H), 2.20 (s, 3H), 1.07 (t, 3H, 7.33 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ172.7, 167.1, 137.6, 137.4, 133.9, 132.0, 130.7, 129.9, 129.6, 128.9, 128.8, 128.7, 127.5, 127.3, 126.7, 81.3, 62.6, 45.0, 37.6, 29.4, 21.5, 16.5

IR (CH_2Cl_2): ν_{CO}: 1755 cm^{-1}, 1633 cm^{-1}

HRMS. Calculated for $C_{27}H_{26}N_2O_2$: 410.19943; found: 410.20071.

Reaction of Münchnone[3] 2a with Ph(H)C=NBn and HCl

(Benzoyl-benzyl-amino)-phenylacetic acid[2] (12.5 mg, 0.036 mmol) was added to a CD_3CN (1 mL) solution of N,N-dicyclohexylcarbodiimide (8.9 mg. 0.043 mmol). To this, now intense yellow solution, was added N-benzyl benzaldimine hydrochloride salt (12.5 mg, 0.054 mmol) and the solution was allowed to heat over 1 hour at 55°C. This results in the formation of a colorless solution, of which, ^{1}H-NMR analysis reveals the formation of **3a** (R_1= -CH_2Ph, R_2=Ph and R_3=Ph) in 99% yield (vs. Internal standard: $(CH_3)_3SiPh$).

^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.73-7.27 (16H, m), δ 7.04-6.89 (5H, m), δ 6.34 (d, 2H, 8Hz), δ 5.56 (s, 1H) δ 4.97 (d, 1H, 16Hz), δ 4.54 (d, 1H, 16Hz), δ 4.35 (d, 1H, 15Hz), δ 3.99(d, 1H, 15Hz),

^{13}C NMR (400 MHz, $CDCl_3$): δ 166.3, δ 165.7, δ 135.6, δ 132.5, δ 132.3, δ 130.2, δ 129.9, δ 129.7, δ 129.5, δ 129.2, δ 129.1, δ 128.8, δ 128.5, δ 128.4, 128.2, δ 128.6, δ 127.6, δ 123.8, δ 84.3, δ 51.6, δ 49.5

IR (KBr): ν_{CO}: 1638 cm^{-1}

Reaction of Münchnone 2a with Ph(H)C=NBn

(Benzoyl-benzyl-amino)-phenylacetic acid (20 mg, 0.043 mmol) was added to a CD_3CN (1 mL) solution of dicyclohexylcarbodiimide (13.1 mg, 0.047 mmol). To this, now intense yellow solution, was added N-benzyl benzaldimine (11.2mg, 0.057mmol) and the solution was allowed to heat over 54 hours at 60°C. ^{1}H-NMR analysis reveals the formation of **1a** in 79% yield (vs. Internal standard: $(CH_3)_3SiPh$).

Reaction of Münchnone 2a with Pd_2dba_3

(Benzoyl-benzyl-amino)-phenylacetic acid (12.5 mg, 0.036 mmol) was added to a CD_3CN (1 mL) solution of N,N-dicyclohexylcarbodiimide (8.9 mg, 0.043 mmol). To this, now intense yellow solution, was added $Pd_2(dba)_3 \cdot CHCl_3$ (1.9 mg, 5 mol%). The solution was allowed to heat over 18 hours at 57°C. ^{1}H-NMR analysis reveals the decomposition of Münchnone by 31%: (vs. Internal standard: $(CH_3)_3SiPh$). Conversely, no decomposition of **2a** was noted under similar conditions in the absence of $Pd_2(dba)_3 \cdot CHCl_3$.

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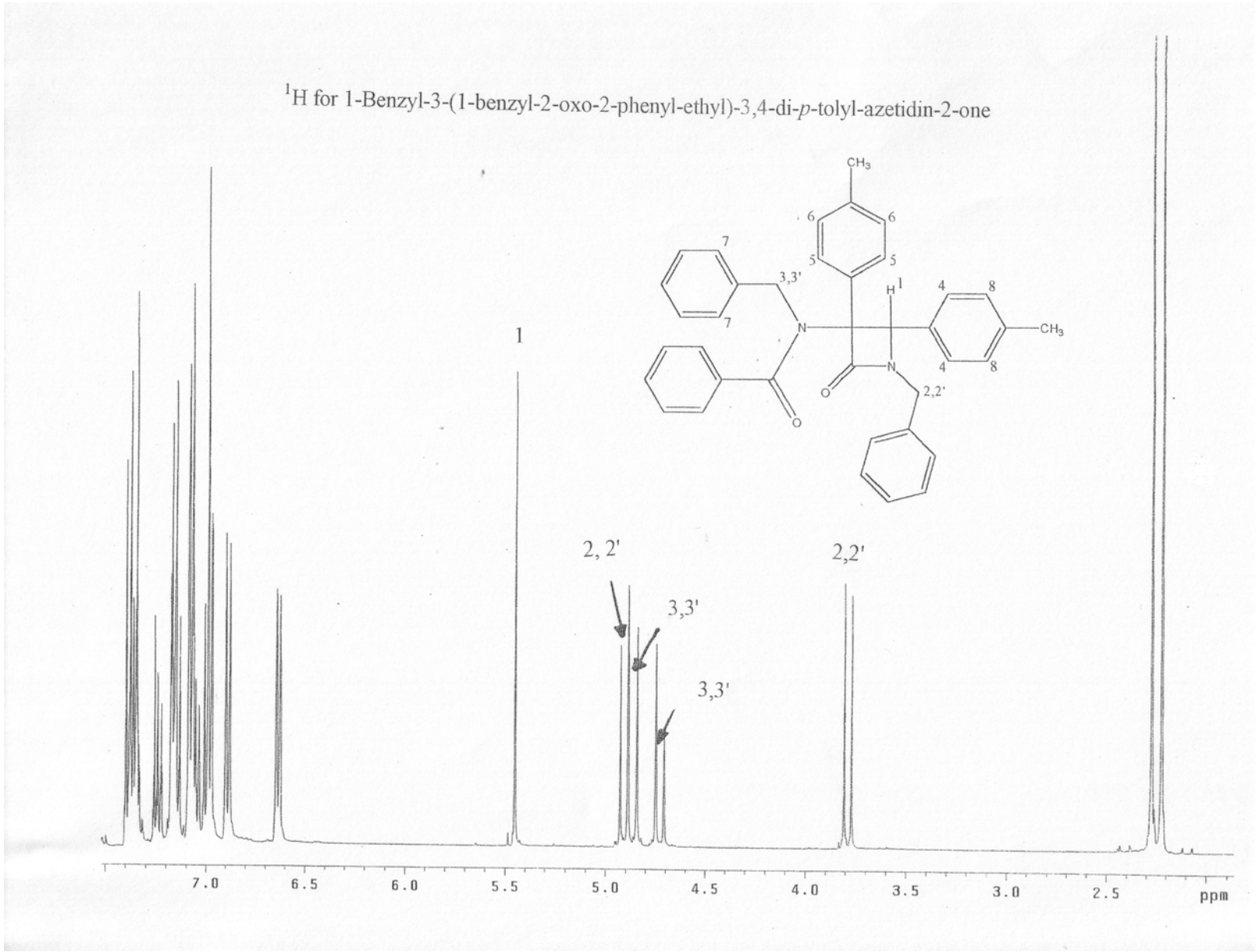
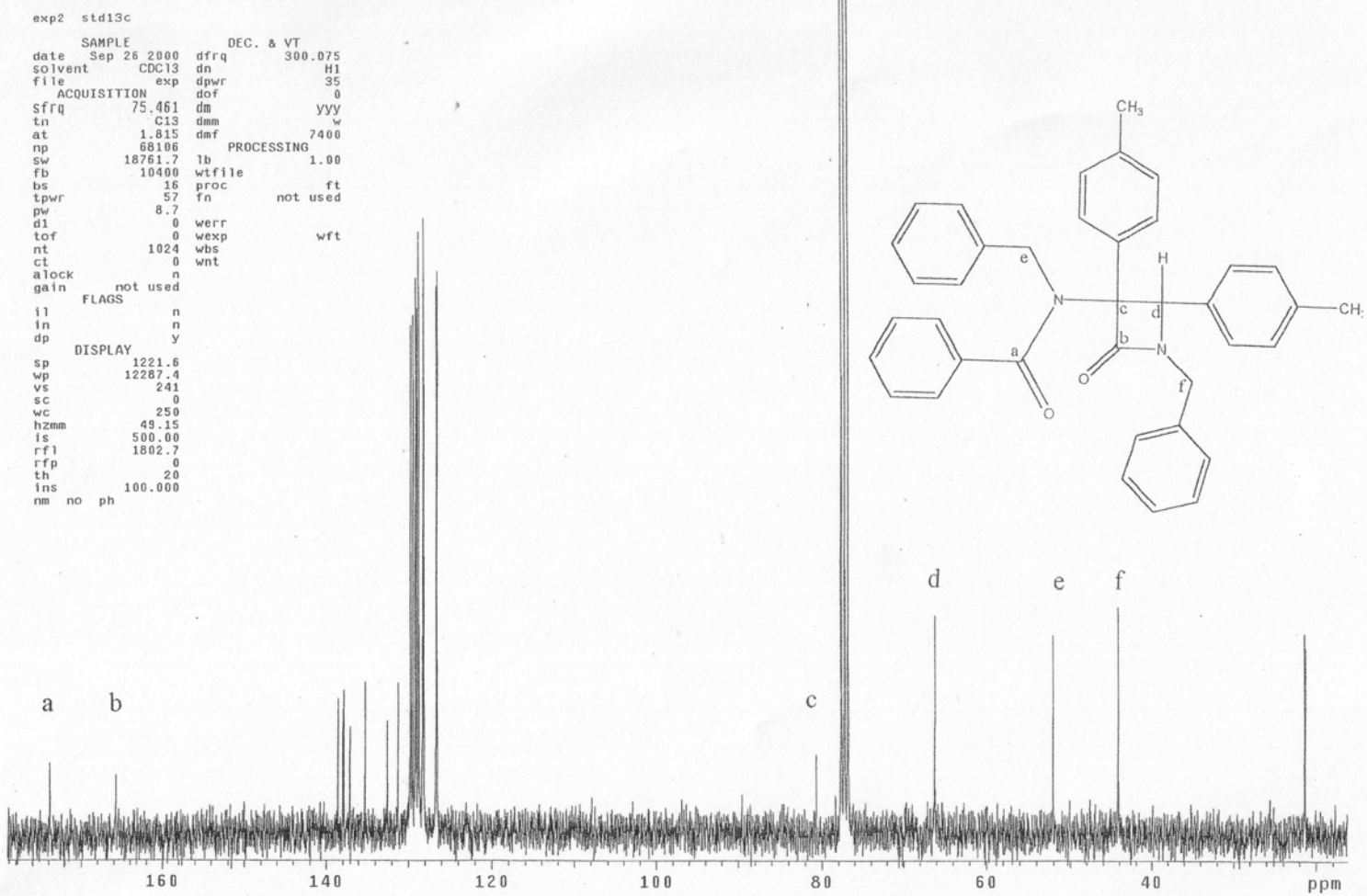

1H for 1-Benzyl-3-(1-benzyl-2-oxo-2-phenyl-ethyl)-3,4-di-p-tolyl-azetidin-2-one
CH3
6
6
7
5
5
3,3'
H
1
4
8
7
N
CH3
4
8
N
O
2,2'
O
1
2, 2'
3,3'
3,3'
2,2'
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
ppm

^{13}C-NMR for 1-Benzyl-3-(1-benzyl-2-oxo-2-phenyl-ethyl)-3,4-di-*p*-tolyl-azetidin-2-one

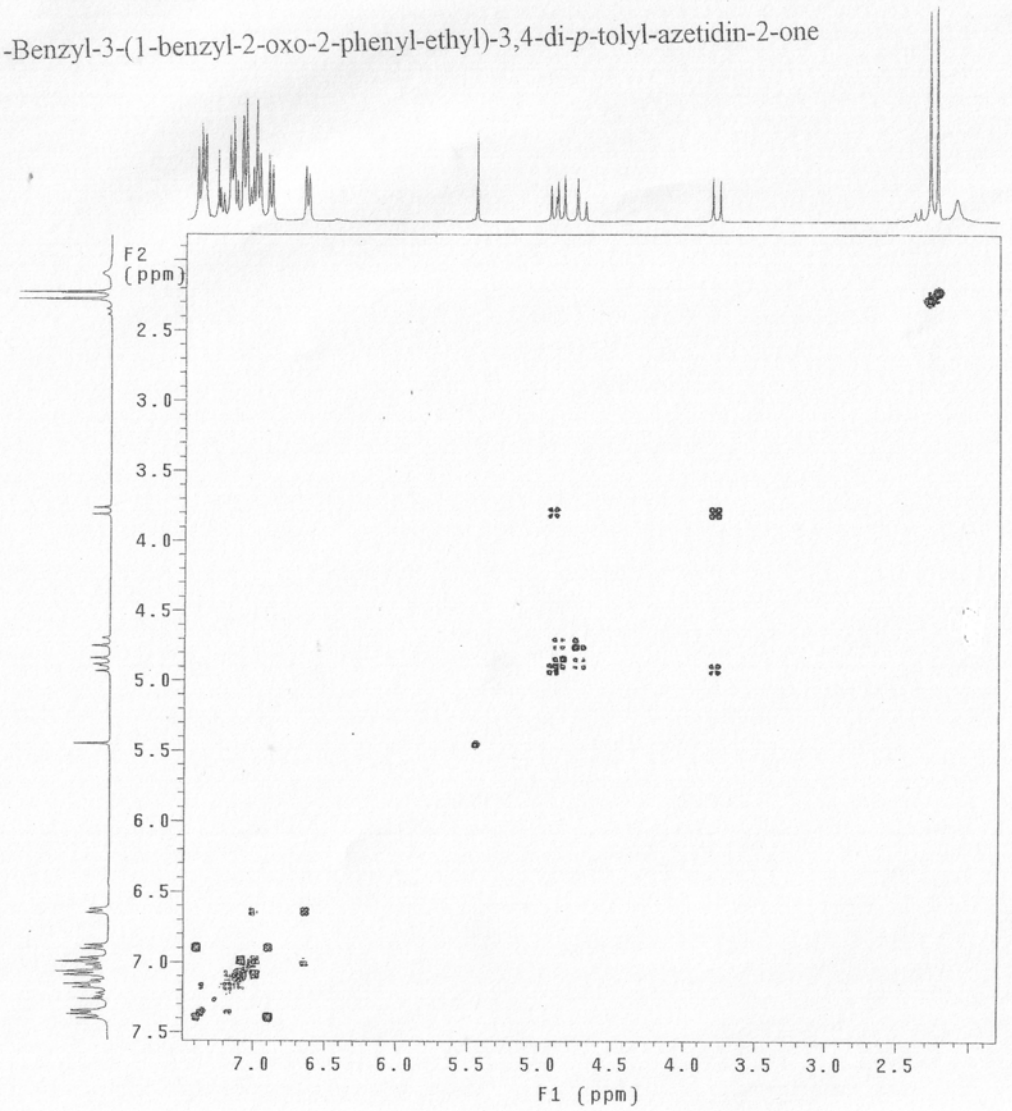


STANDARD 1H OBSERVE

Pulse Sequence: gCOSY
Solvent: CDCl3
Ambient temperature
File: rdh347cosy
Mercury-300 "m300"

PULSE SEQUENCE: gCOSY
Relax. delay 0.800 sec
Acq. time 0.220 sec
Width 2331.0 Hz
2D Width 2331.0 Hz
4 repetitions
128 increments
OBSERVE H1, 300.0738816 MHz
DATA PROCESSING
Sine bell 0.110 sec
F1 DATA PROCESSING
Sine bell 0.055 sec
FT size 2048 x 2048
Total time 10 min, 19 sec

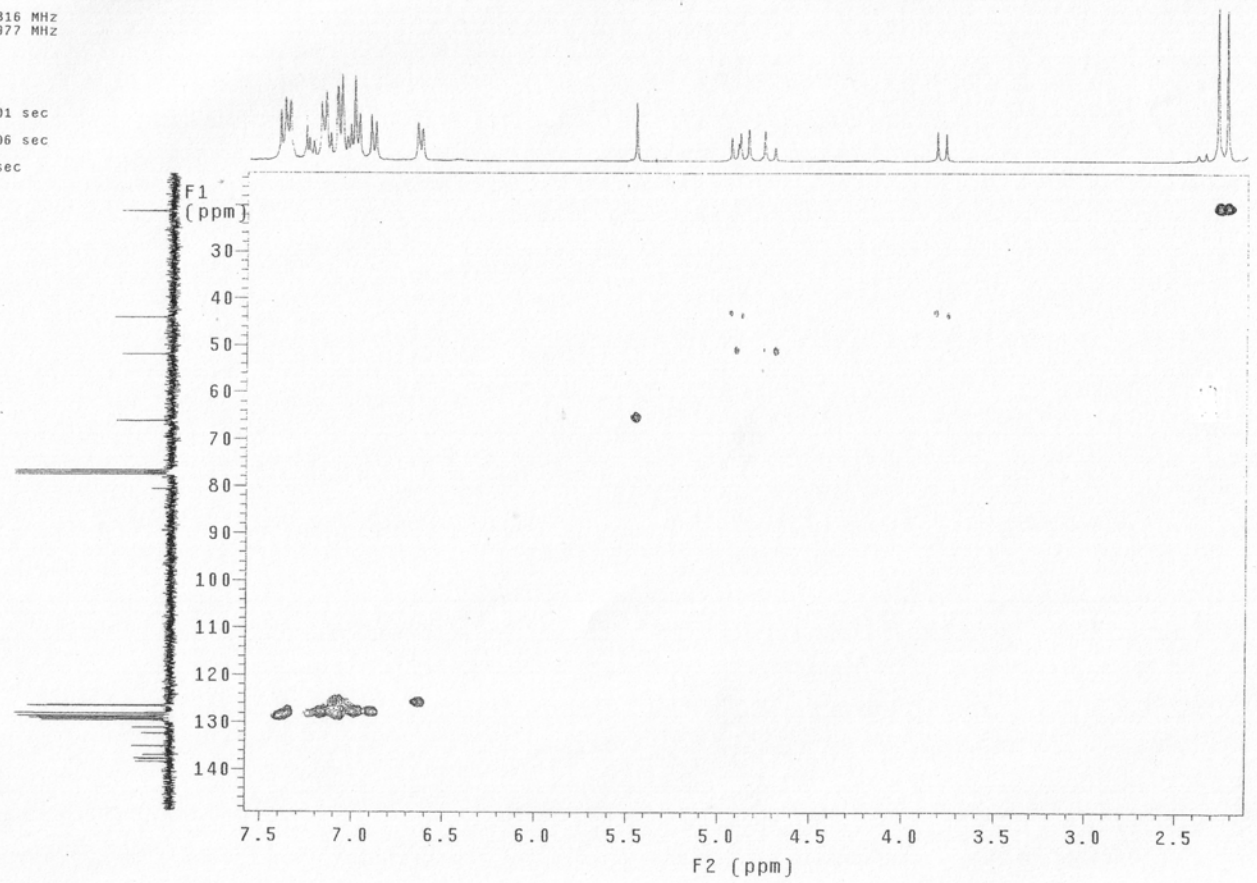
COSY for 1-Benzyl-3-(1-benzyl-2-oxo-2-phenyl-ethyl)-3,4-di-*p*-tolyl-azetidin-2-one



STANDARD 1H OBSERVE

Pulse Sequence: gHMQC
Solvent: CDCl3
Ambient temperature
File: rdhhmqc
Mercury-300 "m300"
PULSE SEQUENCE: gHMQC
Relax. delay 1.000 sec
Acq. time 0.220 sec
Width 2331.0 Hz
2D Width 18761.7 Hz
8 repetitions
2 x 64 increments
OBSERVE H1, 300.0738816 MHz
DECOUPLE C13, 75.4611977 MHz
Power 42 dB
on during acquisition
off during delay
GARP-1 modulated
DATA PROCESSING
Gauss apodization 0.101 sec
F1 DATA PROCESSING
Gauss apodization 0.006 sec
FT size 1024 x 2048
Total time 23 min, 34 sec

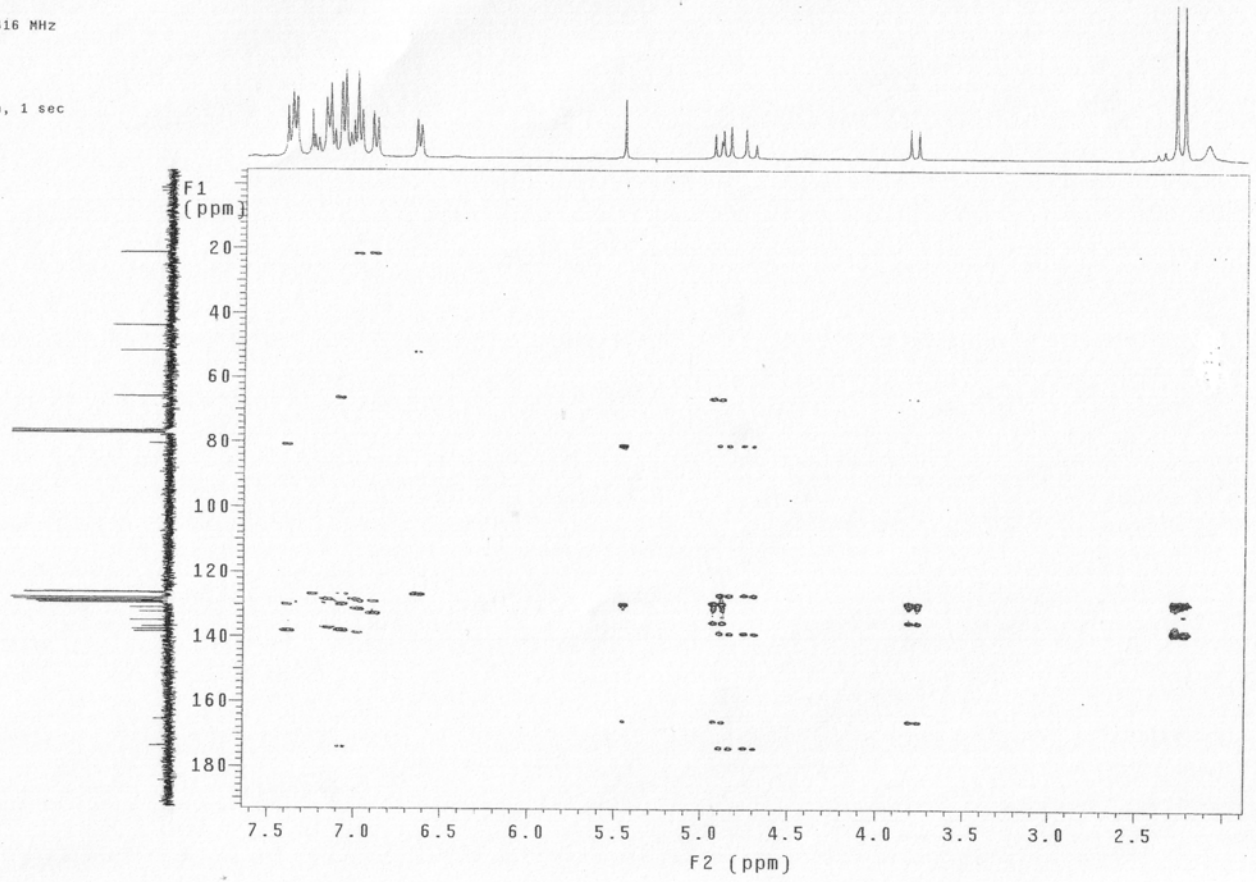
HMQC for 1-Benzyl-3-(1-benzyl-2-oxo-2-phenyl-ethyl)-3,4-di-*p*-tolyl-azetidin-2-one

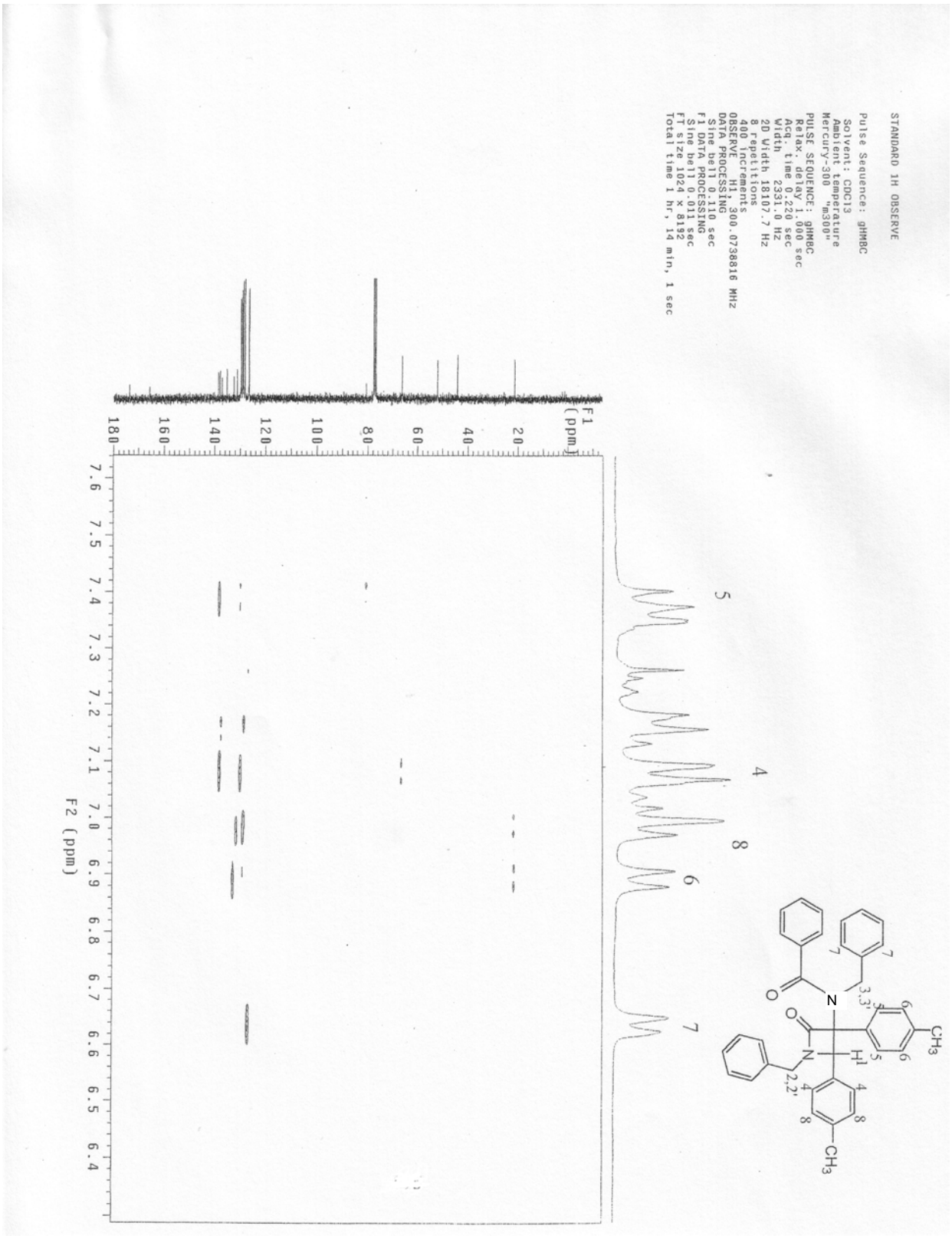


STANDARD 1H OBSERVE

Pulse Sequence: gHMBC
Solvent: CDCl3
Ambient temperature
File: rdhhmbc
Mercury-300 "m300"
PULSE SEQUENCE: gHMBC
Relax. delay 1.000 sec
Mixing 0.700 sec
Acq. time 0.220 sec
Width 2331.0 Hz
2D Width 18107.7 Hz
8 repetitions
400 increments
OBSERVE H1, 300.0738816 MHz
DATA PROCESSING
Sine bell 0.110 sec
F1 DATA PROCESSING
Sine bell 0.044 sec
FT size 1024 x 8192
Total time 1 hr, 14 min, 1 sec

HMBC for 1-Benzyl-3-(1-benzyl-2-oxo-2-phenyl-ethyl)-3,4-di-*p*-tolyl-azetidin-2-one



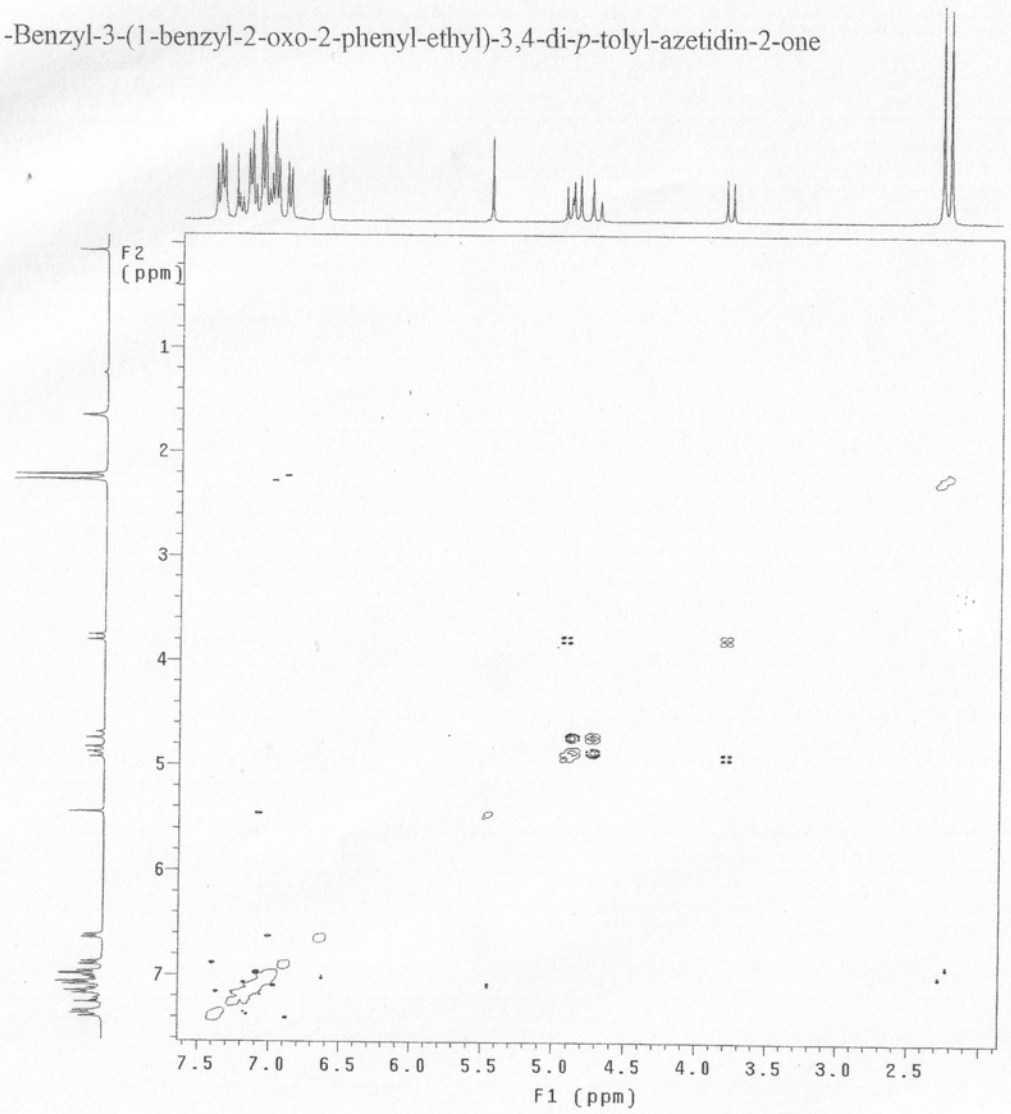

STANDARD 1H OBSERVE
Pulse Sequence: gHMBC
Solvent: CDCl3
Ambient temperature
Mercury-300 "m300"
PULSE SEQUENCE: gHMBC
Relax. delay 1.000 sec
Acq. time 2.220 sec
Width 2331.0 Hz
2D Width 18107.7 Hz
8 repetitions
400 increments
OBSERVE H1, 300.0738816 MHz
DATA PROCESSING
Sine bell 0.110 sec
F1 DATA PROCESSING
Sine bell 0.011 sec
FT size 1024 x 8192
Total time 1 hr, 14 min, 1 sec
F1 (ppm)
F2 (ppm)
N
O
CH3
H1
3,3'
2,2'
4
5
6
7
8

STANDARD 1H OBSERVE

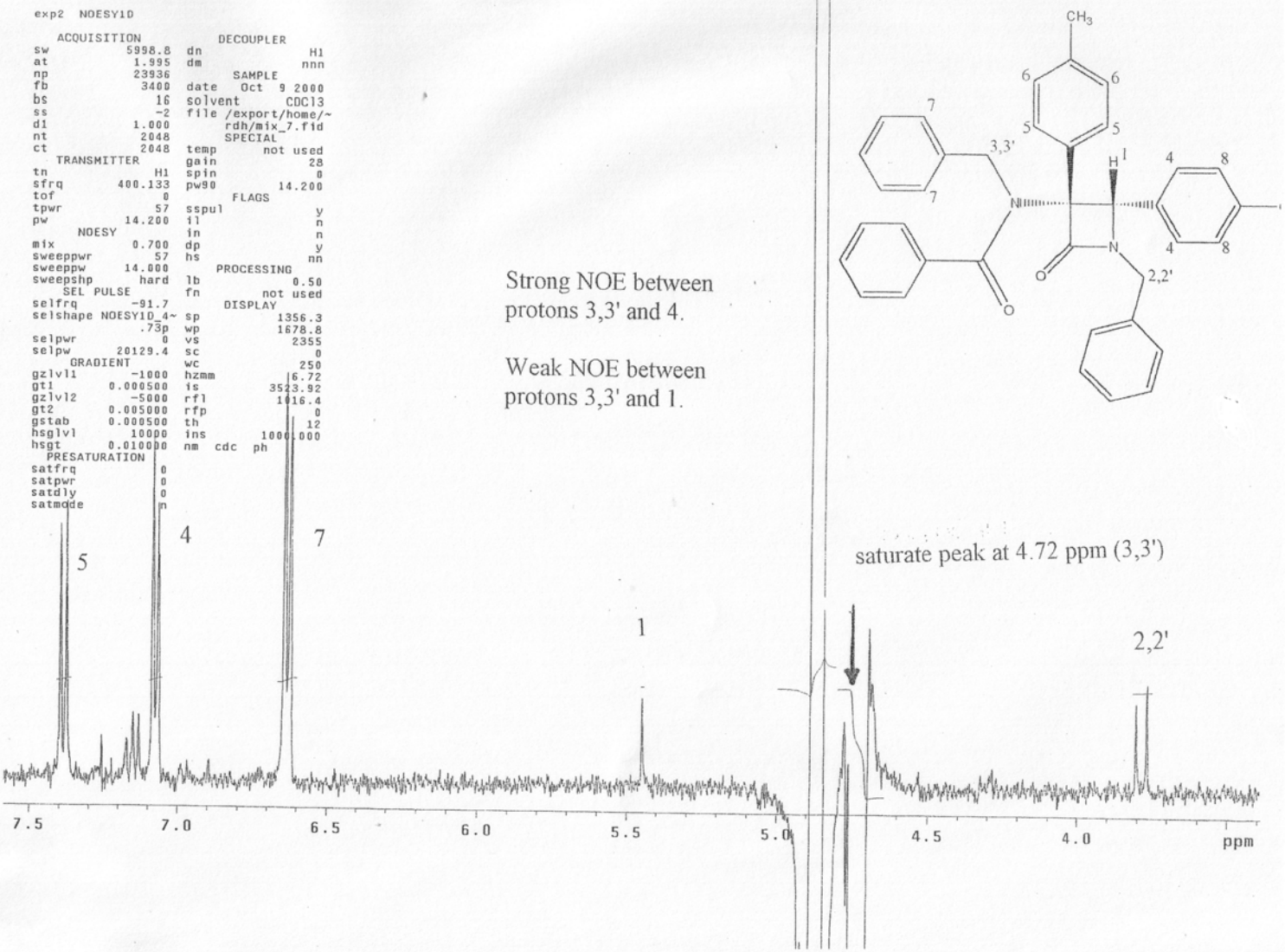
Pulse Sequence: NOESY
Solvent: CDCl3
Ambient temperature
Mercury-300 "m300"

PULSE SEQUENCE: NOESY
Relax. delay 1.500 sec
Mixing 0.700 sec
Acq. time 0.220 sec
Width 2331.0 Hz
2D Width 2331.0 Hz
8 repetitions
2 x 256 increments
OBSERVE H1, 300.0738816 MHz
DATA PROCESSING
Gauss apodization 0.101 sec
F1 DATA PROCESSING
Gauss apodization 0.079 sec
FT size 4096 x 4096
Total time 2 hr, 55 min, 5 sec

NOESY for 1-Benzyl-3-(1-benzyl-2-oxo-2-phenyl-ethyl)-3,4-di-*p*-tolyl-azetidin-2-one



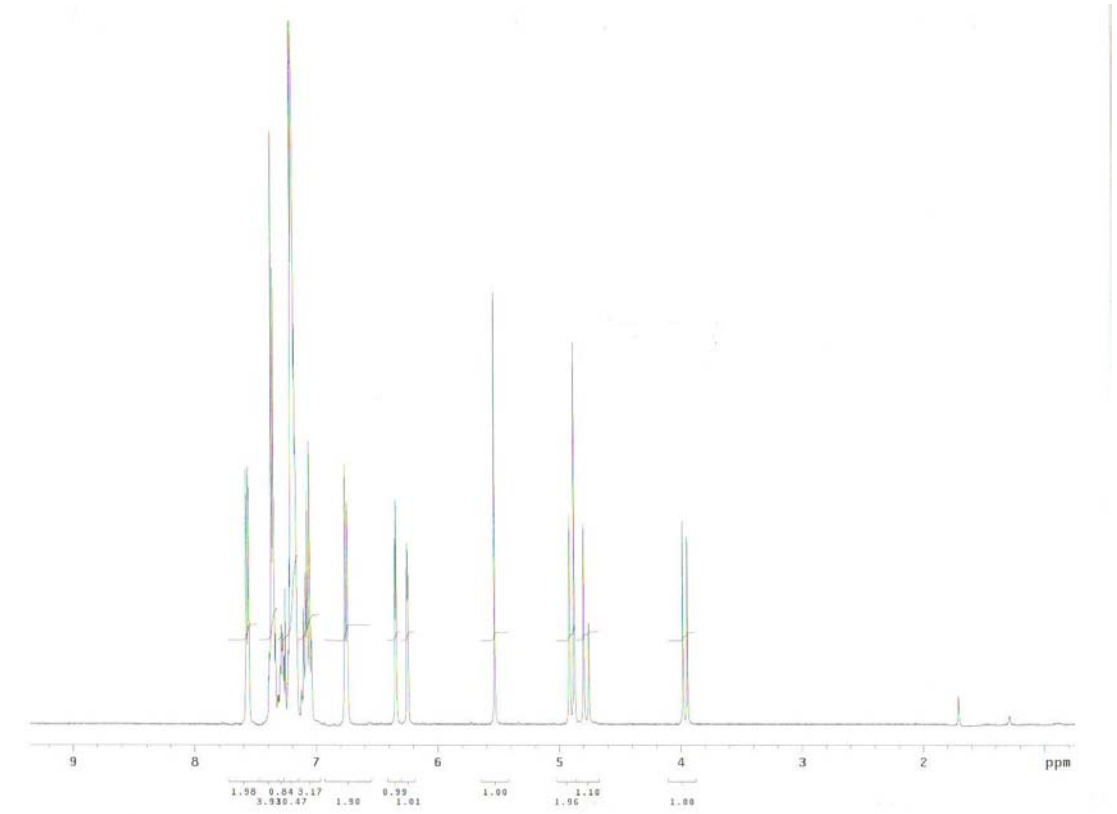
NOESY1D for 1-Benzyl-3-(1-benzyl-2-oxo-2-phenyl-ethyl)-3,4-di-*p*-tolyl-azetidin-2-one

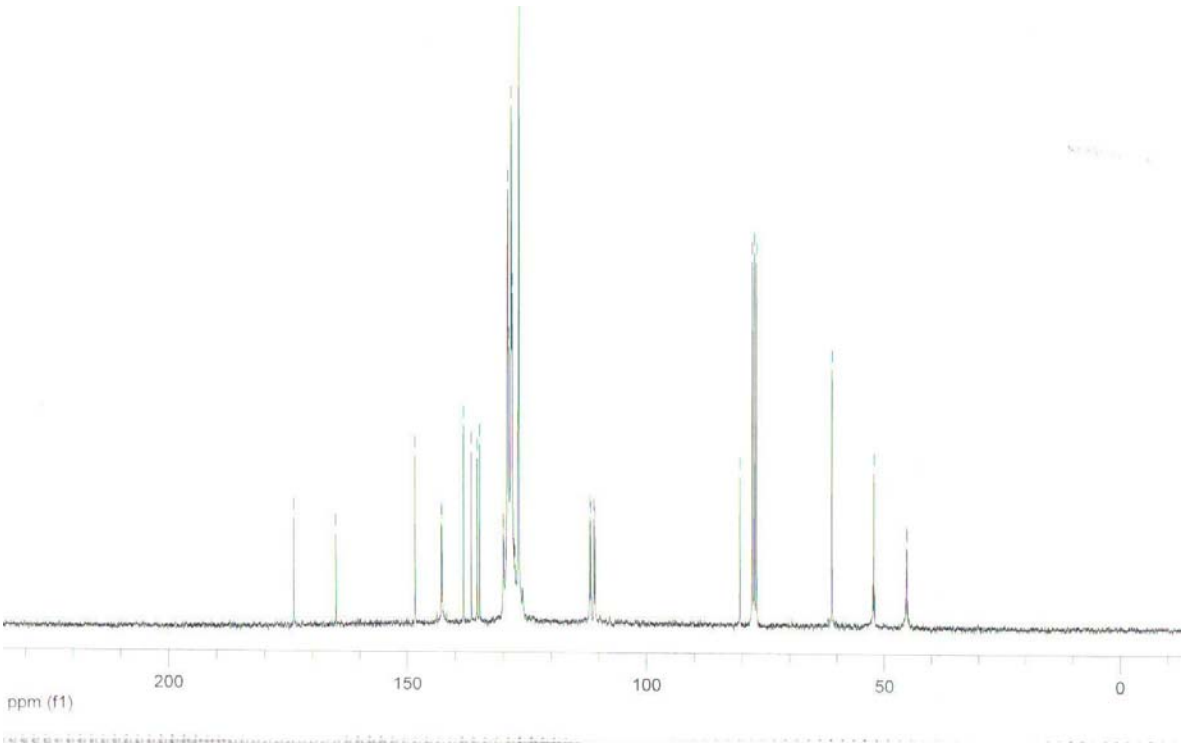


Strong NOE between protons 3,3' and 4.

Weak NOE between protons 3,3' and 1.

^{1}H and ^{13}C NMR Spectra of 1m





^{1}H and ^{13}C NMR Spectra of 1n