Table I. Photostimulated Reaction of Haloarenes with 1-Methyl-2-pyrrolidinone Enolate Ions 2 in Liquid Ammonia[a]

expt	ArX	hν, min	products,[b] % X⁻	3	4
1	PhI	60	85	60[c]	7
2[d]	PhI	180	90	60	6
3[e]	PhI	180	87	*f*	40[c]
4	PhBr	60	85	51	2
5	PhBr	60[g]	5		
6	PhCl	60	80	52	1
7	*p*-IAn[h]	60	80	58[i]	2[j]
8	1-INaph[k]	60	*l*	40[m]	

[a] 15 mmol of 2 and 1 mmol of ArX were dissolved in 300 mL of liquid ammonia, unless otherwise indicated. [b] Determined by GLC unless otherwise indicated. [c] Isolated yield. [d] 8% yield of iodobenzene remained. [e] 10 mmol of 2 and 5 mmol of PhI. [f] Not determined. [g] Dark reaction. [h] *p*-IAn = *p*-iodoanisole. [i] 1-Methyl-3-(*p*-anisyl)-2-pyrrolidinone. [j] 1-Methyl-3,3-(di-*p*-anisyl)-2-pyrrolidinone. [k] 1-INaph = 1-iodonaphthalene. [l] The reaction was quenched with methyl iodide, and 45% yield of naphthalene was found. [m] 1-Methyl-3-(1-naphthyl)-3-methyl-2-pyrrolidinone.

flask was draped with aluminum foil.

Photostimulated Reactions of 1-Methyl-2-pyrrolidinone Enolate Ion 2 with *p*-Iodoanisole. The procedure was similar to the previous reaction. After flash chromatography 1-methyl-3-(*p*-anisyl)-2-pyrrolidinone was isolated as a yellow oil. ^{1}H NMR, mass, and IR spectra were similar to those reported.[13] Also isolated was a yellow oil whose spectral analyses probably indicate the disubstitution product 1-methyl-3,3-(di-*p*-anisyl)-2-pyrrolidinone (2%): MS, *m/e* (rel intensity) 311 (M^+ 56), 254 (50), 252 (90), 223 (100), 165 (37), 145 (44), 115 (44).

Photostimulated Reactions of 1-Methyl-2-pyrrolidinone Enolate Ion 2 with 1-Iodonaphthalene (5). The procedure was similar to the previous reaction. After flash chromatography naphthalene (40% yield) and 1-methyl-3-hydroxy-3-(1-naphthyl)-2-pyrrolidinone were isolated. The substitution product consisted of white crystals, mp 202–204 °C; ^{1}H NMR δ 1.10–1.41 (m, 1 H), 2.60–2.85 (m, 2 H), 3.08 (s, 3 H), 3.16–3.50 (m, 2 H), 7.10–8.52 (m, 7 H); ^{13}C NMR δ 175.31, 136.74, 134.72, 130.59, 129.06, 128.86, 126.05, 125.76, 125.41, 124.13, 123.64, 79.9, 45.67, 35.52, 30.06; IR (NaCl, cm^{-1}) 3279, 2945, 1878, 1399, 1264, 1113, 780, 708; MS, *m/e* (rel intensity) 241 (M^+ 75), 183 (33), 169 (41), 155 (81), 127 (100), 115 (14), 86 (27), 58 (43), 44 (75). Anal. Calcd for $C_{15}H_{15}O_2N$: C, 74.67; H, 6.27. Found: C, 74.42; H, 6.45. We performed a reaction similar to the previous one, but the ammonia was allowed to evaporate under nitrogen, and the residue was dissolved in dichloromethane and chromatographed on silica gel eluted with diethyl ether by using a Chromatotrom, and 1-methyl-3-(1-naphthyl)-2-pyrrolidinone together with a small amount of the oxidized product 6 were isolated, mp 137–139 °C; MS, *m/e* (rel intensity) 225 (M^+ 89), 168 (54), 167 (68), 153 (100), 139 (12), 58 (18), 42 (18); ^{1}H NMR δ 1.85–2.85 (m, 2 H), 3.05 (s, 3 H), 3.40–4.60 (m, 3 H), 7.25–810 (m, 7 H). We performed a reaction similar to the previous one, except that this was quenched with methyl iodide. After flash chromatography naphthalene (45% yield) and 1-methyl-3-(1-naphthyl)-3-methyl-2-pyrrolidinone were isolated, mp 91–93 °C; ^{1}H NMR (CCl_4) δ 1.65 (s, 3 H), 2.42–2.59 (m, 2 H), 2.85 (s, 3 H), 3.02–3.29 (m, 2 H), 7.18–8.05 (m, 7 H), MS, *m/e* (relative intensity) 239 (M^+ 21), 224 (3), 182 (10), 167 (24), 152 (26), 112 (19), 96 (14), 82 (21), 58 (91), 44 (100); IR (NaCl, cm^{-1}) 3045, 2932, 2875, 1682, 1598, 1503; 1455; 1400, 1273, 780, 700.

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Registry No. 1, 872-50-4; 3, 54520-82-0; 4, 20538-39-0; 5, 90-14-2; 6, 123074-45-3; 7, 123074-44-2; PhI, 591-50-4; PhBr, 108-86-1; PhCl, 108-90-7; *p*-IC_6H_4OMe, 696-62-8; 1-methyl-3-(*p*-anisyl)-2-pyrrolidinone, 107770-12-7; 1-methyl-3,3-(di-*p*-anisyl)-2-pyrrolidinone, 123074-43-1; naphthalene, 91-20-3; 1-methyl-3-(1-naphthyl)-2-pyrrolidine, 123074-46-4.

Synthesis of a Truncated A-Unit Analogue for CC-1065[1]

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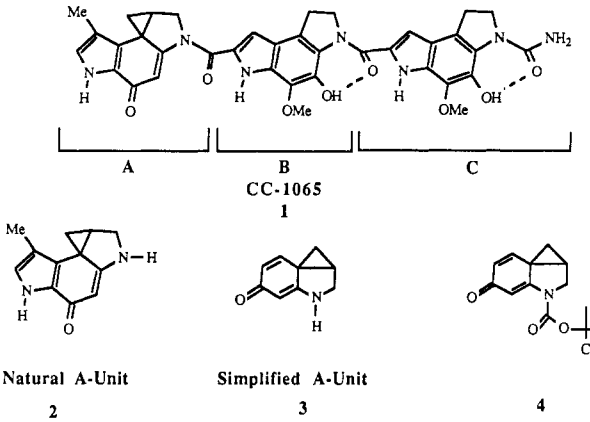
The antibiotic CC-1065 (1) is one of the most active yet toxic antitumor natural products known,[2] and considerable efforts have been directed toward the synthesis of less toxic analogues containing modified B and C units.[3] Since the cyclopropanedienone of the natural A unit 2 is essential for biological activity, our current goal is to synthesize analogues of CC-1065 derived from modified A units. We now report the first synthesis of the parent truncated A-unit dienone 3 from 6-methoxyindole via its acyl derivative 4.[4]



The synthesis of 3 starts from 6-methoxyindole (5),[5] which was converted to 6-methoxygramine (6) by a Mannich reaction with aqueous dimethylamine and formalin in acetic acid (90%) (Scheme I). Methylation of 6 with methyl iodide in benzene gave 6-methoxygramine methiodide (7, 99%),[6] which was converted to nitrile 8 (NaCN, EtOH, reflux, 73%), followed by hydrolysis to acid 9 (NaOH, EtOH, reflux, 80%). The acid 9 was converted to the ester 10 (absolute MeOH, CSA, 99%), which was smoothly reduced with sodium cyanoborohydride in acetic acid,[7] followed by immediate protection with TCBOC-Cl[8] to give the crystalline carbamate 11 (74% yield from indole

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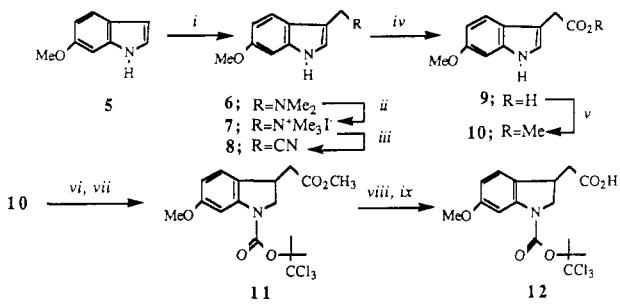
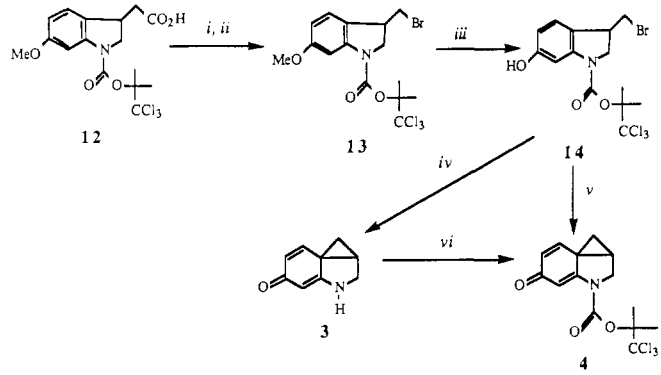
Scheme I[a]



[a] Reagents: (i) $NHMe_2$, CH_2O, AcOH, O °C; (ii) MeI, benzene; (iii) NaCN, EtOH, reflux, N_2; (iv) NaOH, EtOH, reflux, N_2; (v) absolute MeOH, CSA, room temperature; (vi) $NaCNBH_3$, AcOH, room temperature N_2; (vii) TCBOC-Cl, DMAP (cat.), CH_3CN, N_2; (viii) NaOH aq (5%), MeOH; (ix) H_2O, H^+.

Scheme II[a]



[a] Reagents: (i) ClCOCOCl, benzene, room temperature, N_2, 30 min; (ii) 2-mercaptopyridine *N*-oxide, sodium salt, DMAP, CBr_4, benzene, reflux, N_2; (iii) BCl_3·SMe_2, 1,2-dichloroethane, reflux, N_2; (iv) di-2-thienyl ditelluride, $NaBH_4/H_2O$/NaOH, THF, 60 °C; (v) NaOH, H_2O, THF, pH 12.0, 60 °C; (vi) TCBOC-Cl, DMAP, CH_3CN, room temperature.

ester **10**). This compound was hydrolyzed (5% NaOH, MeOH, 40 °C) to the free acid **12**.

At this stage we were set to attempt a Hunsdiecker-type reaction to remove the additional carbon atom and provide a leaving group. Of the procedures available, we selected the Barton protocol.[9] Compound **12** was converted to its acid chloride (ClCOCOCl, benzene, 25 °C), which was directly reacted with the sodium salt of 2-mercaptopyridine *N*-oxide, DMAP, and CBr_4 in refluxing benzene to furnish the bromide **13** (80%) (Scheme II). The bromide **13** was demethylated with boron trichloride–dimethyl sulfide[10] in refluxing 1,2-dichloroethane to furnish bromo phenol **14** (70%). At this stage **14** was set up for the crucial Ar_3-1-type Winstein cyclization.[11,12] We failed to achieve the attempted cyclization with Hunig's base, as well as with triethylamine/water/acetonitrile[13] at room temperature. A variety of other methods were attempted[14] without success but, surprisingly, upon deprotection of the *N*-TCBOC of **14** at 60 °C (di-2-thienyl ditelluride, $NaBH_4$/THF/NaOH),[15] the desired cyclopropanedienone **3** (62%) was obtained. The intermediate *N*-TCBOC derivative **4**, which could be prepared by direct acylation of **3** (TCBOC-Cl, DMAP, CH_3CN, 58%), could be isolated by cyclization of **14** with sodium hydroxide in warm THF (10 mmol of NaOH, pH 12.0, 60 °C, 81%).

The successful acylation of **3** to **4** indicates that **3**, unlike the natural A unit **2**,[3] will be a useful synthon for the synthesis of a number of CC-1065 analogues.

Experimental Section

General. All melting points are uncorrected. All NMR spectra were recorded in $CDCl_3$ unless stated otherwise. The chemical shifts are referenced against TMS as an internal standard (δ = 0). All IR spectra are run as Nujol mulls unless stated otherwise. Elemental analyses (C, H, N) were carried out by Atlantic Microlabs, Atlanta, GA.

6-Methoxygramine 3-Methiodide (7). To a chilled solution of dimethylamine (40% aqueous, 21.85 mL, 191 mmol) and formalin (37% aqueous, 9.8 mL, 125 mmol) in glacial acetic acid was added 6-methoxyindole (**5**) (18.44 g, 121 mmol) in three equal portions, at 0 °C. After being warmed to room temperature and stirred for 4 h, the solution was poured into ice water (500 mL) and basified to pH 12 with 50% NaOH. Crude 6-methoxygramine was extracted with ether (3 × 150 mL), dried (Na_2SO_4), and concentrated. The gramine **6** was used without further purification. Methyl iodide (20 mL, excess) was added to a benzene (400 mL) solution of 6-methoxygramine (**6**) and placed in the dark overnight. The methiodide was filtered, dried under vacuum, and crystallized from benzene to yield 6-methoxygramine methiodide (**7**) (39.6 g, 91.5% from 6-methoxyindole (**5**)): ^1H NMR (DMSO-d_6) δ 3.36 (s, 9 H, N[CH_3]$_3$), 3.78 (s, 3 H, OCH_3), 4.62 (s, 2 H), 6.80 (dd, 1 H, J = 1.8, 8.7 Hz), 6.91 (d, 1 H, J = 1.9 Hz), 11.40 (br s, 1 H); IR (Nujol, cm^{-1}) 3300 (br), 1625, 1565, 1515, 1480, 1453, 1405, 1370, 1340, 1299, 1260, 1200, 1150, 1095, 1070, 1020, 990, 970, 940, 870, 845, 835, 825. Anal. Calcd for $C_{13}H_{19}N_2OI$: C, 45.09; H, 5.53. Found: C, 45.21; H, 5.54.

6-Methoxy-1*H*-indole-3-acetonitrile (8). A solution of 6-methoxygramine methiodide (**7**) (28.2 g, 81.4 mmol), sodium cyanide (8.09; 163 mmol), and ethanol (95%, 600 mL) was refluxed under nitrogen until no more trimethylamine evolved (ca. 24 h). The cooled solution was concentrated and chromatographed (methylene chloride/hexanes, 2:1) to yield 6-methoxy-1*H*-indole-3-acetonitrile (**8**) (12.58 g, 82.9%), which crystallized from absolute ethanol, mp 105 °C: ^1H NMR δ 3.80 (s, 2 H), 3.85 (s, 3 H, OCH_3), 6.83 (d, 1 H, J = 2.1 Hz), 6.88 (s, 1 H), 7.11 (d, 1 H, J = 8.6 Hz), 7.45 (dd, 1 H, J = 2.0, 8.5 Hz), 8.1 (br s, 1 H); IR (cm^{-1}) 3340, 2240, 1625, 1580, 1550, 1500, 1410, 1340, 1295, 1260, 1195, 1165, 1145, 1100, 1070, 1060, 1030, 955, 940, 825, 810, 700, 665, 620, 600; MS (EI) m/e (relative intensity) 187 (M + 1, 9.5), 186 (M^+, 68.4), 172 (10.7), 171 (100.0), 160 (8.2), 144 (5.2), 143 (36.1), 142 (11.1), 117 (5.6), 116 (13.5), 89 (15.0), 78 (15.2), 77 (48.5), 53 (15.2), 51 (15.2). Anal. Calcd for $C_{11}H_{10}N_2O$: C, 70.95; H, 5.41. Found: C, 70.31; H, 5.37.

6-Methoxy-1*H*-indole-3-acetic Acid (9). A solution of 6-methoxy-1*H*-indole-3-acetonitrile (**8**) (11.8 g, 62.9 mmol), ethanol (95%, 500 mL), water (100 mL), and potassium hydroxide (22.0 g) was refluxed under nitrogen until no more ammonia evolved (ca. 36 h). The cooled solution was concentrated and water (200 mL) was added. The solution was acidified to pH 2 with 10% H_2SO_4. The white solid was filtered, dried, and crystallized from methanol/water to yield 6-methoxy-1*H*-indole-3-acetic acid (**9**) (12.8 g, 98.1%), mp 163 °C: ^1H NMR (DMSO-d_6) δ 3.38 (s, 2 H), 3.74 (s, 3 H, OCH_3), 6.63 (dd, 1 H, J = 2.2, 8.6 Hz), 6.84 (d, 1 H, J = 2.0 Hz), 7.07 (s, 1 H), 7.35 (d, 1 H, J = 8.6 Hz), 10.7 (br s, 1 H); IR (cm^{-1}) 3380, 3120, 1695, 1630, 1560, 1505, 1420, 1400, 1360, 1350, 1310, 1270, 1250, 1220, 1200, 1160, 1130, 1100, 1065, 1025, 950, 930, 810, 785, 735, 670, 625; MS (EI) m/e (relative intensity) 206 (M + 1, 21.8), 205 (M^+, 100.0), 162 (12.6), 161 (61.5), 160 (88.7), 147 (8.4), 146 (10.9), 145 (18.0), 117 (41.8), 91 (8.4), 90 (30.1), 89 (15.9). Anal. Calcd for $C_{11}H_{11}NO_3$: C, 64.36; H, 5.40. Found: C, 64.86; H, 5.34.

6-Methoxy-1*H*-indole-3-acetic Acid, Methyl Ester (10). A solution of 6-methoxy-1*H*-indole-3-acetic acid (**9**) (10.0 g, 48.7 mmol), camphorsulfonic acid (50 mg), and absolute methanol (250 mL) was stirred until no starting material remained by TLC (ca.

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(14) t-BuO^- K^+/MeOH, room temperature; NH_4OH/MeOH, room temperature; NaOMe/MeOH, room temperature or 60 °C; n-BuLi/THF, -78 °C; t-BuO^- K^+/THF, 60 °C.
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12 h). The volatiles were removed under reduced pressure, and the crude product was chromatographed (methylene chloride/hexane, 2:1) to yield 6-methoxy-1*H*-indole-3-acetic acid, methyl ester (**10**) (9.89 g, 92.5%), which crystallized from benzene, mp 92 °C: ^{1}H NMR δ 3.69 (s, 3 H, CO_2CH_3), 3.74 (s, 2 H), 3.84 (s, 3 H, OCH_3), 6.78 (d, 1 H, J = 8.9 Hz), 6.84 (s, 1 H), 7.05 (d, 1 H, J = 1.5 Hz), 7.48 (d, 1 H, J = 8.7 Hz), 7.95 (br s, 1 H); IR (cm^{-1}) 3340, 1730, 1690, 1620, 1580, 1550, 1455, 1435, 1430, 1410, 1395, 1365, 1300, 1260, 1239, 1190, 1170, 1125, 1080, 985, 980, 925, 895, 790, 725, 630; MS (EI) m/e (relative intensity) 222 (M + 2, 8.1), 221 (M + 1, 18.6), 220 (M$^+$, 89.7), 161 (11.8), 160 (100.0), 145 (32.3), 117 (50.0), 98 (23.7), 89 (13.5). Anal. Calcd for $C_{12}H_{13}NO_3$: C, 65.74; H, 5.98. Found: C, 65.20; H, 6.02.

6-Methoxy-3-(carbomethoxymethyl)-2,3-dihydro-1*H*-indole-1-carboxylic Acid, 2,2,2-Trichloro-1,1-dimethylethyl Ester (11). To a soluion of 6-methoxy-1*H*-indole-3-acetic acid, methyl ester (**10**) (5.71 g, 26.0 mmol) in glacial acetic acid (100 mL) at 15 °C was added sodium cyanoborohydride in 25-mg portions until no starting material remained by TLC. The crude product was poured into water and basified cautiously with aqueous saturated bicarbonate, to pH 7.5–8.0. The indoline was extracted with ether (3 × 150 mL), dried (Na_2SO_4), and concentrated to a pale yellow oil, which was immediately used without purification. The crude indoline was dissolved in acetonitrile (200 mL), cooled in an ice bath, and treated with triethylamine (7.6 mL, 54.9 mmol), 2,2,2-trichloro-1,1-dimethylethyl chloroformate (8.7 g, 36.5 mmol), and 4-(dimethylamino)pyridine (50 mg) for 12 h under a nitrogen atmosphere. The acetonitrile was removed under reduced pressure and the resulting oil was poured into water (400 mL) and extracted with ether (3 × 150 mL). The ethereal layer was washed with 10% H_2SO_4 (2 × 100 mL), dried (Na_2SO_4), concentrated, and chromatographed (methylene chloride/hexanes, 1:1) to yield carbamate **11** (9.8 g, 88.5%), which was crystallized from methanol, mp 97 °C: ^{1}H NMR δ 2.01 (s, 6 H, $[CH_3]_2$), 2.64 (ddd, 2 H, J = 5.1, 8.6, 16.2 Hz, CH_2CH_3), 3.71 (s, 3 H, CO_2CH_3), 3.75 (m, 2 H, CH, $CHCO_2Me$), 3.82 (s, 3 H, OCH_3), 4.3 (dd, 1 H, J = 8.9, 11.1 Hz), 6.54 (dd, 1 H, J = 2.3, 8.3 Hz), 7.02 (d, 1 H, J = 8.2 Hz), 7.49 (s, 1 H); IR (cm^{-1}) 3100, 1740, 1700, 1615, 1600, 1500, 1490, 1465, 1430, 1400, 1370, 1340, 1310, 1280, 1225, 1190, 1165, 1120, 1040, 1000, 890, 860, 815, 800, 760, 740; MS (EI) m/e (relative intensity) 417 (M + 4, 3.1), 415 (M + 2, 12.0), 423 (M$^+$, 9.8), 352 (15.1), 350 (15.8), 265 (10.4), 206 (10.2), 192 (100.0), 161 (11.0), 160 (24.4), 159 (10.8), 148 (42.5), 147 (13.6), 146 (14.7), 132 (14.4), 123 (14.9), 117 (13.5), 89 (19.9), 77 (11.2). Anal. Calcd for $C_{17}H_{20}Cl_3NO_5$: C, 48.09; H, 4.76. Found: C, 48.19; H, 4.83.

6-Methoxy-3-(carboxymethyl)-2,3-dihydro-1*H*-indole-1-carboxylic Acid, 1-(2,2,2-Trichloro-1,1-dimethylethyl ester) (12). To a solution of ester **11** (6.02 g, 14.6 mmol) in methanol (100 mL) was added 1 N sodium hydroxide (20 mL). The solution was stirred until no starting material was present by TLC (ca. 8 h). The reaction was acidified to pH 2 with 10% sulfuric acid and diluted with water (50 mL). The product was extracted with ether (3 × 25 mL), dried (Na_2SO_4), and concentrated to yield **12** (4.1 g, 70.6%), which was crystallized from methanol (mp 111 °C): ^{1}H NMR δ 2.02 (s, 6 H, $[CH_3]_2$), 2.72 (ddd, 2 H, J = 4.8, 8.8, 16.2 Hz, CH_2CO_2H), 3.77 (m, 2 H), 3.82 (s, 3 H, OCH_3), 4.31 (dd, 1 H, J = 8.9, 11.0 Hz), 6.56 (dd, 1 H, J = 2.3, 8.3 Hz), 7.05 (d, 1 H, J = 8.3 Hz), 7.50 (s, 1 H); IR (cm^{-1}) 2600–2400 (b), 1715, 1700, 1600, 1595, 1495, 1480, 1450, 1430, 1390, 1380, 1300, 1275, 1235, 1200, 1160, 1125, 1115, 1030, 930, 890, 860, 820, 790, 730, 660; MS (EI) m/e (relative intensity) 413 (M + 4, 4.1) 411 (M + 2, 13.0), 409 (M$^+$, 11.8), 352 (5.1), 350 (5.8), 251 (10.4), 193 (10.2), 192 (100.0), 161 (11.0), 160 (14.4), 159 (10.8), 148 (42.5), 147 (13.6), 146 (14.7), 132 (14.4), 123 (14.9), 117 (13.5), 89 (19.9), 77 (11.2). Anal. Calcd for $C_{16}H_{18}Cl_3NO_5$: C, 46.79; H, 4.42. Found: C, 46.34; H, 4.39.

6-Methoxy-3-(bromomethyl)-2,3-dihydro-1*H*-indole-1-carboxylic Acid, 2,2,2-Trichloro-1,1-dimethylethyl Ester (13). To a solution of acid **12** (1.61 g, 3.92 mmol), DMF (3 drops), and benzene (100 mL) was added oxalyl chloride (4.4 mL, 3.95 mmol). After being stirred for 30 min, the yellow-brown solution of acid chloride was evaporated to dryness in vacuo. To the resulting brownish oil were added 2-mercaptopyridine *N*-oxide, sodium salt (780 mg, 4.6 mmol), 4-(dimethylamino)pyridine (25 mg), carbon tetrabromide (5.0 g, 10 mmol), and benzene (50 mL). The solution was evacuated and purged with nitrogen (3×) and was heated to reflux for 4 h. The cooled solution was filtered and concentrated in vacuo. The crude product was chromatographed (methylene chloride/hexanes, 1:1) to yield the bromide **13**, which crystallized from methanol/water (mp 136 °C, 1.4 g, 80.0%): ^{1}H NMR δ 2.02 (s, 6 H, $[CH_3]_2$), 3.37 (t, 2 H, J = 9.4 Hz), 3.71 (m, 1 H), 3.82 (s, 3 H, OCH_3), 4.02 (dd, 1 H, J = 4.8, 12.0 Hz), 4.22 (dd, 1 H, J = 9.3, 11.9 Hz), 6.56 (dd, 1 H, J = 2.2, 8.2 Hz), 7.09 (d, 1 H, J = 8.2 Hz), 7.49 (s, 1 H); IR (cm^{-1}) 1720, 1600, 1490, 1390, 1380, 1370, 1350, 1340, 1290, 1250, 1210, 1150, 1030, 880, 830, 800, 770, 720; MS (EI) m/e (relative intensity) 449 (M + 4, 2.6), 447 (M + 2, 10.1), 446 (M + 1, 3.3), 445 (M$^+$, 11.4), 443 (6.2), 287 (10.3), 285 (9.9), 193 (11.0), 192 (100.0), 162 (9.2), 161 (27.5), 160 (53.8), 159 (13.4), 148 (24.2), 125 (9.9), 12 (17.2), 117 (14.8), 91 (10.1), 89 (17.0), 87 (11.7), 78 (8.6), 57 (8.2). Anal. Calcd for $C_{15}H_{17}BrCl_3NO_3$: C, 40.41; H, 3.85. Found: C, 40.81; H, 3.82.

6-Hydroxy-3-(bromomethyl)-2,3-dihydro-1*H*-indole-1-carboxylic Acid, 2,2,2-Trichloro-1,1-dimethylethyl Ester (14). To a solution of the bromide **13** (1.0 g, 2.24 mmol) in 1,2-dichloroethane (50 mL) was added boron trichloride–dimethyl sulfide complex (1.5 g, excess) in 5 portions. The solution was refluxed until no starting material remained (ca. 14 h). The cooled solution was poured into water (100 mL), and the crude product was extracted with methylene chloride (3 × 100 mL), dried (Na_2SO_4), concentrated, and chromatographed (methylene chloride/ether, 10:1) to yield phenol **14** (80 mg, 83.0%) as a pale brown solid, mp 165 °C: ^{1}H NMR δ 2.02 (s, 6 H, $[CH_3]_2$), 3.40 (dd, 1 H, J = 4, 9.2 Hz), 3.70 (m, 1 H), 3.95 (dd, 1 H, J = 4.8, 9.3 Hz), 4.15 (dd, 1 H, J = 9.2, 9.5 Hz), 5.1 (br s, 1 H, O*H*), 6.50 (dd, 1 H, J = 1.9, 7.8 Hz), 7.06 (d, 1 H, J = 7.5 Hz), 7.38 (s, 1 H); IR (cm^{-1}) 3300, 1690, 1620, 1610, 1615, 1500, 1400, 1380, 1360, 1310, 1270, 1200, 1170, 1160, 1140, 900, 860, 840, 820, 810, 780, 740, 715, 670; MS (EI) m/e (relative intensity) 435 (M + 4, 1.2), 433 (M + 2, 3.3), 431 (M$^+$, 9.9), 397 (1.5), 396 (2.8), 351 (6.7), 253 (9.0), 178 (3.0), 177 (14.4), 174 (12.3), 146 (100.0), 145 (22.8), 134 (17.8), 133 (72.5), 125 (29.7), 124 (12.9), 123 (20.2), 122 (43.2), 118 (10.8), 105 (6.5), 91 (8.2), 89 (8.6), 86 (17.0), 53 (12.7). Anal. Calcd for $C_{14}H_{15}Cl_3NO_3Br$: C, 38.97; H, 3.5. Found: C, 39.10; H, 3.54.

1a,2,3,5-Tetrahydro-1*H*-cycloprop[*c*]indol-5-one (3). A solution of phenol **14** (120 mg, 0.27 mmol), anhydrous tetrahydrofuran (20 mL), and di-2-thienyl ditelluride (50 mg, 0.1 mmol) was warmed to 50 °C. The red solution was treated with an aqueous $NaBH_4$ solution (20%, 2–3 mL containing 3 drops of 20% NaOH, under a nitrogen atmosphere) until a yellow color persisted. The solution was cooled and oxidized with air (red color). The mixture was evaporated to dryness in vacuo. The resulting solid was treated with water and hexane and was filtered. The remaining solid was crystallized from methylene chloride/hexane to give a white solid (mp 79 °C, 24.8 mg, 62.0%): ^{1}H NMR δ 1.49 (m, 1 H), 1.60 (dd, 2 H, J = 2.4, 2.6 Hz), 2.0 (m, 2 H), 3.6 (s, 1 H), 6.14 (d, 1 H, J = 5.0 Hz), 6.92 (dd, 1 H, J = 5.1, 5.3 Hz), 7.43 (d, 1 H, J = 4.9 Hz); IR (cm^{-1}) 3450, 1695; MS (EI) m/e (relative intensity) 148 (M + 1, 0.6), 147 (M$^+$, 68.2), 146 (18.2), 120 (11.8), 119 (10.1), 91 (8.2); UV/vis (EtOH) λ_{max} = 320. Anal. Calcd for C_9H_9NO: C, 73.45; H, 6.16; N, 9.52. Found: C, 73.55; H, 6.19; N, 9.47.

2,2,2-Trichloro-1,1-dimethylethyl Ester Derivative 4. Method 1. A solution of dienone **3** (11.1 mg, 0.075 mmol), 2,2,2-trichloro-1,1-dimethylethyl chloroformate (23.2, 0.076 mmol), and 4-(dimethylamino)pyridine (25 mg) was stirred under a nitrogen atmosphere for 6 h. The resulting solution was concentrated, dissolved in methylene chloride, washed with water, and dried (Na_2SO_4). The organic layer was concentrated and chromatographed (triethylamine-treated SiO_2, 10:1 CH_2Cl_2/Et_2O) to yield **4** (18.8 mg, 58%) as a colorless oil. **Method 2.** A solution of phenol **14** (50 mg, 0.11 mmol) in THF/H_2O (1:1, 10 mL) was treated with NaOH (pH 12.0) and refluxed under a nitrogen atmosphere for 2 h. The resulting solution was concentrated and chromatographed (triethylamine-treated SiO_2, 10:1 CH_2Cl_2/Et_2O) to yield **4** (40.6 mg, 81.3%) as a colorless oil: ^{1}H NMR δ 1.29 (d, 2 H, J = 6.2 Hz), 1.75 (s, 6 H), 2.09 (m, 2 H), 3.80 (m, 1 H), 6.49 (d, 1 H, J = 7.9 Hz), 6.96 (d, 1 H, J = 8.3 Hz), 7.31 (br s, 1 H); IR (cm^{-1}) 1700, 1690, 1600, 1500, 1380, 1310; MS (EI) m/e (relative intensity) 353 (M + 2, 3.7), 351 (M$^+$, 6.4), 319 (17.8), 317 (19.4), 194 (13.8), 193 (69.2), 179 (12.9), 178 (100.0), 176 (21.7), 149 (11.4), 148 (30.7), 146 (14.1), 134 (47.9), 133 (18.3), 132 (10.6), 131 (10.2); UV/vis (EtOH) λ_{max} = 305.

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Registry No. 3, 123380-94-9; 4, 123380-95-0; 5, 3189-13-7; 6, 62467-65-6; 7, 123380-86-9; 8, 23084-35-7; 9, 103986-22-7; 10, 123380-87-0; 11, 123380-90-5; 12, 123380-90-5; 12 acid chloride, 123380-91-6; 13, 123380-92-7; 14, 123380-93-8; CC-1065, 69866-21-3; TCBOC-Cl, 66270-36-8; methyl 6-methoxy-2,3-dihydro-1*H*-indole-3-acetate, 123380-88-1.

Aggregate Structure and Ligand Location Strongly Influence Cu^{2+} Binding Ability of Cationic Metallosurfactants

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Transition-metal metallosurfactants have recently been reported as being effective agents for electron storage,[1] dioxygen complexation,[2] amplification of chemical signals,[3] and catalysis in the cleavage of phosphoric[4] or carboxylic acid[5] esters. On the other hand, aggregates of synthetic surfactants (micelles and, particularly, vesicles) have been investigated with increasing regularity as models of biological membranes.[6] Transition-metal cations permeation across biological membranes is of primary importance, since these ions are involved in several catalytic processes.[7] In this respect, it appears highly relevant to investigate the effect of the aggregate structure and ligand location on the ability of ligand surfactants to bind transition-metal ions. This issue, in particular for Cu^{2+} cations, is addressed in the present paper.

Results and Discussion

For the purposes of this study, we investigated the properties of ligand surfactants with a moderate binding constant for Cu^{2+} ions, and whose complex formation could be easily detected. Accordingly, ligands **1**–**4** were synthesized. They contain the same ligand moiety and cationic headgroup, two thioethereal functions that allow easy spectroscopic monitoring of Cu^{2+} complexation,[8] and only differ in the length of the hydrocarbon chains. The synthetic strategy is outlined in Scheme I.

Ligand **1** is rather soluble in water, where it does not form aggregates, and was synthesized as a reference model. Compound **2** forms micelles[9] (cmc = 7.5×10^{-5} M) and surfactants **3** and **4** form, upon sonication, vesicles[10] (average size as determined by dynamic light scattering measurements and gel-to-liquid crystal phase transition temperature, T_c, were 510 Å, 28 °C and 625 Å, 40 °C, respectively). Inspection of CPK models suggests that, *in the aggregates*, the ligand moiety of the surfactants is located in a hydrophobic region of the organized assembly. The Cu^{2+} binding constants, K_b, of the different ligands have been determined by following the increase in the absorbance of the complex (310–390 nm) upon addition of the ligand to a $Cu(NO_3)_2$ solution (see Experimental Section). The K_b values have been evaluated in two different environments, namely, in CH_3OH, where no aggregates are formed, and in aqueous buffer (4-morpholinoethanesulfonic acid buffer, MES, pH = 6.3) where ligands **2**–**4** form aggregates. The K_b measurements

Scheme I

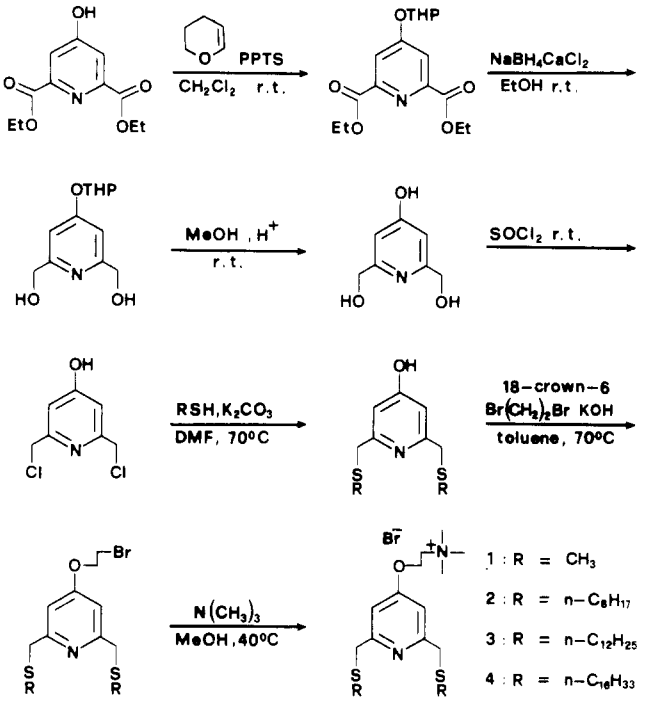

Table I. $Cu(NO_3)_2$ Binding Constants[a] of Surfactants 1–6 in CH_3OH[b] and H_2O (0.05 M MES Buffer, pH = 6.3)

entry	ligand	aggregate structure in H_2O	log K_b	
			H_2O	CH_3OH[b]
1	1	no aggregates	4.7	4.6
2	2	micelles	3.7	4.7
3	2 (1:5 with CTABr)	micelles	2.8	
4	2 (1:10 with CTABr)	micelles	2.7	
5	2 (1:20 with CTABr)	micelles	2.7	
6	3	vesicles	no binding[c]	4.9
7	3 (1:20 with CTABr)	micelles	2.5	
8	4	vesicles	no binding[c]	4.6
9	4 (1:20 with CTABr)	micelles	2.6	
10	5	micelles	3.7	4.7
11	6	vesicles	3.6	

[a] At 25 °C; see the Experimental Section for binding constant determination. [b] With 5% water added. [c] See ref 13.

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