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

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Abstract - Indole reacted with (propargyl alcohol)$Co_2(CO)_6$ 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)$Co_2(CO)_6$ complex **23** provided 3a-(1,1-dimethylpropargyl)hexahydropyrroloindole cobalt complex **9**. Oxidative demetalation of **3**, **11**, and **9** with $Fe(NO_3)_3$ 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] ilamycins,[2] brevianamide E,[3] roquefortine,[4] LL S490β [5] and flustramine A and C[6] which have a 1,1-dimethylallyl group (invert 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-alkylindoles, is crucial for the successful synthesis of these alkaloids. Three methods[7] 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 invert prenyl group.

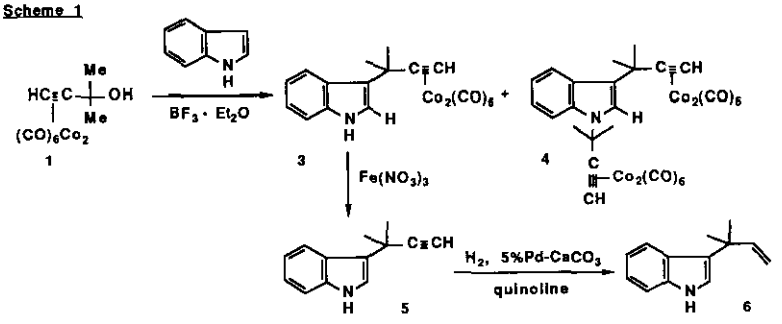
The reaction of cobalt-complexed propargylic alcohols with HBF_4 developed by Nicholas[9] seemed attractive since a cobalt-stabilized carbocation can be reacted with a variety of carbon nucleophiles to provide alkylated products. Recently, Schreiber and coworkers have reported

† 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.[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.

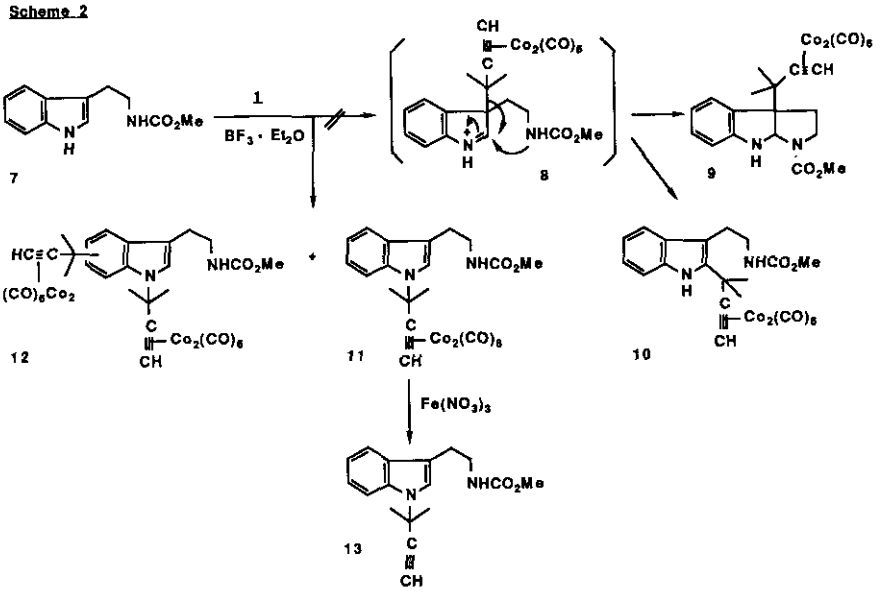
In our first experiment with propargyl dicobalt hexacarbonyl cation, we carried out the reaction of indole with the propargylic alcohol dicobalt hexacarbonyl complex **1** in the presence of BF_3·etherate instead of HBF_4 (tetrafluoroboric acid). The reaction proceeded under ice-salt cooling for 1.5 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 ^1H 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 ^1H-nmr spectrum of **3**, the C-2 proton signal, which was assigned by the selective decoupling method, appeared at δ 7.05 as a doublet with J=1.8Hz. This peak became a singlet upon D_2O addition. The C-4 proton was shifted to down field (δ 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 $Fe(NO_3)_3$·$9H_2O$ in EtOH[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

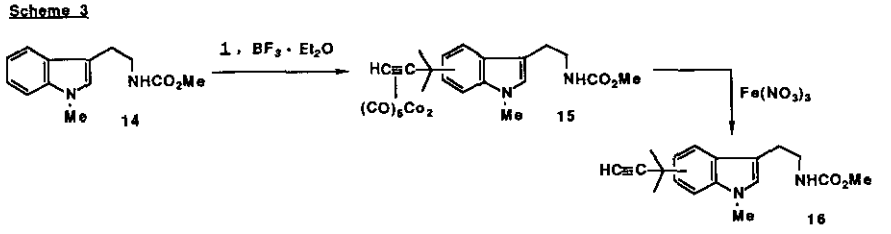


Similar reaction of **1** with N′-methoxycarbonyltryptamine **7** under ice-salt cooling for 3 h did not give the expected compound **9** or **10** but resulted in the formation of N-substituted complex **11** in 77% yield, whereas the reaction at ambient temperature gave a trace amount of disubstituted 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

Scheme 2

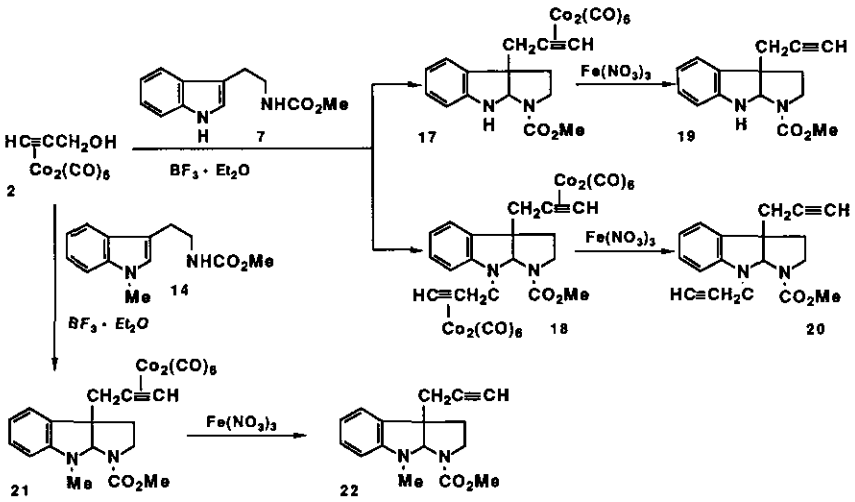


Scheme 3



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 $Fe(NO_3)_3$ 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 bulkyness of **1**. Therefore, the reaction of **7** with the less hindered propargyl complex **2** was carried out in the presence of BF_3•etherate in CH_2Cl_2 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 CH_2Cl_2 at ambient temperature for 4 h, **21** was formed in 69% yield. Treatment of **17**, **18** and **21** with $Fe(NO_3)_3$ provided **19**, **20**, and **22**, respectively (Scheme 4).

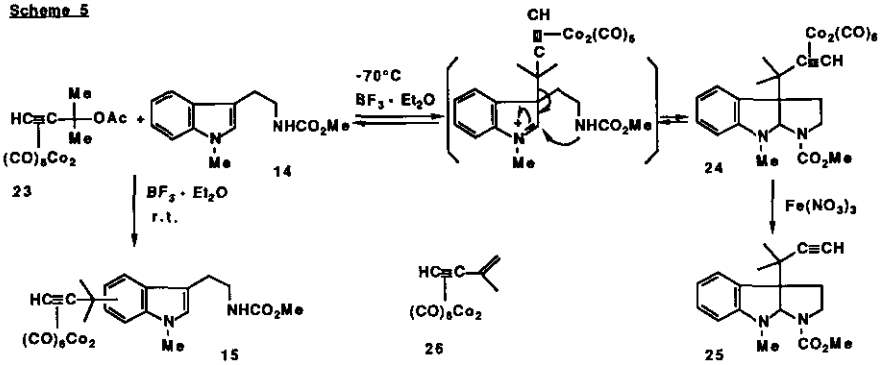
Scheme 4



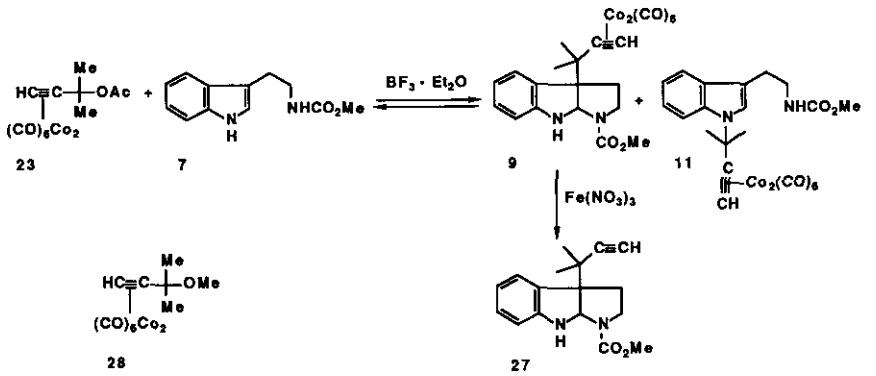
From the above results, steric factors appeared to influence the formation of pyrroloindole cobalt complexes *via* the reaction at the C-3 position of 3-substituted indole derivatives. As 1,1-dimethylpropargyl alcohol dicobalt complex **1** is too bulky to react at the 3-position, it seemed necessary 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**.[9a] 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'-methoxycarbonyltryptamine **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 initialy 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**,[9a, 14] and a trace amount of **15** when dissolved in

BF_3·etherate-CH_2Cl_2 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 $NaHCO_3$ at low temperature (Scheme 5)

Scheme 5



Scheme 6



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 BF_3·etherate in CH_2Cl_2 at ambient temperature, indicating that **9** reverted to **7** more slowly than **24** to **14**. These reactions were also examined in the presence of $EtAlCl_2$, $AlCl_3$, Me_2BBr, $TiCl_4$, $TiCl_4$-DABCO,[13] $SnCl_4$, and $ZnCl_2$. However, the reactions did not proceed, with exception of $TiCl_4$ (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

dicobalt complex **28** with BF_3•etherate[10] gave starting material, and the reaction of **7** with **28** in the presence of $TiCl_4$-DABCO[13] gave **9** in 6.6% yield. Further application of this method to the synthesis of natural products is in progress.

EXPERIMENTAL

Melting points were determined with Yamato MP-1 and Yanagimoto micro melting point apparatus, and are uncorrected. Uv spectra were recorded on a Hitachi 323 spectrophotometer. Ir spectra were obtained with a Hitachi 260-10 spectrophotometer. Mass spectra were recorded on a Hitachi M-60 or a RMU-7M mass spectrometer. Nmr spectra were recorded on a Hitachi R-24B (^{1}H-nmr, 60MHz), a JEOL JNM-FX 270, a JEOL JNM-GX 270 (^{1}H-nmr, 270MHz and ^{13}C-nmr, 67.8MHz), or a JEOL JNM-GSX 500 (^{1}H-nmr, 500MHz) spectrometer. All chemical shifts are reported downfield from TMS as an internal standard and expressed as δ values(ppm). Microanalyses were performed on a Perkin-Elmer 240 C, H, and N analyzer. Unless otherwise noted uv spectra (λ in nm) refer to a solution in 95% EtOH, ir spectra (υ in cm^{-1}) to KBr disks, and nmr spectra to solutions in $CDCl_3$.

Representative alkylation of indole derivative with propargyl alcohol dicobalt hexacarbonyl complexes: 3-Dimethylpropargylindole dicobalt hexacarbonyl complex **3** and 1,3-bis(dimethylpropargyl)indole bis(dicobalt hexacarbonyl)complex **4**[14]

A dry flask was charged with a solution of the indole (0.47 g, 4.01 mmol) in dry CH_2Cl_2 (30 ml) cooled in a ice-salt bath under an argon atmosphere. A solution of (1,1-dimethylpropargyl alcohol)$Co_2(CO)_6$ complex **1**[14] (1.64 g, 4.43 mmol) in dry CH_2Cl_2 (5 ml) and a solution of BF_3•Et_2O (distilled over CaH_2) (1.13 g, 7.96 mmol) in CH_2Cl_2 (5 ml) were added by injection. After stirring for 1.5 h, the reaction mixture was quenched by the addition of saturated $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2. The combined organic extracts were washed with brine and dried over Na_2SO_4 and the solvent was removed by rotary evaporation. Silica gel chromatography (AcOEt/n-Hex=1/5) gave 1.61 g of **3** (86%) and 0.24 g of **4** (7%) as dark red prisms. **3**: mp 116.5~117.5°C (n-Hexane); uv λmax 218, 260^{sh}, 292^{sh}, 346, 410^{sh}nm; ir vmax 3380, 2080, 2050, 2020, 1950, 1450, 740cm^{-1}; ^{1}H-nmr (270MHz) δ 1.83 (6H, s, CH_3CCH_3), 6.30 (1H, s, C≡CH), 7.05 (1H, d, J=1.8Hz, C_2-H, collapses to s with D_2O), 7.18-7.26 (2H, m, C_5, $_6$-H), 7.34 (1H, d, J=8Hz, C_7-H), 7.93 (1H, d, J=7Hz, C_4-H), 7.96 (1H, s, NH, exchangeable); ^{13}C-nmr (67.8MHz) δ 200.0 (s, CO), 137.3 (s, C_{7a}), 125.5 (s, C_{3a}), 125.6 (s, C≡CH), 122.0 (d, C_5 or C_6), 121.3 (d, C_4), 119.2 (d, C_6 or C_5), 120.3 (d, C_2), 111.5 (d, C_7), 110.4 (s, C_3), 74.5 (d, C≡CH), 39.0 (s, CH_3CCH_3), 32.0 (q, CH_3). **4**: mp 133.5~135.5°C (n-Hexane); uv λmax 218^{sh}, 260^{sh}, 305^{sh}, 350nm; ir vmax 3050, 3100, 2980, 2970, 2080, 2050, 2010, 1210, 740cm^{-1}; ^{1}H-nmr (270MHz) δ 1.76 (6H, s, CH_3), 2.07

(6H, s, CH_3), 6.25 (2H, s, C≡CH), 7.12 (1H, s, C_2-H), 7.23-7.14 (2H, m, C_5, $_6$-H), 7.69 (1H, d, J=8Hz, C_7-H), 7.89 (1H, d, J=7Hz, C_4-H).

N-Dimethylpropargyl-N'-methoxycarbonyltryptamine dicobalt 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 CH_2Cl_2 (20 ml) in the presence of BF_3•Et_2O (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, 270^{sh}, 300^{sh}, 352, 410^{sh}nm; ^{1}H-nmr (270MHz) δ 2.13 (6H, s, CH_3CCH_3), 2.92 (2H, t, J=7Hz, CH_2), 3.40-3.50 (2H, m, CH_2N), 3.67 (3H, s, OCH_3), 4.65 (1H, bs, NH), 6.30 (1H, s, C≡CH), 7.14 (1H, s, C_2-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 CH_2Cl_2 (30 ml) carried out in the presence of BF_3•Et_2O (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 recoved 0.12 g of **7** (61%). **12**: uv λmax 303, 350nm; ^{1}H-nmr (270MHz) δ 1.75 (15/2H, s, CH_3), 1.84 (9/2H, s, CH_3), 2.85-2.95 and 3.08-3.14 (2H, m, CH_2), 3.40-3.57 (2H, m, CH_2N), 3.68 (3H, s, OCH_3), 4.60 (3/8H, bs, NH), 4.70 (5/8H, bs, NH), 6.15 (3/8H, s, C≡CH), 6.21 (5/8H, s, C≡CH), 6.25 (1H, s, C≡CH), 7.10(1H, s, C_2-H), 7.38-7.89 (3H, m, arom-H).

N-Methyl-N'-methoxycarbonyldimethylpropargyltryptamine dicobalt 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 CH_2Cl_2 (20 ml) in the presence of BF_3•Et_2O (0.42 g, 3.00 mmol) at -54°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 recoved 0.07 g of **14** (38%). **15**: uv λmax 226, 260^{sh}, 346, 400^{sh}nm; ^{1}H-nmr (270MHz) δ 1.79 (9/2H, s, CH_3CCH_3), 1.80 (3/2H, s, CH_3CCH_3), 2.88-2.97 (2H, m, CH_2), 3.46-3.50 (2H, m, CH_2N), 3.67 (3H, s, NCH_3), 3.75 (9/4H, s, OCH_3), 3.71 (3/4H, s, OCH_3), 4.71 (1H, bs, NHCO), 6.18 (1/4H, s, C≡CH), 6.20 (3/4H, s, C≡CH), 6.85 (1H, s, C_2-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-Methoxycarbonyl-3a-propargyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole dicobalt hexacarbonyl complex **17** and 1-Methoxycarbonyl-3a,8-dipropargyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole bis(dicobalt hexacarbonyl)complex **18**

Similar treatment of N'-methoxycarbonyltryptamine **7** (0.80 g, 3.66 mmol) and (propargyl alcohol)$Co_2(CO)_6$ complex **2** (1.40 g, 4.09 mmol) in CH_2Cl_2 (50 ml) in the presence of BF_3•Et_2O (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 recoved 0.30 g of **7** (38%). **17**: uv λmax 240^{sh}, 290^{sh}, 350nm; ^{1}H-nmr (270MHz) δ 2.24-2.29 (2H, m, CH_2), 3.06-3.13 and 3.62-3.65 (2H, m, NCH_2), 3.42 (1H, d, J=16.5Hz, CH_2C≡CH), 3.53 (1H, d, J=16.5Hz,

$CH_2C{\equiv}CH$), 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, NCHN), 5.72 (1/2H, s, C≡CH), 5.75 (1/2H, s, C≡CH), 6.60 (1H, d, J=8Hz, arom-H), 6.77 (1H, d, J=7Hz, arom-H), 7.07-7.14 (2H, m, arom-H). **18**: uv λmax 250^{sh}, 315^{sh}, 350nm; ^{1}H-nmr (270MHz) δ 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=16Hz, $CH_2C{\equiv}CH$), 3.50 (1H, d, J=16Hz, $CH_2C{\equiv}CH$), 3.76 (3/2H, s, OCH_3), 3.78 (3/2H, s, OCH_3), 4.72-4.90 (2H, m, $NCH_2C{\equiv}CH$), 5.78-5.92 (2H, m, C≡CH), 6.07 (1H, s, NCHN), 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-hexahydropyrrolo[2,3-b]indole dicobalt hexacarbonyl complex **21**

Similar treatment of N-methyl-N′-methoxycarbonyltryptamine **14** (0.25 g, 1.08 mmol) and **2** (0.37 g, 1.08 mmol) in CH_2Cl_2 (30 ml) in the presence of $BF_3{\cdot}Et_2O$ (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 recoved 0.071 g of **14** (19%). **21**: uv λmax 248^{sh}, 308^{sh}, 348, 400^{sh}nm; ^{1}H-nmr (270MHz) δ 2.06-2.18 (2H, m, CH_2), 2.87 (3/2H, s, NCH_3), 2.96 (3/2H, s, NCH_3), 2.96-3.10 and 3.80-3.93 (2H, m, NCH_2), 3.40 (1H, d, J=17Hz, $CH_2C{\equiv}CH$), 3.58 (1H, d, J=17Hz, $CH_2C{\equiv}CH$), 3.72 (3/2H, s, OCH_3), 3.77 (3/2H, s, OCH_3), 5.47 (1/2H, s, NCHN), 5.56 (1/2H, s, NCHN), 5.63 (1/2H, s, C≡CH), 5.68 (1/2H, s, C≡CH), 6.38 (1H, d, J=8Hz, arom-H), 6.69 (1H, dd, J=7, 7Hz, arom-H), 7.01 (1H, d, J=7Hz, arom-H), 7.14 (1H, dd, J=7, 8Hz, arom-H).

Representative alkylation of N′-methoxycarbonyltryptamine with propargyl acetate dicobalt hexacarbonyl complex: 1-Methoxycarbonyl-3a-dimethylpropargyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole dicobalt hexacarbonyl complex **9**

A dry flask was charged with a solution of N′-methoxycarbonyltryptamine **7** (0.50 g, 2.29 mmol) in dry CH_2Cl_2 (80 ml) and cooled to -70°C under an argon atmosphere. A solution of (1,1-dimethylpropargyl acetate)$Co_2(CO)_6$ complex **23**[12, 15] (1.89 g, 4.51 mmol) in dry CH_2Cl_2 (20 ml) and a solution of $BF_3{\cdot}Et_2O$ (distilled over CaH_2) (1.75 g, 12.3 mmol) in dry CH_2Cl_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_2Cl_2. The combined organic extracts were washed with brine and dried over Na_2SO_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**: uv λmax 245^{sh}, 310^{sh}, 350, 385nm; ^{1}H-nmr (500MHz) δ 1.16 (2H, s, CH_3CCH_3), 1.45 (4H, s, CH_3CCH_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, NCHN), 5.46 (2/3H, s, NCHN), 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).

1-Methoxycarbonyl-3a-dimethylpropargyl-8-methyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole dicobalt hexacarbonyl complex **24**

Similar treatment of N-methyl-N'-methoxycarbonyltryptamine **14** (0.40 g, 1.72 mmol) and **23** (1.05 g, 2.51 mmol) in CH_2Cl_2 (20 ml) in the presence of $BF_3 \cdot Et_2O$ (1.85 g, 13.0 mmol) at -90 ~ -80°C for 42 h, followed by addition of saturated $NaHCO_3$ at reaction temperature and work-up as described above, gave 0.20 g of **24** (14%) as a dark red oil and the recoved 0.23 g of **14** (58%). **24**: uv λmax 252, 315, 350^{sh}nm; ^{1}H-nmr (270MHz) δ 1.12 (3H, s, CH_3CCH_3), 1.45 (3H, s, CH_3CCH_3), 2.02-2.08 and 2.22-2.32 (2H, m, CH_2), 2.86 (3/2H, s, NCH_3), 2.94 (3/2H, s, NCH_3), 3.74 (3/2H, s, OCH_3), 3.80 (3/2H, s, OCH_3), 2.86-2.94 and 3.78-4.06 (2H, m, NCH_2), 5.48 (1/2H, s, NCHN), 5.62 (1/2H, s, NCHN), 5.83 (1/2H, s, C≡CH), 5.93 (1/2H, s, C≡CH), 6.37 (1H, d-like, arom-H), 6.67 (1H, t-like, arom-H), 7.09-7.18 (2H, m, arom-H).

Representative oxidative demetalation of propargyl indole dicobalt hexacarbonyl complex with ferric nitrate: Formation of 3-Dimethylpropargylindole **5**

The 3-(1,1-dimethylpropargyl)indole dicobalt hexacarbonyl complex **3** (0.50 g, 1.07 mmol) was dissolved in ethanol (10 ml). Ferric nitrate•$9H_2O$ was added in portions with stirring at ambient temperature until evolution of CO_2 ceased and $Fe(NO_3)_3$ color persisted. This solution was then partitioned between CH_2Cl_2 and H_2O. The aqueous layer was extracted with CH_2Cl_2. The combined organic extracts were washed with water and brine, dried over Na_2SO_4 and concentrated by rotary evaporation. The residue was subjected to silica gel flash chromatography (AcOEt/n-Hex=1/5) to give 0.19 g of **5** (97%) as a pink solid; **5**: uv λmax 222.5, 275^{sh}, 282, 291nm; ir νmax 3400, 3280, 2970, 1620, 1540, 1450, 740cm^{-1}; ^{1}H-nmr (270MHz) δ 1.74 (6H, s, CH_3CCH_3), 2.29 (1H, s, C≡CH), 7.10-7.23 (3H, m, C_2-H and arom-H), 7.34-7.37 (1H, m, arom-H), 7.91 (1H, bs, NH, exchangeable), 7.94 (1H, d, J=8Hz, C_4-H); ms *m/z* (%) 183 (M^+, 53), 168 (100), 141 (18); HRms calcd for $C_{13}H_{13}N$ 183.1046. Found 183.1046 (M^+).

N-Dimethylpropargyl-N'-methoxycarbonyltryptamine **13**:

Similar treatment of **11** (0.24 g, 0.42 mmol) with $Fe(NO_3)_3 \cdot 9H_2O$ in ethanol (10 ml) under ice-salt cooling, followed by work-up as described above, gave **13** (0.12 g) quantitatively as a yellowish oil. This structure of **13** was confirmed by comparison with the sample prepared by the other method.[8]

N-Methyl-N'-methoxycarbonyldimethylpropargyltryptamine **16**

Similar treatment of **15** (0.23 g, 0.40 mmol) with $Fe(NO_3)_3 \cdot 9H_2O$ in ethanol (10 ml) under ice cooling, followed by work-up as described above, gave 0.81 g of **16** (68%) as a colorless oil. **16**: uv λmax 230.5, 283^{sh}, 291nm; ir νmax (neat) 3270, 2950, 2000, 1700, 1520, 870, 790, 770cm^{-1}; ^{1}H-nmr (270MHz) δ 1.68 (9/2H, s, CH_3CCH_3), 1.69 (3/2H, s, CH_3CCH_3), 2.36 (3/4H, s, C≡CH), 2.38 (1/4H, s, C≡CH), 2.95 (2H, t, J=7Hz, CH_2), 3.45-3.55 (2H, m, CH_2N), 3.66 (3H, s, NCH_3), 3.74 (3/4H, s, OCH_3), 3.76 (9/4H, s, OCH_3), 4.74 (1H, bs, NHCO), 6.87 (1H, s, C_2-H),

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 $Fe(NO_3)_3 \cdot 9H_2O$ 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 νmax 3370, 3270, 2940, 1700, 750, 740cm^{-1}; ^{1}H-nmr (270MHz) δ 2.05 (1H, t, J=3Hz, C≡CH), 2.22-2.46 (2H, m, CH_2), 2.52 (1H, dd, J=7, 3Hz, CH_2C≡CH), 2.59 (1H, dd, J=7, 3Hz, CH_2≡CH), 3.02-3.12 and 3.61-3.81 (2H, m, CH_2N), 3.69 (12/7H, s, OCH_3), 3.78 (9/7H, s, OCH_3), 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 $C_{15}H_{16}N_2O_2$: C, 70.10; H, 6.30; N, 10.82. Found: C, 70.10; H, 6.30; N, 10.82.

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 $Fe(NO_3)_3 \cdot 9H_2O$ 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 νmax 3270, 2940, 1680, 740cm^{-1}; ^{1}H-nmr (270MHz) δ 2.03 (1H, t, J=3Hz, CH_2C≡CH), 2.08 (1H, s, NCH_2C≡CH), 2.13-2.35 (2H, m, CH_2), 2.55 (1H, dd, J=17, 3Hz, CH_2C≡CH), 2.65 (1H, dd, J=17, 3Hz, CH_2C≡CH), 3.11-3.19 and 3.82-3.91 (2H, m, NCH_2), 3.73 (18/11H, s, OCH_3), 3.82 (15/11H, s, OCH_3), 4.08-4.37 (2H, m, NCH_2C≡CH), 5.44 (5/11H, s, NCHN), 5.52 (6/11H, s, NCHN), 6.60 (1H, dd, J=7, 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 $C_{18}H_{18}N_2O_2$ 294.1369. Found 294.1368 (M^+); Anal. Calcd for $C_{18}H_{18}N_2O_2$: 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, 0.9 mmol) with $Fe(NO_3)_3 \cdot 9H_2O$ 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 νmax (neat) 3270, 3040, 2940, 1690, 1600, 740cm^{-1}; ^{1}H-nmr (270MHz) δ 2.00 (1H, t, J=3Hz, C≡CH), 2.04-2.33 (2H, m, CH_2), 2.52 (1H, dd, J=17, 3Hz, CH_2C≡CH), 2.54 (1H, dd, J=17, 3Hz, CH_2C≡CH), 2.91 (6/5H, s, NCH_3), 3.91 (9/5H, s, NCH_3), 3.06-3.09 and 3.83-3.94 (2H, m, NCH_2), 3.72 (9/5H, s, OCH_3), 3.78 (6/5H, s, OCH_3), 5.32 (2/5H, s, NCHN), 5.40 (3/5H, s, NCHN), 6.40 (1H, d, J=8Hz, arom-H), 6.66-6.71 (1H, m, arom-H), 7.11-7.17 (2H, 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 $Fe(NO_3)_3 \cdot 9H_2O$ 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 νmax

(neat) 3270, 2960, 2100, 1700, 1600, 740cm^{-1}; ^{1}H-nmr (270MHz) δ 1.02 (9/5H, s, CH_3) and 1.05 (6/5H, s, CH_3) (this splitting of the signals of the methyl protons can be ascribed to hindered rotation about the amide group. At 55°C, the methyl protons appear as a sharp singlet at 1.05), 1.32 (9/5H, s, CH_3) and 1.34 (6/5H, s, CH_3) (1.31, s, at 55°C), 2.03-2.09 and 2.43-2.49 (2H, m, CH_2), 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, NCH_3), 2.99 (6/5H, s, NCH_3), 3.71 (9/5H, s, OCH_3) and 3.78 (6/5H, s, OCH_3)(3.73, s, at 55°C), 2.90-2.99 and 3.81-4.02 (2H, m, NCH_2), 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 $C_{18}H_{22}N_2O_2$ 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 $Fe(NO_3)_3 \cdot 9H_2O$ 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 vmax 3380, 3280, 2970, 2050, 2000, 1689, 1600, 1200, 740cm^{-1}; ^{1}H-nmr (500MHz) δ 1.08(1H, s, CH_3), 1.10 (2H, s, CH_3), 1.33 (1H, s, CH_3), 1.34 (2H, s, CH_3), 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, CH_2), 2.97-3.03 and 3.65-3.82 (2H, m, NCH_2), 3.69 (2H, s, OCH_3), 3.78 (H, s, OCH_3), 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-$CaCO_3$ (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 vigrously stirring for 75 min, and the reaction mixture was filtered through celite. The filtrate was washed with 5%HCl, H_2O, and brine and dried over Na_2SO_4. 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 vmax (neat) 3400, 3060, 3040, 2950, 2910, 2850, 1630, 1610, 1450, 990, 740cm^{-1}; ^{1}H-nmr (60MHz) δ 1.52 (6H, s, CH_3), 5.02 (1H, dd, J=1.5, 11Hz, C=CH_a), 5.15 (1H, dd, J=1.5, 17Hz, C=CH_b), 6.14 (1H, dd, J=11, 17Hz, CH=C), 6.85-7.35 (4H, m, C_2-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 $C_{13}H_{15}N$ 185.1204; Found 185.1204 (M^+).

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