Cobalt-Mediated Macrocyclizations. Facile Synthesis of 2-Oxo-Pyridinophanes via [2 + 2 + 2] Cycloaddition of \( \alpha,\omega \)-Diynes and Isocyanates

Llorente V. R. Boñaga, Han-Cheng Zhang, Diane A. Gauthier, Indrasena Reddy, and Bruce E. Maryanoff*

*Drug Discovery, Johnson & Johnson Pharmaceutical Research & Development, Spring House, Pennsylvania 19477-0776 USA

Supporting Information
Experimental Section

The general methods and characterization data for bis-alkynes 1, 5, 7, 9, and 11 were previously reported. ¹

Typical Procedure for Synthesis of Macroyclic 2-Pyridone-cyclophanes. In a 100-mL round-bottom flask, equipped with a condenser and a three-way stopper connected to a balloon of argon, a mixture of diyne 1 (100 mg, 0.34 mmol, 1 equiv) and β-phenethyl isocyanate (477 mg, 3.24 mmol, 9.7 equiv) was pumped briefly and purged three times with argon. Fifty milliliters of 1,2-dimethoxyethane was then added, followed by a 10-mL solution of CpCo(CO)₂ (12.8 µL, 0.10 mmol, 30 mol %), and the remaining volume of the solvent to provide a final 0.005 M concentration (relative to diyne 1). The resulting light orange solution was then heated at reflux for 24 h. The reaction mixture was then cooled to room temperature. Subsequent removal of the solvents in vacuo, followed by flash chromatography (SiO₂, 3%, 9%, 20%, 33% and 50% ethyl acetate in hexanes, and then 2% methanol in dichloromethane) afforded 69 mg of the para-pyridone cyclophane, 2p (45%) and 34 mg of the meta-pyridone-cyclophane 2m (23%). For best results, newly opened bottles of anhydrous 1,2-dimethoxyethane (EM Science) and CpCo(CO)₂ (Strem Chemicals, Inc.) should be used in the reactions.

![Chemical Structure](image1)

21-Phenethyl-6,15-dioxa-21-aza-tricyclo[18.3.1.08,13]tetracosa-1(23),8(13),9,11,20(24)-pentaen-22-one (2m). ¹H NMR (CDCl₃, 500 MHz): δ 7.12-7.32 (m, 9H), 6.26 (s, 1H), 5.86 (s, 1H), 4.51 (s, 2H), 4.46 (s, 2H), 4.12 (m, 2H), 3.47 (m, 4H), 2.93 (m, 2H), 2.36 (m, 4H), 1.54-1.65 (m, 8H). ¹³C NMR (CDCl₃, 125 MHz): δ 163.83, 153.99, 147.64, 138.57, 136.67, 136.31, 129.16, 128.90, 128.64, 128.59, 127.88, 127.73, 126.65, 116.28, 107.87, 70.60, 70.12, 70.01, 69.88, 45.30, 34.76, 34.40, 31.63, 28.11, 27.58, 26.19, 23.80. IR (neat, cm⁻¹): 2936, 2862, 1652, 1569, 1497, 1454, 1257, 1089, 750, 700. HRMS (FAB) Calcd for C₂₉H₃₅NO₃: 445.59. Found: 446.270070 (MH⁺).

![Chemical Structure](image2)

21-Phenethyl-6,15-dioxa-21-aza-tricyclo[18.2.2.08,13]tetracosa-1(23),8(13),9,11,20(24)-pentaen-22-one (2p). ¹H NMR (CDCl₃, 500 MHz): δ 7.36 (m, 1H), 7.18-7.32 (m, 8H), 7.05 (d, J = 7.0 Hz, 1H), 5.88 (d, J = 7.0 Hz, 1H), 4.328 (s, 2H), 4.327 (s, 2H), 4.23 (br s, 2H), 3.56 (m,
2,2'-Bis-pent-4-ynloxymethyl-biphenyl (3). Compound 3 was prepared similarly as compound 5, in 35% yield. \(^1\)H NMR (CDCl\(_3\), 300 MHz): \(\delta\) 7.14-7.55 (m, 8H), 4.19 (s, 4H), 3.39 (t, \(J = 6.2\) Hz, 4H), 2.23 (td, \(J = 7.2, 2.6\) Hz, 4H), 1.91 (t, \(J = 2.7\) Hz, 2H), 1.68-1.77 (m, 4H). \(^{13}\)C NMR (CDCl\(_3\), 125 MHz): \(\delta\) 139.89, 136.77, 129.97, 128.51, 128.03, 127.46, 84.37, 70.99, 69.38, 68.77, 29.01, 15.68. Anal. Calcd for C\(_{24}\)H\(_{26}\)O\(_2\): C, 83.20, H, 7.56. Found: C, 83.18, H, 7.39.

Compounds 4m. \(^1\)H NMR (CDCl\(_3\), 500 MHz): \(\delta\) 7.57 (d, \(J = 2.5\) Hz, 1H), 7.56 (d, \(J = 3.0\) Hz, 1H), 7.37-7.41 (m, 3H), 7.27-7.31 (m, 3H), 7.19-7.24 (m, 3H), 7.05-7.09 (m, 2H), 6.23 (s, 1H), 5.71 (s, 1H), 4.37 (d, \(J = 11\) Hz, 1H), 4.31 (d, \(J = 10.5\) Hz, 1H), 4.21-4.25 (m, 1H), 4.14 (d, \(J = 3.5\) Hz, 1H), 4.11 (d, \(J = 4.0\) Hz, 1H), 4.05-4.14 (m, 1H), 3.24-3.35 (m, 3H), 3.17-3.21 (m, 1H), 2.96-2.99 (m, 2H), 2.59 (ddd, \(J = 12.0, 8.0, 3.5\) Hz, 1H), 2.47 (ddd, \(J = 11.0, 7.0, 4.0\) Hz, 1H), 2.40 (ddd, \(J = 12.5, 6.0, 3.5\) Hz, 1H), 2.32 (ddd, \(J = 11.0, 5.5, 5.5\) Hz, 1H), 1.79-1.83 (m, 2H), 1.65-1.74 (m, 2H). \(^{13}\)C NMR (CDCl\(_3\), 125 MHz): \(\delta\) 163.88, 153.55, 146.69, 138.93, 138.65, 138.53, 136.32, 129.48, 129.43, 128.89, 128.64, 127.79, 127.71, 127.65, 127.02, 126.81, 126.73, 126.65, 116.30, 109.52, 70.40, 70.11, 68.03, 67.35, 45.46, 34.80, 30.63, 29.04, 28.73, 27.46. HRMS (FAB) Calcd for C\(_{33}\)H\(_{35}\)N\(_2\)O\(_5\): 493.64. Found: 494.270105 (MH\(^+\)).
Compound 4p. $^1$H NMR (CDCl$_3$, 500 MHz): $\delta$ 7.64 (d, $J = 6.5$ Hz, 1H), 7.50 (d, $J = 6.5$ Hz, 1H), 7.38-7.41 (m, 1H), 7.32-7.35 (m, 1H), 7.19-7.29 (m, 6H), 7.00 (dd, $J = 6.0$, 0.5 Hz, 1H), 6.97 (dd, $J = 19.0$, 6.0, Hz, 1H), 6.971 (dd, $J = 19.5$, 6.0, Hz, 1H), 6.85 (d, $J = 6.0$ Hz, 1H), 5.69 (d, $J = 5.5$ Hz, 1H), 4.32 (d, $J = 11.5$ Hz, 1H), 4.31 (d, $J = 11.5$ Hz, 1H), 4.23 (br s, 1H), 4.03 (br s, 1H), 3.77 (d, $J = 12.0$ Hz, 1H), 3.66 (d, $J = 11.5$ Hz, 1H), 3.23 (ddd, $J = 8.5$, 4.5, 4.5 Hz, 1H), 3.18 (ddd, $J = 8.5$, 4.0, 4.0 Hz, 1H), 3.11 (br ddd, $J = 8.0$, 8.0, 8.0 Hz, 1H), 2.95-3.01 (m, 2H), 2.84-2.89 (m, 1H), 2.71-2.79 (m, 1H), 2.58-2.66 (m, 2H), 2.51-2.55 (m, 1H), 1.93-2.02 (m, 2H), 1.78-1.82 (m, 2H). $^{13}$C NMR (CDCl$_3$, 125 MHz): $\delta$ 163.32, 145.09, 138.60, 138.18, 137.75, 137.02, 136.51, 135.74, 129.50, 129.40, 128.90, 128.74, 128.60, 127.67, 127.62, 126.68, 126.60, 126.49, 126.47, 126.45, 107.67, 70.56, 70.49, 69.45, 67.64, 46.12, 34.98, 29.84, 28.36, 27.58, 26.19. HRMS (FAB) Calcd for C$_{33}$H$_{35}$NO$_3$: 493.64. Found: 494.269347 (MH$^+$).

19-Phenylethyl-5,14-dioxoa-19-aza-tricyclo[16.3.1.0$^7$,12]docosa-1(21),7(12),8,10,18(22)-pentaen-20-one (6m). $^1$H NMR (CDCl$_3$, 500 MHz): $\delta$ 7.17-7.38 (m, 9H), 6.28 (s, 1H), 5.96 (s, 1H), 4.50 (s, 2H), 4.49 (s, 2H), 4.17 (br t, $J = 7.4$ Hz, 2H), 3.45 (t, $J = 6.0$ Hz, 2H), 3.41 (t, $J = 5.9$ Hz, 2H), 2.99 (t, $J = 7.6$ Hz, 2H), 2.52 (t, $J = 6.1$ Hz, 4H), 1.93 (quintet, $J = 6.1$ Hz, 2H), 1.87 (quintet, $J = 6.1$ Hz, 2H). $^{13}$C NMR (CDCl$_3$, 125 MHz): $\delta$ 163.98, 153.51, 146.76, 138.63, 136.39, 136.20, 129.42, 129.21, 128.91, 128.64, 128.04, 127.98, 126.65, 116.21, 110.65, 70.63, 70.30, 68.02, 45.65, 34.75, 30.43, 29.04, 28.94, 27.40. IR (neat, cm$^{-1}$): 2926, 2860, 1717, 1658, 1579, 1546, 1454, 1124, 1097, 1076, 752, 701. HRMS (FAB) Calcd for C$_{29}$H$_{31}$NO$_3$: 417.54. Found: 418.239232 (MH$^+$).
19-Phenethyl-5,14-doxia-19-aza-tricyclo[16.2.2.07,12]docosa-1(21),7(12),8,10,18(22)-pentaen-20-one (6p). $^1$H NMR (CDCl$_3$, 500 MHz): δ 7.19-7.33 (m, 9H), 7.02 (d, $J$ = 6.9 Hz, 1H), 5.79 (d, $J$ = 6.9 Hz, 1H), 4.58 (m, 1H), 4.06-4.16 (m, 4H), 3.79-3.84 (m, 1H), 3.45-3.63 (m, 4H), 3.07-3.11 (m, 1H), 2.99-3.05 (m, 1H), 2.84-2.90 (m, 1H), 2.68 (ddd, $J$ = 14.8, 4.8, 4.8 Hz, 1H), 2.40 (ddd, $J$ = 15.3, 9.9, 5.6 Hz, 1H), 2.19-2.26 (m, 1H), 1.83-1.95 (m, 4H). $^{13}$C NMR (CDCl$_3$, 125 MHz): δ 163.43, 145.78, 138.91, 136.59, 136.45, 135.48, 129.82, 128.89, 128.55, 128.24, 128.16, 127.46, 127.07, 126.47, 107.14, 71.32, 69.90, 69.42, 69.28, 46.39, 34.69, 31.61, 30.12, 27.69, 26.71. IR (neat, cm$^{-1}$): 2922, 2860, 1716, 1646, 1595, 1564, 1496, 1454, 1364, 1186, 1124, 1087, 1042, 753, 702. HRMS (FAB) Calcd for C$_{27}$H$_{31}$NO$_3$: 417.54. Found: 418.238755 (MH$^+$).

19-Phenethyl-3,6,13,16-tetraoxa-19-aza-tricyclo[16.2.2.07,12]docosa-1(21),7(12),8,10,18(22)-pentaen-20-one (8). $^1$H NMR (CDCl$_3$, 500 MHz): δ 7.29 (d, $J$ = 6.7 Hz, 1H), 7.23-7.26 (m, 2H), 7.18-7.20 (m, 3H), 6.73-6.80 (m, 3H), 6.67-6.69 (m, 1H), 6.07 (d, $J$ = 6.6 Hz, 1H), 5.08 (d, $J$ = 12.1 Hz, 1H), 4.56 (d, $J$ = 13.6 Hz, 1H), 4.11-4.25 (m, 4H), 4.05 (ddd, $J$ = 11.2, 4.7, 0.8 Hz, 1H), 3.99 (observed d, $J$ = 12.2 Hz, 2H), 3.86 (observed d, $J$ = 13.7 Hz, 1H), 3.85-3.90 (m, 1H), 3.80 (ddd, $J$ = 12.0, 7.5, 0.9 Hz, 1H), 3.76 (ddd, $J$ = 10.7, 4.7, 0.9 Hz, 1H), 3.71 (ddd, $J$ = 12.1, 2.8, 1.2 Hz, 1H), 2.98 (t, $J$ = 7.7 Hz, 2H). $^{13}$C NMR (CDCl$_3$, 125 MHz): δ 163.27, 148.38, 147.88, 143.65, 139.34, 137.32, 129.02, 128.74, 128.49, 126.34, 120.76, 120.24, 112.29, 111.83, 107.90, 70.33, 68.93, 68.64, 67.93, 67.50, 67.28, 46.67, 34.25. Anal. Calcd for C$_{25}$H$_{27}$NO$_3$: C, 71.24, H, 6.46, N, 3.32. Found: C, 70.62, H, 6.51, N, 3.21.

19-Phenethyl-5,14-doxia-19-aza-tricyclo[16.2.2.07,12]docosa-1(21),7(12),8,10,18(22)-pentaene-6,13,20-trione (10). $^1$H NMR (CDCl$_3$, 500 MHz): δ 7.75-7.79 (m, 1H), 7.53-7.57 (m, 1H), 7.46-7.50 (m, 2H), 7.14-7.31 (m, 5H), 6.95 (d, $J$ = 7.0 Hz, 1H), 5.85 (d, $J$ = 7.0 Hz, 1H), 4.53 (ddd, $J$ = 11.4, 5.8, 3.8 Hz, 1H), 4.43 (ddd, $J$ = 11.5, 8.7, 2.9 Hz, 1H), 4.27 (m, 2H), 4.15 (ddd, $J$ = 11.4, 6.6, 3.5 Hz, 1H), 3.82 (ddd, $J$ = 13.2, 9.5, 7.1 Hz, 1H), 3.11 (ddd, $J$ = 13.8, 5.5, 5.5 Hz, 1H), 2.76-2.84 (m, 2H), 2.73 (observed ddd, $J$ = 15.4, 7.1, 5.3 Hz, 1H), 2.57 (ddd, $J$ = 15.5, 7.9, 5.3 Hz, 1H), 2.38-2.46 (m, 1H), 2.35 (ddd, $J$ = 15.1, 9.6, 5.9 Hz, 1H), 2.03-2.20 (m, 3H). $^{13}$C NMR (CDCl$_3$, 125 MHz): δ 167.40, 166.15, 163.32, 144.84, 138.69, 137.06, 131.21, 130.96, 130.74, 129.27, 128.84, 128.77, 128.59, 128.13, 127.68, 126.54, 107.37, 63.65, 63.18,
46.21, 34.36, 29.89, 28.78, 25.04, 23.99. HRMS (FAB) Calcd for C_{27}H_{27}NO_{5}: 445.51. Found: 446.198481 (MH^+).

![Chemical Structure](image1)

19-[2-(2-Thienyl)ethyl]-3,6,13,16-tetraoxa-19-aza-tricyclo[16.2.2.07,12]docosa-1(21),7(12),8,10,18(22)-pentaen-20-one (12). \(^1\)H NMR (CDCl\(_3\), 500 MHz): \(\delta\) 7.28 (d, \(J = 6.7\) Hz, 1H), 7.10 (d, \(J = 5.1\) Hz, 1H), 6.88 (dd, \(J = 5.1, 3.5\) Hz, 1H), 6.70-6.81 (m, 5H), 6.07 (d, \(J = 6.6\) Hz, 1H), 5.06 (d, \(J = 12.2\) Hz, 1H), 4.53 (d, \(J = 13.7\) Hz, 1H), 3.98 (obscured d, \(J = 12.2\) Hz, 1H), 3.87 (obscured d, \(J = 13.8\) Hz, 1H), 3.70-4.07 (m, 10H), 3.23-3.30 (m, 1H), 3.12-3.18 (m, 1H). \(^{13}\)C NMR (CDCl\(_3\), 125 MHz): \(\delta\) 163.25, 148.36, 147.83, 143.76, 141.37, 137.43, 128.76, 127.01, 125.50, 123.77, 120.81, 120.29, 112.31, 111.80, 107.86, 70.34, 68.90, 68.66, 67.90, 67.58, 67.27, 46.80, 27.99. HRMS (FAB) Calcd for C_{23}H_{33}NO_{5}: 427.51. Found: 428.154348 (MH^+).

![Chemical Structure](image2)

19-(4-Methoxybenzyl)-3,6,13,16-tetraoxa-19-aza-tricyclo[16.2.2.07,12]docosa-1(21),7(12),8,10,18(22)-pentaen-20-one (13). \(^1\)H NMR (CDCl\(_3\), 500 MHz): \(\delta\) 7.31 (d, \(J = 6.7\) Hz, 1H), 7.11 (d, \(J = 8.8\) Hz, 2H), 6.73-6.86 (m, 6H), 6.11 (d, \(J = 6.6\) Hz, 1H), 5.63 (d, \(J = 15.5\) Hz, 1H), 5.06 (d, \(J = 12.2\) Hz, 1H), 5.03 (d, \(J = 15.6\) Hz, 1H), 4.74 (d, \(J = 13.5\) Hz, 1H), 4.13-4.21 (m, 2H), 4.06 (ddd, \(J = 11.9, 4.9, 1.1\) Hz, 1H), 4.00 (obscured d, \(J = 12.3\) Hz, 1H), 3.97-4.01 (m, 1H), 3.91-3.95 (m, 1H), 3.91 (obscured d, \(J = 13.5\) Hz, 1H), 3.79-3.87 (m, 2H), 3.75 (m, 1H), 3.73 (s, 3H). \(^{13}\)C NMR (CDCl\(_3\), 125 MHz): \(\delta\) 163.53, 158.61, 148.52, 148.11, 143.62, 137.48, 129.79, 129.17, 128.16, 120.85, 120.24, 113.95, 112.38, 112.09, 108.39, 70.24, 68.95, 68.64, 68.06, 67.52, 55.23, 45.91. HRMS (FAB) Calcd for C_{25}H_{27}NO_{6}: 437.49. Found: 438.191578 (MH^+).
19-Dodecyl-3,6,13,16-tetraoxa-19-aza-tricyclo[16.2.2.07,12]docosa-
1(21),7(12),8,10,18(22)-pentaen-20-one (14). $^1$H NMR (CDCl$_3$, 500 MHz): $\delta$ 7.20 (d, $J = 6.6$ Hz, 1H), 6.64-6.75 (m, 4H), 6.03 (d, $J = 6.6$ Hz, 1H), 4.95 (d, $J = 12.2$ Hz, 1H), 4.76 (d, $J = 13.5$ Hz, 1H), 3.91 (obscured d, $J = 13.6$ Hz, 1H), 3.65-4.11 (m, 11H), 1.42-1.64 (m, 2H), 1.18 (m, 18H), 0.81 (t, $J = 6.9$ Hz, 3H). $^{13}$C NMR (CDCl$_3$, 125 MHz): $\delta$ 162.18, 147.44, 146.94, 142.27, 136.10, 127.81, 119.75, 119.17, 111.33, 110.90, 107.08, 69.33, 67.84, 67.63, 66.88, 66.44, 43.63, 30.91, 28.69, 28.62, 28.61, 28.57, 28.50, 28.34, 28.26, 27.72, 26.19, 21.68, 13.11. HRMS (FAB) Calcd for C$_{29}$H$_{43}$NO$_5$: 485.66. Found: 486.322307 (MH$^+$).

19-Cyclohexyl-3,6,13,16-tetraoxa-19-aza-tricyclo[16.2.2.07,12]docosa-
1(21),7(12),8,10,18(22)-pentaen-20-one (15). $^1$H NMR (CDCl$_3$, 500 MHz): $\delta$ 7.20 (d, $J = 6.5$ Hz, 1H), 6.77-6.83 (m, 2H), 6.74-6.76 (m, 1H), 6.69-6.70 (m, 1H), 6.04 (d, $J = 6.4$ Hz, 1H), 5.01 (d, $J = 12.1$ Hz, 1H), 4.89 (d, $J = 13.7$ Hz, 1H), 3.93-4.09 (m, 5H), 3.95 (obscured d, $J = 12.4$ Hz, 1H), 3.89 (obscured d, $J = 12.0$ Hz, 1H), 3.74-3.80 (m, 3H), 3.48 (m, 1H), 1.92-1.95 (m, 2H), 1.66-1.72 (m, 2H), 1.30-1.39 (m, 2H), 1.15-1.21 (m, 2H), 1.06-1.14 (m, 2H). $^{13}$C NMR (CDCl$_3$, 125 MHz): $\delta$ 164.06, 148.43, 147.78, 143.65, 136.61, 130.18, 120.69, 120.19, 112.17, 111.43, 108.26, 71.04, 68.89, 68.70, 68.12, 67.41, 67.16, 49.17, 33.96, 29.08, 26.66, 25.61, 24.94. HRMS (FAB) Calcd for C$_{25}$H$_{39}$NO$_5$: 399.48. Found: 400.213417 (MH$^+$).

4-(20-Oxo-3,6,13,16-tetraoxa-19-aza-tricyclo[16.2.2.07,12]docosa-
1(21),7(12),8,10,18(22)-pentaen-19-yl)-piperidine-1-carboxylic Acid Benzyl Ester (16). $^1$H NMR (CDCl$_3$, 500 MHz): $\delta$ 7.28-7.38 (m, 5H), 7.21 (d, $J = 6.5$ Hz, 1H), 6.67-6.84 (m, 4H), 6.06
19-Adamantan-1-yl-3,6,13,16-tetraoxa-19-aza-tricyclo[16.2.2.0⁷,12]docosa-
1(21),7(12),8,10,18(22)-pentaen-20-one (17). \(^1\)H NMR (CDCl₃, 500 MHz): \(\delta\) 7.30 (d, \(J = 6.8\)
Hz, 1H), 6.70-6.84 (m, 4H), 6.40 (d, \(J = 6.8\) Hz, 1H), 4.83 (d, \(J = 14.0\) Hz, 1H), 4.65 (d, \(J = 13.6\) Hz,
1H), 4.32 (d, \(J = 14.1\) Hz, 1H), 4.17 (d, \(J = 13.7\) Hz, 1H), 3.89-3.99 (m, 4H), 3.72-3.81 (m,
3H), 3.53-3.59 (m, 1H), 2.53 (br d, \(J = 11.5\) Hz, 2H), 2.29 (br d, \(J = 11.1\) Hz, 2H), 2.08 (br s,
2H), 1.98-2.00 (m, 1H), 1.85-1.88 (m, 2H), 1.70 (br d, \(J = 11.6\) Hz, 2H), 1.58-1.61 (m, 4H). \(^1\)C
NMR (CDCl₃, 125 MHz): \(\delta\) 166.77, 149.08, 148.40, 146.81, 136.73, 130.35, 121.22, 120.46,
113.49, 112.51, 111.81, 72.76, 69.52, 69.09, 68.63, 68.60, 68.08, 67.22, 40.43, 36.22, 30.67.

19-p-Tolyl-3,6,13,16-tetraoxa-19-aza-tricyclo[16.2.2.0⁷,12]docosa-
1(21),7(12),8,10,18(22)-pentaen-20-one (18). \(^1\)H NMR (CDCl₃, 500 MHz): \(\delta\) 7.42 (d, \(J = 6.7\)
Hz, 1H), 7.21-7.25 (m, 1H), 7.10-7.15 (m, 2H), 7.01 (dd, \(J = 8.0, 2.1\) Hz, 1H), 6.76-6.88 (m, 4H),
6.26 (d, \(J = 6.7\) Hz, 1H), 4.97 (d, \(J = 12.3\) Hz, 1H), 4.36 (d, \(J = 13.2\) Hz, 1H), 4.06-4.17 (m, 3H),
4.07 (obscured d, \(J = 12.3\) Hz, 1H), 3.85 (obscured d, \(J = 13.3\) Hz, 1H), 3.77-3.97 (m, 5H), 2.35
(s, 3H). \(^1\)C NMR (CDCl₃, 125 MHz): \(\delta\) 164.06, 148.57, 147.96, 143.84, 138.39, 138.16,
135.27, 130.07, 129.92, 129.60, 129.34, 126.94, 120.81, 120.29, 112.20, 111.62, 107.69, 69.44,
68.52, 68.38, 67.98, 67.93, 66.90, 21.26. HRMS (FAB) Calcd for C₂₄H₂₅NO₅: 407.46. Found:
408.180787 (MH⁺).
19-(4-Methoxyphenyl)-3,6,13,16-tetraoxa-19-aza-tricyclo[16.2.2.07,12]docosa-1(21),7(12),8,10,18(22)-pentaen-20-one (19). \(^1\)H NMR (CDCl\(_3\), 500 MHz): \(\delta\) 7.42 (d, \(J = 6.7\) Hz, 1H), 7.15 (dd, \(J = 8.8, 2.5\) Hz, 1H), 7.04 (dd, \(J = 8.6, 2.5\) Hz, 1H), 6.93 (dd, \(J = 8.6, 2.9\) Hz, 1H), 6.77-6.87 (m, 5H), 6.26 (d, \(J = 6.6\) Hz, 1H), 4.97 (d, \(J = 12.3\) Hz, 1H), 4.38 (d, \(J = 13.3\) Hz, 1H), 4.06-4.17 (m, 4H), 3.77-3.97 (m, 5H), 3.79 (obscured s, 3H), 3.85 (obscured d, \(J = 13.3\) Hz, 1H). \(^1\)\(^3\)C NMR (CDCl\(_3\), 125 MHz): \(\delta\) 164.20, 159.41, 148.59, 147.98, 144.08, 138.16, 131.47, 130.55, 129.61, 128.20, 120.86, 120.31, 114.22, 114.16, 112.23, 111.65, 107.73, 69.47, 68.53, 68.45, 67.97, 66.84, 55.37. HRMS (FAB) Calcd for C\(_{24}\)H\(_{25}\)NO\(_5\): 423.46. Found: 424.176388 (MH\(^+\)).

Single-Crystal X-ray Analysis of 19-Phenethyl-3,6,13,16-tetraoxa-19-azatricyclo[16.2.2.0\textsuperscript{2,2}]docosa-1(21),7,9,11,18(22)-pentaen-20-one (8). Crystals of C\textsubscript{25}H\textsubscript{37}NO\textsubscript{5} (MW = 421.48 Da, colorless square plates), which had been recrystallized from EtOAc, were severely twinned. One of these twinned specimens was cut repeatedly with a razor blade, until a small, mostly single-domain piece was obtained. The diffraction pattern from the principal domain of this crystal did not overlap with the diffraction patterns of other domains. This crystal, at -80±2°C, was orthorhombic, space group P2\textsubscript{1}2\textsubscript{1}2\textsubscript{1} - D (No. 19) with a = 10.325(1) Å, b = 11.651(1) Å, c = 17.868(2) Å, V = 2149.4(4) Å\textsuperscript{3} and Z = 4 (ρ\textsubscript{calc} = 1.302 g·cm\textsuperscript{3}; μ\textsubscript{MoKα} = 0.091 mm\textsuperscript{-1}). A full hemisphere of diffracted intensities (ω-scan width of 0.30°) was measured using graphite-monochromated MoKα radiation on a Bruker SMART APEX CCD Single Crystal Diffraction System. X-rays were provided by a fine-focus sealed x-ray tube operated at 50kV and 35mA. Lattice constants were determined with the Bruker SAINT software package using peak centers for 2466 reflections. A total of 12882 integrated reflection intensities having 2θ(MoKα)< 56.24° were produced using the Bruker program SAINT. A total of 4741 of these were independent and gave R\textsubscript{int} = 0.057. The Bruker SHELXTL-PC software package was used to solve the structure using "direct methods" techniques. All stages of weighted full-matrix least-squares refinement were conducted using F\textsuperscript{2} data with the SHELXTL-PC Version 5 software package. Final agreement factors at convergence are: R\textsubscript{f}(unweighted, based on F) = 0.043 for 3116 independent reflections having 2θ(MoKα)< 56.24° and I>2σ(I); R\textsubscript{f}(unweighted, based on F) = 0.071 and wR\textsubscript{2} (weighted, based on F\textsuperscript{2}) = 0.072 for all 4741 independent reflections having 2θ(MoKα)< 56.24°.

The structural model incorporated anisotropic thermal parameters for all nonhydrogen atoms and isotropic thermal parameters for all hydrogen atoms. All hydrogen atoms were included in the structure factor calculations as idealized atoms (assuming sp\textsuperscript{2} or sp\textsuperscript{3} hybridization of the carbon atoms and C-H bond lengths of 0.95-0.99 Å) "riding" on their respective carbon atoms. The isotropic thermal parameter of each hydrogen atom was fixed at a value 1.2 times the equivalent isotropic thermal parameter of the carbon atom to which it is covalently bonded.
<table>
<thead>
<tr>
<th>Atom</th>
<th>Fractional Coordinates</th>
<th>Equivalent Isotropic Thermal Parameter, U, Å² x 10³</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>10⁴x</td>
<td>10⁴y</td>
</tr>
<tr>
<td>C₁</td>
<td>5930(2)</td>
<td>-1250(2)</td>
</tr>
<tr>
<td>C₂</td>
<td>7165(2)</td>
<td>-1048(2)</td>
</tr>
<tr>
<td>O₃</td>
<td>7003(1)</td>
<td>-205(1)</td>
</tr>
<tr>
<td>C₄</td>
<td>6247(2)</td>
<td>-586(2)</td>
</tr>
<tr>
<td>C₅</td>
<td>5407(2)</td>
<td>385(2)</td>
</tr>
<tr>
<td>O₆</td>
<td>4339(1)</td>
<td>480(1)</td>
</tr>
<tr>
<td>C₇</td>
<td>3463(2)</td>
<td>1330(2)</td>
</tr>
<tr>
<td>C₈</td>
<td>3653(2)</td>
<td>2228(2)</td>
</tr>
<tr>
<td>C₉</td>
<td>2692(2)</td>
<td>3061(2)</td>
</tr>
<tr>
<td>C₁₀</td>
<td>1550(2)</td>
<td>2981(2)</td>
</tr>
<tr>
<td>C₁₁</td>
<td>1339(2)</td>
<td>2072(2)</td>
</tr>
<tr>
<td>C₁₂</td>
<td>2285(2)</td>
<td>1258(2)</td>
</tr>
<tr>
<td>O₁₃</td>
<td>2175(1)</td>
<td>358(1)</td>
</tr>
<tr>
<td>C₁₄</td>
<td>893(2)</td>
<td>75(2)</td>
</tr>
<tr>
<td>C₁₅</td>
<td>973(2)</td>
<td>-995(2)</td>
</tr>
<tr>
<td>O₁₆</td>
<td>1386(1)</td>
<td>-730(1)</td>
</tr>
<tr>
<td>C₁₇</td>
<td>2275(2)</td>
<td>-1538(2)</td>
</tr>
<tr>
<td>C₁₈</td>
<td>3587(2)</td>
<td>-1484(2)</td>
</tr>
<tr>
<td>N₁₉</td>
<td>4321(2)</td>
<td>-507(1)</td>
</tr>
<tr>
<td>C₂₀</td>
<td>5519(2)</td>
<td>-343(2)</td>
</tr>
<tr>
<td>C₂¹</td>
<td>5214(2)</td>
<td>-2209(2)</td>
</tr>
<tr>
<td>C₂₂</td>
<td>4015(2)</td>
<td>-2335(2)</td>
</tr>
<tr>
<td>C₂₃</td>
<td>3927(2)</td>
<td>405(2)</td>
</tr>
<tr>
<td>C₂₄</td>
<td>4491(2)</td>
<td>235(2)</td>
</tr>
<tr>
<td>C₂₅</td>
<td>4247(2)</td>
<td>1269(2)</td>
</tr>
<tr>
<td>C₂₆</td>
<td>5216(2)</td>
<td>2050(2)</td>
</tr>
<tr>
<td>C₂₇</td>
<td>4978(2)</td>
<td>3027(2)</td>
</tr>
<tr>
<td>C₂₈</td>
<td>3762(3)</td>
<td>3233(2)</td>
</tr>
<tr>
<td>C₂₉</td>
<td>2794(2)</td>
<td>2462(2)</td>
</tr>
<tr>
<td>C₃₀</td>
<td>3026(2)</td>
<td>1484(2)</td>
</tr>
<tr>
<td>O₃₁</td>
<td>6153(1)</td>
<td>530(1)</td>
</tr>
</tbody>
</table>
a The numbers in parentheses are the estimated standard deviations in the last significant digit.
b Atoms are labeled in agreement with Figure 1.
c This is one-third of the trace of the orthogonalized \( U_q \) tensor.
Table 2.  Anisotropic Thermal Parameters for Nonhydrogen Atoms in Crystalline 8\(^a\)

<table>
<thead>
<tr>
<th>Atom Type</th>
<th>(U_{11})</th>
<th>(U_{22})</th>
<th>(U_{33})</th>
<th>(U_{23})</th>
<th>(U_{13})</th>
<th>(U_{12})</th>
</tr>
</thead>
<tbody>
<tr>
<td>C(_1)</td>
<td>35(1)</td>
<td>31(1)</td>
<td>33(1)</td>
<td>-3(1)</td>
<td>3(1)</td>
<td>8(1)</td>
</tr>
<tr>
<td>C(_2)</td>
<td>35(1)</td>
<td>47(1)</td>
<td>45(1)</td>
<td>-3(1)</td>
<td>0(1)</td>
<td>8(1)</td>
</tr>
<tr>
<td>O(_3)</td>
<td>38(1)</td>
<td>50(1)</td>
<td>42(1)</td>
<td>-7(1)</td>
<td>0(1)</td>
<td>2(1)</td>
</tr>
<tr>
<td>C(_4)</td>
<td>44(1)</td>
<td>50(1)</td>
<td>38(1)</td>
<td>1(1)</td>
<td>-7(1)</td>
<td>8(1)</td>
</tr>
<tr>
<td>C(_5)</td>
<td>37(1)</td>
<td>44(1)</td>
<td>35(1)</td>
<td>-3(1)</td>
<td>-5(1)</td>
<td>3(1)</td>
</tr>
<tr>
<td>O(_6)</td>
<td>30(1)</td>
<td>38(1)</td>
<td>38(1)</td>
<td>-6(1)</td>
<td>-6(1)</td>
<td>2(1)</td>
</tr>
<tr>
<td>C(_7)</td>
<td>31(1)</td>
<td>30(1)</td>
<td>29(1)</td>
<td>5(1)</td>
<td>5(1)</td>
<td>-2(1)</td>
</tr>
<tr>
<td>C(_8)</td>
<td>40(1)</td>
<td>38(1)</td>
<td>30(1)</td>
<td>-1(1)</td>
<td>4(1)</td>
<td>-6(1)</td>
</tr>
<tr>
<td>C(_9)</td>
<td>49(2)</td>
<td>34(1)</td>
<td>39(1)</td>
<td>-4(1)</td>
<td>11(1)</td>
<td>-4(1)</td>
</tr>
<tr>
<td>C(_10)</td>
<td>43(1)</td>
<td>37(1)</td>
<td>45(1)</td>
<td>2(1)</td>
<td>8(1)</td>
<td>10(1)</td>
</tr>
<tr>
<td>C(_11)</td>
<td>35(1)</td>
<td>42(1)</td>
<td>38(1)</td>
<td>4(1)</td>
<td>0(1)</td>
<td>2(1)</td>
</tr>
<tr>
<td>C(_12)</td>
<td>34(1)</td>
<td>32(1)</td>
<td>30(1)</td>
<td>3(1)</td>
<td>3(1)</td>
<td>1(1)</td>
</tr>
<tr>
<td>O(_13)</td>
<td>30(1)</td>
<td>43(1)</td>
<td>42(1)</td>
<td>-8(1)</td>
<td>-6(1)</td>
<td>3(1)</td>
</tr>
<tr>
<td>C(_14)</td>
<td>29(1)</td>
<td>55(1)</td>
<td>42(1)</td>
<td>-5(1)</td>
<td>-4(1)</td>
<td>3(1)</td>
</tr>
<tr>
<td>C(_15)</td>
<td>34(1)</td>
<td>57(1)</td>
<td>47(1)</td>
<td>-9(1)</td>
<td>0(1)</td>
<td>-6(1)</td>
</tr>
<tr>
<td>O(_16)</td>
<td>42(1)</td>
<td>67(1)</td>
<td>40(1)</td>
<td>-10(1)</td>
<td>-6(1)</td>
<td>8(1)</td>
</tr>
<tr>
<td>C(_17)</td>
<td>50(2)</td>
<td>55(1)</td>
<td>42(1)</td>
<td>-16(1)</td>
<td>-3(1)</td>
<td>-2(1)</td>
</tr>
<tr>
<td>C(_18)</td>
<td>38(1)</td>
<td>35(1)</td>
<td>33(1)</td>
<td>-9(1)</td>
<td>2(1)</td>
<td>2(1)</td>
</tr>
<tr>
<td>N(_19)</td>
<td>37(1)</td>
<td>28(1)</td>
<td>31(1)</td>
<td>0(1)</td>
<td>-3(1)</td>
<td>4(1)</td>
</tr>
<tr>
<td>C(_20)</td>
<td>38(1)</td>
<td>32(1)</td>
<td>30(1)</td>
<td>-4(1)</td>
<td>3(1)</td>
<td>5(1)</td>
</tr>
<tr>
<td>C(_21)</td>
<td>51(2)</td>
<td>27(1)</td>
<td>34(1)</td>
<td>4(1)</td>
<td>5(1)</td>
<td>10(1)</td>
</tr>
<tr>
<td>C(_22)</td>
<td>41(1)</td>
<td>30(1)</td>
<td>39(1)</td>
<td>-3(1)</td>
<td>6(1)</td>
<td>-5(1)</td>
</tr>
<tr>
<td>C(_23)</td>
<td>48(1)</td>
<td>34(1)</td>
<td>36(1)</td>
<td>0(1)</td>
<td>-5(1)</td>
<td>10(1)</td>
</tr>
<tr>
<td>C(_24)</td>
<td>55(2)</td>
<td>43(1)</td>
<td>36(1)</td>
<td>0(1)</td>
<td>1(1)</td>
<td>15(1)</td>
</tr>
<tr>
<td>C(_25)</td>
<td>40(1)</td>
<td>39(1)</td>
<td>29(1)</td>
<td>-6(1)</td>
<td>0(1)</td>
<td>6(1)</td>
</tr>
<tr>
<td>C(_26)</td>
<td>36(1)</td>
<td>62(2)</td>
<td>48(1)</td>
<td>0(1)</td>
<td>-5(1)</td>
<td>2(1)</td>
</tr>
<tr>
<td>C(_27)</td>
<td>56(2)</td>
<td>52(2)</td>
<td>60(2)</td>
<td>9(1)</td>
<td>3(1)</td>
<td>-12(1)</td>
</tr>
<tr>
<td>C(_28)</td>
<td>60(2)</td>
<td>48(1)</td>
<td>42(1)</td>
<td>9(1)</td>
<td>4(1)</td>
<td>9(1)</td>
</tr>
<tr>
<td>C(_29)</td>
<td>42(1)</td>
<td>57(1)</td>
<td>43(1)</td>
<td>5(1)</td>
<td>-6(1)</td>
<td>12(1)</td>
</tr>
<tr>
<td>C(_30)</td>
<td>40(1)</td>
<td>41(1)</td>
<td>42(1)</td>
<td>1(1)</td>
<td>0(1)</td>
<td>-1(1)</td>
</tr>
<tr>
<td>O(_31)</td>
<td>48(1)</td>
<td>34(1)</td>
<td>52(1)</td>
<td>2(1)</td>
<td>0(1)</td>
<td>-7(1)</td>
</tr>
</tbody>
</table>

\(a\) The numbers in parentheses are the estimated standard deviations in the last significant digit.

\(b\) The form of the anisotropic thermal parameter is: \(\exp[-2\pi^2(U_{11}h^2\mathbf{a}^2 + U_{22}k^2\mathbf{b}^2 + U_{33}l^2\mathbf{c}^2 + 2U_{12}hk\mathbf{a}\mathbf{b} + 2U_{13}h\mathbf{a}\mathbf{c} + 2U_{23}k\mathbf{b}\mathbf{c})].\)

\(c\) Atoms are labeled in agreement with Figure 1.
Table 3. Atomic Coordinates for Hydrogen Atoms in Crystalline 8

<table>
<thead>
<tr>
<th>Atom Type&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Fractional Coordinates</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>10&lt;sup&gt;4&lt;/sup&gt;x</td>
</tr>
<tr>
<td>H&lt;sub&gt;2a&lt;/sub&gt;</td>
<td>7454</td>
</tr>
<tr>
<td>H&lt;sub&gt;2b&lt;/sub&gt;</td>
<td>7847</td>
</tr>
<tr>
<td>H&lt;sub&gt;2a&lt;/sub&gt;</td>
<td>6822</td>
</tr>
<tr>
<td>H&lt;sub&gt;2b&lt;/sub&gt;</td>
<td>5700</td>
</tr>
<tr>
<td>H&lt;sub&gt;2a&lt;/sub&gt;</td>
<td>5091</td>
</tr>
<tr>
<td>H&lt;sub&gt;2b&lt;/sub&gt;</td>
<td>5908</td>
</tr>
<tr>
<td>H&lt;sub&gt;2&lt;/sub&gt;</td>
<td>4441</td>
</tr>
<tr>
<td>H&lt;sub&gt;2&lt;/sub&gt;</td>
<td>2833</td>
</tr>
<tr>
<td>H&lt;sub&gt;2&lt;/sub&gt;</td>
<td>900</td>
</tr>
<tr>
<td>H&lt;sub&gt;11&lt;/sub&gt;</td>
<td>535</td>
</tr>
<tr>
<td>H&lt;sub&gt;2a&lt;/sub&gt;</td>
<td>524</td>
</tr>
<tr>
<td>H&lt;sub&gt;2b&lt;/sub&gt;</td>
<td>329</td>
</tr>
<tr>
<td>H&lt;sub&gt;15a&lt;/sub&gt;</td>
<td>1594</td>
</tr>
<tr>
<td>H&lt;sub&gt;15b&lt;/sub&gt;</td>
<td>114</td>
</tr>
<tr>
<td>H&lt;sub&gt;17a&lt;/sub&gt;</td>
<td>2370</td>
</tr>
<tr>
<td>H&lt;sub&gt;17b&lt;/sub&gt;</td>
<td>1919</td>
</tr>
<tr>
<td>H&lt;sub&gt;21&lt;/sub&gt;</td>
<td>5527</td>
</tr>
<tr>
<td>H&lt;sub&gt;22&lt;/sub&gt;</td>
<td>3516</td>
</tr>
<tr>
<td>H&lt;sub&gt;23a&lt;/sub&gt;</td>
<td>4216</td>
</tr>
<tr>
<td>H&lt;sub&gt;23b&lt;/sub&gt;</td>
<td>2970</td>
</tr>
<tr>
<td>H&lt;sub&gt;24a&lt;/sub&gt;</td>
<td>5435</td>
</tr>
<tr>
<td>H&lt;sub&gt;24b&lt;/sub&gt;</td>
<td>4093</td>
</tr>
<tr>
<td>H&lt;sub&gt;26&lt;/sub&gt;</td>
<td>6061</td>
</tr>
<tr>
<td>H&lt;sub&gt;27&lt;/sub&gt;</td>
<td>5659</td>
</tr>
<tr>
<td>H&lt;sub&gt;28&lt;/sub&gt;</td>
<td>3593</td>
</tr>
<tr>
<td>H&lt;sub&gt;29&lt;/sub&gt;</td>
<td>1951</td>
</tr>
<tr>
<td>H&lt;sub&gt;30&lt;/sub&gt;</td>
<td>2343</td>
</tr>
</tbody>
</table>

<sup>a</sup> All hydrogen atoms were included in the structure factor calculations as idealized atoms (assuming sp<sup>2</sup>- or sp<sup>3</sup>-hybridization of the carbon atoms and C-H bond lengths of 0.95 -0.99 Å) "riding" on their respective carbon atoms. The isotropic thermal parameter of each hydrogen atom was fixed at a value 1.2 times the equivalent isotropic thermal parameter of the carbon atom to which it is covalently bonded.

<sup>b</sup> Hydrogen atoms are labeled with the same numerical subscript(s) as the carbon atom to which they are covalently bonded; they also have an additional literal subscript (a or b) where necessary to distinguish between hydrogens bonded to the same carbon atom.
Table 4. Bond Lengths in Crystalline $^8$

<table>
<thead>
<tr>
<th>Type$^b$</th>
<th>Length, Å</th>
<th>Type$^b$</th>
<th>Length, Å</th>
</tr>
</thead>
<tbody>
<tr>
<td>C$_2$-O$_1$</td>
<td>1.432(2)</td>
<td>C$<em>{18}$-N$</em>{19}$</td>
<td>1.381(2)</td>
</tr>
<tr>
<td>O$_3$-C$_4$</td>
<td>1.422(2)</td>
<td>N$<em>{19}$-C$</em>{20}$</td>
<td>1.402(2)</td>
</tr>
<tr>
<td>C$_5$-O$_6$</td>
<td>1.428(2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>O$<em>{13}$-C$</em>{14}$</td>
<td>1.428(2)</td>
<td>N$<em>{19}$-C$</em>{23}$</td>
<td>1.472(2)</td>
</tr>
<tr>
<td>C$<em>{15}$-O$</em>{16}$</td>
<td>1.426(2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>O$<em>{16}$-C$</em>{17}$</td>
<td>1.429(2)</td>
<td>C$<em>{20}$-O$</em>{31}$</td>
<td>1.231(2)</td>
</tr>
<tr>
<td>C$<em>1$-C$</em>{20}$</td>
<td>1.444(2)</td>
<td>C$_7$-C$_6$</td>
<td>1.377(2)</td>
</tr>
<tr>
<td>C$<em>1$-C$</em>{21}$</td>
<td>1.345(3)</td>
<td>C$<em>7$-C$</em>{12}$</td>
<td>1.410(3)</td>
</tr>
<tr>
<td>O$_6$-C$_7$</td>
<td>1.367(2)</td>
<td>C$_8$-C$_9$</td>
<td>1.399(3)</td>
</tr>
<tr>
<td>C$<em>{12}$-O$</em>{13}$</td>
<td>1.368(2)</td>
<td>C$<em>9$-C$</em>{10}$</td>
<td>1.366(3)</td>
</tr>
<tr>
<td>C$_1$-C$_2$</td>
<td>1.504(3)</td>
<td>C$<em>{10}$-C$</em>{11}$</td>
<td>1.386(3)</td>
</tr>
<tr>
<td>C$_4$-C$_5$</td>
<td>1.502(3)</td>
<td>C$<em>{11}$-C$</em>{12}$</td>
<td>1.377(3)</td>
</tr>
<tr>
<td>C$<em>{14}$-C$</em>{15}$</td>
<td>1.494(2)</td>
<td>C$<em>{12}$-C$</em>{22}$</td>
<td>1.344(2)</td>
</tr>
<tr>
<td>C$<em>{17}$-C$</em>{18}$</td>
<td>1.503(3)</td>
<td>C$<em>{21}$-C$</em>{22}$</td>
<td>1.409(3)</td>
</tr>
<tr>
<td>C$<em>{23}$-C$</em>{24}$</td>
<td>1.526(2)</td>
<td>C$<em>{25}$-C$</em>{26}$</td>
<td>1.377(3)</td>
</tr>
<tr>
<td>C$<em>{24}$-C$</em>{25}$</td>
<td>1.507(3)</td>
<td>C$<em>{25}$-C$</em>{30}$</td>
<td>1.386(3)</td>
</tr>
<tr>
<td>C$<em>{29}$-C$</em>{30}$</td>
<td>1.382(3)</td>
<td>C$<em>{26}$-C$</em>{27}$</td>
<td>1.390(3)</td>
</tr>
</tbody>
</table>

$^b$ The numbers in parentheses are the estimated standard deviations in the last significant digit.

$^b$ Atoms are labeled in agreement with Figure 1.
Table 5. Bond Angles in Crystalline 8

<table>
<thead>
<tr>
<th>Type $^b$</th>
<th>Angle, (deg)</th>
<th>Type $^b$</th>
<th>Angle, (deg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>O$_2$C$_1$C$_2$</td>
<td>111.9(2)</td>
<td>O$<em>{12}$C$</em>{11}$C$_{12}$</td>
<td>124.3(2)</td>
</tr>
<tr>
<td>C$_4$O$_5$C$_2$</td>
<td>114.0(1)</td>
<td>O$<em>{13}$C$</em>{12}$C$_7$</td>
<td>116.0(2)</td>
</tr>
<tr>
<td>O$_5$C$_6$C$_5$</td>
<td>109.0(2)</td>
<td>C$<em>{16}$C$</em>{12}$C$_7$</td>
<td>119.8(2)</td>
</tr>
<tr>
<td>O$_6$C$_5$C$_4$</td>
<td>107.8(2)</td>
<td>C$<em>{22}$C$</em>{18}$N$_{19}$</td>
<td>120.7(2)</td>
</tr>
<tr>
<td>C$_7$O$_6$C$_5$</td>
<td>116.5(1)</td>
<td>C$<em>{22}$C$</em>{18}$C$_{17}$</td>
<td>121.3(2)</td>
</tr>
<tr>
<td>C$<em>{12}$O$</em>{13}$C$_{14}$</td>
<td>116.3(2)</td>
<td>N$<em>{19}$C$</em>{18}$C$_{17}$</td>
<td>117.9(2)</td>
</tr>
<tr>
<td>O$<em>{13}$C$</em>{14}$C$_{15}$</td>
<td>107.7(2)</td>
<td>C$<em>{16}$N$</em>{19}$C$_{20}$</td>
<td>122.3(2)</td>
</tr>
<tr>
<td>O$<em>{16}$C$</em>{15}$C$_{14}$</td>
<td>110.3(2)</td>
<td>C$<em>{18}$C$</em>{19}$C$_{23}$</td>
<td>122.2(2)</td>
</tr>
<tr>
<td>C$<em>{15}$O$</em>{16}$C$_{17}$</td>
<td>114.3(2)</td>
<td>C$<em>{20}$N$</em>{19}$C$_{23}$</td>
<td>115.5(2)</td>
</tr>
<tr>
<td>O$<em>{16}$C$</em>{17}$C$_{18}$</td>
<td>112.5(2)</td>
<td>O$<em>{31}$C$</em>{20}$N$_{19}$</td>
<td>119.9(2)</td>
</tr>
<tr>
<td>N$<em>{19}$C$</em>{23}$C$_{24}$</td>
<td>112.4(2)</td>
<td>O$<em>{31}$C$</em>{20}$C$_{1}$</td>
<td>124.3(2)</td>
</tr>
<tr>
<td>C$<em>{25}$C$</em>{24}$C$_{23}$</td>
<td>111.1(2)</td>
<td>N$<em>{19}$C$</em>{20}$C$_{1}$</td>
<td>115.9(2)</td>
</tr>
<tr>
<td>C$<em>{21}$C$</em>{20}$C$_{21}$</td>
<td>120.1(2)</td>
<td>C$<em>{21}$C$</em>{22}$</td>
<td>121.9(2)</td>
</tr>
<tr>
<td>C$<em>{22}$C$</em>{21}$C$_{2}$</td>
<td>123.4(2)</td>
<td>C$<em>{28}$C$</em>{25}$C$_{30}$</td>
<td>118.1(2)</td>
</tr>
<tr>
<td>C$<em>{20}$C$</em>{25}$C$_{2}$</td>
<td>116.5(2)</td>
<td>C$<em>{20}$C$</em>{25}$C$_{24}$</td>
<td>121.1(2)</td>
</tr>
<tr>
<td>O$_6$C$_5$C$_6$</td>
<td>125.3(2)</td>
<td>C$<em>{20}$C$</em>{23}$C$_{24}$</td>
<td>120.8(2)</td>
</tr>
<tr>
<td>O$<em>{12}$C$</em>{12}$C$_{12}$</td>
<td>115.5(2)</td>
<td>C$<em>{23}$C$</em>{26}$C$_{27}$</td>
<td>121.1(2)</td>
</tr>
<tr>
<td>C$<em>{10}$C$</em>{9}$C$_{8}$</td>
<td>120.3(2)</td>
<td>C$<em>{25}$C$</em>{27}$C$_{26}$</td>
<td>120.1(2)</td>
</tr>
<tr>
<td>C$<em>{10}$C$</em>{9}$C$_{8}$</td>
<td>120.2(2)</td>
<td>C$<em>{25}$C$</em>{22}$C$_{27}$</td>
<td>119.3(2)</td>
</tr>
<tr>
<td>C$<em>{10}$C$</em>{9}$C$_{11}$</td>
<td>120.0(2)</td>
<td>C$<em>{28}$C$</em>{29}$C$_{30}$</td>
<td>120.9(2)</td>
</tr>
<tr>
<td>C$<em>{11}$C$</em>{10}$C$_{10}$</td>
<td>120.5(2)</td>
<td>C$<em>{28}$C$</em>{30}$C$_{25}$</td>
<td>120.5(2)</td>
</tr>
</tbody>
</table>

$^a$ The numbers in parentheses are the estimated standard deviations in the last significant digit.

$^b$ Atoms are labeled in agreement with Figure 1.
Table 6. Torsion Angles in Crystalline 8

<table>
<thead>
<tr>
<th>Type&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Angle, (deg)</th>
<th>Type&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Angle, (deg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C&lt;sub&gt;21&lt;/sub&gt;-C&lt;sub&gt;1&lt;/sub&gt;-C&lt;sub&gt;2&lt;/sub&gt;-O&lt;sub&gt;3&lt;/sub&gt;</td>
<td>-107.7(2)</td>
<td>C&lt;sub&gt;17&lt;/sub&gt;-C&lt;sub&gt;18&lt;/sub&gt;-N&lt;sub&gt;19&lt;/sub&gt;-C&lt;sub&gt;20&lt;/sub&gt;</td>
<td>175.9(2)</td>
</tr>
<tr>
<td>C&lt;sub&gt;20&lt;/sub&gt;-C&lt;sub&gt;1&lt;/sub&gt;-C&lt;sub&gt;2&lt;/sub&gt;-O&lt;sub&gt;3&lt;/sub&gt;</td>
<td>71.7(2)</td>
<td>C&lt;sub&gt;22&lt;/sub&gt;-C&lt;sub&gt;14&lt;/sub&gt;-N&lt;sub&gt;19&lt;/sub&gt;-C&lt;sub&gt;23&lt;/sub&gt;</td>
<td>175.5(2)</td>
</tr>
<tr>
<td>C&lt;sub&gt;1&lt;/sub&gt;-C&lt;sub&gt;2&lt;/sub&gt;-O&lt;sub&gt;3&lt;/sub&gt;-C&lt;sub&gt;4&lt;/sub&gt;</td>
<td>71.2(2)</td>
<td>C&lt;sub&gt;17&lt;/sub&gt;-C&lt;sub&gt;18&lt;/sub&gt;-N&lt;sub&gt;19&lt;/sub&gt;-C&lt;sub&gt;23&lt;/sub&gt;</td>
<td>-7.1(3)</td>
</tr>
<tr>
<td>C&lt;sub&gt;2&lt;/sub&gt;-O&lt;sub&gt;3&lt;/sub&gt;-C&lt;sub&gt;5&lt;/sub&gt;-C&lt;sub&gt;6&lt;/sub&gt;</td>
<td>-141.7(2)</td>
<td>C&lt;sub&gt;18&lt;/sub&gt;N&lt;sub&gt;19&lt;/sub&gt;-C&lt;sub&gt;20&lt;/sub&gt;O&lt;sub&gt;31&lt;/sub&gt;</td>
<td>178.3(2)</td>
</tr>
<tr>
<td>O&lt;sub&gt;2&lt;/sub&gt;-C&lt;sub&gt;4&lt;/sub&gt;-C&lt;sub&gt;5&lt;/sub&gt;-O&lt;sub&gt;6&lt;/sub&gt;</td>
<td>77.9(2)</td>
<td>C&lt;sub&gt;23&lt;/sub&gt;N&lt;sub&gt;19&lt;/sub&gt;-C&lt;sub&gt;20&lt;/sub&gt;O&lt;sub&gt;31&lt;/sub&gt;</td>
<td>1.1(2)</td>
</tr>
<tr>
<td>C&lt;sub&gt;6&lt;/sub&gt;-C&lt;sub&gt;5&lt;/sub&gt;-O&lt;sub&gt;6&lt;/sub&gt;-C&lt;sub&gt;7&lt;/sub&gt;</td>
<td>-179.6(2)</td>
<td>C&lt;sub&gt;18&lt;/sub&gt;N&lt;sub&gt;19&lt;/sub&gt;-C&lt;sub&gt;20&lt;/sub&gt;C&lt;sub&gt;1&lt;/sub&gt;</td>
<td>-1.1(2)</td>
</tr>
<tr>
<td>C&lt;sub&gt;3&lt;/sub&gt;-O&lt;sub&gt;6&lt;/sub&gt;-C&lt;sub&gt;7&lt;/sub&gt;-C&lt;sub&gt;8&lt;/sub&gt;</td>
<td>13.9(2)</td>
<td>C&lt;sub&gt;23&lt;/sub&gt;N&lt;sub&gt;19&lt;/sub&gt;-C&lt;sub&gt;20&lt;/sub&gt;C&lt;sub&gt;1&lt;/sub&gt;</td>
<td>-178.3(2)</td>
</tr>
<tr>
<td>C&lt;sub&gt;3&lt;/sub&gt;-O&lt;sub&gt;5&lt;/sub&gt;-C&lt;sub&gt;7&lt;/sub&gt;-C&lt;sub&gt;12&lt;/sub&gt;</td>
<td>-166.7(2)</td>
<td>C&lt;sub&gt;31&lt;/sub&gt;C&lt;sub&gt;1&lt;/sub&gt;-C&lt;sub&gt;20&lt;/sub&gt;O&lt;sub&gt;31&lt;/sub&gt;</td>
<td>-175.5(2)</td>
</tr>
<tr>
<td>O&lt;sub&gt;5&lt;/sub&gt;-C&lt;sub&gt;7&lt;/sub&gt;-C&lt;sub&gt;8&lt;/sub&gt;-C&lt;sub&gt;9&lt;/sub&gt;</td>
<td>178.9(2)</td>
<td>C&lt;sub&gt;2&lt;/sub&gt;C&lt;sub&gt;1&lt;/sub&gt;-C&lt;sub&gt;20&lt;/sub&gt;O&lt;sub&gt;31&lt;/sub&gt;</td>
<td>5.1(3)</td>
</tr>
<tr>
<td>C&lt;sub&gt;12&lt;/sub&gt;-C&lt;sub&gt;7&lt;/sub&gt;-C&lt;sub&gt;8&lt;/sub&gt;-C&lt;sub&gt;9&lt;/sub&gt;</td>
<td>-0.4(3)</td>
<td>C&lt;sub&gt;21&lt;/sub&gt;N&lt;sub&gt;19&lt;/sub&gt;C&lt;sub&gt;20&lt;/sub&gt;N&lt;sub&gt;19&lt;/sub&gt;</td>
<td>3.8(2)</td>
</tr>
<tr>
<td>C&lt;sub&gt;12&lt;/sub&gt;-C&lt;sub&gt;9&lt;/sub&gt;-C&lt;sub&gt;10&lt;/sub&gt;-C&lt;sub&gt;11&lt;/sub&gt;</td>
<td>0.8(3)</td>
<td>C&lt;sub&gt;27&lt;/sub&gt;C&lt;sub&gt;1&lt;/sub&gt;-C&lt;sub&gt;20&lt;/sub&gt;N&lt;sub&gt;19&lt;/sub&gt;</td>
<td>-175.6(2)</td>
</tr>
<tr>
<td>C&lt;sub&gt;12&lt;/sub&gt;-C&lt;sub&gt;10&lt;/sub&gt;-C&lt;sub&gt;11&lt;/sub&gt;-C&lt;sub&gt;12&lt;/sub&gt;</td>
<td>-1.5(3)</td>
<td>C&lt;sub&gt;20&lt;/sub&gt;C&lt;sub&gt;1&lt;/sub&gt;-C&lt;sub&gt;21&lt;/sub&gt;C&lt;sub&gt;22&lt;/sub&gt;</td>
<td>-4.1(3)</td>
</tr>
<tr>
<td>C&lt;sub&gt;10&lt;/sub&gt;-C&lt;sub&gt;11&lt;/sub&gt;-C&lt;sub&gt;12&lt;/sub&gt;-O&lt;sub&gt;13&lt;/sub&gt;</td>
<td>-177.6(2)</td>
<td>N&lt;sub&gt;19&lt;/sub&gt;C&lt;sub&gt;18&lt;/sub&gt;-C&lt;sub&gt;22&lt;/sub&gt;C&lt;sub&gt;21&lt;/sub&gt;</td>
<td>1.4(3)</td>
</tr>
<tr>
<td>C&lt;sub&gt;10&lt;/sub&gt;-C&lt;sub&gt;11&lt;/sub&gt;-C&lt;sub&gt;12&lt;/sub&gt;-C&lt;sub&gt;7&lt;/sub&gt;</td>
<td>1.9(3)</td>
<td>C&lt;sub&gt;17&lt;/sub&gt;C&lt;sub&gt;18&lt;/sub&gt;-C&lt;sub&gt;22&lt;/sub&gt;C&lt;sub&gt;21&lt;/sub&gt;</td>
<td>-175.9(2)</td>
</tr>
<tr>
<td>O&lt;sub&gt;1&lt;/sub&gt;-C&lt;sub&gt;7&lt;/sub&gt;-C&lt;sub&gt;12&lt;/sub&gt;-O&lt;sub&gt;13&lt;/sub&gt;</td>
<td>-0.8(2)</td>
<td>C&lt;sub&gt;21&lt;/sub&gt;C&lt;sub&gt;21&lt;/sub&gt;-C&lt;sub&gt;22&lt;/sub&gt;C&lt;sub&gt;18&lt;/sub&gt;</td>
<td>1.4(3)</td>
</tr>
<tr>
<td>C&lt;sub&gt;12&lt;/sub&gt;-C&lt;sub&gt;7&lt;/sub&gt;-C&lt;sub&gt;12&lt;/sub&gt;-O&lt;sub&gt;13&lt;/sub&gt;</td>
<td>178.6(1)</td>
<td>C&lt;sub&gt;14&lt;/sub&gt;N&lt;sub&gt;19&lt;/sub&gt;C&lt;sub&gt;23&lt;/sub&gt;C&lt;sub&gt;24&lt;/sub&gt;</td>
<td>-92.0(2)</td>
</tr>
<tr>
<td>O&lt;sub&gt;5&lt;/sub&gt;-C&lt;sub&gt;7&lt;/sub&gt;-C&lt;sub&gt;12&lt;/sub&gt;-C&lt;sub&gt;11&lt;/sub&gt;</td>
<td>179.6(2)</td>
<td>C&lt;sub&gt;26&lt;/sub&gt;N&lt;sub&gt;19&lt;/sub&gt;C&lt;sub&gt;23&lt;/sub&gt;C&lt;sub&gt;24&lt;/sub&gt;</td>
<td>85.1(2)</td>
</tr>
<tr>
<td>C&lt;sub&gt;10&lt;/sub&gt;-C&lt;sub&gt;12&lt;/sub&gt;-C&lt;sub&gt;11&lt;/sub&gt;-C&lt;sub&gt;12&lt;/sub&gt;</td>
<td>-0.9(3)</td>
<td>N&lt;sub&gt;19&lt;/sub&gt;C&lt;sub&gt;23&lt;/sub&gt;-C&lt;sub&gt;24&lt;/sub&gt;C&lt;sub&gt;25&lt;/sub&gt;</td>
<td>-171.1(2)</td>
</tr>
<tr>
<td>C&lt;sub&gt;11&lt;/sub&gt;-C&lt;sub&gt;12&lt;/sub&gt;-O&lt;sub&gt;13&lt;/sub&gt;-C&lt;sub&gt;14&lt;/sub&gt;</td>
<td>-18.2(2)</td>
<td>C&lt;sub&gt;23&lt;/sub&gt;C&lt;sub&gt;24&lt;/sub&gt;-C&lt;sub&gt;25&lt;/sub&gt;C&lt;sub&gt;26&lt;/sub&gt;</td>
<td>103.0(2)</td>
</tr>
<tr>
<td>C&lt;sub&gt;12&lt;/sub&gt;-C&lt;sub&gt;12&lt;/sub&gt;-O&lt;sub&gt;13&lt;/sub&gt;-C&lt;sub&gt;14&lt;/sub&gt;</td>
<td>162.3(2)</td>
<td>C&lt;sub&gt;23&lt;/sub&gt;C&lt;sub&gt;24&lt;/sub&gt;-C&lt;sub&gt;25&lt;/sub&gt;C&lt;sub&gt;26&lt;/sub&gt;</td>
<td>-74.6(2)</td>
</tr>
<tr>
<td>C&lt;sub&gt;12&lt;/sub&gt;-C&lt;sub&gt;13&lt;/sub&gt;-C&lt;sub&gt;14&lt;/sub&gt;-C&lt;sub&gt;15&lt;/sub&gt;</td>
<td>-174.1(1)</td>
<td>C&lt;sub&gt;20&lt;/sub&gt;-C&lt;sub&gt;25&lt;/sub&gt;-C&lt;sub&gt;26&lt;/sub&gt;C&lt;sub&gt;27&lt;/sub&gt;</td>
<td>0.1(3)</td>
</tr>
<tr>
<td>O&lt;sub&gt;13&lt;/sub&gt;-C&lt;sub&gt;14&lt;/sub&gt;-C&lt;sub&gt;15&lt;/sub&gt;-O&lt;sub&gt;16&lt;/sub&gt;</td>
<td>-79.9(2)</td>
<td>C&lt;sub&gt;24&lt;/sub&gt;C&lt;sub&gt;25&lt;/sub&gt;-C&lt;sub&gt;26&lt;/sub&gt;C&lt;sub&gt;27&lt;/sub&gt;</td>
<td>-177.5(2)</td>
</tr>
<tr>
<td>C&lt;sub&gt;14&lt;/sub&gt;-C&lt;sub&gt;15&lt;/sub&gt;-O&lt;sub&gt;16&lt;/sub&gt;-C&lt;sub&gt;17&lt;/sub&gt;</td>
<td>140.2(2)</td>
<td>C&lt;sub&gt;25&lt;/sub&gt;C&lt;sub&gt;26&lt;/sub&gt;-C&lt;sub&gt;27&lt;/sub&gt;C&lt;sub&gt;28&lt;/sub&gt;</td>
<td>0.6(3)</td>
</tr>
<tr>
<td>C&lt;sub&gt;15&lt;/sub&gt;-C&lt;sub&gt;16&lt;/sub&gt;-C&lt;sub&gt;17&lt;/sub&gt;-C&lt;sub&gt;18&lt;/sub&gt;</td>
<td>-70.4(2)</td>
<td>C&lt;sub&gt;26&lt;/sub&gt;C&lt;sub&gt;27&lt;/sub&gt;-C&lt;sub&gt;28&lt;/sub&gt;C&lt;sub&gt;29&lt;/sub&gt;</td>
<td>-0.8(4)</td>
</tr>
<tr>
<td>O&lt;sub&gt;16&lt;/sub&gt;-C&lt;sub&gt;17&lt;/sub&gt;-C&lt;sub&gt;18&lt;/sub&gt;-C&lt;sub&gt;22&lt;/sub&gt;</td>
<td>110.0(2)</td>
<td>C&lt;sub&gt;27&lt;/sub&gt;C&lt;sub&gt;28&lt;/sub&gt;-C&lt;sub&gt;29&lt;/sub&gt;C&lt;sub&gt;30&lt;/sub&gt;</td>
<td>0.4(3)</td>
</tr>
<tr>
<td>O&lt;sub&gt;16&lt;/sub&gt;-C&lt;sub&gt;17&lt;/sub&gt;-C&lt;sub&gt;18&lt;/sub&gt;-N&lt;sub&gt;19&lt;/sub&gt;</td>
<td>-67.3(2)</td>
<td>C&lt;sub&gt;28&lt;/sub&gt;C&lt;sub&gt;29&lt;/sub&gt;-C&lt;sub&gt;30&lt;/sub&gt;C&lt;sub&gt;31&lt;/sub&gt;</td>
<td>0.3(3)</td>
</tr>
<tr>
<td>C&lt;sub&gt;22&lt;/sub&gt;-C&lt;sub&gt;18&lt;/sub&gt;-N&lt;sub&gt;19&lt;/sub&gt;-C&lt;sub&gt;20&lt;/sub&gt;</td>
<td>-1.5(3)</td>
<td>C&lt;sub&gt;26&lt;/sub&gt;-C&lt;sub&gt;25&lt;/sub&gt;-C&lt;sub&gt;30&lt;/sub&gt;C&lt;sub&gt;29&lt;/sub&gt;</td>
<td>-0.6(3)</td>
</tr>
<tr>
<td>C&lt;sub&gt;25&lt;/sub&gt;-C&lt;sub&gt;24&lt;/sub&gt;-C&lt;sub&gt;30&lt;/sub&gt;-C&lt;sub&gt;29&lt;/sub&gt;</td>
<td>177.0(2)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> The numbers in parentheses are the estimated standard deviations in the last significant digit.
<sup>b</sup> Atoms are labeled in agreement with Figure 1.
Compound 6m: Inverse HETCOR
Compound 6m: $^{13}$C NMR (125 MHz)

Current Data Parameters
NAME  500_May09-2003
EXPD  05
PROCNO  1

F2 - Acquisition Parameters
Date_  20030510
Time_  22.54
INSTRM_ spec1
PROBHO_ 5 mm GNP IH/1
PULPROG_ zgpp30
TD_  65536
SOLVENT_ CCl3
NS_  24576
DS_  4
SMH_  272.2727 Hz
FIDRES_ 0.346791 Hz
AG_  1.4418420 sec
RG_  512
DW_  22.000 usec
DE_  6.000 usec
TE_  300.0 K
DI_  1.50000000 sec
d11_  0.03000000 sec
d12_  0.00000000 sec

------------- CHANNEL f1 -------------
NUCl_  13C
P1_  9.10 usec
PL1_  5.00 dB
SF01_  125.7684264 MHz

------------- CHANNEL f2 -------------
CPDPROG_ wait16
NUC2_  1H
PCPD2_  116.00 usec
PL2_  6.00 dB
PL12_  24.00 dB
PL13_  27.00 dB
SF02_  500.1320005 MHz

F2 - Processing parameters
SM_  65536
SF_  125.7577856 MHz
MDW_  EM
SBB_  0.50 Hz
LB_  0
GB_  0
PC_  1.40

TD NMR plot parameters
CX_  20.00 cm
F1P_  165.000 ppm
F1_  20795.04 Hz
F2P_  0.000 ppm
F2_  0.00 Hz
PPMCM_  8.25000 ppm/cm
HzCM_  1037.50171 Hz/cm
Compound 8: $^1$H NMR (500 MHz)

Current Data Parameters
NAME: 500X0617-2002
PROCNO: 30
PROCAD: 1

F2 - Acquisition Parameters
Data: 20021017
Time: 23.20
INSTRUM: SPECT
PROBD: 5 mm NMR 2H
PULPROG: r600
TD: 600.36
SOV: CDCl3
FD: 8
DG: 2
SNH: 6009.615 Hz
FRES: 0.291669 Hz
AG: 5.4526453 sec
INC: 114
DN: 83.200 uscct
DE: 0.00 uscct
TC: 300.0 K
DT: 1.0000000 sec

************* CHANNEL F1 *************
NC1: 1H
PL1: 14.50 uscct
SF01: 500.1325000 MHz

F2 - Processing parameters
SI: 32768
SF: 500.1300141 MHz
KOH: 10
SSB: 1
LB: 0.30 Hz
UB: 0
RC: 1.00

ID NMR plot parameters
CH: 32.00 cm
FIP: 0.000 ppm
FI: 4001.04 Hz
FJP: 0.200 ppm
F2: 100.30 Hz
RPMIN: 0.20273 ppm/cm
H: 0.39599 Hz/cm
Compound 8: $^{13}$C NMR (125 MHz)