Acylation, Cyanoethylation and Alkylation of Methyl and Phenyl Indolylmagnesium Salts: Influence of the Substituents on the *C*- and *N*-Reaction Products

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Analysis of the influence of the substitution on indolylmagnesium salts in the reaction with benzoyl chloride, acrylonitrile and methyl iodide, giving the *C*- and *N*-derivatives, have been carried out. The yield in the *C*- and *N*-product depends upon the electronic character and position of the substituent (methyl or phenyl) on the indole ring and of the ethereal solvent as well as the concentration and molar ratio of the reagents. The 2- or 3-phenyl substituted indolylmagnesium salts with acrylonitrile always gave the 1-(2-cyanoethyl)indole derivative.

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The *N*-alkylation of heterocyclic compounds bearing an N-H acidic hydrogen such as pyrrole or indole is generally performed by treatment of the heterocycle with the appropriate base and an alkylating agent [1]. However, the indolyl anion exhibits ambident behavior as a nucleophile, and substantial quantities of the *C*- and *N*-alkylated products can be obtained [2]. Some factors influence the relative *N*- to *C*-alkylation: a) the cation of the indolyl salt (*N*-alkylation generally predominates when the cation is sodium or potassium ion, while *C*-alkylation usually predominates with harder cations [3] like magnesium or lithium; b) the solvent [4]; and c) the alkylating agent (active allylic or benzylic halides generally afford a greater proportion of *C*-alkylated material [5]).

Furthermore, it has been reported that *N*-alkylindoles can be obtained in excellent yield using the indolyl salts under phase-transfer conditions in the presence of crown ethers or polyethylene glycols or their dialkyl ethers or quaternary ammonium ions [2a-c,6,7].

On the other hand, alkoxyindolylmagnesium halides couple with α-chloroacetamides, ethyl chloroformate, acyl chlorides, and nitroethenes [8a-c] generally in low yields.

Moreover, 2,3-dimethylindole and 1,2,3,4-tetrahydrocarbazole afford the corresponding 3*H*-indole derivative, albeit in low yield [9]. Recently we reported the specific *C*-methylation of the 1,2,3,4-tetrahydrocarbazolylmagnesium salt and structural analogues in good yields [10].

However, the stereoelectronic influence of the substituents on the indole ring in the acylation, cyanoethylation and alkylation have not been well established. The regioselective alkylation or acylation of the indole ring is a strategic point and a key step in alkaloid synthesis as the intramolecular cyclization to prepare the E ring of aspidospermidine, in which we are interested.

Benzoylation of Indolylmagnesium Derivatives with Benzoyl Chloride.

The indolylmagnesium salts were prepared in 0.3 or 0.45 *M* concentration by reaction of the indole derivative **1a-b** with methylmagnesium iodide in diethyl ether or tetrahydrofuran respectively in quantitative yield, under rigorous dryness and an argon atmosphere [11]. The indolylmagnesium salt affinity for small amounts of oxygen in the inert reaction atmosphere has been analyzed and applied [7,10].

Table 1

Benzoylation of the Indolylmagnesium Derivatives

Compound	Solvent	Indole/ Benzoyl Chloride	Product	%
Indole **1a**	Diethyl ether	1:1	**5a**	45
Indole **1a**	Diethyl ether	1:3	**5a**	75
Indole **1a**	Tetrahydrofuran	1:1	**5a**	20
2-Methylindole **1b**	Diethyl ether	1:1	**4b**	72
2-Methylindole **1b**	Diethyl ether	1:2	**4b**	91
2-Methylindole **1b**	Tetrahydrofuran	1:2	**4b**	50
2-Methylindole **1b**	Toluene	1:3	**4b**	79
3-Methylindole **1c**	Diethyl ether	1:2	**2c**	85
2,3-Dimethylindole **1d**	Diethyl ether	1:2	**2d**	45
			3d	39

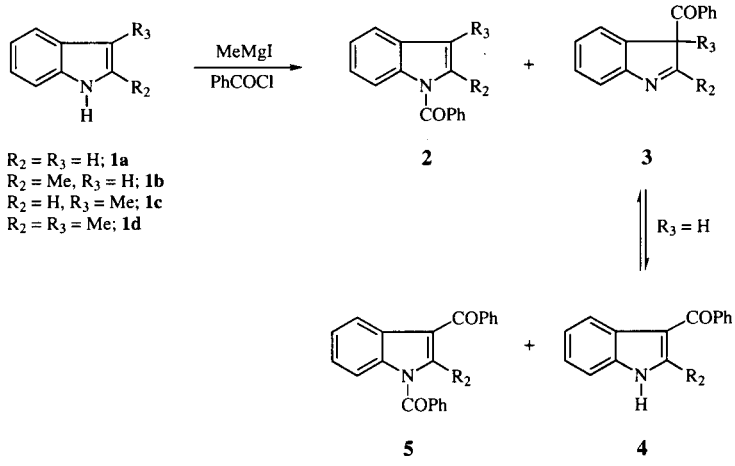
The benzoylation was carried out by addition of a solution of benzoyl chloride, in diethyl ether (or tetrahydrofuran) to the corresponding indolylmagnesium salt. In this way, the reaction of the indolylmagnesium iodide and benzoyl chloride gives 1,3-dibenzoylindole **5a**, as the unique product in moderate yield which decreases with the polarity of the ethereal solvent [12], but considerably increases with the benzoyl chloride concentration, Table 1. Thus, the 1,3-dibenzoylindole **5a** proceeds by attack of the enhanced carbanionic character on position 3 of the indolylmagnesium salt to the benzoyl chloride giving **3a**, that is in equilibrium with the NH indole **4a**, and transforms into **5a** by the fast *N*-benzoylation in the presence of the Grignard reagent, Scheme 1.

Compound **4b** is an orange crystalline solid that exhibits an anomalous infrared and ^{1}H-nmr spectra due to the intermolecular hydrogen bridge between the NH and CO groups. The structure was confirmed by X-ray diffraction analysis [13].

In contrast, the reaction of 3-methylindolyl magnesium iodide in diethyl ether and benzoyl chloride, only gives 1-benzoyl-3-methylindole **2c**, in good yield, while 2,3-dimethylindolylmagnesium iodide in diethyl ether and benzoyl chloride, gives both 1-benzoyl-2,3-dimethyl indole **2d** and 3-benzoyl-2,3-dimethyl-3*H*-indole **3d**, practically in the same amount.

The influence of methyl substitution in the above reaction can be analyzed by comparison with the unsubstituted indole. Thus, the presence of a methyl substituent on position 2 enhances the yield and regioselectivity in the *C*-benzoylation product; the *N*-benzoyl derivative was never detected. In contrast, a methyl substituent on position 3 enhances *N*-benzoylation, and the *C*-benzoyl derivative was never detected, Table 1 and Scheme 1.

Scheme 1
Benzoylation of Indolylmagnesium Salts



Moreover, 2-methylindolylmagnesium iodide in diethyl ether and benzoyl chloride gives only 3-benzoyl-2-methylindole **4b** in excellent yield, Table 1. The yield of the reaction increases with the amount of the benzoyl chloride in diethyl ether but decreases with the polarity of the ethereal solvent [12]. Toluene is also a remarkably good solvent in this reaction, Table 1.

On the basis of the experiences with 2-methyl and 3-methyl derivatives, the reaction of 2,3-dimethylindolyl-

Table 2
Cyanoethylation of the Indolylmagnesium Salts

Compound	Solvent	Indole/ Acrylonitrile	Product	%
2-Methylindole **1b**	Tetrahydrofuran	1:1.5	**9b**	36
			8b	54
2-Methylindole **1b**	Tetrahydrofuran	1:3	**9b**	46
			8b	30
3-Methylindole **1c**	Tetrahydrofuran	1:4	**6c**	58
2,3-Dimethylindole **1d**	Tetrahydrofuran	1:3	**7d**	64
2-Phenylindole **1e**	Tetrahydrofuran	1:2	**6e**	75
3-Phenylindole **1f**	Tetrahydrofuran	1:2	**6f**	85
2-Methyl-3-phenylindole **1g**	Tetrahydrofuran	1:3	**6g**	78
3-Methyl-2-phenylindole **1h**	Tetrahydrofuran	1:4	**6h**	85

magnesium and benzoyl chloride agrees well with the expected activation on the 3 and 1 positions of the indole ring respectively by both methyl substituents, Scheme 1.

Cyanoethylation of Indolylmagnesium Salts.

The reaction of the indolylmagnesium salts with α-haloacetonitriles is used for the preparation of tryptamines and alkaloids [14]. Some indolylmagnesium compounds add to nitriles to give ketones on hydrolysis [15]. The behavior of an acrylonitrile as an electrophile in the reaction with the indolylmagnesium halides is now examined.

The indolylmagnesium salts in tetrahydrofuran, prepared with the corresponding indole **1b-h** and *n*-butylmagnesium chloride in tetrahydrofuran, and acrylonitrile as a soft acid substrate [3], under rigorous dryness and argon atmosphere [10,11], gives the cyanoethyl derivative in moderately good yield, Table 2.

The use of *n*-butylmagnesium chloride in tetrahydrofuran has some advantages: a) gives a homogeneous solution; and b) avoids the anionic polymerization of the acrylonitrile. In contrast, the insolubility of methylmagnesium iodide (in diethyl ether) for the required concentrations and their anionic catalyst activity in diethyl ether (or diethyl ether: dichloromethane [16]) produces important amounts of polymerized acrylonitrile as an insoluble yellow solid.

The cyanoethylation of the indolylmagnesium salts shows some differences with the benzoylation studied. The reaction of 2-methylindolylmagnesium chloride with acrylonitrile, gives a mixture of 1,3-di(2-cyanoethyl)-2-methylindole **9b** and 3-(2-cyanoethyl)-2-methylindole **8b**. Moreover, the ratio **9b/8b** increases with the acrylonitrile concentration, Table 2, and thus, the formation of the 1,3-disubstituted product **9b** proceeds from the 3-(2-cyanoethyl) intermediate **7b** that is in equilibrium with the NH indole **8b** which in the presence of the Grignard reagent and excess acrylonitrile transforms into the *N*-cyanoethylation product **9b**, Scheme 2. On this basis, the presence of a methyl substituent on position 2 enhances the *C*-cyanoethylation, Table 2 and Scheme 2.

The reaction between 3-methylindolylmagnesium chloride and acrylonitrile gives the 1-(2-cyanoethyl)-3-methylindole **6c** as the only alkylation product. Thus, the presence of the methyl substituent on position 3 enhances the formation of the *N*-cyanoethyl derivative, Table 2 and Scheme 2.

However, the reaction of 2,3-dimethylindolylmagnesium chloride and acrylonitrile gives only 3-(2-cyanoethyl)-2,3-dimethyl-3*H*-indole **7d**.

On the basis of these observations with 2-methyl and 3-methyl derivatives, the results of the reaction with the 2,3-dimethyl derivative is evidence that only the methyl substituent on position 2 exhibits important activation on position 3 of the indole ring, Scheme 2.

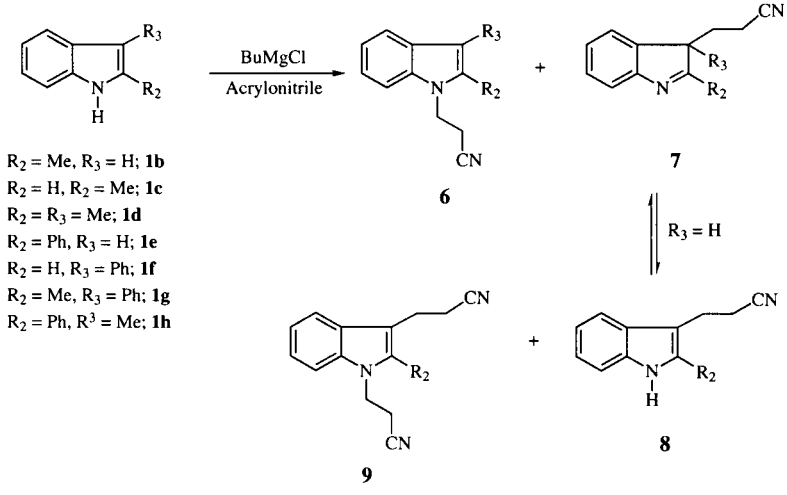
On the other hand, the influence of the phenyl substitution in the indolylmagnesium salt on the cyanoethylation was also studied.

The influence of the phenyl and methyl substituents both on positions 2 or 3 of the indolylmagnesium salts have been also studied in the cyanoethylation reaction. In this way, the 2-methyl-3-phenyl (or 3-methyl-2-phenyl) salts of the indoles **1g** (or **1h**) and acrylonitrile always gives the 1-cyanoethyl derivative **6g** (or **6h**) as the only cyanoethylation product in good yield, Table 2, Scheme 2. Then, a phenyl substituent on position 2 or 3 induces the formation of the *N*-cyanoethylation product and the activation effect of the methyl substituent on position 2 is completely eliminated by the withdrawing effect of the phenyl substituent, Table 2 and Scheme 2.

Methylation of Indolylmagnesium Salts.

The methylation of the indole ring was carried out with the corresponding indolylmagnesium salts (0.3 *M*) in

Scheme 2
Cyanoethylation of Indolylmagnesium Salts



diethyl ether and methyl iodide. In this way, 2-methylindolylmagnesium iodide, prepared by reaction of 2-methylindole with a solution of methylmagnesium iodide in diethyl ether, was treated with methyl iodide to give 2,3-dimethylindole **1d** and 1,2-dimethylindole **10** as the alkylation products. However, larger amounts of methyl iodide increases the yield of **1d** and 1,2-dimethylindole **10** and furthermore 2,3,3-trimethyl-3*H*-indole **11** in low yield. Compound **11** was obtained from the reaction of the indolylmagnesium salt of **1d** and methyl iodide. Thus, the methyl substituent on position 2 regloselectively induces the formation of the *N*-alkylation product, Table 3.

Table 3
Methylation of the Indolylinagnesium Salts

Compound	Solvent	Indole/ Methyl iodide	Product	%
2-Methylindole **1b**	Diethyl ether	1:1	**1d**	24
			10	45
2-Methylindole **1b**	Diethyl ether	1:4	**1d**	32
			10	54
			11	5
2,3-Dimethylindole **1d**	Diethyl ether	1:9	**11**	78

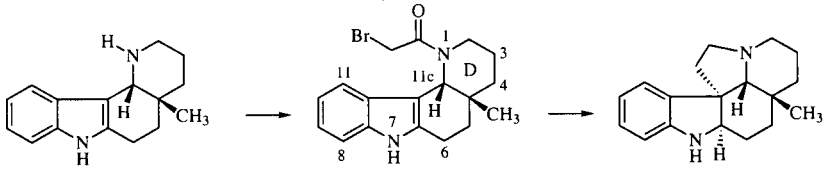
In the same way, the reaction of 2,3-dimethylindolylmagnesium iodide (0.3 *M*) in diethyl ether and methyl iodide, gives the 2,3,3-trimethyl-3*H*-indole as an orange oil in good yield as the single reaction product. Hence, the 2,3-dimethyl substitution in the indolylmagnesium salt enhances the formation of the *C*-alkylation product which agrees well with the methylation of 2,3-polymethylene-1*H*-indolylmagnesium halides [10]. The last alkylation reaction studied was adapted to the 2,3-dialkylated indole system **13**, Scheme 3.

in excellent yield starting from the *cis* tetracyclic derivative **12** with bromoacetyl chloride in toluene in the presence of triethylamine.

Compound **13** exists in a conformational equilibrium (2:1 ratio by ^{1}H-nmr) due to the rotamers of the amide group in contrast with the NH derivative. The nmr spectrum exhibits an anisotropic effect on the proton at C11c by the CO group that appears as two singlets at 5.50 (main) and 4.70 ppm (C=O on opposite sides to C11c, Scheme 3). Moreover, two NH signals at 8.65 and 8.45 appear in the spectrum as broad singlets in a 2:1 ratio. Also, the infrared spectrum exhibits two absorption bands of the NH group at 3390 and 3280 cm^{-1} that give evidence for the existence of two rotamers.

Although the structure of the main rotamer shows the bromo methyl group at an appropriate distance (crystallographic molecular models) for the intramolecular 5-*exo*-*trig*-cyclization [19], the indolylmagnesium salt of **13** in tetrahydrofuran or toluene, is not transformed into the cyclization product and practically all the starting product was recovered. The increase of the ionicity of the *N*-metal bond (Li, or Na, in tetrahydrofuran or toluene) was unsuccessful.

Scheme 3
Intramolecular Alkylation of the Indolylmagnesium Salt of **13**



12 **13** **14**

Having efficiently solved the stereochemistry at the C/D ring junction of **12** [18], the total synthesis of the 20-methyl analogue of aspidospermidine **14** was undertaken by intramolecular *C*-alkylation of the indolylmagnesium salt to the E-ring.

The alkylation of tetracyclic compound **12** with 1,2-dibroethane was unsuccessful [18]. In this way a more reactive 1-bromoacetyl-4a-methyl-*cis*-2,3,4,4a,5,6,7,11c-octahydro-1*H*-pyrido[3,2-*c*]carbazole **13** was synthesized

EXPERIMENTAL

Melting points were determined on a Reichert hotstage microscope and are uncorrected. The ir spectra (FT) were obtained as neat films between sodium chloride plates or

potassium bromide pellets or a Nujol suspension. The nmr spectra were recorded at 200 MHz. Chemical shifts are given in δ units. Deuteriochloroform with tetramethylsilane as internal standard was used as the solvent, unless otherwise noted. Mass spectral analyses were recorded by electron impact at 70 eV. Yields are given on isolated products. Materials were obtained from commercial suppliers and used without further purification. All substituted indoles were prepared satisfactorily by the Fischer reaction from the phenylhydrazones of the appropriate ketones and were purified by column chromatography.

Benzoylation of the Methylindolylmagnesium Iodide Derivatives. General Procedure.

To a solution of methylmagnesium iodide (1.9 mmoles) in diethyl ether was added the indole derivative (1.9 mmoles) in diethyl ether (1 ml) and the mixture was stirred for 1 hour. A solution of benzoyl chloride (1.9 mmoles) in diethyl ether (1 ml) was added and after 6 hours, the mixture was hydrolyzed with a saturated aqueous ammonium chloride solution and extracted twice with diethyl ether (10 ml). The combined organic extracts were washed with 10% sodium hydroxide solution, dried over magnesium sulfate. After filtration the solvent was evaporated at reduced pressure to give a residual brown oil that was purified on a silica gel column *via* cromatography using ethyl acetate-hexane (1:3) as the eluent.

1,3-Dibenzoylindole **5a**.

Indolylmagnesium iodide and benzoyl chloride give 1,3-dibenzoylindole **5a** as a white solid (45%), mp 171-172°, (Rf, 0.55); ^{1}H nmr (deuteriochloroform): δ 7.4-7.7 (m, 8H), 7.7-7.9 (m, 5H), 8.25-8.35 (m, 2H); ir (Nujol): 1690, 1635, 760, 755, 710 cm^{-1}; ms: (70 eV) m/z 339 (M$^+$, 12), 325 (35), 105 (100), 77 (57).

Anal. Calcd for $C_{22}H_{15}NO_2$: C, 81.21; H, 4.65; N, 4.31. Found: C, 81.09; H, 5.35; N, 3.97.

3-Benzoyl-2-methylindole **4b**.

2-Methylindolylmagnesium iodide and benzoyl chloride gave 3-benzoyl-2-methylindole **4b** as an orange solid (91%), mp 181-182°, (Rf, 0.25); ^{1}H nmr (deuteriochloroform): δ 2.50 (s, 3H), 7.10 (m, 2H), 7.35 (m, 2H), 7.50 (m, 3H), 7.70 (m, 2H); ir (potassium bromide): 3260-3100, 1595, 1570, 800, 750, 730, 705 cm^{-1}; ms: (70 eV) m/z 236 (18), 235 (M$^+$, 100), 234 (12), 157 (9), 104 (9).

Anal. Calcd. for $C_{16}H_{13}NO$: C, 81.68; H, 5.57; N, 5.95. Found: C, 81.14; H, 5.88; N, 5.45.

1-Benzoyl-3-methylindole **2c**.

3-Methylindolylmagnesium iodide and benzoyl chloride give 1-benzoyl-3-methylindole **2c** as a green oil (85%), (Rf, 0.58); ^{1}H nmr (deuteriochloroform): δ 2.25 (s, 3H, CH_3), 7.05 (s, 1H, H-2), 7.35 (m, 2H), 7.50 (m, 4H), 7.70 (d, 2H, J = 7.3 Hz), 8.40 (d, 1H, J = 8.0 Hz); ir (film): 1680, 750, 725, 700 cm^{-1}; ms: (70 eV) m/z 235 (M$^+$, 41), 105 (100), 77 (54).

Anal. Calcd. for $C_{16}H_{13}NO$: C, 81.68; H, 5.57; N, 5.95. Found: C, 81.23; H, 5.25; N, 5.55.

1-Benzoyl-2,3-dimethylindole (**2d**) and 3-Benzoyl-2,3-dimethylindole (**3d**).

2,3-Dimethylindolylmagnesium iodide and benzoyl chloride give 1-benzoyl-2,3-dimethylindole (45%) and 3-benzoyl-2,3-dimethylindole (39%) as oils.

1-Benzoyl-2,3-dimethylindole **2d**.

This compound (Rf, 0.65) had ^{1}H nmr (deuteriochloroform): δ 2.20 (s, 3H), 2.30 (s, 3H), 7.00 (m, 2H), 7.15 (m, 2H), 7.50 (m, 3H), 7.70 (m, 2H); ir (film): 1680, 750, 720, 700 cm^{-1}.

Anal. Calcd for $C_{17}H_{15}NO$: C, 81.89; H, 6.06; N, 5.62. Found: C, 81.60; H, 6.34; N, 5.37.

3-Benzoyl-2,3-dimethylindole **3d**.

This compound (Rf, 0.42) had ^{1}H nmr (deuteriochloroform): δ 1.45 (s, 3H); 2.70 (s, 3H), 7.0-7.5 (m, 9H); ir (film): 1720, 1600, 1580, 750, 710 cm^{-1}.

Anal. Calcd. for $C_{17}H_{15}NO$: C, 81.89; H, 6.06; N, 5.62. Found: C, 81.55; H, 5.75; N, 5.67.

Cyanoethylation of Indolylmagnesium Chloride Salts. General Procedure.

To a solution of *n*-butylmagnesium chloride in tetrahydrofuran (2 *M*), 3.4 ml (6.9 mmoles), under an argon atmosphere, was added the appropriate indole derivative (6.9 mmoles) in dry tetrahydrofuran (11 ml). After 1 hour at room temperature acrylonitrile was added in the same molar ratio. The mixture was stirred at room temperature for 24 hours. The reaction was hydrolyzed with a saturated aqueous solution of ammonium chloride and extracted with dichloromethane. The organic layer was dried over anhydrous magnesium sulfate and after filtration the solvent was removed to give a residual brown oil that was purified by column chromatography using ethyl acetate:hexane (1:3) as the eluent.

1,3-Di(2-cyanoethyl)-2-methylindole (**8b**) and 3-(2-Cyanoethyl)-2-methylindole (**9b**).

The reaction of 2-methylindolylmagnesium chloride and acrylonitrile during 2 hours gave two products. When the molar ratio of 2-methylindolyl chloride to acrylonitrile was 1:1.5; 1,3-di(2-cyanoethyl)-2-methylindole **9b** was obtained as a white solid (327 mg, 36%), mp 142-143°, (Rf, 0.36) and 3-(2-cyanoethyl)-2-methylindole **8b** was also obtained as a white solid (563 mg, 54%), mp 78-79° (Rf, 0.13). When the molar ratio of 2-methylindolylmagnesium chloride to acrylonitrile was 1:3, 1,3-di(2-cyanoethyl)-2-methylindole **9b** (404 mg, 46%) and 3-(2-cyanoethyl)-2-methylindole **8b** (227 mg, 30%) were the products.

1,3-Di(2-cyanoethyl)-2-methylindole **9b**.

This compound had ^{1}H nmr (deuteriochloroform): δ 2.50 (s, 3H), 2.61 (t, 2H, J = 7.2 Hz), 2.75 (t, 2H, J = 6.9 Hz), 3.12 (t, 2H, J = 7.2 Hz), 4.43 (t, 2H, J = 6.9 Hz), 7.20 (m, 3), 7.51 (m, 1H, H-7); ir (potassium bromide): 2250, 690 cm^{-1}; ms: (70 eV) m/z 237 (M$^+$, 19), 197 (100), 157 (25), 156 (20).

Anal. Calcd. for $C_{15}H_{15}N_3$: C, 75.92; H, 6.37; N, 17.71. Found: C, 75.77; H, 6.03; N, 17.41.

3-(2-Cyanoethyl)-2-methylindole **8b**.

This compound had ^{1}H nmr (deuteriochloroform): δ 2.45 (s, 3H), 2.65 (t, 2H, J = 6.0 Hz), 3.08 (t, 2H, J = 6.0 Hz), 7.12 (m, 2H, ArH), 7.28 (m, 1H, ArH), 7.42 (m, 1H, ArH), 7.88 (s, 1H, NH); ir (potassium bromide): 3340, 2240, 740 cm^{-1}; ms: (70 eV) m/z 184 (M$^+$, 20), 144 (100), 143 (13), 115 (6), 77 (6).

Anal. Calcd. for $C_{12}H_{12}N_2$: C, 78.23; H, 6.57; N, 15.21. Found: C, 78.01; H, 6.20; N, 14.79.

1-(2-Cyanoethyl)-3-methylindole **6c**.

3-Methylindolylmagnesium chloride and acrylonitrile (1:3) gave 1-(2-cyanoethyl)-3-methylindole **6c** as an orange solid (360

mg, 58%), mp 72-74°, (Rf, 0.4); ^{1}H nmr (deuteriochloroform): δ 2.31 (s, 3H), 2.74 (t, 2H, J = 6.3 Hz), 4.35 (t, 2H, J = 6.3 Hz), 6.90 (s, 1H), 7.20 (m, 3H), 7.58 (m, 1H); ir (Nujol): 2260, 790 cm^{-1}; ms: (70 eV) m/z 184 (M$^+$, 42), 144 (100), 128 (5), 115 (9).

Anal. Calcd. for $C_{12}H_{12}N_2$: C, 78.23; H, 6.57; N, 15.21. Found: C, 78.11; H, 6.74; N, 14.95.

3-(2-Cyanoethyl)-2,3-dimethyl-3*H*-indole **7d**.

2,3-Dimethylindolylmagnesium chloride and acrylonitrile (1:3) gave 3-(2-cyanoethyl)-2,3-dimethyl-3*H*-indole **7d** as an orange oil (400 mg, 64%), (Rf, 0.3); ^{1}H nmr (deuteriochloroform): δ 1.30 (s, 3H), 1.60 (t, 2H, J = 6.9 Hz), 2.25 (m, 2H), 2.30 (s, 3H), 7.20 (m, 2H), 7.40 (m, 1H), 7.60 (m, 1H); ir (film): 2240, 1570, 760 cm^{-1}; ms: (70 eV) m/z 198 (M$^+$, 26), 158 (100), 143 (15), 115 (24), 77 (12).

Anal. Calcd. for $C_{13}H_{14}N_2$: C, 78.75; H, 7.12; N, 14.13. Found: C, 78.45; H, 7.05; N, 14.35.

1-(2-Cyanoethyl)-2-phenylindole **6e**.

2-Phenylindolylmagnesium and acrylonitrile (1:2) gave 1-(2-cyanoethyl)-2-phenylindole **6e** as a yellow solid (808 mg, 75%), mp 87-89°, (Rf, 0.49); ^{1}H nmr (deuteriochloroform): δ 2.51 (t, 2H, J = 6.6 Hz), 4.48 (t, 2H, J = 6.6 Hz), 6.55 (s, 1H), 7.21 (m, 3H), 7.65 (m, 1H); ir (potassium bromide): 2240, 760, 750, 690 cm^{-1}.

Anal. Calcd. for $C_{17}H_{14}N_2$: C, 82.90; H, 5.73; N, 11.37. Found: C, 82.79; H, 5.45; N, 11.15.

1-(2-Cyanoethyl)-3-phenylindole **6f**.

3-Phenylindolylmagnesium chloride and acrylonitrile (1:2) gave 1-(2-cyanoethyl)-3-phenylindole **6f** as a white solid (959 mg, 85%), mp 76-77°, (Rf, 0.32); ^{1}H nmr (deuteriochloroform): δ 2.79 (t, 2H, J = 6.8 Hz), 4.42 (t, 2H, J = 6.8 Hz), 7.29 (m, 5H), 7.45 (m, 2H), 7.66 (m, 2H), 7.98 (m, 1H); ir (potassum bromide): 2240, 760, 740, 700 cm^{-1}; ms (70 eV): m/z 246 (M$^+$, 60), 206 (100), 178 (15), 128 (14).

Anal. Calcd. for $C_{17}H_{13}N_2$: C, 83.24; H, 5.34; N, 11.42. Found: C, 83.02; H, 5.54; N, 11.22.

1-(2-Cyanoethyl)-2-methyl-3-phenylindole **6g**.

2-Methyl-3-phenylindolylmagnesium chloride and acrylonitrile (1:3) gave 1-(2-cyanoethyl)-2-methyl-3-phenylindole **6g** as a brown solid (887 mg, 78%), mp 89-90°, (Rf, 0.35); ^{1}H nmr (deuteriochloroform): δ 2.52 (s, 3H), 2.81 (t, 2H, J = 6.4 Hz), 4.50 (t, 2H, J = 6.4 Hz), 7.18 (m, 1H), 7.25 (m, 1H), 7.31 (m, 1H), 7.50 (m, 5H), 7.60 (m, 1H); ir (potassium bromide): 2240, 770, 740, 700 cm^{-1}; ms: (70 eV) m/z 260 (M$^+$, 52), 220 (100), 204 (18), 178 (8).

Anal. Calcd. for $C_{18}H_{16}N_2$: C, 83.04; H, 6.19; N, 10.76. Found: C, 82.78; H, 6.40; N, 10.52.

1-(2-Cyanoethyl)-3-methyl-2-phenylindole **6h**.

3-Methyl-2-phenylindolylmagnesium chloride and acrylonitrile (1:4) gave 1-(2-cyanoethyl)-3-methyl-2-phenylindole **6h** as a white solid (905 mg, 85%), mp 87-88°, (Rf, 0.53); ^{1}H nmr (deuteriochloroform): δ 2.23 (s, 3H), 2.50 (t, 2H, J = 7.3 Hz), 4.83 (t, 2H, J = 7.3 Hz), 7.2-7.7 (m, 9H); ir (Nujol): 2250, 760, 740, and 705 cm^{-1}; ms: (70 eV) m/z 260 (M$^+$, 59), 220 (100), 205 (43), 204 (36).

Anal. Calcd. for $C_{18}H_{16}N_2$: C, 83.04; H, 6.19; N, 10.76. Found: C, 82.82; H, 5.99; N, 10.93.

Methylation of the Indolylmagnesium Salts.

2,3-Dimethylindole (**1d**) and 1,2-dimethylindole (**10**).

To a solution of methylmagnesium iodide (3.8 mmoles) in diethyl ether (5 ml), was added a solution of 2-methylindole (500 mg, 3.8 mmoles) in diethyl ether (5 ml) and after 1 hour at room temperature a solution of methyl iodide (0.24 ml, 3.8 mmoles) in diethyl ether (2.5 ml) was added dropwise. The mixture was stirred at room temperature for 24 hours and then hydrolyzed with a saturated aqueous ammonium chloride solution and extracted with dichloromethane. The extracts were dried over anhydrous magnesium sulfate and after filtration, the solvent was removed to give a brown oil which was purified by column chromatography using dichloromethane as the eluent giving two alkylation products: 2,3-dimethylindole **1d** in 24% yield, mp 105-106° and 1,2-dimethylindole **10** as an oil in 45% yield.

2,3,3-Trimethyl-3*H*-indole **11**.

To a solution of methylmagnesium iodide (2.08 mmoles) in diethyl ether (5 ml), was added a solution of 2,3-dimethylindole (301 mg, 2.08 mmoles) in diethyl ether (1 ml) and after 1 hour was added dropwise a solution of methyl iodide (1.20 ml, 19.3 mmoles) in diethyl ether (1 ml) and then stirred at room temperature for 24 hours. The mixture was hydrolyzed with a saturated aqueous solution of ammonium chloride and then extracted with dichloromethane (15 ml). The extracts were dried over anhydrous magnesium sulfate and after filtration of the solvent was removed to give a brown oil which was purified by column chromatography using ethyl acetate:hexane 1:1 as the eluent. 2,3,3-Trimethyl-3*H*-indole **11** was obtained as an orange oil (256.7 mg, 78%); ^{1}H nmr (deuteriochloroform): δ 1.29 (s, 6H), 2.72 (s, 3H), 7.20 (m, 3H), 7.50 (m, 1H); ir (film): 1570, 750 cm^{-1}; ms: (70 eV) m/z 159 (M$^+$, 12), 158 (19), 144 (100), 129 (19), 91 (16), 77 (14).

Anal. Calcd. for $C_{11}H_{13}N$: C, 82.97; H, 8.23; N, 8.80. Found: C, 82.59; H, 8.45; N, 7.50.

1-Bromoacetyl-4a-methyl-*cis*-2,3,4,4a,5,6,7,11c-octahydro-1*H*-pyrido[3,2-*c*]carbazole **13**.

In a Schlenk tube under rigorous dryness and an argon atmosphere and in an ice-water bath was placed a solution of the 4a-methyl-*cis*-2,3,4,4a,5,6,7,11c-octahydro-1*H*-pyrido[3,2-*c*]carbazole **12** [16], (70 mg, 0.3 mmoles) in dichloromethane (5 ml). Then triethylamine (0.04 ml, 0.3 mmoles) and bromoacetyl chloride (0.02, 0.3 mmoles) were added to the reaction mixture which was stirred at 0° for 2 hours and then was treated with water (10 ml) and extracted with dichloromethane (15 ml). The organic layer was dryed over magnesium sulfate and after filtration the solvent was removed and the 1-bromoacetylderivative **13** was obtained as a pale yellow solid (98 mg, 93%), mp 79-81°, (ethyl acetate, Rf, 0.82); ^{1}H nmr (deuteriochloroform): δ 1.00 (s, 3H), 1.18 (s, 3H), 1.2-2.0 (m, 4H), 2.6-2.9 (m, 4H), 3.61 (m, 1H), 4.0-4.5 (m, 3H), 4.72 (s, 1H), 5.50 (s, 1H), 6.95-7.35 (m, 4H), 8.46 (br s, 1H), 8.65 (br s, 1H); ir (potassium bromide): 3390, 3280, 1615, 740 cm^{-1}.

Anal. Calcd. for $C_{17}H_{21}N_2OBr$: C, 58.46; H, 6.06; N, 8.02. Found: C, 58.12; H, 6.34; N, 7.79.

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