THE NICHOLAS REACTION OF INDOLES. PROPARGYLATION OF INDOLES WITH (PROPA RGYL)DICOBALT HEXACARBONYL CATIONS †

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Abstract - Indole reacted with (propargyl alcohol)Co₂(CO)₆ complex 1 to give 3-(1,1-dimethylpropargyl)indole 3, whereas N'-methoxycarbonyltryptamine 7 gave the corresponding N-substituted derivative 11. The reaction of 7 with (propargyl acetate)Co₂(CO)₆ complex 23 provided 3a-(1,1-dimethylpropargyl)hexahydropyrroloindole cobalt complex 9. Oxidative demetalation of 3, 11, and 9 with Fe(NO₃)₃ gave 5, 13, and 27, respectively. Hydrogenation of 5 afforded the corresponding 3-(1,1-dimethylallyl)indole 6.

There are a number of indole alkaloids such as echinulin,¹ ilamycin,² brevianamide E,³ roquefortine,⁴) LL S490β⁵) and flustamine A and C⁶) which have a 1,1-dimethylallyl group (inert prenyl group) at the 2- or 3-position of the indole ring. Foreseeing selection of an appropriate reagent and conditions for introducing a prenyl group into the indole ring, specially at the 3-position of 3-alkyindoles, is crucial for the successful synthesis of these alkaloids. Three methods⁷) have been reported for introduction of the inverted prenyl group to the indole ring at the 2 or 3 position, which include the rearrangement of 1-prenyl-, 2-prenylthio-, or 3-prenylthioindole derivatives, direct synthesis of 2-(1,1-dimethylallyl)indole from appropriate aniline derivatives, and 1,1-dimethylpropargylation of tryptamine derivatives.⁸) As part of our current interest in the search for new biologically active indole derivatives, we thought it worthwhile to focus our attention on the development of new methods for the synthesis of indoles bearing an inverted prenyl group.

The reaction of cobalt-complexed propargyl alcohols with HBF₄ developed by Nicholas⁹) seemed attractive since a cobalt-stabilized carbocation can be reacted with a variety of carbon nucleophiles to provide alkylated products. Recently, Schreiber and coworkers have reported

† We dedicate this paper to the memory of Professor Tetsuji Kametani.
the modified Nicholas reaction which involves the reaction of cobalt-complexed propargylic ethers with Lewis acids.\textsuperscript{10} Here, we report, in full, an investigation of the reaction of indole and tryptamine derivatives with various propargyl dicobalt hexacarbonyl complexes in the presence of Lewis acids.

In our first experiment with propargyl dicobalt hexacarbonyl cation, we carried out the reaction of indole with the propargylic alcohol dicobalt hexacarbonyl complex 1 in the presence of BF\textsubscript{3}·etherate instead of HBF\textsubscript{4} (tetrafluoroboric acid). The reaction proceeded under ice-salt cooling for 1.5 h to give the expected 3-(1,1-dimethylpropargyl)indole complex 3 in 86\% yield accompanied by a small amount (7\%) of the disubstituted complex 4. The $^1$H and $^{13}$C-nmr spectra of 3 and 4 confirmed the presence of 1,1-dimethylpropargyl substituent at the 3-position of indole. In the $^1$H-nmr spectrum of 3, the C-2 proton signal, which was assigned by the selective decoupling method, appeared at $\delta$ 7.05 as a doublet with $J$=1.8Hz. This peak became a singlet upon D\textsubscript{2}O addition. The C-4 proton was shifted to down field ($\delta$ 7.93, $J$=7.0Hz), reflecting the deshielding effect by the presence of the propargyl dicobalt group at the 3-position. Treatment of the complex 3 with an excess of Fe(NO\textsubscript{3})\textsubscript{3}·9H\textsubscript{2}O in EtOH\textsuperscript{11} afforded the corresponding 3-(1,1-dimethylpropargyl)indole 5 in nearly quantitative yield (97\%). Catalytic hydrogenation of 5 using Lindlar catalyst gave 3-(1,1-dimethylallyl)indole 6 quantitatively (Scheme 1).

![Scheme 1](image)

Similar reaction of 1 with N′-methoxycarbonyltryptamine 7 under ice-salt cooling for 3 h did not give the expected compound 9 or 10 but resulted in the formation of N-substituted complex 11 in 77\% yield, whereas the reaction at ambient temperature gave a trace amount of disubstituted complex 12 (0.8\%) together with 11 (35\%) (Scheme 2). On the other hand, the aromatic substitution reaction on the benzene ring occurred preferentially to give 15 in 32\% yield when
N-methyl-N'-methoxycarbonyltryptamine 14 was treated with 1 at -54°C for 26 h (Scheme 3). The structures of 11 and 15 were confirmed by converting them with Fe(NO₃)₃ to the corresponding dimethylpropargyltryptamines 13 and 16, respectively. The nmr spectra of 12, 15, and 16 indicated that these compounds consisted of two or more positional isomers which, however, could not be separated. The failure to obtain either 9 or 10 suggested that the formation of 8 was prevented by the bulkiness of 1. Therefore, the reaction of 7 with the less hindered propargyl complex 2 was carried out in the presence of BF₃-etherate in CH₂Cl₂ with ice-salt cooling for 9 h and the expected 3a-propargyl-1-methoxycarbonyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole dicobalt complex 17 and 3a,8-dipropargyl complex 18 were obtained in 40% and 9% yields, respectively. Likewise, when 14 was mixed with 2 in CH₂Cl₂ at ambient temperature for 4 h, 21 was formed in 69% yield. Treatment of 17, 18 and 21 with Fe(NO₃)₃ provided 19, 20, and 22, respectively (Scheme 4).
From the above results, steric factors appeared to influence the formation of pyrroloindole cobalt complexes via the reaction at the C-3 position of 3-substituted indole derivatives. As 1,1-dimethylpropargyl alcohol dicobalt complex 1 is too bulky to react at the 3-position, it seemed necessary to increase the reactivity of 1. Expectedly, more reactive 1,1-dimethylpropargyl acetate dicobalt complex 23 was prepared in an excellent yield (above 90%) from 1,1-dimethylpropargyl acetate\(^{12}\) and dicobalt octacarbonyl in hexane at ambient temperature. However, we failed to purify 23 by silica gel column chromatography due to its facile elimination of AcOH to give \(26_5\). Therefore freshly prepared crude 23 was used for the reaction with indoles which was found to proceed at lower temperature in the presence of BF\(_3\)-etherate. Thus, when N-methyl-N'-methoxy-carbonyltryptamine 14 was treated with the complex 23 at -90°C to -80°C for 42 h, 3a-(1,1-dimethylpropargyl)hexahydropyrroloindole dicobalt complex 24 (14%) was formed and a 58% yield of 14 was recovered. Similar treatment of 14 with 23 followed by oxidative demetalation at ambient temperature gave 3a-(1,1-dimethylpropargyl)pyrroloindole 25 in 27% over all yield from 14. Tlc examination showed that 24 converted to 14 even at low temperature in the presence of Lewis acid like BF\(_3\)-etherate. Accordingly, when the reaction mixture was allowed to warm from -85°C to 20°C for 38 h, 24 was not obtained. Instead, 15 was obtained in 58% yield along with 30% recovery of 14, indicating that at higher temperature, the initially formed complex 24 at lower temperature reverted to 14 and the 1,1-dimethylpropargyl dicobalt hexacarbonyl cation which underwent substitution reaction at the benzene ring to give the complex 15. Furthermore, the complex 24 decomposed to 14 (68%), \(26_5\), \(9a_5\), 14) and a trace amount of 15 when dissolved in...
BF3·etherate-CH2Cl2 solution at ambient temperature for 15 min. Therefore, in order to isolate the complex 24, the reaction mixture has to be quenched rapidly with saturated NaHCO3 at low temperature (Scheme 5).

Similar reaction of 7 with the acetate complex 23 at -70°C for 28 h produced the N-substituted complex 11 as the main product in 88% yield, but the pyrroloindole complex 9 was obtained in 12% yield which was decomplexed in 93% yield to give 27 (Scheme 6). Treatment of 7 with 23 at low temperature (-90°C, 24 h, and -70°C, 24 h) followed by immediate demetalation in one pot gave 27 (14%) and 13 (78%). TLC examination showed that the complex 9 converted to 7 and 11 after 8.5 h when treated with BF3·etherate in CH2Cl2 at ambient temperature, indicating that 9 reverted to 7 more slowly than 24 to 14. These reactions were also examined in the presence of EtAlCl2, AlCl3, Me2BBr, TiCl4, TiCl4-DABCO,13) SnCl4, and ZnCl2. However, the reactions did not proceed, with exception of TiCl4 (6eq) / DABCO (1eq) (70°C, 22.5 h) with which the excepted adduct 9 was formed in 4.9% yield. Additionally, attempted reaction of 7 with 1,1-dimethylpropargyl methyl ether.
EXPERIMENTAL

Symbols of natural products in progress.

Further application of this method to the hydroboration of 2-functionalized 10-phenyl-2-naphthalenone with ZnCl₂ and TFAA, and the reaction of 7 with 2 in dichloromethane in the presence of TIOAc-DABCO, gave product 8 in 65% yield. Further application of this method to the preparation of various other compounds is in progress.
(6H, s, CH₃), 6.25 (2H, s, C=C=CH), 7.12 (1H, s, C₂-H), 7.23-7.14 (2H, m, C₅, C₆-H), 7.69 (1H, d, J=8Hz, C₇-H), 7.89 (1H, d, J=7Hz, C₄-H).

N-Dimethylpropargyl-N'-methoxycarbonyltryptamine diacobalt hexacarbonyl complex 11 and bis(dimethylpropargyl)-N'-methoxycarbonyltryptamine bis(dicobalt hexacarbonyl)complex 12

Similar treatment of N'-methoxycarbonyltryptamine 7 (0.18 g, 0.81 mmol) and 1 (0.40 g, 1.05 mmol) in CH₂Cl₂ (20 ml) in the presence of BF₃·Et₂O (0.23 g, 1.62 mmol) under ice-salt cooling for 3 h, followed by work-up as described above, gave 0.35 g of 11 (77%) as a dark red oil. 11: uv λmax 222, 270sh, 300th, 352, 410thnm; ¹H-nmr (270MHz) δ 2.13 (6H, s, CH₃C=CH), 2.92 (2H, t, J=7Hz, CH₂), 3.40-3.50 (2H, m, CH₂N), 3.67 (3H, s, OCH₃), 4.65 (1H, bs, NH), 6.30 (1H, s, C=C=CH), 7.14 (1H, s, C₂-H), 7.24-7.09 (2H, m, arom-H), 7.56 (1H, d, J=7Hz, arom-H), 7.73 (1H, d, J=8Hz, arom-H). Similar reaction of 7 (0.20 g, 0.92 mmol) and 1 (0.51 g, 1.38 mmol) in CH₂Cl₂ (30 ml) carried out in the presence of BF₃·Et₂O (0.1 g, 0.74 mmol) at ambient temperature for 24 h, gave 0.19 g of 11 (35%), 0.006 g of 12 (0.8%) as dark red oils, and the recovered 0.12 g of 7 (61%). 12: uv λmax 303, 350nm; ¹H-nmr (270MHz) δ 1.75 (15/2H, s, CH₃), 1.84 (9/2H, s, CH₂), 2.85-2.95 and 3.08-3.14 (2H, m, CH₂), 3.40-3.57 (2H, m, CH₂N), 3.68 (3H, s, OCH₃), 4.60 (3/5H, bs, NH), 7.10 (3/5H, s, C=C=CH), 6.21 (5/6H, s, C=C=CH), 6.25 (1H, s, C=C=CH), 7.10(1H, s, C₂-H), 7.38-7.89 (3H, m, arom-H).

N-Methyl-N'-methoxycarbonyldimethylpropargyltryptamine diacobalt hexacarbonyl complex 15

Similar treatment of N-methyl-N'-methoxycarbonyltryptamine 14 (0.19 g, 0.81 mmol) and 1 (0.40 g, 1.05 mmol) in CH₂Cl₂ (20 ml) in the presence of BF₃·Et₂O (0.42 g, 3.00 mmol) at -5°C for 26 h, followed by work-up as described above, gave 0.15 g of 15 (32%) as a dark red oil and the recovered 0.07 g of 14 (38%). 15: uv λmax 226, 260th, 346, 400thnm; ¹H-nmr (270MHz) δ 1.79 (9/2H, s, CH₃C=CH), 1.80 (3/2H, s, CH₃C=CH), 2.88-2.97 (2H, m, CH₂), 3.46-3.50 (2H, m, CH₂N), 3.67 (3H, s, NCH₃), 3.75 (9/4H, s, OCH₃), 3.71 (3/4H, s, OCH₃), 4.71 (1H, bs, NHCO), 6.18 (1/4H, s, C=C=CH), 6.20 (3/4H, s, C=C=CH), 6.85 (1H, s, C₂-H), 7.20-7.62 (3H, m, arom-H). The nmr spectrum of 15 also suggested this consist of two positional isomers which failed to be separated by silica gel chromatography.

1-Methoxycarbohydr-3a-propargyl-1,2,3,3a,8a-hexahydropyrrole[2,3-b]indole dicobalt hexacarbonyl complex 17 and 1-Methoxycarbohydr-3a,8a-dipropargyl-1,2,3,3a,8a-hexahydropyrrole[2,3-b]indole bis(dicobalt hexacarbonyl)complex 18

Similar treatment of N'-methoxycarbonyltryptamine 7 (0.80 g, 3.66 mmol) and (propargyl alcohol)Co₂(CO)₆ complex 2 (1.40 g, 4.09 mmol) in CH₂Cl₂ (50 ml) in the presence of BF₃·Et₂O (0.88 g, 6.20 mmol) under ice-salt cooling for 9 h, followed by work-up as described above, gave 0.80 g of 17 (40%), 0.30 g of 18 (9%) as dark red oils, and the recovered 0.30 g of 7 (38%). 17: uv λmax 240sh, 290th, 350nm; ¹H-nmr (270MHz) δ 2.24-2.29 (2H, m, CH₂), 3.06-3.13 and 3.62-3.65 (2H, m, NCH₃), 3.42 (1H, d, J=16.5Hz, CH₂C=CH), 3.53 (1H, d, J=16.5Hz,
\( \text{CH}_2\text{C} \equiv \text{CH} \), 3.69 (3/2H, s, OCH\(_3\)), 3.77 (3/2H, s, OCH\(_3\)), 4.67 (1/2H, s, NH, exchangeable), 5.10 (1/2H, s, NH, exchangeable), 5.30-5.31 (1H, m, NCH\(_3\)), 5.72 (1/2H, s, C=CH), 5.75 (1/2H, s, C=CH), 6.60 (1H, d, \( J=8\text{Hz} \), arom-H), 6.77 (1H, d, \( J=7\text{Hz} \), arom-H), 7.07-7.14 (2H, m, arom-H).

18: \( \text{uv}\; \lambda_{\text{max}} \; 250\text{th}, \; 315\text{th}, \; 350\text{nm} \); \( ^1\text{H-nmr} \; (270\text{MHz}) \; \delta \; 2.02-2.20 \) (2H, m, CH\(_2\)), 3.12-3.17 and 3.79-3.80 (2H, m, NCH\(_2\)), 3.39 (1H, d, \( J=16\text{Hz} \), CH\(_2\)C=CH), 3.50 (1H, d, \( J=16\text{Hz} \), CH\(_2\)C=CH), 3.76 (3/2H, s, OCH\(_3\)), 3.78 (3/2H, s, OCH\(_3\)), 4.72-4.90 (2H, m, NCH\(_2\)C=CH), 5.78-5.92 (2H, m, C=CH), 6.07 (1H, s, NCH\(_3\)), 6.68-6.72 (1H, m, arom-H), 7.03-7.21 (3H, m, arom-H).

**1-Methoxycarbonyl-3a-propargyl-8-methyl-1,2,3,3a,8,8a-hexahydropropyrrrolo[2,3-b]indole dicobalt hexacarbonyl complex 21**

Similar treatment of N-methyl-N'-methoxycarbonyl tryptamine 14 (0.25 g, 1.08 mmol) and 2 (0.37 g, 1.08 mmol) in CH\(_2\)Cl\(_2\) (30 ml) in the presence of BF\(_3\cdot\)Et\(_2\)O (0.33 g, 2.16 mmol) at ambient temperature for 4 h, followed by work-up as described above, gave 0.41 g of 21 (69%) as a dark red oil and the recovered 0.071 g of 14 (19%).

Representative alkylation of N'-methoxycarbonyltryptamine with propargyl acetate dicobalt hexacarbonyl complex: 1-Methoxycarbonyl-3a-dimethylpropargyl-1,2,3,3a,8,8a-hexahydropropyrrrolo[2,3-b]indole dicobalt hexacarbonyl complex 29

A dry flask was charged with a solution of N'-methoxycarbonyltryptamine 7 (0.50 g, 2.29 mmol) in dry CH\(_2\)Cl\(_2\) (80 ml) and cooled to -70°C under an argon atmosphere. A solution of (1,1-dimethylpropargylacetate)CO\(_2\)(CO)\(_6\) complex 23\(^{12, \; 15}\) (1.89 g, 4.51 mmol) in dry CH\(_2\)Cl\(_2\) (20 ml) and a solution of BF\(_3\cdot\)Et\(_2\)O (distilled over CaH\(_2\)) (1.75 g, 12.3 mmol) in dry CH\(_2\)Cl\(_2\) (5 ml) were added dropwise. After stirring for 28 h, the reaction mixture was quenched by the addition of saturated NaHCO\(_3\). The aqueous layer was extracted with CH\(_2\)Cl\(_2\). The combined organic extracts were washed with brine and dried over Na\(_2\)SO\(_4\) and the solvent was removed by rotary evaporation. Silica gel chromatography (AcOEt/n-Hex=1/5) gave 0.15 g of 9 (12%) and 1.07 g of 11 (88%) as dark red oils. 9: \( \text{uv}\; \lambda_{\text{max}} \; 245\text{th}, \; 310\text{th}, \; 350, \; 385\text{nm} \); \( ^1\text{H-nmr} \; (500\text{MHz}) \; \delta \; 1.16 \) (2H, s, CH\(_3\)CCH\(_3\)), 1.45 (4H, s, CH\(_3\)CCH\(_3\)), 2.08-2.32 and 2.40-2.54 (2H, m, CH\(_2\)), 2.79-2.03 and 3.54-3.85 (2H, m, NCH\(_2\)), 3.69 (2H, s, OCH\(_3\)), 3.77 (1H, s, OCH\(_3\)), 4.60 (1/3H, s, NH), 5.05 (2/3H, s, NH), 5.42 (1/3H, s, NCH\(_3\)), 5.46 (2/3H, s, NCH\(_3\)), 6.01 (1/3H, s, C=CH), 6.06 (2/3H, s, C=CH), 6.58-6.63 (1H, m, arom-H), 6.74-6.77 (1H, m, arom-H), 7.03-7.17 and 7.21-7.24 (2H, m, arom-H).
Similar treatment of N-methyl-N-methoxybenzylcholine-triptamine 14 (0.40 g, 1.72 mmol) and 23 (1.05 g, 2.51 mmol) in the presence of BF₃·Et₂O (1.85 g, 13.0 mmol) at -90-80°C for 42 h, followed by addition of saturated NaHCO₃ at reaction temperature and work-up at described above, gave 0.20 g of 24 (14%).

As a dark red oil and the red oil was obtained (1.2 g of 14 (59%), 34: uv 253, 315, 350 μm; 1H-nmr (270 MHz), 8.1:1.2:1.43 (H, s, CH₃CH₃CH₂CH₃), 2.0:2.2:0.8 and 2.2:2.1:2.3:2.2:2 (H, m, CH₂, CH₂), 3.26 (2H, s, NCH₃), 3.14 (2H, s, OCH₃), 2.86-2.94 and 3.7:3.4:3.06 (H, m, NH, NCH₃, CH₂), 5.4-5.8 (1H, d, J=8 Hz, H₂), 5.93 (1H, s, CH₃C=N), 6.37 (H, d, J=8 Hz, CH₂).

6.67 (1H, d, J=8 Hz), 7.0-7.1:7.8 (2H, m, aromatic). 

Representative oxidative demethylation of prepared dimethyltriptamine complex with ferric nitrate.

Formation of 3-Dimethylbenzylcholine-2,4-Methoxytriptamine-1-3

The 3-Dimethylbenzylcholine-2,4-Methoxytriptamine-1 complex 3 (0.30 g, 1.07 mmol) was dissolved in 20 ml of CO₂-free chloroform and added to the solution of the ferric nitrate-H₂O in ethanol (10 ml). Ferric nitrate-H₂O was added to the solution of the ferric nitrate-H₂O in ethanol (10 ml). The solution was then portioned between chloroform and H₂O. The organic layer was dried over Na₂SO₄ and concentrated by rotary evaporation. The residue was subjected to silica gel flash chromatography (AQA-Eth/Hex=1:2) to give 0.19 g of 5 (97%), 1H-nmr (270MHz), 8:1.7:4 (6H, s, CH₃CH₃CH₂CH₃), 7.94 (1H, dt, J=8 Hz, C₃H₃CH₂, 4.4 Hz, CH₃CH3CH2CH3), 7.44-7.57 (1H, m, aromatic), 7.69 (1H, d, J=8 Hz, CH₃CH₂), 7.91 (1H, br, NH), 10H (15). 0H (5). 

C₂H₅N. 0.83:1.046 (M)+

N-Methyl-N-methoxybenzylcholine-triptamine 15

Similar treatment of 11 (0.24 g, 0.44 mmol) with Fe(OH)₃·H₂O in ethanol (10 ml) under ice-salt cooling, followed by work-up as described above, gave 0.12 g of 16 (88%), m/z 163 (M+), 37, 26, 24, 22, 20, 18, 17, 15, 7, 6, 5, 4, 3, 2, 1. 

C₃H₇N. 0.83:1.046 (M)+

N-Methyl-N-methoxybenzylcholine-triptamine 16

Similar treatment of 15 (0.23 g, 0.40 mmol) with Fe(OH)₃·H₂O in ethanol (10 ml) under ice-salt cooling, followed by work-up as described above, gave 0.12 g of 16 (88%), m/z 163 (M+), 37, 26, 24, 22, 20, 18, 17, 15, 7, 6, 5, 4, 3, 2, 1. 

C₃H₇N. 0.83:1.046 (M)+
7.24-7.32 (1H, m, arom-H), 7.44-7.52 (1H, m, arom-H), 7.73 (1H, d, J=2Hz, arom-H); ms m/z (%) 298 (M⁺, 31), 210 (100), 143 (5).

1-Methoxycarbonyl-3a-propargyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole 19

Similar treatment of 17 (0.89 g, 1.56 mmol) with Fe(NO₃)₃+9H₂O in ethanol (20 ml) at ambient temperature, followed by work-up as described above, gave 0.41 g of 19 (99%) as colorless needles. 19: mp 95~97°C (AcOEt-n-Hexane); uv λmax 244, 299nm; ir vmax 3370, 3270, 2940, 1700, 750, 740cm⁻¹; ¹H-nmr (270MHz) δ 2.05 (1H, t, J=3Hz, C=CH), 2.22-2.46 (2H, m, CH₂), 2.52 (1H, dd, J=7, 3Hz, CH₂C=CH), 2.59 (1H, dd, J=7, 3Hz, CH₂=CH), 3.02-3.12 and 3.61-3.81 (2H, m, CH₂N), 3.69 (12/7H, s, OCH₃), 3.78 (9/7H, s, OCH₃), 4.73 (3/7H, s, NH), 5.15 (4/7H, s, NH), 5.22 (3/7H, s, NCHN), 5.26 (4/7H, s, NCHN), 6.61 (1H, d, J=8Hz, arom-H), 6.73-6.80 (1H, m, arom-H), 7.07-7.18 (2H, m, arom-H); ms m/z (%) 256 (M⁺, 94), 217 (100), 130 (59), 77 (16). Anal. Calcd for C₁₅H₁₆N₂O₂: C, 70.10; H, 6.30; N, 9.28. Found: C, 70.10; H, 6.30; N, 9.28.

1-Methoxycarbonyl-3a,8-dipropargyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole 20

Similar treatment of 18 (0.51 g, 0.59 mmol) with Fe(NO₃)₃+9H₂O in ethanol (15 ml) at ambient temperature, followed by work-up as described above, gave 0.16 g of 20 (90%) as colorless oil. 20: uv λmax 249, 300nm; ir vmax 3370, 2940, 1700, 750, 740cm⁻¹; ¹H-nmr (270MHz) δ 2.03 (1H, t, J=3Hz, CH₂C=CH), 2.08 (1H, s, NCH₂C=CH), 2.13-2.35 (2H, m, CH₂), 2.55 (1H, dd, J=17, 3Hz, CH₂C=CH), 2.65 (1H, dd, J=17, 3Hz, CH₂=CH), 3.11-3.19 and 3.82-3.91 (2H, m, NCH₂), 3.73 (18/11H, s, OCH₃), 3.82 (15/11H, s, OCH₃), 4.08-4.17 (2H, m, NCH₂C=CH), 5.44 (5/11H, s, NCHN), 5.52 (6/11H, s, NCHN), 6.60 (1H, dd, J=2, 1Hz, arom-H), 6.79 (1H, dd, J=8, 1Hz, arom-H), 7.16-7.22 (2H, m, arom-H); ms m/z (%) 294 (M⁺, 78), 255 (100), 216 (40), 180 (66), 168 (77), 115 (20); HRms calcd for C₁₈H₁₈N₂O₂ 294.1368. Found 294.1368 (M⁺); Anal. Calcd for C₁₈H₁₈N₂O₂: C, 73.45; H, 6.07; N, 9.52. Found: C, 73.14; H, 6.34; N, 9.24.

1-Methoxycarbonyl-3a-propargyl-8-methyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole 22

Similar treatment of 21 (0.51 g, 0.59 mmol) with Fe(NO₃)₃+9H₂O in ethanol (15 ml) under ice cooling, followed by work-up as described above, gave 0.19 g of 22 (78%) as a colorless oil. 22: uv λmax 253, 308nm; ir vmax (neat) 3270, 3040, 2940, 1690, 1600, 740cm⁻¹; ¹H-nmr (270MHz) δ 2.00 (1H, t, J=3Hz, C=CH), 2.04-2.33 (2H, m, CH₂), 2.52 (1H, dd, J=17, 3Hz, CH₂C=CH), 2.54 (1H, dd, J=17, 3Hz, CH₂=CH), 2.91 (6/5H, s, NCH₂), 3.91 (9/5H, s, NCH₃), 3.06-3.09 and 3.83-3.94 (2H, m, NCH₂), 3.72 (9/5H, s, OCH₃), 3.78 (6/5H, s, OCH₃), 5.32 (2/5H, s, NCHN), 5.40 (3/5H, s, NCHN), 6.49 (1H, d, J=8Hz, arom-H), 6.66-6.71 (1H, m, arom-H); ms m/z (%) 270 (M⁺, 100), 231 (95), 216 (18), 144 (65), 115 (11).

1-Methoxycarbonyl-3a-dimethylpropargyl-8-methyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole 25

Similar treatment of 24 (0.18 g, 0.33 mmol) with Fe(NO₃)₃+9H₂O in ethanol (10 ml) under ice cooling, followed by work-up as described above, gave 0.06 g of 25 (61%) as a colorless oil. 25: uv λmax 255, 310nm; ir vmax
This work was purified by flash chromatography at 55°C. The methyl protons appear as a sharp singlet at 1.05 (9/5H, s, CH₃) and 1.34 (6/5H, s, CH₃) (1.31, s, at 55°C), 2.03-2.09 and 2.43-2.49 (2H, m, CH₂), 2.17 (2/5H, s, C=CH) and 2.18 (3/5H, s, C=CH) (2.16, s, at 55°C), 2.90 (9/5H, s, NCH₃), 2.99 (6/5H, s, NCH₃), 3.71 (9/5H, s, OCH₃) and 3.78 (6/5H, s, OCH₃) (3.73, s, at 55°C), 2.90-2.99 and 3.81-4.02 (2H, m, NCH₂), 5.51 (2/5H, s, NCHN) and 5.60 (3/5H, s, NCHN) (5.55, s, at 55°C), 6.35 (1H, d-like, arom-H), 6.64 (1H, t-like, arom-H), 7.09-7.16 (2H, m, arom-H); ms m/z (%) 298 (M⁺, 20), 231 (100), 216 (4), 171 (12), 144 (29); HRMs calcd for C₁₃H₁₈N₂O₂ 298.1676. Found 298.1671 (M⁺).

1-Methoxycarbonyl-3a-dimethylpropargyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole 27

Similar treatment of 9 (0.13 g, 0.25 mmol) with Fe(NO₃)₃·9H₂O in ethanol (10 ml) under ice cooling, followed by work-up as described above, gave 0.07 g of 27 (93%) as a yellowish oil. 27: uv λmax 245, 300nm; ir v max 3380, 3280, 2970, 2050, 2000, 1689, 1600, 1200, 740cm⁻¹; ¹H-nmr (500MHz) δ 1.08 (1H, s, CH₃), 1.10 (2H, s, CH₃), 1.33 (1H, s, CH₃), 1.34 (2H, s, CH₃), 2.19 (1/3H, s, C=CH), 2.20 (2/3H, s, C=CH), 2.13-2.18 and 2.56-2.66 (2H, m, CH₂), 2.97-3.03 and 3.65-3.82 (2H, m, NCH₂), 3.69 (2H, s, OCH₃), 3.78 (H, s, OCH₃), 4.63 (1/3H, s, NH, exchangeable), 5.09 (2/3H, s, NH, exchangeable), 5.42 (1/3H, s, NCHN), 5.48 (2/3H, s, NCHN), 6.57-6.58 (1H, m, arom-H), 6.71-6.75 (1H, m, arom-H), 7.08-7.15 (2H, m, arom-H); ms m/z (%) 284 (M⁺, 21), 217 (100), 157 (14), 130 (19). These spectral data were identical with those obtained by our previous method.⁸

Reduction of 3-(1,1-dimethylpropargyl)indole 5 to 3-(1,1-dimethylallyl)indole 6

5% Pd-CaCO₃ (4 mg) and quinoline (0.02 ml) were added to the flask charged with 3-(1,1-dimethylpropargyl)-indole 5 (66.7 mg, 0.36 mmol) and dry benzene (10 ml) under a nitrogen atmosphere. Hydrogen was introduced with vigorously stirring for 75 min, and the reaction mixture was filtered through celite. The filtrate was washed with 5%HCl, H₂O, and brine and dried over Na₂SO₄. After concentration by rotary evaporation, the residue was purified by flash chromatography (AcOEt/n-Hex=1/5) to give 6 (67.8 mg) quantitatively as a pinkish oil. ⁶:¹⁶

uv λmax 223.5, 278, 283, 292nm; ir v max (neat) 3400, 3060, 3040, 2950, 2910, 2850, 1630, 1610, 1450, 990, 740cm⁻¹; ¹H-nmr (60MHz) δ 1.52 (6H, s, CH₃), 5.02 (1H, dd, J=1.5, 11Hz, C=CH₂), 5.15 (1H, dd, J=1.5, 17Hz, C=CH₃), 6.14 (1H, dd, J=11, 17Hz, CH=CH), 6.85-7.35 (4H, m, C₂-H and arom-H), 7.64-7.70 (1H, m, arom-H), 7.78 (1H, bs, NH); ms m/z (%) 185 (M⁺, 39), 170 (100), 158 (39), 155 (18), 143 (16), 115 (13); HRMs calcd for C₁₃H₁₅N 185.1204; Found 185.1204 (M⁺).

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REFERENCES AND NOTES


14. The formation of ene-yne complex 26 was observed in all experiments. mp 31.5~33.5°C (sublimed), ir v max 2090, 2040, 2010, 1630, 1450cm⁻¹; ¹H-nmr (270MHz) δ 2.07 (3H, s, CH₃), 5.29 (1H, s, C=C=CH₂), 5.39 (1H, s, C=CH₂), 6.19 (1H, s, C=CH₂).


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