A Biomimetic Approach To The Discorhabdin Alkaloids; Total Syntheses of Discorhabdins C and E and Dethiadiscorhabdin D.

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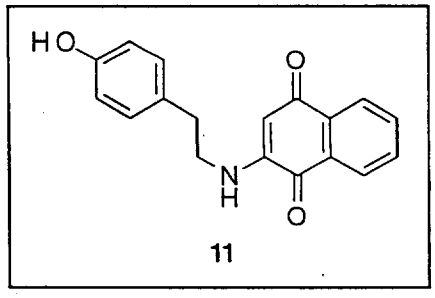
SUPPORTING INFORMATION

Experimental

General. All reactions involving air-sensitive reagents were performed under a nitrogen atmosphere. Flash chromatography[1] was carried out using Merck 60 230-400 mesh silica gel, and thin layer chromatography was carried out on Merck silica gel 60 F-254 glass plates. Reagents were used as received from commerical suppliers unless otherwise noted. Organic extracts were dried with magnesium sulfate, filtered, and concentrated under reduced pressure with a rotary evaporator. Unless otherwise indicated, IR spectra were obtained as thin films on NaCl plates. NMR spectra were obtained in $CDCl_3$ except where noted. ^1H NMR spectral data are tabulated in the order: muliplicity (s, singlet; br s, broad singlet; d, doublet; t, triplet; q, quartet; m, multiplet), number of protons, coupling constants in Hertz. All melting points are uncorrected. Mass spectra were recorded at the University of California Berkeley (UCB) using fast atom bombardment. Elemental analyses were performed by the Microanalytical Laboratory operated by the UCB College of Chemistry.

2-[2-(4-Hydroxyphenyl)ethylamino]naphthoquinone (11). A solution of 5-methoxynaphthoquinone [2] (5.0 g, 26.5 mmol) and tyramine (3.7 g, 26.8 mmol) in ethanol was heated to reflux and stirred for 6 h. Then the reaction solution was slowly cooled to rt, during which time the product separated in orange needles. The suspension was cooled in an ice bath for 15 min and then the mixture was filtered and washed with cold ethanol to provide **11** (6.02 g, 77%). The filtrate was concentrated *in vacuo*, and the remaining brown residue was recrystallized from hot ethanol to obtain a second crop (0.85 g, 11%), mp 172 °C. IR: 3354, 1678, 1604, 1567, 1513 cm^{-1}. ^1H NMR (500 MHz): δ 2.10 (br s, 1), 2.90 (t, 2, *J*=7.0), 3.41 (q, 2, *J*=6.9), 5.78 (s, 1), 5.96 (br s, 1), 6.81 (d, 2, *J*=8.4), 7.08 (d, 2, *J*=8.4), 7.61 (t, 1, *J*=7.5), 7.73 (t, 1, *J*=7.5), 8.02 (d, 1, *J*=7.7), 8.10 (d, 1, *J*=7.7). ^{13}C NMR (100 MHz): δ 33.5, 43.9, 100.8, 115.8, 126.2, 126.3, 129.7, 129.8, 130.5, 132.0, 133.6, 134.8, 147.9, 154.8, 181.7, 183.1. Anal. Calcd for $C_{18}H_{15}NO_3$: C, 73.71; H, 5.15; N, 4.78. Found: C, 73.66; H, 5.19; N, 4.79.



11

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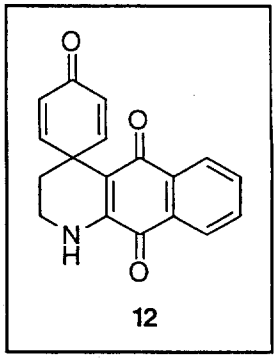
1. Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

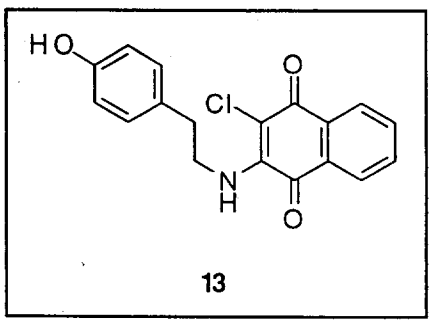
2. (a) Smith, L. I.; Hoehn, H. H. *J. Am. Chem. Soc.* **1941**, *63*, 1178. (b) *Elsevier's Encyclopedia of Organic Chemistry*; Radt, F., Ed.; Elsevier Publishing Company: New York, 1952; Series III, Vol. 12b, p. 3054.

Spirodienone naphthoquinone (12). To a solution of **11** (200 mg, 0.68 mmol) in acetonitrile (7 mL) was added triethylamine (0.29 mL, 2.1 mmol) followed by $CuCl_2 \cdot 2H_2O$ (116 mg, 0.68 mmol). Oxygen was bubbled through the stirring suspension for 12 h, and then stirring was continued under an oxygen blanket for 12 h. The reaction solution was filtered through SiO_2 and washed with ethyl acetate. The filtrate was concentrated *in vacuo* to provide **12** (180 mg, 90%) as a bright red-orange solid, mp 269-270 °C. IR: 3335, 1657, 1596, 1564, 1512, 1334, 1305 cm^{-1}. ^1H NMR (500 MHz): δ 1.95 (t, 2, *J*=5.8), 3.60 (br s, 2), 6.34 (br s, 1), 6.41 (d, 2, *J*=9.9), 6.97 (d, 2, *J*=9.8), 7.60 (t, 1, *J*=7.6), 7.71 (t, 1, *J*=7.5), 8.02 (d, 1, *J*=7.5), 8.03 (d, 1, *J*=7.7). ^{13}C NMR (100 MHz): δ 34.0, 37.6, 39.7, 109.7, 126.0, 126.5, 128.0, 129.9, 132.0, 133.6, 135.1, 145.1, 153.0, 179.4, 180.7, 185.5. Anal. Calcd for $C_{18}H_{13}NO_3$: C, 74.22; H, 4.50; N, 4.81. Found: C, 74.15; H, 4.70; N, 4.73.



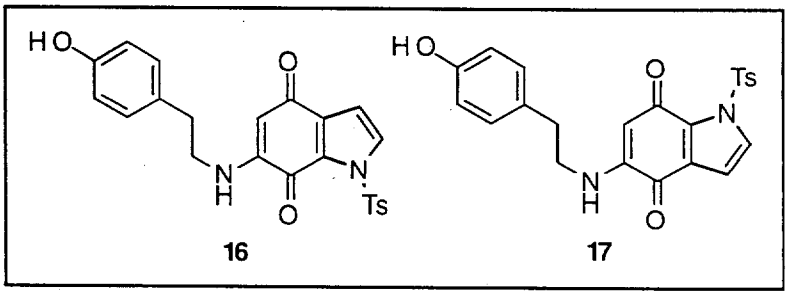
12

2-Chloro-3-[2-(4-hydroxyphenyl)ethylamino]naphthoquinone (13). To a solution of **11** (150 mg, 0.51 mmol) in acetonitrile (5 mL) was added $CuCl_2 \cdot 2H_2O$ (131 mg, 0.77 mmol). The resulting suspension was stirred under O_2 for 20 h. The acetonitrile was then removed *in vacuo* and the dark orange residue was purified by flash chromatography (35% ethyl acetate in hexanes) to provide **13** (72 mg, 43%) as a red solid. IR: 3325, 1679, 1601, 1567, 1514, 1339 cm^{-1}. ^1H NMR (400 MHz): δ 2.91 (t, 2, *J*=7.1), 4.07 (m, 2), 6.11 (br s, 1), 6.81 (d, 2, *J*=8.5), 7.10 (d, 2, *J*=8.5), 7.62 (t, 1, *J*=7.6), 7.72 (t, 1, *J*=7.6), 8.00 (d, 1, *J*=7.6), 8.14 (d, 1, *J*=7.6). ^{13}C NMR (100 MHz) (d_6-DMSO): δ 35.8, 45.5, 108.6, 115.1, 125.6, 126.2, 128.3, 129.4, 129.7, 131.9, 132.4, 134.6, 145.1, 155.7, 175.1, 180.0. Anal. Calcd for $C_{18}H_{14}ClNO_3$: C, 65.96; H, 4.31; N, 4.27. Found: C, 65.72; H, 4.35; N, 4.42.



13

6-[2-(4-Hydroxyphenyl)ethylamino]-1-(*p*-toluenesulfonyl)indole-4,7-dione (16) and 5-[2-(4-Hydroxyphenyl)ethylamino]-1-(*p*-toluenesulfonyl)-indole-4,7-dione (17). To a solution of 4,7-indoloquinone **15** (100 mg, 0.33 mmol) in acetonitrile (3.5 mL) was added tyramine (137 mg, 1.00 mmol). The resulting suspension was heated to 60-70 °C and stirred vigorously open to the air. Over 20 min the reaction solution turned from yellow to dark red. The reaction mixture was then filtered through SiO_2 while still slightly warm and washed with ethyl acetate until all the red color had eluted into the filtrate. The filtrate was then concentrated *in vacuo* almost to dryness, and the residue was taken up in a small amount of CH_2Cl_2 and loaded onto a flash SiO_2 column. Elution with

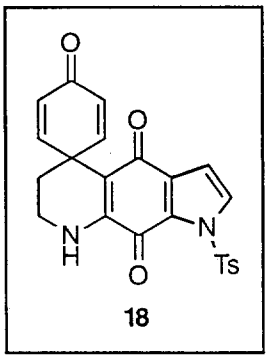


30→50% ethyl acetate in hexanes resulted in the isolation of **16** (87 mg, 60%) and **17** (45 mg, 31%). The more polar material (**16**) was a red powder, mp 168 °C; while the less polar material (**17**) was isolated as a red glass, mp 209 °C.

Isomer 16: IR: 3345, 3201, 1671, 1589, 1514, 1424, 1366 cm^{-1}. ^1H NMR (400 MHz): δ 2.44 (s, 3), 2.82 (t, 2, *J*=7.0), 3.29 (q, 2, *J*=6.0), 5.35 (s, 1), 5.87 (br s, 1), 6.73 (d, 1, *J*=3.1), 6.79 (d, 2, *J*=8.4), 7.03 (d, 2, *J*=8.4), 7.35 (d, 2, *J*=8.1), 7.79 (d, 1, *J*=3.1), 7.98 (d, 2, *J*=8.4). ^{13}C NMR (100 MHz) (d_6-acetone): δ 21.6, 33.7, 45.1, 96.8, 108.8, 116.1, 116.2, 127.9, 129.6, 130.3, 130.5, 130.7, 132.4, 135.1, 147.3, 149.0, 156.9, 171.0, 180.9. Anal. Calcd for $C_{23}H_{20}N_2SO_5$: C, 63.29; H, 4.62; N, 6.42. Found: C, 63.26; H, 4.70; N, 6.52.

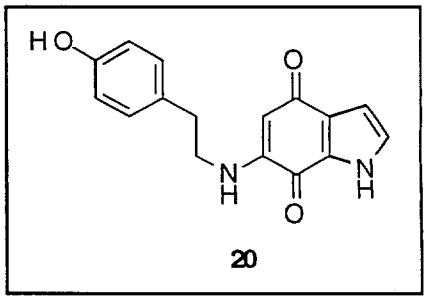
Isomer 17: IR: 3362, 3148, 1682, 1595, 1537, 1514, 1460, 1377 cm^{-1}. ^1H NMR (400 MHz): δ 2.40 (s, 3), 2.79 (t, 2, *J*=7.2), 3.24 (q, 2, *J*=6.9), 5.19 (s, 1), 5.77 (br t, 1, *J*=5.7), 6.65 (d, 1, *J*=3.3), 6.76 (d, 2, *J*=8.5), 6.99 (d, 2, *J*=8.5), 7.32 (d, 2, *J*=8.1), 7.68 (d, 1, *J*=3.3), 8.01 (d, 2, *J*=8.4). ^{13}C NMR (100 MHz): d 21.7, 33.2, 44.1, 97.4, 107.2, 115.8, 126.8, 127.8, 129.1, 129.4, 129.5, 129.7, 132.6, 134.2, 145.9, 147.0, 154.8, 175.2, 178.7. Anal. Calcd for $C_{23}H_{20}N_2SO_5$: C, 63.29; H, 4.62; N, 6.42. Found: C, 63.29; H, 4.67; N, 6.30.

1-(*p*-Toluenesulfonyl)-4,5,6,7,8,9-hexahydro-1*H*-pyrrolo[3,2*g*]-quinoline-4,9-dione-5-spiro-4'-cyclohexa-2',5'-dien-1'-one (18). To a solution of **16** (45 mg, 0.10 mmol) in acetonitrile (1 mL) was added triethylamine (43 μL, 0.31 mmol) followed by $CuCl_2 \cdot 2H_2O$ (18 mg, 0.10 mmol). Oxygen was bubbled through the stirring reaction solution until no starting material persisted (7 h). The reaction mixture was then filtered through SiO_2 and washed with 15% methanol in CH_2Cl_2. The filtrate was concentrated *in vacuo* to provide **18** (42 mg, 93%) as a purple solid. IR: 3297, 3138, 1684, 1661, 1577, 1509, 1321 cm^{-1}. ^1H NMR (CD_2Cl_2) (400 MHz): δ 1.82 (t, 2, *J*=5.8), 2.44 (s, 3), 3.47 (m, 2), 6.22 (d, 2, *J*=10.0), 6.24 (br s, 1), 6.62 (d, 1, *J*=3.1), 6.83 (d, 2, *J*=10.0), 7.37 (d, 2, *J*=8.1), 7.77 (d, 1, *J*=3.1), 7.97 (d, 2, *J*=8.4). ^{13}C NMR (100 MHz) (d_6-DMSO): δ 21.1, 32.7, 37.1, 39.4, 102.9, 108.6, 125.7, 126.5, 128.3, 130.0, 132.2, 133.4, 134.2, 146.1, 146.3, 155.0, 168.9, 176.2, 185.1. Anal. Calcd for $C_{23}H_{18}N_2SO_5$: C, 63.58; H, 4.18; N, 6.45. Found: C, 63.39; H, 4.28; N, 6.28.



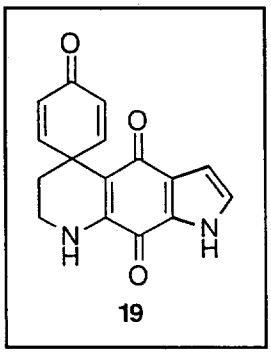
18

6-[2-(4-Hydroxyphenyl)ethylamino]indole-4,7-dione (20). To a solution of **16** (175 mg, 0.40 mmol) in methanol (5 mL) was added 2 mL of a 1M aq. KOH solution. The reaction solution was stirred for 45 min. The reaction was then quenched with aq. sat. NH_4Cl and diluted with CH_2Cl_2. The layers were separated, and the aqueous layer was extracted once with CH_2Cl_2. The combined organics were dried and concentrated *in vacuo*, and the remaining residue was filtered through SiO_2 and washed with ethyl acetate. The filtrate was concentrated *in vacuo* to provide **20** (94 mg, 83%) as a



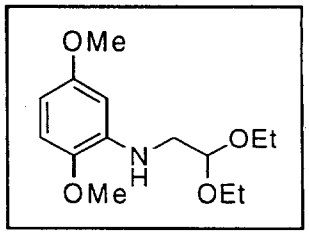
20

dark purple solid. IR: 3298, 2484, 1661, 1589, 1515, 1393, 1241 cm^{-1}. ^1H NMR (d_4-methanol) (400 MHz): δ 2.73 (t, 2, *J*=7.1), 3.25 (t, 2, *J*=7.1), 5.11 (s, 1), 6.39 (d, 1, *J*=2.6), 6.62 (d, 2, *J*=8.5), 6.96 (d, 2, *J*=8.5), 7.01 (d, 1, *J*=2.6). ^{13}C NMR (400 MHz) (d_4-methanol): δ 34.2, 45.5, 96.5, 108.9, 116.4, 128.6, 130.1, 130.2, 130.6, 130.7, 150.9, 157.1, 172.6, 185.7. Anal. Calcd for $C_{16}H_{14}N_2O_3$: C, 68.08; H, 5.00; N, 9.92. Found: C, 67.91; H, 5.25; N, 9.60.



19

4,5,6,7,8,9-Hexahydro-1*H*-pyrrolo[3,2*g*]quinoline-4,9-dione-5-spiro-4'-cyclohexa-2',5'-dien-1'-one (19). To a suspension of **18** (27 mg, 0.062 mmol) in methanol (4 mL) was added NaOMe in methanol (0.3 mL of a 4M solution). After stirring for 30 min, the reaction mixture was diluted with CH_2Cl_2 and quenched with aq. sat. NH_4Cl. The layers were separated and the aqueous layer was extracted twice with CH_2Cl_2. The combined organics were dried and concentrated *in vacuo*. The residue was dissolved in CH_2Cl_2 and loaded onto a SiO_2 column. Elution with ethyl acetate provided **19** (14 mg, 81%) as a dark red solid. IR: 3318, 3137, 1652, 1575, 1544, 1505, 1403, 1317 cm^{-1}. ^1H NMR (d_6-DMSO): δ 1.71 (m, 2), 3.39 (m, 2), 6.10 (d, 2, *J*=10.0), 6.28 (m, 1), 7.04 (d, 2, *J*=10.0), 7.22 (m, 1), 7.92 (br s, 1), 12.6 (br s, 1). ^{13}C NMR (100 MHz) (d_6-DMSO): δ 33.2, 36.9, 39.1, 103.2, 107.7, 126.2, 127.2, 128.3, 129.0, 146.1, 155.7, 170.8, 178.4, 185.2. Anal. Calcd for $C_{16}H_{12}N_2O_3$: C, 68.57; H, 4.32; N, 9.99. Found: C, 68.49; H, 4.50; N, 9.74.



2-(2,5-Dimethoxyanilino)acetaldehyde diethyl acetal.[3] To a solution of 2,5-dimethoxyaniline (1.54g, 10 mmol) in DMF (12.5 mL) was added bromoacetaldehyde diethyl acetal (1.55 mL, 10 mmol), followed by $NaHCO_3$ (850 mg, 10 mmol). The reaction mixture was then heated to reflux using a sand bath that was maintained between 155-160 °C. After stirring for 46 h, the reaction was cooled to rt and quenched with H_2O. The solution was extracted with diethyl ether, and the organics were dried and concentrated *in vacuo*. The resulting brown residue was purified by flash chromatography (5% ethyl acetate in hexanes) to produce 2-(2,5-dimethoxyanilino)-acetaldehyde diethyl acetal (2.0 g, 74%) as a colorless liquid that turned pale blue upon standing. IR: 3421, 1615, 1523, 1461, 1247, 1217 cm^{-1}. ^1H NMR (400 MHz): δ 1.24 (t, 6, *J*=7.1), 3.25 (d, 2, *J*=5.6), 3.57-3.77 (m, 4), 3.75 (s, 3), 3.80 (s, 3), 4.72 (t, 1, *J*=5.6), 6.18 (dd, 1, *J*=8.6, 2.6), 6.28 (br s, 1), 6.67 (d, 1, *J*=8.6). ^{13}C NMR (100 MHz): δ 15.4, 46.2, 55.5, 56.0, 62.4, 63.7, 98.4, 99.5, 100.9, 110.1, 141.8, 154.7. Anal. Calcd for $C_{14}H_{23}NO_4$: C, 62.43; H, 8.61, N, 5.20. Found: C, 62.25; H, 8.66; N, 5.18.

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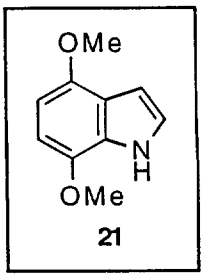
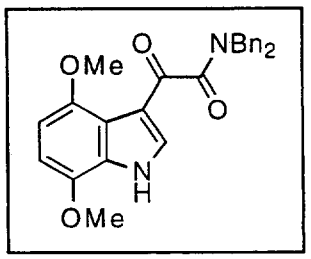
3. Cherif, M.; Cotelle, P.; Catteau, J. P. *Heterocycles* **1992**, *34*, 1749. We discovered discrepancies between the reported characterization data and our data. Therefore, our complete procedure and full analytical data are reported here.



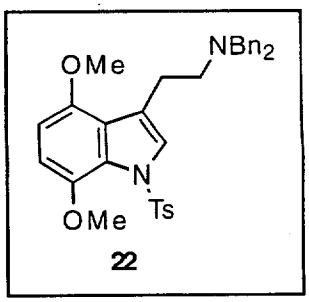
21

4,7-Dimethoxyindole (21).[2] To a solution of 2-(2,5-dimethoxyanilino)acetaldehyde diethyl acetal (1.0 g, 3.7 mmol) in dry hexane (9 mL) at 0 °C under a nitrogen atmosphere was added triethylamine (0.78 mL, 5.6 mmol) followed by freshly distilled trifluoroacetic anhydride (0.63 mL, 4.5 mmol). The yellow biphasic reaction solution was then allowed to warm to rt and stirred for 25 min. The reaction was quenched with water and diluted with diethyl ether. The organics were washed once with water, dried, and concentrated *in vacuo*. The resulting yellow oil was dissolved in xylenes (25 mL), and this solution was degassed and placed under argon. The degassed solution was then cannulated into a round-bottomed flask containing polyphosphoric acid (1.5 mL), and the reaction was heated to reflux with stirring. After the reflux had been maintained for 45 min, the reaction mixture was cooled slightly, and the xylene solution was decanted from the blackened polyphosphoric acid. Removal of the xylenes with a rotary evaporator provided the crude trifluoroacetylindole, which upon purification by flash chromatography (8% ethyl acetate in hexanes) lost the trifluoroacetyl group to provide 310 mg (47%) of 4,7-dimethoxyindole (**21**) as white needles, mp 119 °C. IR: 3370, 1526, 1463, 1353, 1262, 1086 cm^{-1}. ^1H NMR (400 MHz): δ 3.93 (s, 3), 3.93 (s, 3), 6.40 (d, 1, *J*=8.3), 6.52 (d, 1, *J*=8.3), 6.64 (dd, 1, *J*=3.0, 2.4), 7.12 (t, 1, *J*=2.7), 8.40 (br s, 1). ^{13}C NMR (100 MHz): δ 55.6, 98.7, 100.3, 101.4, 119.9, 122.5, 127.6, 141.1, 147.7. Anal. Calcd for $C_{10}H_{11}NO_2$: C, 67.78; H, 6.26; N, 7.90. Found: C, 67.63; H, 6.35; N, 7.60.



N,N-Dibenzyl-4,7-dimethoxyindole-3-glyoxamide. To a solution of dimethoxy indole **21** (1.0 g, 5.65 mmol) in ethyl ether (18 mL) at 0 °C, was added oxalyl chloride (1.08 g, 8.47 mmol) slowly dropwise. The resulting dark orange solution was warmed to rt and stirred for 5 h, during which time a yellow precipitate formed. The solution was recooled to 0 °C and dibenzylamine (3.34 g, 16.95 mmol) was added dropwise. After the addition, the reaction mixture was stirred at rt overnight. The reaction suspension became thick during this time. An extractive workup was performed using ethyl acetate/aq. sat. $NaHCO_3$. The organics were dried and concentrated *in vacuo*. Flash chromatography of the residue (20%→40% ethyl acetate/ hexanes) provided N,N-dibenzyl-4,7-dimethoxyindole-3-glyoxamide (1.52 g, 63%) as yellow plates, mp 143-145 °C. IR: 3251, 1632, 1520, 1452 cm^{-1}. ^1H NMR (500MHz): δ 3.70 (s, 3), 3.85 (s, 3), 4.47 (s, 2), 4.60 (s, 2), 6.52 (d, 1, *J*=8.3), 6.59 (d, 1, *J*=8.4), 7.27-7.38 (m, 10), 7.89 (s, 1), 9.42 (br s, 1). ^{13}C NMR (125 MHz): δ 45.9, 50.6, 55.7, 56.2, 103.3, 103.9, 116.1, 116.3, 127.5, 127.9, 128.6, 128.7, 128.7, 128.7, 134.0, 135.5, 136.4, 140.8, 148.3, 169.0, 186.1. Anal. Calcd for $C_{26}H_{24}N_2O_4$: C, 72.88; H, 5.65; N, 6.54. Found: C, 72.49; H, 5.72; N, 6.35.

N,N-Dibenzyl-4,7-dimethoxy-1-(*p*-toluenesulfonyl)tryptamine (22).



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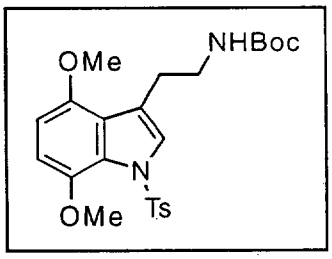
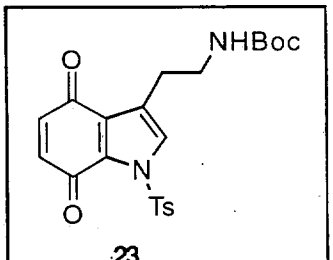
To a solution of the foregoing product (818 mg, 1.91 mmol) in THF (30 mL) at 0 °C was added $LiAlH_4$ (581 mg, 15.3 mmol). The suspension was heated at a reflux for 5 h. Then the reaction solution was cooled back to 0 °C and quenched by the slow addition of 0.6 mL H_2O, 0.6 mL 15% NaOH, and 1.8 mL H_2O. The aluminum salts were filtered through Celite and washed with THF. The filtrate was concentrated *in vacuo* and the remaining residue was concentrated from toluene three times. The crude tryptamine was then dissolved in THF (20 mL) and NaH (240 mg, 6.0 mmol) was added to the solution. After stirring for 25 min, tosyl chloride (500 mg, 2.6 mmol) was added and the reaction was stirred 12 h. The solution was cooled to 0 °C and quenched slowly with aqueous saturated $NaHCO_3$. When bubbling ceased, the reaction was diluted with water and ethyl acetate. The layers were separated, and the aqueous layer was extracted once with ethyl acetate. The combined organics were dried and concentrated *in vacuo*. Flash chromatography of the residue (10→15% ethyl acetate/hexanes) provided the N-tosyl indole **22** (930 mg, 84%) as a pale yellow, foamy oil. IR: 1509, 1357, 1099 cm^{-1}. ^1H NMR (500 MHz): δ 2.38 (s, 3), 2.82 (t, 2, *J*=7.3), 3.05 (t, 2, *J*=7.3), 3.61 (s, 6), 3.67 (s, 4), 6.40 (d, 1, *J*=8.6), 6.55 (d, 1, *J*=8.6), 7.20-7.30 (m, 8), 7.37-7.39 (m, 4), 7.51 (s, 1), 7.71 (d, 2, *J*=8.4). ^{13}C NMR (125 MHz): δ 21.6, 24.6, 54.3, 55.2, 56.4, 58.4, 103.2, 107.6, 119.0, 123.0, 124.9, 126.3, 126.7, 127.1, 128.1, 128.7, 129.2, 137.7, 140.0, 141.8, 143.8, 148.7. Anal. Calcd for $C_{33}H_{34}N_2SO_4$: C, 71.46; H, 6.18; N, 5.05. Found: C, 71.76; H, 6.53; N, 5.07.

4,7-Dimethoxy-3-[2-[(*tert*-butoxycarbonyl)amino]ethyl]-1-(*p*-toluenesulfonyl)indole.



A suspension of dibenzyltryptamine **22** (460 mg, 0.83 mmol) and $Pd(OH)_2$ (50 mg) in ethanol (5 mL) was stirred for 20 h under a H_2 balloon. The reaction was filtered through Celite and the filtrate was concentrated *in vacuo*. The resulting residue was dissolved in CH_2Cl_2 (14 mL) and di-*t*-butyl dicarbonate (200 mg, 0.91 mmol) was added. After stirring for 30 min, the reaction solution was concentrated *in vacuo*, and the residue was eluted through a short plug of SiO_2 (25% ethyl acetate/ hexanes). The crude product (240 mg, 61%) was used directly in the next step. ^1H NMR (400 MHz): δ 1.43 (s, 9), 2.38 (s, 3), 3.01 (t, 2, *J*=6.5), 3.45 (m, 2), 3.61 (s, 3), 3.83 (s, 3), 4.72 (br s, 1), 6.49 (d, 1, *J*=8.6), 6.58 (d, 1, *J*=8.6), 7.24 (d, 2, *J*=8.2), 7.53 (s, 1), 7.70 (d, 2, *J*=8.2).

3-[2-[(*tert*-Butoxycarbonyl)amino]ethyl]-1-(*p*-toluenesulfonyl)-indole-4,7-dione (23).

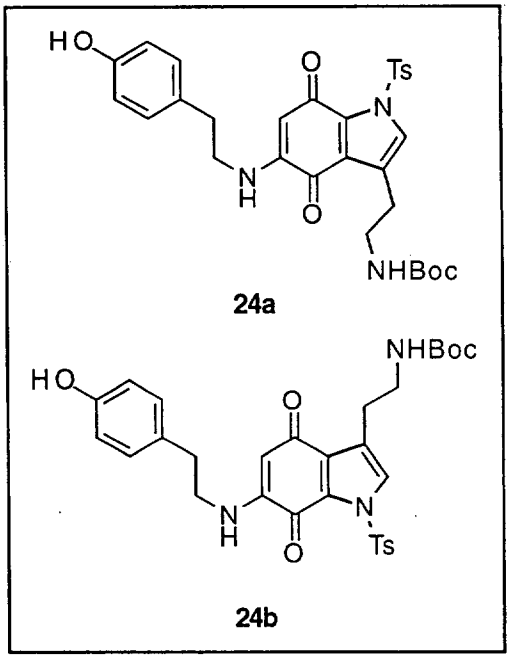


23

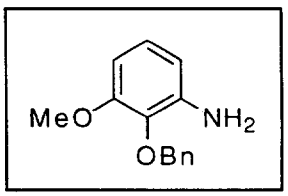
To a stirring solution of the foregoing dimethoxytryptamine (240 mg, 0.51 mmol) in CH_3CN (3 mL) was added a solution of ceric ammonium nitrate (890 mg, 1.53 mmol) in water (2 mL). The bright orange reaction solution was stirred for 45 min, then diluted with CH_2Cl_2 and water. The layers were separated, and the organics were dried and concentrated *in vacuo*. Flash chromatography of the residue (25% ethyl acetate/ hexanes)

provided quinone **23** (181 mg, 80%) as a yellow-orange oil that darkened upon standing. IR: 3386, 1702, 1662, 1596, 1490, 1388 cm^{-1}. ^1H NMR (400 MHz): δ 1.41 (s, 9), 2.43 (s, 3), 2.96 (t, 2, *J*=6.5), 3.39 (m, 2), 4.69 (br s, 1), 6.51 (d, 1, *J*=10.2), 6.55 (d, 1, *J*=10.2), 7.35 (d, 2, *J*=8.3), 7.65 (s, 1), 8.02 (d, 2, *J*=8.3). ^{13}C NMR (125 MHz): δ 21.8, 25.9, 28.4, 40.1, 79.3, 114.0, 122.8, 127.8, 128.1, 129.1, 129.7, 133.8, 136.2, 137.0, 146.2, 155.9, 174.7, 184.4.

5-[[2-(4-Hydroxyphenyl)ethyl]amino]-3[2-(*tert*-butoxycarbonyl)-amino]ethyl]-1-(*p*-toluenesulfonyl)indole-4,7-dione (24a) and 6-[[2-(4-hydroxyphenyl)ethyl]amino]-3[2-(*tert*-butoxycarbonyl)amino]ethyl]-1-(*p*-toluene-sulfonyl)indole-4,7-dione (24b). To a solution of quinone **23** (80 mg, 0.18 mmol) in CH_3CN (3 mL) was added tyramine (74 mg, 0.54 mmol). Oxygen gas was then bubbled through the solution while it was stirred at reflux for 75 min. After cooling the reaction slightly, it was filtered through a SiO_2 column and eluted with ethyl acetate. Concentration of the dark red filtrate provided quinones **24a** and **b** as an inseparable mixture (3:2) of regioisomers (103 mg, 95%). IR: 3366, 1676, 1597, 1515, 1493, 1368 cm^{-1}. ^1H NMR (500 MHz): (major isomer) δ 1.42 (s, 9), 2.40 (s, 3), 2.80 (t, 2, *J*=6.8), 2.90 (t, 2, *J*=6.5), 3.25 (t, 2, *J*=6.5), 3.38 (m, 2), 4.67 (br s, 1), 5.24 (s, 1), 5.77 (t, 1, *J*=6.0), 6.77 (d, 2, *J*=8.3), 6.99 (d, 2, *J*=8.4), 7.31 (d, 2, *J*=8.3), 7.50 (s, 1), 7.98 (d, 2, *J*=8.3). (minor isomer) δ 1.42 (s, 9), 2.43 (s, 3), 2.79 (t, 2, *J*=6.8), 2.97 (t, 2, *J*=6.5), 3.25 (t, 2, *J*=6.5), 3.38 (m, 2), 4.87 (br s, 1), 5.16 (s, 1), 5.72 (t, 1, *J*=6.0), 6.77 (d, 2, *J*=8.3), 6.99 (d, 2, *J*=8.4), 7.33 (d, 2, *J*=8.3), 7.64 (s, 1), 7.96 (d, 2, *J*=8.3) ^{13}C NMR (125 MHz): δ 21.7, 21.8, 25.7, 26.1, 28.4, 33.2, 33.4, 40.0, 40.6, 44.0, 44.4, 79.3, 79.5, 97.1, 97.2, 115.8, 122.0, 123.5, 124.4, 125.8, 127.3, 128.8, 129.0, 129.3, 129.4, 129.6, 129.7, 130.2, 130.8, 133.0, 133.9, 134.3, 145.8, 146.1, 147.1, 147.7, 155.0, 156.2, 170.0, 175.0, 179.6, 183.3. Anal. Calcd for $C_{30}H_{33}N_3SO_7$: C, 62.16; H, 5.74; N, 7.25. Found: C, 62.15; H, 6.00; N, 7.15.



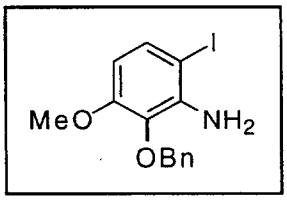
2-Benzyloxy-3-methoxyaniline. To a solution of 2-nitroguaiacol[4] (5.33 g, 31.5 mmol) in DMF (100 mL) was added benzyl bromide (5.39 g, 31.5 mmol) and K_2CO_3 (13.1 g, 94.6 mmol). The resulting suspension was heated to 90 °C and stirred for 3 h. After cooling, the reaction solution was diluted with ethyl ether and water. The layers were separated, and the organics were washed twice with water. The organics were then dried and concentrated *in vacuo* to give the benzyl ether as a yellow liquid which was used directly in the next step without further purification. IR: 1532, 1362, 1271 cm^{-1}. ^1H NMR (400



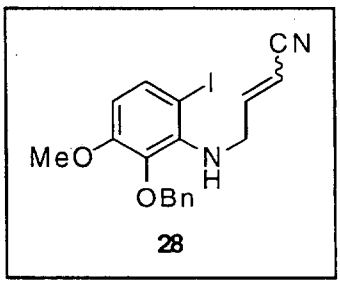
4. Thompson, M. J.; Zeegers, P. J. *Tetrahedron*, **1990**, *46*, 2661.

MHz): δ 3.94 (s, 3), 5.18 (s, 2), 7.12-7.17 (m, 2), 7.32-7.41 (m, 4), 7.49-7.51 (m, 2). ^{13}C NMR (100 MHz): δ 56.4, 75.9, 116.0, 116.1, 123.9, 128.3, 128.4, 128.6, 136.4, 141.4, 145.4, 154.3. The crude benzyl ether was suspended in ethanol (30 mL) and water (10 mL). To this mixture was added iron (12.8 g) and concentrated HCl (0.3 mL), and the slurry was stirred vigorously at a reflux for 40 min. After cooling to rt, the reaction mixture was filtered through a Büchner funnel and washed with ethanol. The filtrate was concentrated *in vacuo*, and the residue was partitioned between ethyl ether and water. The organics were dried and concentrated to provide aniline **35** (6.86 g, 95%) as a yellow oil. IR: 3469, 3372, 1612, 1478 cm^{-1}. ^{1}H NMR (400 MHz): δ 3.80 (br s, 2), 3.88 (s, 3), 5.04 (s, 2), 6.40 (d, 2, *J*=9.0), 6.90 (t, 1, *J*=8.1), 7.34-7.43 (m, 3), 7.51-7.53 (m, 2). ^{13}C NMR (100 MHz): δ 55.6, 74.2, 102.2, 108.7, 124.1, 127.9, 128.2, 128.3, 134.8, 137.8, 140.8, 153.0. Anal. Calcd for $C_{14}H_{15}NO_2$: C, 73.34; H, 6.59; N, 6.11. Found: C, 73.04; H, 6.49; N, 5.87.

6-Benzyloxy-2-iodo-5-methoxyaniline. A biphasic mixture of diethyl ether (180 mL), aqueous saturated Na_2CO_3, and the foregoing 2-benzyloxy-3-methoxyaniline aniline (6.09 g, 27 mmol) was stirred in the dark. To this mixture was added ICl (6.2 g, 38 mmol) in ether (30 mL). The reaction solution was stirred for 1 h, and then the layers were separated. The organic layer was washed three times with fresh saturated Na_2SO_3 solution. The organics were then dried and concentrated *in vacuo*. The residue was dissolved in a minimum amount of CH_2Cl_2 and loaded onto a silica column. Elution with 10% ether in hexanes provided 6-benzyloxy-2-iodo-5-methoxyaniline (6.8 g, 72%) as white crystals, mp 57 °C. IR: 3468, 3351, 2837, 1600, 1480 cm^{-1}. ^{1}H NMR (400 MHz): δ 3.79 (br s, 2), 3.85 (s, 3), 5.00 (s, 2), 6.23 (d, 1, *J*= 8.8), 7.32 (d, 1, *J*=8.8), 7.35-7.48 (m, 5). ^{13}C NMR (100 MHz): δ 55.9, 74.1, 74.6, 104.7, 128.2, 128.4, 128.5, 133.2, 134.7, 137.5, 141.2, 153.1. Anal. Calcd for $C_{14}H_{14}INO_2$: C, 47.34; H, 3.97; N, 3.94. Found: C, 47.43; H, 4.14; N, 3.88.



N-Crotononitrile-6-benzyloxy-2-iodo-5-methoxyaniline (28). To a solution of the foregoing iodoaniline (8.72 g, 24.6 mmol) in acetone/water (85:15) (60 mL) was added bromocrotononitrile[5] (5.84 g, 40 mmol) and $NaHCO_3$ (6.7 g, 80 mmol). The resulting mixture was stirred at reflux for 36 h, adding additional bromocrotononitrile (2 g) every 12 h. The dark reaction mixture was then cooled and diluted with diethyl ether and water. The layers were separated, and the organics were washed once with water. The organics were dried and concentrated *in vacuo*. Flash chromatography of the residue (30% diethyl ether in hexanes) provided nitrile aniline **28** (8.91 g, 86%) as a mixture of *cis* and *trans* isomers. IR: 3343, 2222, 1576 cm^{-1}. ^{1}H NMR (400 MHz): (trans isomer) δ 3.84 (s, 3), 3.93 (dd, 2, *J*=4.8, 2.0), 4.94 (s, 2), 5.53 (dt, 1, *J*=16.3,

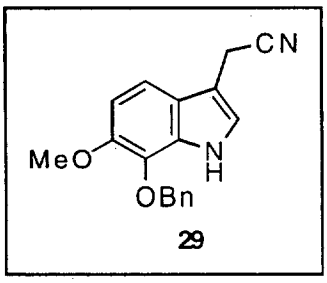


28

5. Bromocrotononitrile was prepared as a mixture of *cis* and *trans* isomers by heating a solution of crotonitrile, NBS, and AIBN overnight in CCl_4. The product was used crude after filtration and evaporation of the solvent.

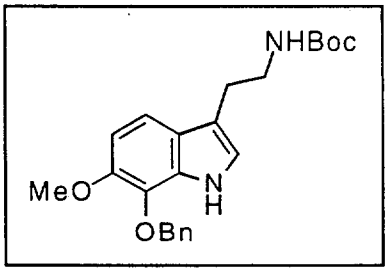
1.8), 6.36 (d, 1, *J*=8.8), 6.64 (dt, 1, *J*=16.3, 4.8), 7.32-7.45 (m, 6). (cis isomer) δ 3.84 (s, 3), 4.17 (dd, 2, *J*=6.6,1.5), 4.98 (s, 2), 5.28 (dt, 1, *J*=11.1, 1.5), 6.37 (d, 1, *J*=8.8), 6.49 (dt, 1, *J*=11.1, 6.6), 7.32-7.45 (m, 6). ^{13}C NMR (125 MHz): δ 47.8, 48.5, 56.0, 56.0, 74.7, 74.8, 80.6, 81.2, 99.8, 100.2, 107.5, 107.7, 115.3, 117.3, 128.2, 128.3, 128.4, 128.4, 128.5, 128.5, 134.0, 134.1, 137.0, 137.0, 138.6, 139.0, 142.0, 142.2, 152.4, 152.9, 154.1, 154.1. Anal. Calcd for $C_{18}H_{17}IN_2O_2$: C, 51.45; H, 4.08; N, 6.67. Found: C, 51.41; H, 4.36; N, 6.39.

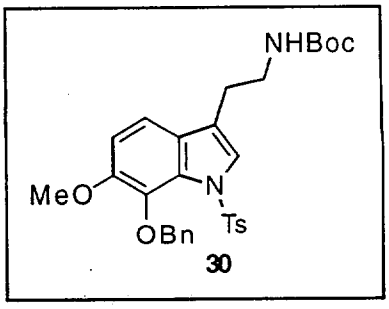
[(7-Benzyloxy-6-methoxy)-3-indolyl]acetonitrile (29). To a degassed solution of nitrile aniline **28** (5.0 g, 11.9 mmol) in CH_3CN (120 mL) was added $Pd(OAc)_2$ (134 mg, 0.60 mmol), triethylamine (3.3 mL, 23.8 mmol), and tri-*o*-tolylphosphine (360 mg, 1.2 mmol). The solution was stirred at reflux for 3 h, and then the solvent was removed *in vacuo*. The residue was partitioned between diethyl ether and water, and the layers were separated. The organics were washed once with water, dried, and concentrated. Flash chromatography of the residue (35% diethyl ether in hexanes) provided indole **29** (3.08 g, 89%) as a yellow oil. IR: 3352, 2252 cm^{-1}. ^{1}H NMR (400 MHz): δ 3.76 (d, 2, *J*=1.0), 3.96 (s, 3), 5.19 (s, 2), 6.93 (d, 1, *J*=8.6), 7.01 (t, 1, *J*=1.2), 7.23 (d, 1, *J*=8.6), 7.34-7.45 (m, 5), 7.92 (br s, 1). ^{13}C NMR (100 MHz): δ 14.4, 57.4, 75.4, 104.7, 108.8, 113.1, 118.1, 122.4, 122.5, 128.2, 128.3, 128.6, 131.5, 133.4, 137.9, 147.7. Anal. Calcd for $C_{18}H_{16}N_2O_2$: C, 73.96; H, 5.52; N, 9.58. Found: C, 74.21; H, 5.75; N, 9.19.



29

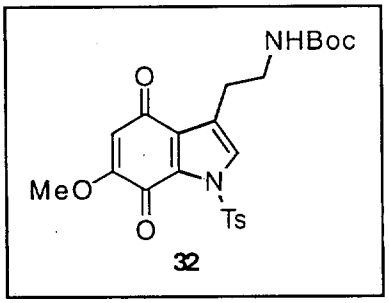
7-Benzyloxy-6-methoxy-3[2-(*tert*-butoxycarbonylamino)-ethyl]indole. To a solution of $LiAlH_4$ (3.2 g, 84 mmol) in diethyl ether (100 mL) at 0 °C was added indole **29** (3.5 g, 12.0 mmol) as a diethyl ether solution (30 mL). The resulting mixture was warmed to rt and stirred for 30 min. After recooling the reaction solution to 0 °C, it was quenched by the slow addition of H_2O (3.2 mL), 15% NaOH (3.2 mL), and H_2O (9.6 mL). The aluminum salts were filtered through Celite and washed with ether. The filtrate was then concentrated *in vacuo*, and the residue was dissolved in CH_2Cl_2 (50 mL). To this solution was added di-*t*-butyl-dicarbonate (2.67 g, 12.0 mmol), and the solution was stirred for 20 min. The solvent was removed *in vacuo*, and the residue was purified by flash chromatography (40% diethyl ether in hexanes) to provide 7-benzyloxy-6-methoxy-3[2-(*tert*-butoxycarbonylamino)ethyl]indole (3.76 g, 79%) as a colorless foamy oil. IR: 3367, 1693 cm^{-1}. ^{1}H NMR (500 MHz): δ 1.43 (s, 9), 2.88 (t, 2, *J*=6.7), 3.42 (br s, 2), 3.95 (s, 3), 4.57 (br s, 1), 5.18 (s, 2), 6.85 (d, 1, *J*=2.0), 6.87 (d, 1, *J*=8.6), 7.24 (d, 1, *J*=8.6), 7.30-7.47 (m, 5), 7.79 (br s, 1). ^{13}C NMR (125 MHz): δ 25.9, 28.4, 40.7, 57.5, 75.3, 79.1, 108.2, 113.2, 113.8, 121.6, 124.1, 128.1, 128.3, 128.5, 131.4, 133.5, 138.1, 147.3, 155.9. Anal. Calcd for $C_{23}H_{28}N_2O_4$: C, 69.68; H, 7.12; N, 7.07. Found: C, 69.37; H, 7.02; N, 7.30.





30

7-Benzyloxy-6-methoxy-3[2-(*tert*-butoxycarbonyl)amino]-ethyl]-1-(*p*-toluenesulfonyl)indole (30). To a solution of the foregoing incole (330 mg, 0.83 mmol) in DMF (10 mL) at 0 °C was added NaH (170 mg, 4.2 mmol). The resulting greenish-gray mixture was stirred at rt for 30 min, then recooled to 0 °C. *p*-Toluenesulfonic anhydride (540 mg, 1.6 mmol) was added to the reaction mixture, and the solution was stirred at rt for 20 min. After cooling to 0 °C, the reaction was quenched with aqueous saturated $NaHCO_3$ until bubbling ceased. The solution was diluted with ethyl ether and water, and the layers were separated. The organics were washed once with water, then dried and concentrated *in vacuo*. Flash chromatography of the residue (CH_2Cl_2) provided tosylated indole **30** (350 mg, 76%) as a colorless foamy gum. IR: 3419, 1706, 1364, 1172 cm^{-1}. ^1H NMR (400 MHz): δ 1.47 (s, 9), 2.26 (s, 3), 2.86 (t, 2, *J*=6.8), 3.44 (br s, 2), 3.85 (s, 3), 4.67 (br s, 1), 5.14 (s, 2), 6.91 (d, 1, *J*=8.5), 6.98 (d, 2, *J*=8.2), 7.19 (d, 1, *J*=8.5), 7.34-7.43 (m, 3), 7.51-7.60 (m, 5). ^{13}C NMR (100 MHz): δ 21.4, 25.7, 28.4, 40.3, 56.9, 74.7, 79.4, 110.3, 114.1, 117.6, 125.5, 127.6, 127.7, 127.9, 128.1, 128.8, 129.3, 129.3, 136.1, 136.5, 138.2, 143.8, 150.9, 155.9. Anal. Calcd for $C_{30}H_{34}N_2SO_6$: C, 65.44; H, 6.22; N, 5.09. Found: C, 65.78; H, 5.95; N, 4.92.



32

6-Methoxy-3-[2-(*tert*-butoxycarbonyl)-amino]ethyl]-1-(*p*-toluenesulfonyl)indole-4,7-dione (32). A solution of tryptamine **30** (2.0 g, 3.64 mmol) and Pd/C (0.8 g) in ethyl acetate (30 mL) was stirred under an atmosphere of hydrogen for 90 min. The reaction mixture was then filtered through Celite and washed with ethyl acetate. The filtrate was concentrated *in vacuo*, and the residue was dissolved in acetone (180 mL). This acetone solution was then rapidly added to a stirring suspension of freshly prepared Fremy's salt[6] (6.8g, 25.4 mmol) and K_2HPO_4 (3.0 g, 22.1 mmol) in water (180 mL). The orange mixture was stirred for 17 h. After this time, most of the acetone was removed *in vacuo* and the remaining suspension was extracted with CH_2Cl_2 (3 x 200 mL). The organics were dried and concentrated to produce quinone **32** as a yellow solid (1.42 g, 82%). ^1H NMR: δ 1.40 (s, 9), 2.40 (s, 3), 2.95 (t, 2, *J*=6.8), 3.38 (t, 2, *J*=6.7), 3.76 (s, 3), 4.73 (br s, 1), 5.69 (s, 1), 7.32 (d, 2, *J*=8.3), 7.66 (s, 1), 8.03 (d, 2, *J*=8.3). ^{13}C NMR (125 MHz): δ 21.7, 25.9, 28.3, 40.2, 56.8, 79.3, 106.7, 122.9, 128.6, 129.2, 129.3, 129.6, 129.7, 133.5, 146.1, 155.9, 159.5, 169.0, 184.0. The ^1H NMR data agree with the previously published data.[7]

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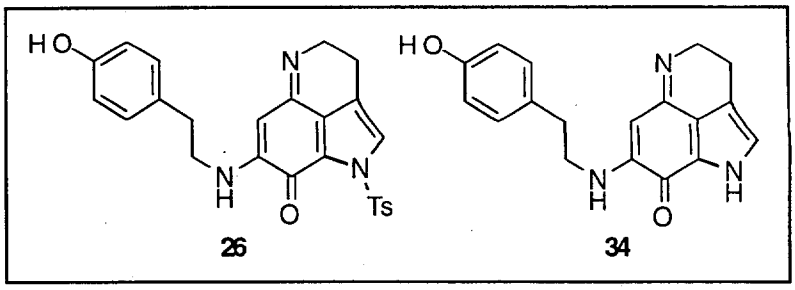
6. Zimmer, H.; Lankin, D. C.; Horgan, S. W. *Chem. Rev.* **1971**, *71*, 229.

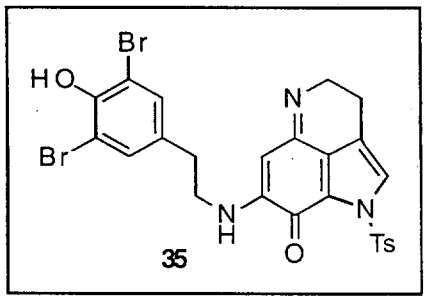
7. Sadanandan, E. V.; Pillai, S. K.; Lakshmikantham, M. V.; Billimoria, A. D.; Culpepper, J. S.; Cava, M. P. *J. Org. Chem.* **1995**, *60*, 1800.



1-(*p*-Toluenesulfonyl)-7-[[2-(4-hydroxyphenyl)ethyl]amino]-1,3,4,8-tetrahydropyrrolo[4.3.2-*de*]quinolin-8-one (26) and Makaluvamine D (34). Quinone **32** (300 mg, 0.64 mmol) was stirred in a mixture of 4:1 CH_2Cl_2:TFA (10 mL) for 2 h. The solvent mixture was then removed *in vacuo*, and the yellow solid residue was suspended in freshly distilled absolute EtOH (60 mL). While this mixture began to heat to reflux, $NaHCO_3$ (320 mg) and molecular sieves were added. After stirring for 10 min, tyramine•HCl (220 mg, 1.27 mmol) was added and the reaction mixture was stirred at reflux for 2 h. The ethanol was removed *in vacuo* to provide the crude product as a darkly colored residue. Flash chromatography (90:10:0.1/CH_2Cl_2: MeOH:TFA) provided 230 mg (62%) of phenol **26** as a purple solid, and 46 mg (17%) of makaluvamine D (**34**) as a red solid.

Phenol 26: IR: 1679, 1632, 1561, 1397 cm^{-1}. ^1H NMR (d_4-methanol) (500 MHz): δ 2.33 (s, 3), 2.73 (t, 2, *J*=7.4), 2.87 (t, 2, *J*=7.3), 3.41 (t, 2, *J*=7.4), 3.72 (t, 2, *J*=7.3), 5.34 (s, 1), 6.57 (d, 2, *J*=8.5), 6.91 (d, 2, *J*=8.5), 7.34 (d, 2, *J*=8.1), 7.76 (s, 1), 7.97 (d, 2, *J*=8.5). ^{13}C NMR (d_4-methanol) (125 MHz): δ 19.0, 21.7, 34.3, 43.5, 46.8, 86.1, 116.5, 119.9, 124.5, 129.1, 129.8, 130.1, 130.2, 130.9, 131.2, 134.7, 148.7, 154.3, 157.5, 157.9, 167.2. HRMS calcd for $C_{25}H_{24}N_3SO_4$ 462.1488, found 462.1496.

Makaluvamine D (34): IR: 3278, 1675, 1628, 1554, 1401 cm^{-1}. ^1H NMR (d_4-methanol) (400 MHz): δ 2.87 (t, 2, *J*=7.4), 2.94 (t, 2, *J*=7.5), 3.54 (t, 2, *J*=7.3), 3.63 (t, 2, *J*=7.5), 5.37 (s, 1), 6.71 (d, 2, *J*=8.5), 7.06 (d, 2, *J*=8.5), 7.14 (s, 1). ^{13}C NMR (d_4-methanol) (125 MHz): δ 19.5, 34.3, 44.1, 46.5, 85.2, 116.5, 120.2, 123.9, 125.4, 127.2, 129.9, 130.8, 154.9, 157.4, 159.6, 168.4. HRMS calcd for $C_{18}H_{18}N_3O_2$ 308.1399, found 308.1406. The spectral data match the previously reported values.[8]



1-(*p*-Toluenesulfonyl)-7-[[2-(3,5-dibromo-4-hydroxyphenyl)-ethyl]amino]-1,3,4,8-tetrahydropyrrolo[4.3.2-*de*]-quinolin-8-one (35). The foregoing procedure was carried out with dibromotyr-amine•HBr[9] in place of tyramine•HCl to obtain dibromophenol **35** (47%) as a purple solid. IR: 3310, 1684, 1633, 1561 cm^{-1}. ^1H NMR (d_4-methanol) (500 MHz): δ 2.42 (s, 3), 2.81 (t, 2, *J*=7.1), 2.97 (t, 2, *J*=7.4), 3.52 (t, 2, *J*=7.1), 3.83 (t, 2, *J*=7.4), 5.43 (s, 1), 7.29 (s, 2), 7.42 (d, 2, *J*=8.5), 7.83 (s, 1), 8.06 (d, 2, *J*=8.5). ^{13}C NMR (d_4-methanol) (125 MHz): δ 18.9, 21.7, 33.5, 43.5, 46.0, 86.4, 112.3, 119.8, 124.4, 129.0, 130.0, 130.2, 131.2, 133.3, 133.8, 134.6, 148.6, 151.2, 154.3, 157.9,

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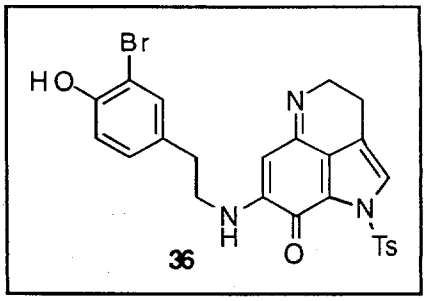
8. Radisky, D. C.; Radisky, E. S.; Barrows, L. R.; Copp, B. R.; Kramer, R. A.; Ireland, C. M. *J. Am. Chem. Soc.* **1993**, *115*, 1632.

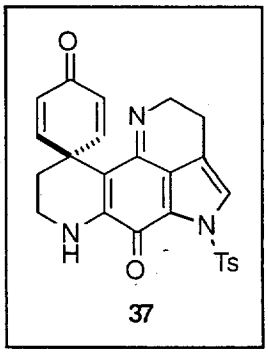
9. Zeynek, *Hoppe-Seyler's Z. Physiol. Chem.* **1921**, *114*, 283.

167.0. HRMS calcd for $C_{25}H_{22}N_3SO_4Br_2$ 617.9698, found 617.9709.



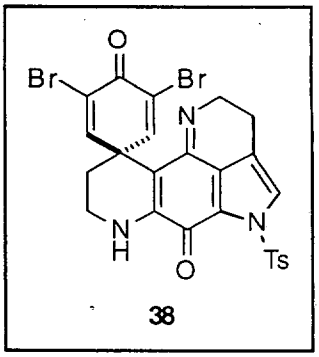
36

1-(*p*-Toluenesulfonyl)-7-[[2-(3-bromo-4-hydroxylphenyl)-ethyl]amino]-1,3,4,8-tetrahydropyrrolo[4.3.2-*de*]quinolin-8-one (36). The same procedure was followed as for phenol **26** using bromotyramine•HBr[10] in place of tyramine•HCl, providing bromophenol **36** (46%) as a purple solid. IR: 1681, 1633, 1557 cm^{-1}. ^1H NMR (d_4-methanol) (400 MHz): δ 2.29 (s, 3), 2.68 (t, 2, *J*=7.2), 2.83 (t, 2, *J*=7.4), 3.38 (t, 2, *J*=7.2), 3.69 (t, 2, *J*=7.4), 5.29 (s, 1), 6.34 (d, 1, *J*=8.3), 6.87 (dd, 1, *J*=8.3, 2.1), 7.12 (d, 1, *J*=2.1), 7.30 (d, 2, *J*=8.1), 7.70 (s, 1), 7.93 (d, 2, *J*=8.4). ^{13}C NMR (d_4-methanol) (125 MHz): δ 18.9, 21.7, 33.9, 43.5, 46.4, 86.3, 110.8, 117.5, 119.9, 124.4, 129.1, 130.1, 130.2, 131.2, 131.6, 134.4, 134.7, 148.7, 154.3, 154.4, 157.9, 167.1. HRMS calcd for $C_{25}H_{23}N_3SO_4Br$ 540.0593, found 540.0587.



37

1-(*p*-Toluenesulfonyl)di(debromo)discorhabdin C (37). Oxygen was bubbled through a stirring solution of phenol **26** (180 mg, 0.312 mmol) in CH_3CN (10 mL). To this solution was added $CuCl_2•2H_2O$ (160 mg, 0.936 mmol) followed by triethylamine (126 mg, 1.25 mmol). The resulting suspension was stirred with oxygen bubbling through it for 1 h. Then the reaction was diluted with 90:10:0.1 CH_2Cl_2:MeOH:TFA (30 mL) and preabsorbed onto SiO_2. The preabsorbed SiO_2 was then eluted through a SiO_2 column with 90:10:0.1 CH_2Cl_2:MeOH:TFA. Concentration *in vacuo* of the purple eluted fractions provided spirodienone **37** as a purple solid (161 mg, 90%). IR: 3318, 1687, 1663, 1597, 1555 cm^{-1}. ^1H NMR (d_4-methanol) (500 MHz): δ 1.77 (t, 2, *J*=5.3), 2.24 (s, 3), 2.70 (t, 2, *J*=7.0), 3.49 (t, 2, *J*=5.3), 3.56 (t, 2, *J*=7.0), 6.25 (d, 2, *J*=9.6), 6.92 (d, 2, *J*=9.6), 7.24 (d, 2, *J*=8.2), 7.70 (s, 1), 7.88 (d, 2, *J*=8.2). ^{13}C NMR (d_4-methanol) (125 MHz): δ 19.1, 21.7, 35.4, 39.9, 40.6, 44.5, 95.5, 120.8, 124.1, 130.2, 130.3, 131.0, 131.2, 131.3, 134.6, 148.7, 152.4, 153.1, 154.4, 165.5, 185.7. HRMS calcd for $C_{25}H_{22}N_3SO_4$ 460.1331, found 460.1338.



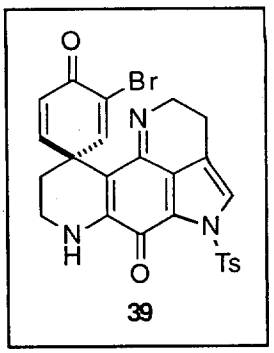
38

1-(*p*-Toluenesulfonyl)discorhabdin C (38). The same procedure was followed as above using dibromophenol **35** in place of phenol **26**, providing dibromospirodienone **38** (81%) as a magenta solid. IR: 3303, 1681, 1596, 1555, 1326 cm^{-1}. ^1H NMR (d_4-methanol) (400 MHz): δ 1.92 (t, 2, *J*=5.2), 2.30 (s, 3), 2.79 (t, 2, *J*=7.1), 3.54 (t, 2, *J*=5.2), 3.62 (t, 2, *J*=7.2), 7.31 (d, 2, *J*=8.2), 7.49 (s, 2), 7.78 (s, 1), 7.95 (d, 2, *J*=8.3). ^{13}C NMR (d_4-methanol) (125 MHz): δ 19.0, 21.7, 35.0, 39.8, 44.7, 45.9, 94.3, 120.9, 124.0, 124.6, 130.1, 130.2, 130.3, 131.2, 134.6, 148.7, 151.9, 153.2, 154.4, 165.2, 172.6. HRMS calcd for

10. Zeynek, *Hoppe-Seyler's Z. Physiol. Chem.* **1921**, *114*, 283.

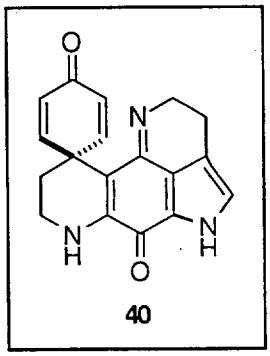
$C_{25}H_{20}N_3SO_4Br_2$ 615.9541, found 615.9516.

1-(*p*-Toluenesulfonyl)discorhabdin E (39). The foregoing procedure was followed using bromophenol **36** in place of phenol **26**, providing bromospirodienone **39** (84%) as a purple solid. IR: 3332, 1666, 1597, 1554, 1326 cm^{-1}. ^1H NMR (d_4-methanol) (400 MHz): δ 1.82-1.92 (m, 2), 2.30 (s, 3), 2.77 (t, 2, *J*=7.4), 3.54 (t, 2, *J*=5.7), 3.62 (t, 2, *J*=7.3), 6.39 (d, 1, *J*=9.9), 6.96 (dd, 1, *J*=9.9, 2.7), 7.31 (d, 2, *J*=8.0), 7.48 (d, 1, *J*=2.7), 7.77 (s, 1), 7.95 (d, 2, *J*=8.5). ^{13}C NMR (d_4-methanol) (125 MHz): δ 19.0, 21.7, 35.3, 39.8, 43.7, 44.6, 94.9, 120.9, 124.1, 127.0, 129.9, 130.2, 130.2, 130.3, 131.2, 134.6, 148.7, 151.8, 152.1, 153.1, 154.4, 165.4, 178.5. HRMS calcd for $C_{25}H_{21}N_3SO_4Br$ 538.0436, found 538.0428.



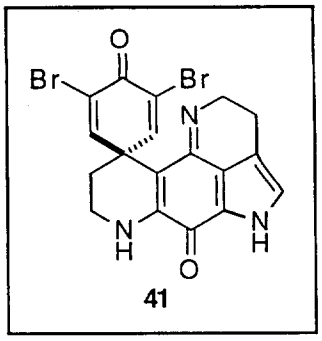
39

Di(debromo)discorhabdin C (40). To a solution of tosyldienone **37** (100 mg, 0.17 mmol) in methanol (15 mL) was added 0.4 mL of NaOMe in MeOH (approximately 4 M). This resulting suspension was stirred for 50 min and then quenched by the dropwise addition of TFA until a purple color persisted. The reaction mixture was diluted with CH_2Cl_2 (40 mL) and preabsorbed onto SiO_2. The preabsorbed SiO_2 was eluted through a SiO_2 column with CH_2Cl_2:MeOH:TFA (90:10:0.1). Concentration *in vacuo* of the slower eluting fractions provided the crude product, which was further purified by flash chromatography (10% MeOH/CH_2Cl_2) to provide dienone **40** (59 mg, 80%) as a green solid that produced purple solutions in protic solvents. IR: 3300, 1679, 1620, 1592, 1547 cm^{-1}. ^1H NMR (d_4-methanol) (400 MHz): δ 1.89 (t, 2, *J*=5.7), 2.75 (t, 2, *J*=7.4), 3.60 (t, 2, *J*=5.7), 3.66 (t, 2, *J*=7.4), 6.35 (d, 2, *J*=9.9), 7.06 (s, 1), 7.09 (d, 2, *J*=10.0). ^{13}C NMR (d_4-methanol) (125 MHz): δ 19.5, 35.6, 39.6, 40.8, 45.1, 94.3, 121.3, 124.8, 125.2, 127.7, 130.9, 153.2, 153.8, 156.3, 166.8, 185.9. HRMS calcd for $C_{18}H_{16}N_3O_2$ 306.1243, found 306.1250.



40

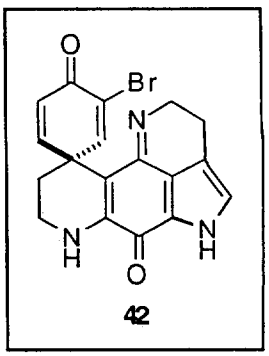
Discorhabdin C (41). The foregoing procedure was followed using dibromospirodienone **38** in place of spirodienone **37**, providing discorhabdin C (**41**) (77%) as a red solid. IR: 1675, 1588, 1541, 1326, 1024 cm^{-1}. ^1H NMR (d_4-methanol) (400 MHz): δ 2.00 (t, 2, *J*=5.7), 2.80 (t, 2, *J*=7.4), 3.61 (t, 2, *J*=5.6), 3.68 (t, 2, *J*=7.4), 7.10 (s, 1), 7.62 (s, 2). ^{13}C NMR (d_4-methanol) (125 MHz): δ 19.5, 35.2, 39.5, 45.3, 46.1, 93.2, 120.2, 121.4, 124.3, 124.8, 127.8, 152.7, 153.8, 156.3, 166.5, 172.8. HRMS calcd for $C_{18}H_{14}N_3O_2Br_2$ 461.9453, found 461.9451. The spectral data are identical to the reported isolation data.[11]



41

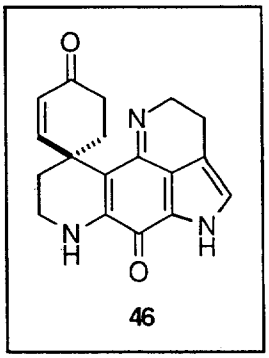
11. Perry, N. B.; Blunt, J. W.; McCombs, J. D.; Munro, M. H. G. *J. Org. Chem.* **1986**, *51*, 5476.

Discorhabdin E (42). The foregoing procedure was followed using bromospirodienone **39** in place of spirodienone **37**, providing discorhabdin E (**42**) as a red solid in 67% yield. IR: 1679, 1590, 1544, 1416, 1328, 1025 cm^{-1}. ^1H NMR (d_4-methanol) (400 MHz): d 2.05 (m, 2), 2.87 (t, 2, *J*=7.5), 3.70 (t, 2, *J*=5.7), 3.77 (t, 2, *J*=7.5), 6.54 (d, 1, *J*=9.9), 7.18 (s, 1), 7.19 (dd, 1, *J*=9.9, 2.6), 7.70 (d, 1, *J*=2.6). ^{13}C NMR (d_4-methanol) (125 MHz): δ 19.8, 35.7, 39.9, 44.2, 45.5, 94.0, 121.6, 125.1, 125.5, 127.0, 128.0, 129.9, 152.8, 153.2, 154.1, 156.6, 166.9, 179.0. HRMS calcd for $C_{18}H_{15}N_3O_2Br$ 384.0348, found 384.0344. The spectral data are identical to the reported isolation data.[12]



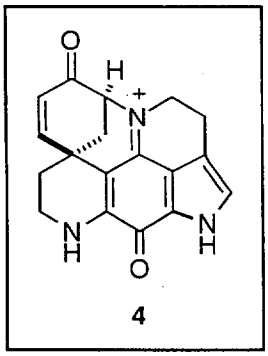
42

Enone 46. A suspension of dienone **40** (30 mg, 0.72 mmol) and 10% Pd/C (5 mg) in methanol (5 ml) was stirred under hydrogen for exactly 5 min. During this time, the reaction solution turned from dark purple to colorless. Then the solution was filtered through Celite, and the purple color returned. The filtrate was concentrated *in vacuo*, and the residue was purified by flash chromatography (10% $MeOH/CH_2Cl_2$) to provide enone **46** (21 mg, 69%) as a green solid that produced purple solutions in protic solvents. IR: 1681, 1592, 1544, 1441, 1332 cm^{-1}. ^1H NMR (d_4-methanol) (500 MHz): δ 1.76 (app tdd, 1, *J*=12.5, 4.8, 1.5), 2.17-2.21 (m, 1), 2.27 (ddd, 1, *J*=14.0, 3.4, 2.1), 2.41-2.47 (m, 2), 2.73 (ddd, 1, *J*=21.0, 16.0, 4.9), 2.83-2.93 (m, 2), 3.58 (ddd, 1, *J*=15.7, 12.5, 3.5), 3.70 (ddd, 1, *J*=15.3, 4.8, 2.0), 3.75-3.86 (m, 2), 6.17 (d, 1, *J*=10.2), 6.92 (dd, 1, *J*=10.2, 2.2), 7.16 (s, 1). ^{13}C NMR (d_4-methanol) (125 MHz): δ 19.5, 29.0, 30.6, 33.7, 36.4, 39.2, 44.9, 101.2, 121.2, 124.9, 125.0, 127.5, 131.4, 153.2, 155.6, 156.2, 167.0, 199.7. HRMS calcd for $C_{18}H_{16}N_3O_2$ 308.1399, found 308.1396.



46

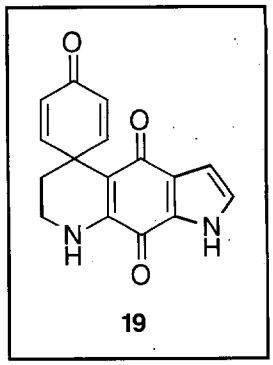
5,8-Di(dethio)discorhabdin D (4). To a solution of enone **46** (18 mg, 0.043 mmol) in 3.5 mL of 5:1 $CHCl_3$:TFA was added phenyltrimethylammonium tribromide (18 mg, 0.047 mmol). The resulting mixture was stirred for 70 min. The solvent was removed *in vacuo*, and the residue was dissolved in 7 mL of methanol. This purple solution was filtered through a plug of basic alumina, producing an orange-red filtrate. The orange solution was allowed to sit at rt for 1 h. After this time, the methanol was removed *in vacuo*. Flash chromatography of the residue (10% $MeOH/CH_2Cl_2$) provided immonium salt **4** (13 mg, 73%) as a green solid that produced purple solutions in protic solvents. IR: 1675, 1594, 1567, 1536, 1413, 1334 cm^{-1}. ^1H NMR (d_4-methanol) (500 MHz): δ 1.80 (ddd, 1, *J*=13.7, 11.5, 5.8), 2.13 (ddd, 1, *J*=13.1, 3.2, 2.5), 2.17 (ddd, 1, *J*=13.7, 3.9, 1.9), 2.63 (app dt, 1, *J*=13.1, 2.4), 2.97-3.13 (m, 2), 3.79-4.02 (m, 4), 4.28 (t, 1, *J*=2.5), 6.09 (d, 1, *J*=10.1), 7.11 (s, 1), 7.29 (dd, 1, *J*=10.1, 2.4). ^{13}C NMR (d_4-methanol) (125 MHz): δ 20.6, 30.1, 30.7,



4

12. Perry, N. B.; Blunt, J. W.; Munro, M. H. G; Higa, T.; Sakai, R. *J. Org. Chem.* **1988**, *53*, 4127.

37.1, 39.6, 51.8, 64.5, 95.6, 119.2, 124.1, 125.1, 125.7, 127.5, 150.2, 150.6, 155.5, 167.2, 190.1. HRMS calcd for $C_{18}H_{16}N_3O_2$ 306.1243, found 306.1249.



19

Single-Crystal X-Ray Analysis of 4,5,6,7,8,9-Hexahydro-1*H*-pyrrolo-[3,2*g*]quinoline-4,9-dione-5-spiro-4'-cyclohexa-2',5'-dien-1'-one (19): The compound crystallizes in the centrosymmetric monoclinic space group $P2_1/n$ with four formula units of $C_{16}H_{12}N_2O_3$ in the unit cell. The structure is well-behaved with reasonable bond lengths and angles.

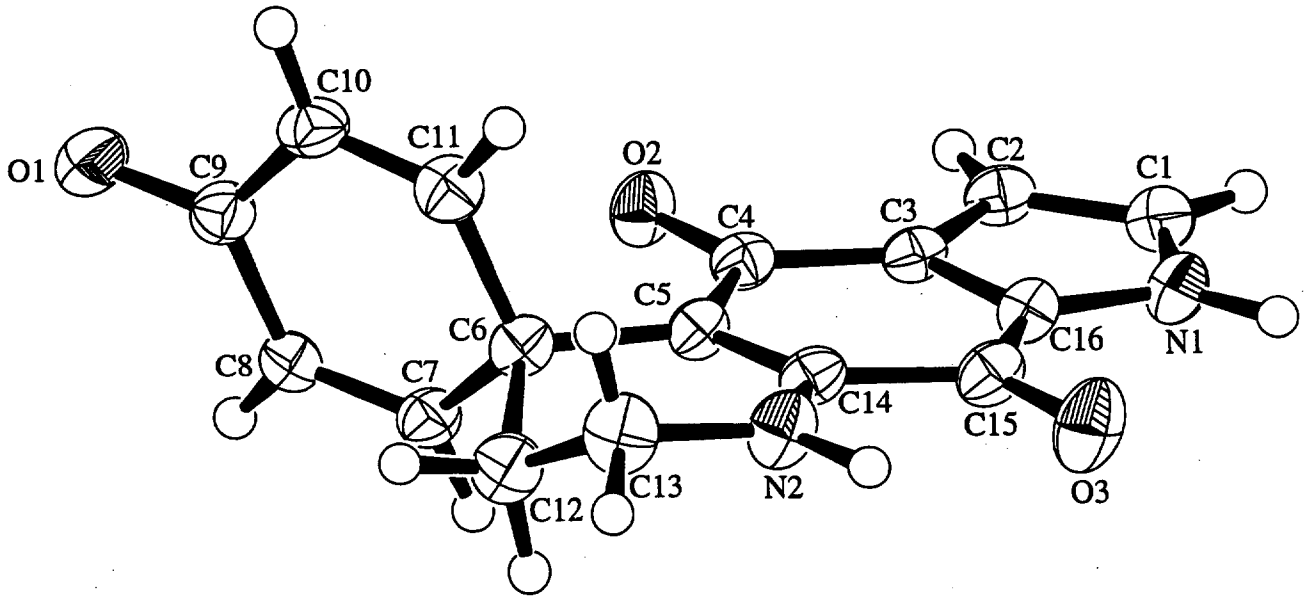
A network of molecules is built up in the *ac* plane through hydrogen bonding. Each molecule participates in hydrogen bonding with four other molecules using the following connectivities:

N(1)-H(1)...O(1) (N(1)...O(1) distance = 2.774 Å)

N(2)-H(2)...O(2) (N(2)...O(2) distance = 2.929 Å)

The hydrogen atoms in the structure were located but not refined. Their positions were adjusted to reflect ideallized geometries 0.95 Å away from the atom to which they were attached. H(1), the hydrogen attached to N(1), was located in the plane formed by N(1), C(1),and C(16), and H(2), the hydrogen atom attached to N(2), was located in the plane formed by N(2), C(13), and C(14). Consequently, the positions of H(1) and H(2) were fixed to correspond to sp^2 hybridization on N(1) and N(2).

ORTEP Represenation:



Data Collection

A red plate-like crystal of $C_{16}N_2O_3H_{12}$ having approximate dimensions of 0.44 x 0.30 x 0.04 mm was mounted on a glass fiber. All measurements were made on a Siemens SMART[10] diffractometer with graphite monochromated Mo-Kα radiation.

Cell constants and an orientation matrix for data collection, obtained from a least-squares refinement using the measured positions of 3421 reflections with $I > 10\sigma$ in the range $3.00 < 2\theta < 45.00°$, corresponded to a primitive monoclinic cell with dimensions:

$a = 7.6696(3)\ \AA$

$b = 9.6900(4)\ \AA \qquad \beta = 95.396(2)°$

$c = 17.8595(7)\ \AA$

$V = 1321.41(8)\ \AA^3$

For Z = 4 and F.W. = 280.28, the calculated density is 1.41 g/cm^3. The systematic absences of:

h0l: $h+l \neq 2n$

0k0: $k \neq 2n$

uniquely determine the space group to be:

$P2_1/n$ (#14)

The data were collected at a temperature of -95 $\pm$ 1°C. Frames corresponding to an arbitrary hemisphere of data were collected using ω scans of 0.30° counted for a total of 10 seconds each.

Data Reduction

Data were integrated using the program SAINT[11] with box parameters of 1.6x1.6x0.6° to a maximum 2θ value of 52.3°. The data were corrected for Lorentz and polarization effects. No decay correction was applied. An empirical absorption correction based on comparison of redundant and equivalent data and an elipsoidal model of the absorption surface was applied using the program XPREP[12] (Tmax=0.98, Tmin=0.89). The 6394 integrated and corrected reflections were averaged to yield 2499 unique data (R_{int} = 0.034).

Structure Solution and Refinement

The structure was solved by direct methods[1] and expanded using Fourier techniques[2]. The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included but not refined. The final cycle of full-matrix least-squares refinement[3] was based on 1630 observed reflections ($I > 3.00\sigma(I)$) and 190 variable parameters and converged (largest parameter shift was 0.00 times its esd) with unweighted and weighted agreement factors of:

$$R = \Sigma||Fo| - |Fc||/\Sigma|Fo| = 0.036$$

$$R_w = \sqrt{(\Sigma w(|Fo| - |Fc|)^2/\Sigma wFo^2)} = 0.048$$

The standard deviation of an observation of unit weight[4] was 1.71. The weighting scheme was based on counting statistics and included a factor (p = 0.030) to downweight the intense reflections. Plots of $\Sigma w(|Fo| - |Fc|)^2$ versus $|Fo|$, reflection order in data collection, sin θ/λ and various classes of indices showed no unusual trends. The maximum and minimum peaks on the final difference Fourier map corresponded to 0.16 and -0.22 $e^-/\AA^3$, respectively.

Neutral atom scattering factors were taken from Cromer and Waber[5] . Anomalous dispersion effects were included in Fcalc[6]; the values for Δf' and Δf" were those of Creagh and McAuley[7]. The values for the mass attenuation coefficients are those of Creagh and Hubbel[8]. All calculations were performed using the teXsan[9] crystallographic software package of Molecular Structure Corporation.

References

(1) SIR92: Altomare, A., Burla, M.C., Camalli, M., Cascarano, M., Giacovazzo, C., Guagliardi, A., Polidori, G. (1994). J. Appl. Cryst., in preparation.

(2) DIRDIF92: Beurskens, P.T., Admiraal, G., Beurskens, G., Bosman, W.P., Garcia-Granda, S., Gould, R.O., Smits, J.M.M. and Smykalla, C. (1992). The DIRDIF program system, Technical Report of the Crystallography Laboratory, University of Nijmegen, The Netherlands.

(3) Least-Squares:

Function minimized: $\Sigma w(|Fo| - |Fc|)^2$

where w = $\frac{1}{\sigma^2(Fo)} = \frac{4Fo^2}{\sigma^2(Fo^2)}$

(4) Standard deviation of an observation of unit weight:

$$\sqrt{\Sigma w(|Fo| - |Fc|)^2/(No - Nv)}$$

where: No = number of observations

Nv = number of variables

(5) Cromer, D. T. & Waber, J. T.; "International Tables for X-ray Crystallography", Vol. IV, The Kynoch Press, Birmingham, England, Table 2.2 A (1974).

(6) Ibers, J. A. & Hamilton, W. C.; Acta Crystallogr., 17, 781 (1964).

(7) Creagh, D. C. & McAuley, W.J .; "International Tables for Crystallography", Vol C, (A.J.C. Wilson, ed.), Kluwer Academic Publishers, Boston, Table 4.2.6.8, pages 219-222 (1992).

(8) Creagh, D. C. & Hubbell, J.H..; "International Tables for Crystallography", Vol C, (A.J.C. Wilson, ed.), Kluwer Academic Publishers, Boston, Table 4.2.4.3, pages 200-206 (1992).

(9) teXsan: Crystal Structure Analysis Package, Molecular Structure Corporation (1985 & 1992).

(10) SMART Area-Detector Software Package; Siemens Industrial Automation, Inc.: Madison, WI, (1995)

(11) SAINT: SAX Area-Dectector Integration Program; V4.024; Siemens Industrial Automation, Inc.: Madison, WI, (1995)

(12) XPREP (v 5.03) Part of the SHELXTL Crystal Structure Determination Package; Siemens Industrial Automation, Inc.: Madison, WI, (1995)

EXPERIMENTAL DETAILS

A. Crystal Data

Empirical Formula	$C_{16}N_2O_3H_{12}$
Formula Weight	280.28
Crystal Color, Habit	Red, plate
Crystal Dimensions	0.44 X 0.30 X 0.04 mm
Crystal System	monoclinic
Lattice Type	Primitive
No. of Reflections Used for Unit Cell Determination (2θ range)	3421 (3.0 - 45.0°)
Lattice Parameters	a = 7.6696(3)Å
	b = 9.6900(4) Å
	c = 17.8595(7) Å
	β = 95.396(2)°
	V = 1321.41(8) Å^3
Space Group	$P2_1/n$ (#14)
Z value	4
D_{calc}	1.409 g/cm^3
F_{000}	584.00
μ(MoKα)	0.99 cm^{-1}

B. Intensity Measurements

Diffractometer	SMART
Radiation	MoKα (λ = 0.71069 Å) graphite monochromated

Crystal to Detector Distance	60 mm
Temperature	-95.0°C
Scan Type	ω (0.3°/frame)
Scan Rate	10.0 sec./frame
$2\theta_{max}$	52.3°
No. of Reflections Measured	Total: 6394 Unique: 2499 (R_{int} = 0.034)
Corrections	Lorentz-polarization Absorption (Tmax=0.98, Tmin=0.89)

C. Structure Solution and Refinement

Structure Solution	Direct Methods (SIR92)
Refinement	Full-matrix least-squares
Function Minimized	$\Sigma w(\|Fo\| - \|Fc\|)^2$
Least Squares Weights	$\frac{1}{\sigma^2(Fo)} = \frac{4Fo^2}{\sigma^2(Fo^2)}$
p-factor	0.030
Anomalous Dispersion	All non-hydrogen atoms
No. Observations (I>3.00σ(I))	1630
No. Variables	190
Reflection/Parameter Ratio	8.58
Residuals: R; Rw; Rall	0.036 ; 0.048 ; 0.060
Goodness of Fit Indicator	1.71
Max Shift/Error in Final Cycle	0.00
Maximum peak in Final Diff. Map	0.16 $e^-/\AA^3$
Minimum peak in Final Diff. Map	-0.22 $e^-/\AA^3$

Table 1. Atomic coordinates and B_{iso}/B_{eq}

atom	x	y	z	B_{eq}
O(1)	0.5714(2)	-0.0669(2)	0.71891(9)	3.32(4)
O(2)	0.5290(2)	0.1945(2)	0.93766(8)	2.42(3)
O(3)	-0.0773(2)	0.3505(2)	1.04492(9)	3.23(4)
N(1)	0.2665(2)	0.4528(2)	1.11129(10)	2.17(4)
N(2)	-0.0934(2)	0.1878(2)	0.9242(1)	2.27(4)
C(1)	0.4430(3)	0.4714(2)	1.1217(1)	2.25(5)
C(2)	0.5214(3)	0.3943(2)	1.0696(1)	2.20(5)
C(3)	0.3865(2)	0.3247(2)	1.0255(1)	1.82(4)
C(4)	0.3889(2)	0.2287(2)	0.9618(1)	1.75(4)
C(5)	0.2207(2)	0.1771(2)	0.9291(1)	2.16(4)
C(6)	0.2169(3)	0.0721(2)	0.8654(1)	1.98(4)
C(7)	0.3465(3)	-0.0420(2)	0.8827(1)	1.98(5)
C(8)	0.4558(3)	-0.0878(2)	0.8351(1)	2.24(5)
C(9)	0.4692(3)	-0.0214(2)	0.7629(1)	2.36(5)
C(10)	0.3577(3)	0.0983(2)	0.7450(1)	2.60(5)
C(11)	0.2434(3)	0.1404(2)	0.7918(1)	2.31(5)
C(12)	0.0328(3)	0.0002(3)	0.8588(1)	2.77(5)
C(13)	-0.1165(3)	0.1018(3)	0.8578(1)	2.95(5)
C(14)	0.0669(2)	0.2230(2)	0.9544(1)	1.97(5)
C(15)	0.0629(3)	0.3186(2)	1.0214(1)	2.56(5)
C(16)	0.2306(3)	0.3635(2)	1.0527(1)	2.06(4)
H(1)	0.1825	0.4948	1.1399	2.6024
H(2)	-0.1934	0.2200	0.9467	2.7292
H(3)	0.5026	0.5285	1.1591	2.6944
H(4)	0.6433	0.3889	1.0642	2.6446
H(5)	0.3505	-0.0842	0.9308	2.3735
H(6)	0.5271	-0.1658	0.8485	2.6830
H(7)	0.3668	0.1468	0.6993	3.1194
H(8)	0.1738	0.2190	0.7777	2.7700
H(9)	0.0274	-0.0600	0.9005	3.3233
H(10)	0.0201	-0.0518	0.8135	3.3233
H(11)	-0.2241	0.0529	0.8574	3.5440
H(12)	-0.1182	0.1578	0.8142	3.5440

$$B_{eq} = \frac{8}{3}\pi^2(U_{11}(aa^*)^2 + U_{22}(bb^*)^2 + U_{33}(cc^*)^2 + 2U_{12}aa^*bb^*\cos\gamma + 2U_{13}aa^*cc^*\cos\beta + 2U_{23}bb^*cc^*\cos\alpha)$$

Table 2. Anisotropic Displacement Parameters

atom	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
O(1)	0.0500(10)	0.0425(10)	0.0420(10)	0.0019(8)	0.0210(8)	0.0038(8)
O(2)	0.0208(7)	0.0413(9)	0.0386(9)	0.0017(7)	0.0078(7)	-0.0056(7)
O(3)	0.0252(9)	0.069(1)	0.048(1)	0.0045(8)	0.0104(8)	-0.0130(9)
N(1)	0.0283(10)	0.041(1)	0.0288(10)	0.0029(9)	0.0058(7)	-0.0025(9)
N(2)	0.0199(9)	0.051(1)	0.036(1)	0.0001(9)	0.0027(8)	-0.0054(10)
C(1)	0.030(1)	0.035(1)	0.029(1)	-0.0027(10)	-0.0011(9)	0.002(1)
C(2)	0.022(1)	0.033(1)	0.031(1)	-0.0006(9)	0.0030(9)	0.005(1)
C(3)	0.022(1)	0.028(1)	0.025(1)	0.0015(9)	0.0035(9)	0.0058(9)
C(4)	0.024(1)	0.028(1)	0.026(1)	0.0033(9)	0.0025(9)	0.0059(10)
C(5)	0.023(1)	0.031(1)	0.025(1)	0.0013(9)	0.0024(9)	0.0013(9)
C(6)	0.024(1)	0.033(1)	0.027(1)	-0.0004(10)	0.0017(9)	0.0006(10)
C(7)	0.033(1)	0.030(1)	0.024(1)	-0.0003(10)	0.0010(9)	0.0029(10)
C(8)	0.032(1)	0.025(1)	0.030(1)	0.0007(10)	0.0032(9)	0.001(1)
C(9)	0.031(1)	0.033(1)	0.030(1)	-0.0067(10)	0.0056(10)	-0.002(1)
C(10)	0.038(1)	0.035(1)	0.025(1)	-0.004(1)	0.0009(10)	0.006(1)
C(11)	0.031(1)	0.034(1)	0.028(1)	0.0021(10)	-0.0028(10)	0.0029(10)
C(12)	0.032(1)	0.042(1)	0.036(1)	-0.006(1)	0.003(1)	-0.004(1)
C(13)	0.024(1)	0.051(2)	0.042(1)	-0.005(1)	-0.002(1)	-0.008(1)
C(14)	0.023(1)	0.035(1)	0.027(1)	-0.0024(9)	0.0024(9)	0.002(1)
C(15)	0.022(1)	0.039(1)	0.032(1)	0.0036(10)	0.0056(9)	0.002(1)
C(16)	0.026(1)	0.033(1)	0.025(1)	0.0029(9)	0.0019(9)	-0.0003(10)

The general temperature factor expression:

$$\exp(-2\pi^2(a^{*2}U_{11}h^2 + b^{*2}U_{22}k^2 + c^{*2}U_{33}l^2 + 2a^*b^*U_{12}hk + 2a^*c^*U_{13}hl + 2b^*c^*U_{23}kl))$$

Table 3. Bond Lengths(Å)

atom	atom	distance	atom	atom	distance
O(1)	C(9)	1.242(2)	O(2)	C(4)	1.240(2)
O(3)	C(15)	1.230(2)	N(1)	C(1)	1.361(3)
N(1)	C(16)	1.366(3)	N(2)	C(13)	1.447(3)
N(2)	C(14)	1.340(2)	C(1)	C(2)	1.376(3)
C(2)	C(3)	1.410(3)	C(3)	C(4)	1.472(3)
C(3)	C(16)	1.384(3)	C(4)	C(5)	1.454(3)
C(5)	C(6)	1.525(3)	C(5)	C(14)	1.376(2)
C(6)	C(7)	1.500(3)	C(6)	C(11)	1.503(3)
C(6)	C(12)	1.569(3)	C(7)	C(8)	1.325(3)
C(8)	C(9)	1.452(3)	C(9)	C(10)	1.458(3)
C(10)	C(11)	1.330(3)	C(12)	C(13)	1.509(3)
C(14)	C(15)	1.515(3)	C(15)	C(16)	1.421(3)

Table 4. Bond Lengths(Å)

atom	atom	distance	atom	atom	distance
N(1)	H(1)	0.95	N(2)	H(2)	0.95
C(1)	H(3)	0.95	C(2)	H(4)	0.95
C(7)	H(5)	0.95	C(8)	H(6)	0.95
C(10)	H(7)	0.95	C(11)	H(8)	0.95
C(12)	H(9)	0.95	C(12)	H(10)	0.95
C(13)	H(11)	0.95	C(13)	H(12)	0.95

Table 5. Bond Angles(°)

atom	atom	atom	angle	atom	atom	atom	angle
C(1)	N(1)	C(16)	108.4(2)	C(13)	N(2)	C(14)	120.9(2)
N(1)	C(1)	C(2)	109.1(2)	C(1)	C(2)	C(3)	107.0(2)
C(2)	C(3)	C(4)	132.2(2)	C(2)	C(3)	C(16)	106.7(2)
C(4)	C(3)	C(16)	121.1(2)	O(2)	C(4)	C(3)	120.8(2)
O(2)	C(4)	C(5)	122.3(2)	C(3)	C(4)	C(5)	116.9(2)
C(4)	C(5)	C(6)	118.9(2)	C(4)	C(5)	C(14)	120.9(2)
C(6)	C(5)	C(14)	120.3(2)	C(5)	C(6)	C(7)	111.9(2)
C(5)	C(6)	C(11)	111.4(2)	C(5)	C(6)	C(12)	107.9(2)
C(7)	C(6)	C(11)	111.3(2)	C(7)	C(6)	C(12)	105.2(2)
C(11)	C(6)	C(12)	108.9(2)	C(6)	C(7)	C(8)	124.2(2)
C(7)	C(8)	C(9)	121.5(2)	O(1)	C(9)	C(8)	120.4(2)
O(1)	C(9)	C(10)	122.3(2)	C(8)	C(9)	C(10)	117.3(2)
C(9)	C(10)	C(11)	120.9(2)	C(6)	C(11)	C(10)	124.4(2)
C(6)	C(12)	C(13)	112.8(2)	N(2)	C(13)	C(12)	109.4(2)
N(2)	C(14)	C(5)	124.6(2)	N(2)	C(14)	C(15)	112.8(2)
C(5)	C(14)	C(15)	122.6(2)	O(3)	C(15)	C(14)	120.4(2)
O(3)	C(15)	C(16)	125.2(2)	C(14)	C(15)	C(16)	114.4(2)
N(1)	C(16)	C(3)	108.8(2)	N(1)	C(16)	C(15)	127.2(2)
C(3)	C(16)	C(15)	124.0(2)				

Table 6. Bond Angles(°)

atom	atom	atom	angle	atom	atom	atom	angle
C(1)	N(1)	H(1)	125.8	C(16)	N(1)	H(1)	125.8
C(13)	N(2)	H(2)	119.5	C(14)	N(2)	H(2)	119.5
N(1)	C(1)	H(3)	125.4	C(2)	C(1)	H(3)	125.4
C(1)	C(2)	H(4)	126.5	C(3)	C(2)	H(4)	126.5
C(6)	C(7)	H(5)	117.9	C(8)	C(7)	H(5)	117.9
C(7)	C(8)	H(6)	119.3	C(9)	C(8)	H(6)	119.3
C(9)	C(10)	H(7)	119.5	C(11)	C(10)	H(7)	119.6
C(6)	C(11)	H(8)	117.7	C(10)	C(11)	H(8)	117.8
C(6)	C(12)	H(9)	108.6	C(6)	C(12)	H(10)	108.6
C(13)	C(12)	H(9)	108.6	C(13)	C(12)	H(10)	108.6
H(9)	C(12)	H(10)	109.5	N(2)	C(13)	H(11)	109.5
N(2)	C(13)	H(12)	109.5	C(12)	C(13)	H(11)	109.4
C(12)	C(13)	H(12)	109.5	H(11)	C(13)	H(12)	109.5

Table 7. Torsion Angles(°)

atom	atom	atom	atom	angle	atom	atom	atom	atom	angle
O(1)	C(9)	C(8)	C(7)	-179.3(2)	O(1)	C(9)	C(10)	C(11)	176.7(2)
O(2)	C(4)	C(3)	C(2)	0.5(3)	O(2)	C(4)	C(3)	C(16)	179.9(2)
O(2)	C(4)	C(5)	C(6)	2.9(3)	O(2)	C(4)	C(5)	C(14)	-176.3(2)
O(3)	C(15)	C(14)	N(2)	3.5(3)	O(3)	C(15)	C(14)	C(5)	-175.6(2)
O(3)	C(15)	C(16)	N(1)	-2.9(4)	O(3)	C(15)	C(16)	C(3)	179.3(2)
N(1)	C(1)	C(2)	C(3)	-0.4(2)	N(1)	C(16)	C(3)	C(2)	-0.2(2)
N(1)	C(16)	C(3)	C(4)	-179.8(2)	N(1)	C(16)	C(15)	C(14)	177.7(2)
N(2)	C(13)	C(12)	C(6)	-55.9(2)	N(2)	C(14)	C(5)	C(4)	175.4(2)
N(2)	C(14)	C(5)	C(6)	-3.8(3)	N(2)	C(14)	C(15)	C(16)	-177.1(2)
C(1)	N(1)	C(16)	C(3)	0.0(2)	C(1)	N(1)	C(16)	C(15)	-178.1(2)
C(1)	C(2)	C(3)	C(4)	179.9(2)	C(1)	C(2)	C(3)	C(16)	0.4(2)
C(2)	C(1)	N(1)	C(16)	0.2(2)	C(2)	C(3)	C(4)	C(5)	-179.5(2)
C(2)	C(3)	C(16)	C(15)	178.0(2)	C(3)	C(4)	C(5)	C(6)	-177.2(2)
C(3)	C(4)	C(5)	C(14)	3.7(3)	C(3)	C(16)	C(15)	C(14)	-0.1(3)
C(4)	C(3)	C(16)	C(15)	-1.6(3)	C(4)	C(5)	C(6)	C(7)	46.9(2)
C(4)	C(5)	C(6)	C(11)	-78.3(2)	C(4)	C(5)	C(6)	C(12)	162.2(2)
C(4)	C(5)	C(14)	C(15)	-5.7(3)	C(5)	C(4)	C(3)	C(16)	0.0(3)
C(5)	C(6)	C(7)	C(8)	-133.1(2)	C(5)	C(6)	C(11)	C(10)	130.6(2)
C(5)	C(6)	C(12)	C(13)	48.2(2)	C(5)	C(14)	N(2)	C(13)	-3.5(3)
C(5)	C(14)	C(15)	C(16)	3.8(3)	C(6)	C(5)	C(14)	C(15)	175.2(2)
C(6)	C(7)	C(8)	C(9)	5.5(3)	C(6)	C(11)	C(10)	C(9)	-0.1(3)
C(7)	C(6)	C(5)	C(14)	-133.9(2)	C(7)	C(6)	C(11)	C(10)	5.0(3)
C(7)	C(6)	C(12)	C(13)	167.8(2)	C(7)	C(8)	C(9)	C(10)	0.2(3)
C(8)	C(7)	C(6)	C(11)	-7.7(3)	C(8)	C(7)	C(6)	C(12)	110.1(2)
C(8)	C(9)	C(10)	C(11)	-2.9(3)	C(10)	C(11)	C(6)	C(12)	-110.6(2)
C(11)	C(6)	C(5)	C(14)	100.9(2)	C(11)	C(6)	C(12)	C(13)	-72.8(2)
C(12)	C(6)	C(5)	C(14)	-18.6(3)	C(12)	C(13)	N(2)	C(14)	33.3(3)
C(13)	N(2)	C(14)	C(15)	177.4(2)					

Table 8. Non-bonded Contacts out to 3.60 Å

atom	atom	distance	ADC	atom	atom	distance	ADC
O(1)	N(1)	2.774(2)	55404	O(1)	N(2)	3.506(2)	54602
O(1)	C(13)	3.521(3)	54602	O(1)	C(1)	3.595(3)	55404
O(2)	N(2)	2.929(2)	65501	O(2)	C(13)	3.310(3)	65501
O(2)	C(1)	3.420(3)	66703	O(2)	C(7)	3.580(2)	65703
O(3)	C(2)	3.179(2)	45501	O(3)	C(16)	3.423(3)	56703
O(3)	C(15)	3.424(3)	56703	O(3)	O(3)	3.569(4)	56703
O(3)	N(1)	3.572(2)	56703	C(1)	C(4)	3.563(3)	66703
C(2)	C(2)	3.214(4)	66703	C(2)	C(3)	3.320(3)	66703
C(2)	C(8)	3.419(3)	65703	C(3)	C(8)	3.516(3)	65703

The ADC (atom designator code) specifies the position of an atom in a crystal. The 5-digit number shown in the table is a composite of three one-digit numbers and one two-digit number: TA (first digit) + TB (second digit) + TC (third digit) + SN (last two digits). TA, TB and TC are the crystal lattice translation digits along cell edges a, b and c. A translation digit of 5 indicates the origin unit cell. If TA = 4, this indicates a translation of one unit cell length along the a-axis in the negative direction. Each translation digit can range in value from 1 to 9 and thus ±4 lattice translations from the origin (TA=5, TB=5, TC=5) can be represented.

The SN, or symmetry operator number, refers to the number of the symmetry operator used to generate the coordinates of the target atom. A list of symmetry operators relevant to this structure are given below.

For a given intermolecular contact, the first atom (origin atom) is located in the origin unit cell and its position can be generated using the identity operator (SN=1). Thus, the ADC for an origin atom is always 55501. The position of the second atom (target atom) can be generated using the ADC and the coordinates of the atom in the parameter table. For example, an ADC of 47502 refers to the target atom moved through symmetry operator two, then translated -1 cell translations along the a axis, +2 cell translations along the b axis, and 0 cell translations along the c axis.

An ADC of 1 indicates an intermolecular contact between two fragments (eg. cation and anion) that reside in the same asymmetric unit.

Symmetry Operators:

(1)	X,	Y,	Z	(2)	1/2-X,	1/2+Y,	1/2-Z
(3)	-X,	-Y,	-Z	(4)	1/2+X,	1/2-Y,	1/2+Z

Table 9. Least Squares Planes

Plane number 1

Atoms defining plane	Distance
O(1)	-0.020(2)
C(6)	-0.060(2)
C(7)	0.034(2)
C(8)	0.013(2)
C(9)	0.012(2)
C(10)	0.040(2)
C(11)	0.008(2)

Plane number 2

Atoms defining plane	Distance
N(2)	-0.043(3)
C(5)	0.041(3)
C(6)	-0.039(3)
C(13)	0.036(3)
C(14)	-0.004(3)
Additional Atoms	**Distance**
C(12)	-0.636
C(11)	1.319

Plane number 3

Atoms defining plane	Distance
O(2)	-0.004(2)
O(3)	0.011(3)
C(3)	-0.009(3)
C(4)	0.006(3)
C(5)	0.031(3)
C(14)	-0.035(3)
C(15)	-0.010(3)
C(16)	0.0006(9)
Additional Atoms	**Distance**
N(1)	-0.020
N(2)	-0.107
C(2)	-0.042
C(6)	0.113

Plane number 4

Atoms defining plane	Distance
N(1)	0.000(2)
C(1)	0.002(3)
C(2)	-0.002(3)
C(3)	0.002(3)
C(16)	-0.0001(9)
Additional Atoms	**Distance**
C(4)	-0.001
C(15)	-0.039

Plane number 5

Atoms defining plane	Distance
N(1)	-0.005(2)
N(2)	-0.036(3)
C(1)	-0.064(3)
C(2)	-0.085(3)
C(3)	-0.029(3)
C(4)	-0.022(3)
C(5)	0.035(3)
C(6)	0.110(3)
C(13)	-0.129(3)
C(14)	0.005(3)
C(15)	0.039(3)
C(16)	0.0168(9)
Additional Atoms	**Distance**
C(12)	0.615

Summary

plane	mean deviation	χ^2
1	0.0266	1663.1
2	0.0325	697.4
3	0.0131	297.2
4	0.0012	1.4
5	0.0479	5612.5

Dihedral angles between planes (°)

plane	1	2	3	4
2	74.08			
3	102.21	174.72		
4	101.04	173.75	1.18	
5	103.16	176.30	1.60	2.56