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Preparation of 2-Substituted Pyrroles and Indoles by Regioselective Alkylation and Deprotection of 1-(2-Trimethylsilylethoxymethyl)pyrrole and 1-(2-Trimethylsilylethoxymethyl) indole.

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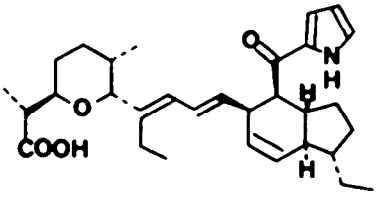
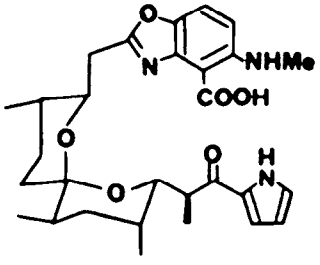
Abstract: After N-alkylation of pyrrole and indole with 2-trimethylsilylethoxymethyl chloride the products of the reaction could be regioselectively deprotonated with n-butyllithium at the 2-position. Reaction of the resulting anions with acid chlorides, lactones, silyl chlorides or aldehydes gave addition products, some of which were deprotected to the parent pyrrole or indole using anhydrous tetra-n-butylammonium fluoride.

Various natural products, for example, indanomycin (X-14547A) (1) and calcimycin (A-23187) (2) contain a 2-acylpyrrole unit. While there are several excellent methods in the literature[1-9] for the introduction of this group, not all are compatible with complex natural product synthesis.



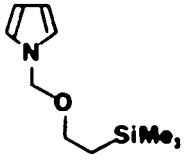
(1)



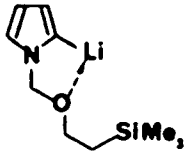
(2)

During our work on the total synthesis of (1) we needed to introduce the 2-acylpyrrole group by means of a ring opening reaction of a lactone with a suitably protected 2-lithiopyrrole anion.[10] The pyrrole protecting group had to be sufficiently robust to withstand subsequent synthetic steps yet be removed under mild conditions such that there would be no epimerisation of any of the carefully introduced chiral centres.

Since existing literature procedures were considered unsatisfactory we chose to study the use of 2-trimethylsilylethoxymethyl (SEM) as a nitrogen protecting group for pyrrole as in compound (3). We reasoned that this group would facilitate deprotonation at the 2-position via the chelated species (4) and permit reaction with electrophilic species, yet be easily removable at the end of the reaction sequence. Here we report full details and further examples of our study in this area together with related chemistry of SEM-indole (5)[6,11].



(3)



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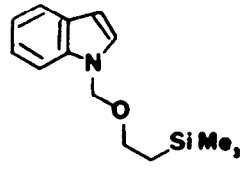


(5)

Results and Discussion

Although SEM had not been previously used as a protecting group for nitrogen it was readily introduced by treating pyrrole with sodium hydride in dimethylformamide (DMF)/ dimethylsulphoxide (DMSO) followed by reaction with SEM-chloride[12]. Previously we showed that SEM-pyrrole (3) could be regioselectively deprotonated at the 2-position using n-butyllithium in dimethoxyethane (DME) at 0°C and reacted with the appropriate lactone for the indanomycin synthesis.[10]

Subsequent to our initial publication of the above results Muchowski[6] reported the preparation of both SEM-pyrrole and SEM-indole and in an isolated example attempted deprotonation using t-butyllithium in hexane at -10°C with poor results. During our early studies we also noticed that the use of t-BuLi, s-BuLi, LDA, KDA and LTMP in solvents such as ether and THF with HMPA and TMEDA were inferior to our published nBuLi/DME Method.

In Table 1 we report several additional examples of the reaction of 2-lithio-SEM-pyrrole with various electrophiles such as acyl chlorides, silyl chlorides, lactones and aldehydes to give reasonable yields of the corresponding addition products (6) - (11). Prompted by these encouraging results we have also studied the related preparation of SEM-indole (5) and its selective deprotonation at the 2-position. SEM-indole (5) was obtained in 98% yield in a similar procedure to that used for SEM-pyrrole. Deprotonation of (5) was also best achieved by the slow addition of n-butyllithium to a DME solution of SEM-indole at -10 to -15°C. The resulting orange 2-lithio anion was reacted with electrophiles at -25°C to give addition products (12)-(16) (Table 2).

Table 1 **Reaction of 2-Lithio-SEM-pyrrole with Electrophiles**

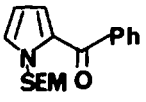
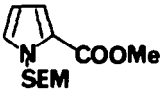
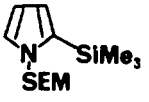
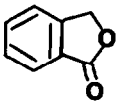
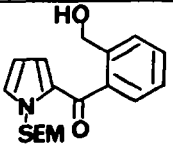
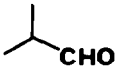
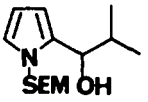
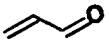
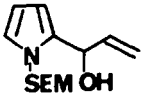
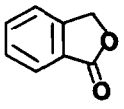
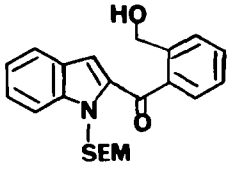
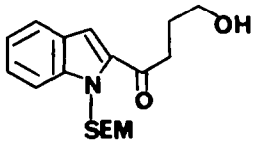
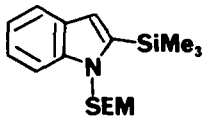
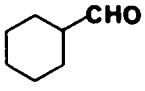
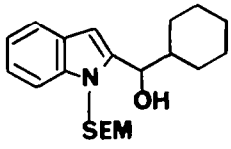
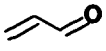
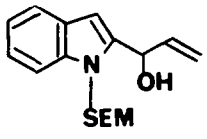
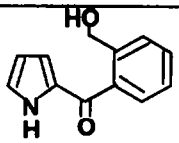
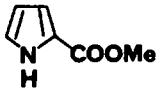
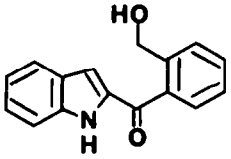
Electrophile	Product		Yield (%)
PhCOCl		(6)	40
MeOOCCl		(7)	42
Me_3SiCl		(8)	40
		(9)	64
		(10)	52
		(11)	40

Table 2 **Reaction of 2-Lithio-SEM-indole with Electrophiles**

Electrophile	Product		Yield (%)
		(12)	65
		(13)	65
Me_3SiCl		(14)	57
		(15)	70
		(16)	63

The SEM-protecting group in both the pyrrole and indole adducts prepared above and in the earlier indanomycin synthesis proved to be remarkably stable to a variety of reaction conditions, even towards the normal deprotection methods, for example, lithium tetrafluoroborate in acetonitrile at -70°C[12] or caesium fluoride in HMPA[13]. Deprotection however, can be achieved by the use of freshly prepared anhydrous tetra- n-butylammonium fluoride (TBAF). The anhydrous TBAF was prepared by azeotropic removal of water from the commercially available trihydrate using benzene (or toluene) on a rotary evaporator at temperatures below 50°C followed by heating (<50°) under high vacuum for 12h.[14] The residual yellow oil was then dissolved in a minimum amount of dry THF and introduced directly into the deprotection reactions via syringe at 0°C. Only three representative examples of this deprotection procedure are reported here (Table 3) all of which proceed in acceptable yields.

Table 3 **Deprotection Reaction using Anhydrous Tetra-n-butylammonium Fluoride**

Starting Material	Product	Yield (%)
(9)	 (17)	56
(7)	 (18)	51
(12)	 (19)	78

The combined use of the SEM-group to protect the pyrrole nitrogen atom and direct lithiation to the 2-position has already been shown to be valuable in natural product synthesis[10]. We further believe the method reported herein for the selective 2-substitution of the indole ring will find similar future applications.

EXPERIMENTAL

^{1}H n.m.r. spectra were recorded on Bruker WH-250 and JEOL FX90Q spectrometers in deuteriochloroform solutions.

Infra-red spectra were recorded on a Perkin-Elmer 938G spectrophotometer as liquid films or in chloroform solutions.

Mass spectra were obtained on a VG Micromass 7070B instrument. Melting points were determined on a Kofler Hot-Stage instrument and are uncorrected.

Column chromatography was carried out on Kieselgel 60(230-400 mesh) under pressure eluting with petroleum ether (b.pt 40-60°C) - diethyl ether mixtures.

All solvents were dried by standard methods and distilled before use. All solutions were dried over anhydrous magnesium sulphate.

Preparation of 1-(2-Trimethylsilylethoxymethyl)pyrrole (3).- Freshly distilled pyrrole (2.1 ml, 30 mmol) was added dropwise to an ice-cold suspension of sodium hydride (1.92 g of a 60% dispersion in mineral oil, prewashed with 3 x 10 ml 30-40°C pet. ether, 48 mmol) in a dimethylformamide (DMF) (80 ml) - dimethylsulphoxide (DMSO) (16 ml) mixture. The solution was allowed to warm to room temperature and when hydrogen evolution had ceased, was cooled to 0°C and 2-trimethylsilylethoxymethyl chloride (7.96 ml, 45 mmol) added dropwise. The solution was then stirred at room temperature for 30 min. before pouring into water (100 ml) and ice (25 g). The aqueous layer was separated and extracted with ether (3 x 100 ml) and the combined organic extracts washed with water before being dried and concentrated to an oil. Column chromatography eluting with 99% pet. ether - 1% ether gave N-SEM-pyrrole (3) (4.9 g, 83%) as a colourless liquid: b.pt. 76°C (1.5 mm Hg); ν_{max} (film) 2954, 1495, 1270, 1250, 1070, 860, 835 and 720 cm^{-1}; ^{1}H n.m.r. δ (250 MHz) 0.0 (9H, s, $SiMe_3$), 1.1 (2H, t, J = 8 Hz, CH_2Si), 3.6 (2H, t, J = 8 Hz, OCH_2), 5.3 (2H, s, NCH_2O), 6.2 (2H, dd, J = 2, 2 Hz, H3 and H4), and 6.9 (2H, dd, J = 2,2Hz, H2 and H5).

Preparation of 1-(2-Trimethylsilylethoxymethyl)indole (5).- Preparation by the method described above. N-SEM- indole (98%) was obtained as a clear oil after column chromatography eluting with 99% pet. ether - 1% ether: ν_{max} (film) 2952, 1460, 1303, 1248, 1076, 860, 836 and 740 cm^{-1}; ^1H n.m.r. δ (250 MHz) 0.0 (9H, s, $SiMe_3$), 0.93 (2H, t, J = 8 Hz, CH_2Si), 3.51 (2H, t, J = 8 Hz, OCH_2), 5.50 (2H, s, NCH_2O), 6.58 (1H, dd, J = 3, 0.6 Hz, H3), 7.19 (1H, s, H2), 7.19 (1H, dt, J = 6.8, 1.3 Hz, H5), 7.29 (1H, dt, J = 6.8, 1.3 Hz, H6), 7.54 (1H, br.d, J = 7.5 Hz, H7), and 7.68 (1H, br.d, J = 7.5 Hz, H4).

General Method for Substitution of the 2-Position of SEM-pyrrole.- SEM-pyrrole (3) (0.208g, 1.05 mmol) was dissolved in dimethoxyethane (DME) (1 ml) under argon at -5°C-0°C. To this solution was added n-butyllithium (0.75 ml of a 1.55M solution in hexane, 1.16 mmol) dropwise over 8 min. The resulting pale yellow solution was then allowed to stir for a further 8 min at -5°C-0°C before being added via cannula to a solution of the appropriate electrophile (0.53 mmol) in DME (1 ml) at -5°C. The resulting mixture was allowed to stir for 30 min, being monitored by t.l.c. before being poured into saturated aqueous ammonium chloride solution (10 ml). This mixture was extracted with ether (3 x 20 ml), the ether extracts combined, dried, concentrated and purified by column chromatography (Yield calc. on recovered SEM-pyrrole).

1-(2-Trimethylsilylethoxymethyl)-2-benzoyl pyrrole (6).- Compound (6) (40%) was obtained as a clear oil after column chromatography: ν_{max} (film) 2952, 1630, 1411, 1248, 1083, 837, 724, and 698 cm^{-1}; ^1H n.m.r. δ (90 MHz) 0.0 (9H, s, $SiMe_3$), 0.9 (2H, t, J = 8 Hz, CH_2Si), 3.61 (2H, t, J = 8 Hz, OCH_2), 5.82 (2H, s, NCH_2O), 6.25 (1H, m, H4), 6.78 (1H, m, H5), and 7.2-7.9 (6H, m, H3 and PhH); m/z 301 (M^+), 228 (M^+-TMS), 200 (M^+-CH_2CH_2TMS), 184 (M^+-OCH_2CH_2TMS), 105 (PhC = O^+), and 77 (Ph^+). Found M^+ 301.1506, $C_{17}H_{23}NO_2Si$ requires M^+ 301.1498.

1-(2-Trimethylsilylethoxymethyl)-2-carbomethyoxy pyrrole (7).- Compound (7) (42%) was obtained as a clear oil after column chromatography: ν_{max} (film) 2951, 1707, 1437, 1412, 1320, 1116, 1081, 859, 836, 742, and 693 cm^{-1}; ^1H n.m.r. δ (90 MHz) 0.00 (9H, s, $SiMe_3$), 0.9 (2H, m, CH_2Si), 3.55 (2H, m, OCH_2), 3.85 (3H, s, CO_2Me), 5.7 (2H, s, NCH_2O), 6.2 (1H, m, H4), and 7.0 (2H, m, H3 and H5); m/z 255 (M^+), 196 (M^+-CO_2Me), 182 (M^+-TMS), 139 (M^+-$CHOCH_2SiMe_3$), 80 ($C_5H_6N^+$), and 73 (TMS^+). Found M^+ 255.1284, $C_{12}H_{21}NO_3Si$ requires M^+ 255.1290.

1-(2-Trimethylsilylethoxymethyl)-2-trimethylsilyl pyrrole (8).- Compound (8) (40%) was obtained as a clear oil after column chromatography: ν_{max} (film) 2954, 1275, 1249, 1122, 1086, 837, 760, 722, and 632 cm^{-1}; ^1H n.m.r. δ (90 MHz) 0.0 (9H, s, $SiMe_3$), 0.3 (9H, s, pyrrole-$SiMe_3$), 0.9 (2H, t, J = 8 Hz, CH_2Si), 3.40 (2H, t, J = 8 Hz, OCH_2), 5.20 (2H, s, NCH_2O), 6.18 (1H, m, H4), 6.45 (1H, m, H3), and 6.92 (1H, m, H5); m/z 269 (M^+), 254 (M^+-CH_3), 196 (M^+-TMS), 152 (M^+-OCH_2CH_2TMS), and 73 (TMS^+). Found M^+ 269.1626, $C_{13}H_{27}NOSi$ requires M^+ 269.1631.

1-(2-Trimethylsilylethoxymethyl)-2-o-hydroxymethyl benzoyl pyrrole (9).- Compound (9) (64%) was obtained as a clear oil after column chromatography: ν_{max} (film) 3446, 2952, 1625, 1411, 1330, 1246, 1082, 916, 836, and 743 cm^{-1}; ^1H n.m.r. δ (90 MHz) 0.0 (9H, s, $SiMe_3$), 0.92 (2H, t, J = 8 Hz, CH_2Si), 3.62 (2H, t, J = 8 Hz, OCH_2), 3.90 (1H, t, J = 6.5, OH), 4.53 (2H, d, J = 6.5 Hz, $PhCH_2$), 5.72 (2H, s, NCH_2O), 6.21 (1H, m, H4), 6.65 (1H, m, H5), 7.21 (1H, m, H3), and 7.21-7.68 (4H, m, PhH); m/z 331 (M^+), 313 (M^+-H_2O), 258 (M^+-TMS) and 135 (ArC=O). Found M^+ 331.1606, $C_{18}H_{25}NO_3Si$ requires M^+ 331.1603.

1-(2-Trimethylsilylethoxymethyl)-2-(1-hydroxy-2-methylpropyl) pyrrole (10).- Compound (10) (52%) was obtained as a clear oil after column chromatography: ν_{max} (film) 3435, 2955, 1177, 1077, 836, and 710 cm^{-1}; ^1H n.m.r. δ (250 MHz) 0.0 (9H, s, $SiMe_3$), 0.87 (2H, m, CH_2Si), 0.87 (3H, d, J = 6.5 Hz, CH_3), 1.12 (3H, d, J = 6.5 Hz, CH_3), 2.18 (1H, m, $CHMe_2$), 2.53 (1H, d, J = 4 Hz, OH), 3.44 (2H, d, J = 8 Hz, OCH_2), 4.33 (1H, dd, J = 8, 4 Hz, CH-OH), 5.28 (1H, d, J = 11 Hz, NCHO), 5.31 (1H, d, J = 11 Hz, NCHO), 6.07 (1H, dd, J = 3.7, 3 Hz, H4), 6.14 (1H, dd, J = 3.7, 2 Hz, H3), and 6.68 (1H, dd, J = 3, 2 Hz, H5); m/z 269 (M^+), 251 (M^+-H_2O), 226 (M^+-C_3H_7), and 152 (M^+-$C_6H_{13}OSi$). (Found: C, 62.16; H, 10.36; N, 5.32%. $C_{14}H_{27}NO_2Si$ requires C, 62.40; H, 10.10; N, 5.20%).

1-(2-Trimethylsilylethoxymethyl)-2-(1'-hydroxy prop-2'-enyl pyrrole (11).- Compound (11) (40%) was obtained as a clear oil after column chromatography: ν_{max} (film) 3418, 2952, 1276, 1249, 1080, 922, 860, 836, and 717 cm^{-1}; ^1H n.m.r. δ (250 MHz) 0.0 (9H, s, $SiMe_3$), 0.92 (2H, m, CH_2Si), 3.17 (1H, br.d, J = 5 Hz, OH), 3.49 (2H, m, OCH_2), 5.27 (1H, d, J = 10.5 Hz, NCHO), 5.27-5.33 (2H, m, anti-H3' and CH-OH), 5.37 (1H, d, J = 10.5 Hz, NCHO), 5.49 (1H, dt, J = 16, 1.5 Hz, syn-H3'), 6.25-6.07 (3H, m, H4, H5 and H2'), and 6.75 (1H, dd, J = 3, 1.8 Hz, H3); m/z 253 (M^+), 180 (M^+-TMS), 152 (M^+-CH_2CH_2TMS), 137 ($C_8H_{11}NO$), and 80 ($C_5H_6N^+$). Found: C, 61.86; H, 9.23; N, 5.58%. $C_{13}H_{23}NO_2Si$ requires C, 61.62; H, 9.15; N, 5.53%).

General Method for Substitution at the 2-Position of SEM-indole (5).- SEM-indole (5) (0.247g, 1 mmol) was dissolved in DME (1 ml) under argon at -10°C. To this solution was added n-butyllithium (0.76 ml of 1.44N solution in hexane, 1.1 mmol) dropwise over 8 min. The resulting orange solution was allowed to stir for a further 8 min. while warming to -5°C. This mixture was then cooled to -20°C before being added, via cannula, to a stirred solution of the appropriate electrophile (0.5 mmol) in DME (1 ml) at -20°C. The resulting mixture was allowed to stir at -10°C for 30 min then poured into saturated aqueous ammonium chloride solution (10 ml). This mixture was extracted with ether (3 x 20 ml), the ether extracts combined, dried, concentrated and purified by column chromatography (Yield calc. on recovered SEM-indole).

1-(2-Trimethylsilylethoxymethyl)-2-o-hydroxymethyl benzoyl indole (12).- Compound (12) (65%) was obtained as a clear oil after column chromatography: ν_{max} (film) 3446, 2951, 1635, 1511, 1400, 1347, 1250, 1122, 1092, 1076, 860, 836, and 744 cm^{-1}; ^1H n.m.r. δ (250 MHz) 0.0 (9H, s, $SiMe_3$), 0.92 (2H, t, J = 9 Hz, CH_2Si), 3.62 (2H, t, J = 9 Hz, $-OCH_2-$), 3.72 (1H, br.t, J = 9 Hz, OH), 4.62 (2H, d, J = 7 Hz, CH_2-OH), 6.1 (2H, s, NCH_2O), 6.95 (1H, d, J = 0.8 Hz, H3), 7.20 (1H, ddd, J = 8, 7, 0.8 Hz, H6), and 7.37-7.70 (7H, m, H4, H5, H7 and other aromatics); m/z 381 (M^+), 363 (M^+-H_2O), 262 (M^+-H_2O-$C_5H_{13}Si$), 246 (M^+-H_2O-$C_5H_{13}OSi$), 233 (M^+-OH-$C_6H_{15}OSi$), and 73 ($SiMe_3^+$). (Found: C, 69.25; H, 7.34; N, 3.96%. $C_{22}H_{27}NO_3Si$ requires C, 69.26; H, 7.13; N, 3.67%.)

1-(2-Trimethylsilylethoxymethyl)-2-(4'hydroxy butanoyl)indole (13).- Compound (13) (65%) was obtained as a clear oil after column chromatography: ν_{max} (film) 3426, 2951, 1653, 1476, 1248, 1072, 834, and 736 cm^{-1}; ^1H n.m.r. δ (250 MHz) 0.0 (9H, s, $SiMe_3$), 0.88 (2H, m, CH_2Si), 2.02 (2H, qn, J = 6.3 Hz, H3'), 2.20 (1H, br.s, OH), 3.13 (2H, t, J = 6.8 Hz, H4'), 3.53 (2H, m, OCH_2), 3.74 (2H, t, J = 5.6 Hz, H4'), 6.00 (2H, s, NCH_2O), 7.19 (1H, ddd, J = 7.8, 6.8, 0.9 Hz, H6), 7.39 (2H, m, H3, H5), 7.55 (1H, dd, J = 8.4, 0.6 Hz, H7), and 7.68 (1H, br.d, J = 7.8 Hz, H4); m/z 333 (M^+), 315 (M^+-H_2O), 260 (M^+-TMS), 246 (M^+-CH_2TMS), and 59 ($CH_2CH_2CH_2OH^+$). Found M^+ 333.1766, $C_{18}H_{27}NO_3Si$ requires M^+ 333.1760.

1-(2-Trimethylsilylethoxymethyl)-2-trimethylsilyl indole (14).- Compound (14) (57%) was obtained as a clear oil after column chromatography: ν_{max} (film) 2953, 1465, 1249, 1167, 1081, 839, 750, 735, and 633 cm^{-1}; ^1H n.m.r. δ (250 MHz) 0.0 (9H, s, $SiMe_3$), 0.43 (9H, s, indole - $SiMe_3$), 0.95 (2H, m, CH_2Si), 3.53 (2H, m, OCH_2), 5.59 (2H, s, NCH_2O), 6.80 (1H, d, J = 1 Hz, H3), 7.14 (1H, ddd, J = 7.8, 6.8, 1 Hz, H5), 7.26 (1H, ddd, J = 7.8, 6.8, 1 Hz, H6), 7.51 (1H, br.d, J = 8 Hz, H7), and 7.64 (1H, br.t, J = 7 Hz, H4); m/z 319 (M^+), 246 (M^+ - TMS), 202 (M^+-$C_5H_{13}OSi$), 188 (M^+-$C_6H_{15}OSi$), 115 (M^+-$C_6H_{15}OSi$ - TMS), and 73 (TMS^+) (Found: C, 64.17; H, 8.97; N, 4.55%. $C_{17}H_{29}NOSi_2$ requires C, 63.89; H, 9.15; N, 4.38%).

1-(2-Trimethylsilylethoxymethyl)-2-cyclohexylhydroxymethylindole (15).- Compound (15) (70%) was obtained as a clear oil after column chromatography: ν_{max} (film) 3422, 2924, 2852, 1457, 1310, 1249, 1072, 859, 836 and 736 cm^{-1}; ^1H n.m.r. δ (250 MHz) 0.0 (9H, s, $SiMe_3$), 0.9 (2H, dd, J = 9, 7Hz, CH_2Si), 1.0-2.1 (10H, m, cyclohexyl CH_2), 2.28 (1H, br.d, J = 14 Hz, cyclohexyl CH), 2.82 (1H, br.s, OH), 3.56 (2H, dd, J = 9.5, 7.5 Hz, OCH_2), 4.60 (1H, br.d, J = 9 Hz, CH-OH), 5.60 (2H, s, NCH_2O), 6.52 (1H, s, H3), 7.17 (1H, dt, J = 7.5, 1.25 Hz, H5), 7.27 (1H, ddd, J = 7.5, 5.4, 1.25 Hz, H6), 7.46 (1H, br.d, J = 7.5 Hz, H8) and 7.62 (1H, br.d, J = 7.5 Hz, H4); m/z 359 (M^+), 341 (M^+-H_2O), 276 (M^+-cyclohexyl), 242 (M^+-$C_5H_{13}Si$), 224 (M^+-H_2O-$C_5H_{13}OSi$), and 73 (TMS^+). (Found: C, 69.70; H, 9.47; N, 4.63%. $C_{21}H_{33}NO_2Si$ requires C, 70.15; H, 9.25; N, 3.91%) Found M^+ 359.2272, $C_{21}H_{33}NO_2Si$ requires M^+ 359.2281.

1-(2-Trimethylsilylethoxymethyl-2-(1'-hydroxy prop-2'-enyl) indole (16).- Compound (16) (63%) was obtained as a clear oil after column chromatography: ν_{max} (film) 3422, 2951, 2894, 1637, 1457, 1309, 1249, 1072, 859, 835 and 737 cm^{-1}; ^1H n.m.r. δ (250 MHz) 0.0 (9H, s, $SiMe_3$), 0.92 (2H, m, CH_2Si), 3.40 (1H, d, J = 4.5 Hz, OH), 3.54 (2H, t, J = 6.8 Hz, OCH_2), 5.38 (1H, dt, J = 10, 1.5 Hz, anti H3'), 5.46-5.60 (3H, m, NCHO, CH-OH and syn-H3'), 5.67 (1H, d, J = 10 Hz, NCHO), 6.27 (1H, ddd, J = 16, 10, 4.5 Hz, H2'), 6.52 (1H, s, H3), 7.14 (1H, m, H6), 7.25 (1H, ddd, J = 7.9, 5.6, 1.1 Hz, H5), 7.43 (1H, br.d, J = 7.5 Hz, H7), and 7.60 (1H, br.d, J = 7.5 Hz, H4); m/z 303 (M^+), 286 (M^+-OH), 230 (M^+-TMS), 186 (M^+-$C_5H_{13}OSi$), and 130 (indole nucleus$^+$). (Found: C, 67.20; H, 8.54; N, 4.70%. $C_{17}H_{25}NO_2Si$ requires C, 67.28; H, 8.30; N, 4.62%).

General Method for the Deprotection of 2-Substituted SEM-protected Pyrroles and Indoles.- The substrate (1.12 x 10^{-4} mol) was dissolved in THF (1 ml) at 0°C and anhydrous tetra-n-butylammonium fluoride (0.5 ml of a 2.2N solution in THF) was added dropwise. The reaction was monitored by tlc until completion, then poured into a water (10 ml) ether (20 ml) mixture. The aqueous layer was re-extracted with ether (2 x 20 ml) and the ether extracts combined, washed with brine (20 ml), dried, concentrated to give a pale solid which was purified by column chromatography.

2-o-Hydroxymethylbenzoyl pyrrole (17).- Compound (17) (56%) was obtained as a pale pink solid after column chromatography: m.pt. 120°C; ν_{max} ($CHCl_3$) 3446, 2995, 1606, 1399, 1333, 1112, 1084, 1040, 1013, and 898 cm^{-1}; ^1H n.m.r. δ (250 MHz) 4.17 (1H, t, J = 7.5 Hz, OH), 4.58 (2H, d, J = 7.5 Hz, Ph-CH_2), 6.33 (1H, m, H5), 6.77 (1H, m, H4), 7.21 (1H, m, H3), 7.36-7.55 (3H, m, aromatic H3', H4', H5'), 7.76 (1H, br.d, J = 7 Hz, aromatic H6'), and 10.16 (1H, br.s, NH); m/z 201 (M^+), 183 (M^+-H_2O), 135 ($C_8H_6O_2$), and 94 (M^+-C_7H_7O). (Found: C, 67.20; H, 8.54; N, 4.70%. $C_{17}H_{25}NO_2Si$ requires C, 67.28; H, 8.30; N, 4.62%).

2-Carbomethoxypyrrole (18).- Compound (18) (51%) was obtained as a white solid after column chromatography: m.pt. 69°C; ν_{max} ($CHCl_3$) 3457, 3311, 2991, 1684, 1443, 1406, 1322, 1188, 1165, 1131, 1110, 1078, 1033, and 985 cm^{-1}; ^1H n.m.r. δ (90 MHz) 3.9 (3H, s, CO_2CH_3), 6.25 (1H, m, H5), 7.0 (2H, m, H3 and H4) and 9.0-9.6 (1H, br.s, NH); m/z 125 (M^+), 94 (M^+-OMe), and 66 (M^+-CO_2Me). Found M^+ 125.0471, $C_6H_7NO_2$ requires M^+ 125.0476.

2-(o-Hydroxymethyl)benzoyl indole (19).- Compound (19) (78%) was obtained as a white solid after column chromatography: ν_{max} ($CHCl_3$) 3450, 2995, 1617, 1568, and 1518 cm^{-1}; ^1H n.m.r. δ (90 MHz) 3.80 (1H, br.m., -OH), 4.65 (2H, br.d, J = 5Hz, $-CH_2-O$), 7.0-7.9 (9H, m, aromatics), and 9.40 (1H, br.s, NH); m/z 251 (M^+), 233 (M^+-H_2O), 144 (C_9H_6NO), and 134 ($C_8H_6O_2$). Found M^+ 251.0946, $C_{16}H_{13}NO_2$ requires M^+ 251.0946.

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