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Molecular structure and reactivity of the 1,2-dihydrocarbazol-4(3*H*)-one: X-ray crystal structure of N-methyl and N-(p-methylbenzenesulfonyl) derivatives

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Synthesis and reactivity analysis of the 1,2-dihydrocarbazol-4(3H)-one, and the N-methyl, N-tosyl and 2,2-dimethyl derivatives have been carried out. Molecular structures of the N-methyl and N-tosyl derivatives have been analyzed by X-ray diffraction. Crystals of the N-methyl derivative are monoclinic, space group $P2_1/c$, a = 8.868(1), b = 16.652(1), c = 7.5440(4) Å, β = 113.657(3). Crystals of the N-tosyl derivative are monoclinic, $P2_1/c$, a = 12.0016(3), b = 8.9178(2), c = 16.0485(4) Å, β = 104.372(2). An extended conjugation from the carbonyl group to the nitrogen atom and an envelope conformation for the common cyclohexenone fragment are evident in both cases. Oximation and Beckmann rearrangement, and etherification of the carbonyl group is reported.

KEY WORDS: Synthesis, reactivity, tetrahydrocarbazol-4-one.

Introduction

Tetrahydrocarbazoles are important synthons for alkaloids synthesis.[1a] An apparent route to prepare 4-substituted alkylidene derivatives of the 4(3H)-1,2-dihydrocarbazole is the Wittig reaction between a suitable ylide and the 1,2-dihydrocarbazol-4(3H)-one. Thus, synthesis of this 4-oxocarbazole derivative, has been outlined as a functionalized intermediate. In this way, we have investigated the reactivity of this carbonyl group with nucleophiles as the corresponding Wittig ylides to form the 4-(N,N-dimethylaminoalkyl)-1,2,3,4-tetrahydrocarbazol derivatives which are potential intermediates for aspidosperma alkaloids synthesis[1a] or show the structural requirements of the antidepressant drugs.[1b]

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Experimental

M.p.s were measured in a hot-stage microscope and are uncorrected. The ir spectra were registered on a Pye-Unicam SP1100 spectrophotometer and the nmr spectra were obtained with a Bruker WH-200-SY (200 MHz) instrument. Mass spectra were obtained in a Hewlett-Packard 5985 gc-ms system. Elemental analysis were performed with Perkin-Elmer 240 elemental analyzer. The solvents and reagents were purified in the usual way. Yields are given after column chromatography.

Synthesis of 1,2-dihydrocarbazol-4(3H)-one, 1

A solution of 2,3-dichloro-5,6-dicyanobenzoquinone, 4.54 g (0.02 moles) in 30 ml of tetrahydrofuran was dropped at 0°C on a solution of 1,2,3,4-tetrahydrocarbazole, 1.71 g (0.01 mol) in 65 ml of tetrahydrofuran-water (9:1). The mixture was stirred first during 30 min at 0°C and finally 5 h at room-temperature.

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Then, 9.0 g of powdered potassium carbonate was added to the mixture and stirred during 1 hr. Solvent was evaporated, providing a residual brown solid, which was chromatographed on a silica gel column eluted with ethyl acetate–chloroform (4 : 1) to give 1,2-dihydrocarbazol-4(3H)-one, and 3,4-dihydrocarbazol-1(2H)-one, as colorless crystalline products recrystallized from ethanol, mp 220-222°C (lit[2] 221-222°C) and 168–170 in 89 and 2% yield, respectively (Scheme 1). 1,2-dihydrocarbazol-4(3H)-one, **1**. Found: C, 77.49; H, 6.08; N, 7.91. $C_{12}H_{11}NO$ requires C, 77.81; H, 5.99; N, 7.56; ν_{max}(KBr) 3400-2100 (br, NH), 1605 (C=O) and 750 (Ar) cm^{-1}; ν_{max}($HCCl_3$) 3455 (br, NH), 1647 (C=O), 750 (Ar) cm^{-1}. Nmr, δ_H ($DCCl_3$): 8.55 (1H, br s, NH), 8.22 (1H, m, 5-H), 7.3 (3H, m, 6-H, 7-H, 8-H), 2.98 (2H, t, 1-CH_2, J 6.18 Hz), 2.60 (2H, t, 3-CH_2, J 6.35 Hz), 2.25 (2H, m, 2-CH_2). M/z (70 eV): 185 (M^+, 71), 158(11), 157(100), 143(18), 130(11), 129(84), 128(25), 102(19), 77(10), 51(11).

3,4-dihydrocarbazol-1(2H)-one. Found: C, 77.56; H, 6.12; N, 7.80. $C_{12}H_{11}NO$ requires C, 77.81; H, 5.99; N, 7.56. ν_{max}(Nujole): 3700-2700 (br, assoc. NH), 1630 (C=O), 750(Ar). Nmr, δ_H ($DCCl_3$) 8.3 (br s, 1H, NH), 7.2 (m, 4H, Ar), 3.02 (t, 2H, 4-CH_2, J 6.0 Hz), 2.68 (t, 2H, 2-CH_2, J 6.0 Hz), 2.26 (m, 2H, 3-CH_2). M/z, (70 eV) 185 (M^+, 25), 171 (34), 170 (100), 168 (41), 157 (25), 129 (54), 105 (34), 97 (84), 85 (45).

Synthesis of 9-Methyl-1,2-dihydrocarbazol-4(3H)-one, 2

To a suspension of 0.27 g (1.46 mmol) of 1,2-dihydrocarbazol-4(3H)-one in 50 ml of an aqueous solution of sodium hydroxide (10%) stirred at 60–70°C for 30 min, was dropped during 2 hr, 3 ml of Me_2SO_4. After the addition, the mixture was stirred for 2 more hr, cooled, and extracted twice with dichloromethane. The organic extracts were washed with water, dried with magnesium sulfate, and finally the solvent was removed to give a slightly yellow solid which was recrystallized from methanol–water. The 9-methyl-1,2-dihydrocarbazol-4(3H)-one was obtained as a crystalline colorless solid, mp 194–196°C, in 89% yield on the starting indole **1**. Found: C, 77.94; H, 6.44; N, 6.85. $C_{13}H_{13}NO$ requires C, 78.36; H, 6.58; N, 7.03. ν_{max}(KBr): 1640 (C=O), 750 (Ar). Nmr, δ_H ($CDCl_3$) 8.24 (1H, m, 5-H), 7.20 (3H, m, 6-H, 7-H, 8-H), 3.65 (3H, s, CH_3), 2.88 (2H, t, J 6.20HZ, 1-CH_2), 2.54 (2H, t, J 3.36Hz, 3-CH_2), 2.22 (2H, m, 2-CH_2). Nmr, δ_C (50.3 MHz; $CDCl_3$) 193.63 (C=O), 151.76 (9a-C), 137.34 (8a-C), 124.71 (4b-C), 122.86 (6-C), 122.45 (5-C), 121.55 (7-C), 112.59 (4a-C), 109.01 (8-C), 37.77 (3-C), 29.73 (CH_3-N), 23.22 (1-C), 22.07 (2-C).

C(3)-Deuteration of 2

Accurate assignation of the methylene groups in the nmr spectrum (benzylic type and α-carbonyl methylenes) and in the mass fragmentation spectrum, was possible by only deuteration of the α-methylene to the carbonyl group. A solution of 30 mg of **2** and 1 mg of potassium hydroxide in 2 ml of dioxane-deuterium oxide (1 : 1) was stirred at room temperature for 170 h. Analysis by ^{1}H-nmr shows that **2** has interchanged two protons in 80% yield.

Synthesis of 9-p-toluensulphonyl-1,2-dihydrocarbazol-4(3H)-one, 3

In a previously flamed flask bottom were placed 0.18 g (1.0 mmol) of 1,2-dihydrocarbazol-4(3H)-one, and 0.05 g (2.1 mmol) of sodium hydride in 50 ml of THF, under argon atmosphere. The mixture was stirred at room temperature for 20 min, increased to 75°C and then, dropped into a solution of 0.60 g (3.1 mmol) of p-toluensulfonyl chloride in 15 ml of THF and stirred for 2 hr more. Solvent was removed and the crude residual solid was chromatographed in a silica gel column using dichloromethane as eluent. Compound **3** was obtained as a white solid, recrystallized from ethanol, mp 147–149°C in 95% yield on the starting indole **1**. Found: C, 67.04; H, 4.89; N, 3.78; S, 9.12. $C_{19}H_{17}NSO_3$ requires C, 67.27; H, 5.05; N, 4.13; S, 9.45; ν_{max}(KBr): 1670 (C=O), 755 (Ar). Nmr, δ_H ($CDCl_3$) 8.21 (1H, m, 5-H), 7.2 (3H, m, 6-H, 7-H, 8-H), 3.33 (2H, t, J 6.16Hz, 1-CH_2), 2.56 (2H, t, J 6.52Hz, 3-CH_2), 2.21 (2H, m, 2-CH_2) and tolyl group at 7.76 (2H, m, Ar-H, 7.30 (2H, m, Ar-H), 2.36 (3H, s, CH_3). Nmr, δ_C (50.3 MHz, $CDCl_3$) 194.98 (C=O), 150.90 (9a-C), 135.55 (8a-C), 125.79 (4b-C), 125.35 (6-C), 124.94 (5-C), 121.90 (7-C), 118.07 (4a-C), 113.87 (8-C), 37.88 (3-C), 24.54 (1-C), 23.21 (2-C) and tolyl group at 145.77 (para-C), 135.96 (C-S), 130.25 (two meta-C), 126.62 (two ortho-C), 21.63 (CH_3).

a. Reaction of the 1,2-dihydrocarbazol-4(3H)-ones 1-4 with hydroxylamine.

a.1. Reaction of 1 with hydroxylamine. General procedure. A mixture of 1 g (5.4 mmol) of **1**, 0.562 g (8.1 mmol) of hydroxylamine hydrochloride and 0.662 g (8.1 mmol) of sodium acetate in 10.6 ml of methanol and 4.6 ml of H_2O, under argon atmosphere, was warmed at the reflux temperature for 30 h. The reaction mixture was poured in 35 ml of H_2O–ice and a white precipitate was formed. The solid was filtrated and recrystallized from methanol-water (1 : 1), giving the oxime **5**, 1.026 g, 95% yield as a white solid, mp 203–205°C (lit[3] 208-210°C).

Nmr, δ_H (MeOD): 7.95 (1H, m, 8-H), 7.3 (1H, m, 5-H), 7.1 (2H, m, 6-H, 7-H), 2.85 (2H, t, J 6.3 Hz, 3-CH_2), 2.05 (2H, m, 1-CH_2), 1.2 (2H, t, J 7.5 Hz, 2-CH_2). Ir (KBr) 3410 (OH st), 1620 (C=N st), 1420 and 1490 (OH), 840 (N–O st). M/z, (70 eV) 200 (M^+, 100), 183 (21), 168 (15), 167 (13), 156 (30), 155 (68), 128 (15), 115 (6), 101 (8), 51 (3).

a.2. Reaction of 2 with hydroxylamine. Following the General procedure indicated in **a.1**, 0.733 g (3,6 mmol) of **2** and 0.412 g (5.9 mmol) of hydroxylamine hydrochloride for 15 h give the oxime **6**, 0.750 g, 95% as a white solid, recrystallized from methanol–water (1 : 1), mp 228-230°C. (Found: C, 72.54; H, 6.12; N, 12.81. $C_{12}H_{12}N_2O$ requires C, 72.88; H, 6.59; N, 13.07%). Nmr, δ_H ($CDCl_3$) 8.1 (1H, m, 8-H), 7.25 (3H, m, 5-H, 6-H, 7-H), 3.7 (3H, s, CH_3-N), 2.85 (4H, m, 1-CH_2, 3-CH_2), 2.1 (2H, q, J 6.8 Hz, 2-CH_2). ν_{max} (KBr) 3300 (OH st), 1630 (C=N st), 1450 and 1470 (OH), 885 (N-O st). M/z, (70 eV) 214 (M^+, 100), 197 (19), 182 (12), 170 (36), 169 (48), 157 (7), 140 (8), 127 (9), 115 (13), 101 (5), 51 (2).

a.3. Reaction of 3 with hydroxylamine. Following the General Procedure indicated in **a.1**, 0.3 g (0.887 mmol) of **3** and 0.13 g (1.8 mmol) of hydroxylamine hydrochloride for 9 h of reaction give the oxime **7**, 0.310 g (quantitative yield) as a white solid, recrystallized from methanol-water (1 : 1), mp 145–147°C. (Found: C, 64.23; H, 5.32; N, 7.86. $C_{19}H_{18}N_2O_3S$ requires C, 64.41; H, 5.12; N, 7.90; S, 9.03%). Nmr δ_H ($CDCl_3$) 8.2 (1H, m, 8-H), 8.1 (1H, m, 5-H), 7.7 and 7.25 (4H, Ar-Ts), 7.3 (2H, m, 6-H, 7-H), 3.2 (2H, t, J 6.8 Hz, 3-CH_2), 2.8 (2H, t, J 6.8 Hz, 1-CH_2), 2.35 (3H, s, CH_3-Ts), 2.0 (2H, m, 2-CH_2). Ir (KBr) 3310 (OH st), 1630 (C=N st), 1460 (OH), 1375 and 1100 (S=O st). M/z (70 eV) 354 (M^+, 84), 337 (3), 199 (100), 182 (42), 171 (13), 167 (21), 155 (39), 127 (25), 115 (12), 101 (6), 91 (63, 65 (24), 51 (3).

a.4. Reaction of 4 with hydroxylamine. Following the General Procedure indicated in **a.1**, 0.6 g (2.8 mmol) of **4** and 0.291 g (4.25 mmol) of hydroxylamine hydrochloride for 28 h give oxime **8**, 0.58 (90%) as a brown solid, recrystallized from methanol-water (1 : 1), mp 215-217°C. (Found: C, 73.58; H, 7.14; N, 12.05. requires C, 73.66; H, 7.07; N, 12.27%). Nmr δ_H ($DCCl_3$) 8.2 (1H, br s, NH), 8.00 (1H, m, 8-H), 7.30 (1H, m, 5-H), 7.21 (2H, m, 6-H, 7-H), 2.70 (2H, s, 3-CH_2), 2.61 (2H, s, 1-CH_2), 1.15 (6H, s, gem. Me_2). ν_{max} (KBr) 3310 (OH st), 1630 (C=N st), 1450 (OH), 900 (N-O st). M/z, (70 eV) 228 (M^+, 100), 212 (9), 196 (7), 169 (37), 155 (43), 130 (10), 101 (5), 51 (1).

b. Beckmann rearrangement of the oximes 5-8 in PPA

b.1. Rearrangement of 5 in PPA. General procedure. In a flask, previously flamed and under argon atmosphere, were placed 1.5 g (10.5 mmol) of phosphorous pentoxide and 1.5 ml of orthophosphoric acid (85%) at 120-130°C with stirring up to complete dissolution. Then, 0.65 g (3.5 mmol) of the oxime **5** was added and warmed at 150–160°C for 30 min. After cooling the mixture was poured in 150 ml of water–ice and the solid formed quickly filtered off. The solid was treated with 8 ml of NaOH 2N and 10 ml of ethanol with stirring for 2 h. The organic layer was extracted with dichloromethane, dried with $MgSO_4$, and decanted. Solvent was removed under vacuum to give a solid which was chromatographed in a silica gel column using dichloromethane–ethyl acetate (50 : 3) as eluent. The oxime unchanged was isolated and then the polarity of the eluent phase was increased with 30% ehtanol. 0.357 g, 55% of 3,4,5,6-tetrahydroazepino [4,3-b] indol-1(2H)-one **9**, was isolated, as a white solid, recrystallized from ethanol, mp 214-216°C (lit[3] 210°C).

Nmr δ_H (MeOD) 8.11 (1H, m, 7-H), 7.82 (1H, s, NHCO), 7.20 (1H, m, 10-H), 7.01 (2H, m, 8-H, 9-H), 3.25 (2H, m, 3-CH_2), 3.10 (2H, t, J 7.6 Hz, 5-CH_2), 2.05 (2H, m, 4-CH_2). ν_{max} (KBr) 3300-3000 (br, NH st), 1630 (CO, amide st), 1450 (NH, amide). M/z, (70 eV) 200 (M^+, 100), 171 (30), 170 (88), 157 (29), 144 (19), 143 (22), 130 (26), 115 (29), 102 (10), 51 (6).

b.2. Rearrangement of 6 in PPA. Following the General Procedure referred in **b.1**, 0.55 g (2.7 mmol) of **6** in polyphosphoric acid (33 g of P_2O_5 in 15 ml of orthophosphoric, 85%) at 150–160°C, after column chromatography, gave 0.304 g, 63.4% of the 9-methyl-3,4,5,6-tetrahydroazepino [4,3-b] indol-1(2H)-one **10**, as an slightly yellow solid, recrystallized from ethanol, mp 266–269°C. (Found C, 72.45; H, 6.45; N, 12.88.

requires C, 72.88; H, 6.59; N, 13.07%). Nmr δ_H ($DDCl_3$) 8.45 (1H, m 7-H), 7.21 (3H, m, 8-H, 9-H, 10-H), 6.7 (1H, br s, NHCO), 3.7 (3H, s, CH_3-N), 3.36 (2H, m, 3-CH_2), 3.08 (2H, t, J 7.3 Hz, 5-CH_2), 2.2 (2H, m, 4-CH_2). ν_{max} (KBr) 3280-3200 (br, NH st), 1625 (CO st, amide), 1470 and 1440 (NH, amide). M/z, (70 eV) 214 (M^+, 100), 185 (24), 184 (93), 171 (28), 158 (19), 157 (12), 154 (11), 144 (59), 130 (13), 129 (12), 128 (19), 115 (23), 93 (16), 81 (23), 77 (13), 58 (33), 51 (6).

b.3. Rearrangement of 7 in PPA. Following the General Procedure referred in **b.1**, 0.31 g (0.875 mmol) of **7** in polyphosphoric acid (22.2 g of P_2O_5 in 9.8 ml of orthophosphoric acid, 85%) at 150–160°C, after column chromatography, gave 0.244 g, 78% of 9-tosyl-3,4,5,6-tetrahydroazepino [4,3-b] indol-1(2H)-one, **11**, as a white solid recrystallized from ethanol, mp 265–270°C. (Found: C, 64.20; H, 4.98; N, 7.63. requires C, 64.41; H, 5.12; N, 7.90%). Nmr δ_H ($DCCl_3$) 8.9 (1H, br s, NHCO), 8.4 and 7.8 (4H, Ar and Ts), 7.8 (1H, m, 7-H), 7.6 (1H, m, 10-H), 7.3 (2H, m, 9-H, 8-H), 3.4 (2H, m, 2-CH_2), 3.2 (2H, q, J 6.8 Hz, 5-CH_2), 2.4 (3H, s, CH_3-Ts), 2.1 (2H, m, 4-CH_2). ν_{max} (KBr) 3400 (br, NH st), 1615 (CO st, amide), 1460 (NH, amide). M/z (70 eV) 354 (M^+, 91), 325 (38), 324 (82), 311 (30), 296 (22), 284 (11), 268 (17), 227 (13), 217 (12), 199 (16), 169 (51), 157 (21), 140 (36), 129 (44), 115 (46), 91 (74), 69 (82), 57 (100), 51 (15).

b.4. Rearrangement of 8 in PPA. Following the General Procedure referred in **b.1**, 0.438 g (1.92 mmol) of **8** in polyphosphoric acid (28.8 g of P_2O_5 in 12.72 ml of orthophosphoric acid, 85%) at 150–160°C, after column chromatography gave 0.221 g, 49% of 2,2-dimethyl-6(H)-3,5-dihydroazepino[4,3-b]indol-1(2H)-one, **12**, as a white solid, recrystallized from ethanol, mp 265–270°C. (Found: C, 73.33; H, 6.89; N, 12.32. requires C, 73.66; H, 7.07; N, 12.27%). Nmr δ_H ($DCCl_3$) 8.05 (1H, m, 7-H), 7.28 (1H, m, 10-H), 7.05 (2H, m, 8-H, 9-H), 2.90 (2H, s, 3-CH_2), 2.77 (2H, s, 5-CH_2), 1.00 (6H, s, Me_2). ν_{max} (Film) 3300–3100 (br, NH st), 1615 (CO, st amide), 1470–1450 (CH_2 as), 1235 (−CMe_2), 1480 (NH, amide). M/z, (70 eV) 228 (M^+, 95), 213 (19), 199 (29), 198 (47), 185 (27), 184 (100), 171 (15), 170 (19), 167 (14), 158 (26), 130 (43), 129 (43), 128 (33), 115 (17), 102 (28), 77 (22).

c. Ethanolic etherification of the enolic form of 1: preparation of 4-ethoxycyclohexano[b]indole, 13

In a flask, previously flamed, were placed 1.5 g (10.5 mmol) of P_2O_5 and 1.5 ml of orthophosphoric acid (85%), warmed at 60°C up to complete solution. Then was added a solution of 0.1 g (0.54 mmol) of 1,2-dihydrocarbazol-4(3H)-one in 20 ml of ethanol and the mixture was warmed at 100°C for 24 h. Finally the mixture was hydrolysed with 2 ml of water–ice, extracted with dichloromethane, dried with $MgSO_4$, and decanted. Solvent was removed under vacuum and the residual green oil was extracted in toluene and chromatographed in a silica gel column using dichloromethane-ethyl acetate (5:1) as eluent. The 4-ethoxy derivative **13** was obtained as a yellow oil, 40 mg, 35% yield (picrate, recrystallized from ethanol, mp 104–107°C). (Found: C, 78.45; H, 6.78; N, 6.42. $C_{14}H_{15}NO$ requires C, 78.84; H, 7.09; N, 6.57%) Nmr δ_H ($DCCl_3$) 8.45 (1H, m, 8-H), 7.45 (1H, m, 5-H), 7.25 (2H, m, 6-H, 7-H), 2.90 (2H, t, J 6.7 Hz, 1-CH_2), 2.75 (2H, t, J 6.7 Hz, 3-CH_2), 2.66 (2H, q, J 7.4 Hz, CH_2-CH_3), 2.05 (2H, dt or q, J 6.7 Hz, 2-CH_2), 1.22 (3H, t, J 7.4 Hz, CH_3CH_2). ν_{max} (Film) 1700–1680 (C=N st), 1460 (CH_2 as), 1375 (CH_3 st), 1180 (C=C-O-C st as), 760 (Ar ortho disubst). M/z, (70 eV) 213 (M^+, 31), 198 (22), 170 (26), 168 (8), 158 (25), 143 (14), 127 (65), 111 (25), 99 (100), 81 (44), 51 (4).

Structural solution

Crystals for X-ray diffraction were obtained by slow evaporation of an ethanol solution of **2** (or **3**). Summary of the X-ray crystal data collection and processing parameters are given in Table 1.

Results and discussion

Synthesis of the 1,2-dihydrocarbazol-4(3H)-one (**1**) and its 2,2-dimethyl derivative (**4**) were carried out by means of the Fischer reaction from its respective monophenylhydrazone of the cyclohexane-1,3-dione,[2] (**1**) or of the 5,5-dimethyl-cyclohexane-1,3-dione (dimedone) (**4**) in 51 and 43% yield respectively.

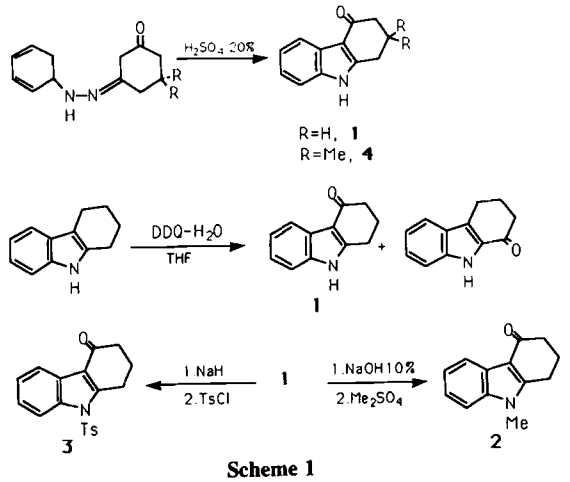
Synthesis of **1** was also carried out in good yield by means of the oxidation of 1,2,3,4-tetrahydrocarbazole with 2,3-dichloro-5,6-dicyanoquinone in an identical manner to that indicated previously.[8]

Synthesis of **2** and **3** was undertaken starting of **1** with the $NaOH/Me_2SO_4$ system and with the NaH/tosyl chloride system respectively, in good yields, Scheme 1.

Molecular structure of **1** was analyzed by X-ray diffraction.[2] The molecule is strongly associated forming molecular aggregates with intermolecular N-hydrogen-oxygen bridges between the N-H of the indole and the carbonyl group in an anti-form.

Table 1. Crystal Data and Summary of Intensity Data Collection and Structure Refinement.

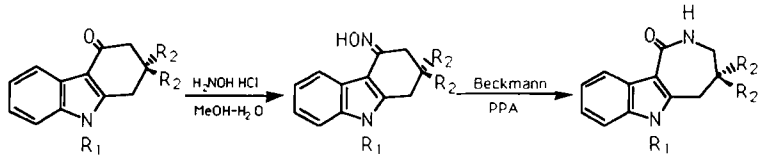
	Data for **2**	Data for **3**
Cmpd.,	N-methyl-1,2-dihydrocarbazol-4(3*H*)-one,	N-tosyl-1,2-dihydrocarbazol-4(3*H*)-one
Color/shape,	colorless/prismatic	colorless/prismatic
For. wt.,	$C_{13}H_{13}NO$, 199.27	$C_{19}H_{17}NSO_3$, 339.43
Space group,	monoclinic, $P2_1/c$	monoclinic, $P2_1/c$
Temp., °C,	20	20
Cell constants	(63 reflections, within $2 < \theta < 68°$)	
	a, 8.868(1) Å,	*a*, 12.0016(3) Å,
	b, 16.652(1) Å,	*b*, 8.9178(2) Å,
	c, 7.5440(4) Å,	*c*, 16.0485(4) Å,
	β, 113.657(3)	β, 104.372(2) deg,
	Cell vol. 1020.4(2)	Cell vol, 1660.9(1) $Å^3$
Formula units/unit cell,	Z, 4	Z, 4
D_{calc} g cm^3,	1.30(1)	1.35(1)
μ_{calc} cm^{-1},	6.121	18.227
Diffractometer/Scan,	Four-circle, Philips PW 1100, $\omega/2\theta$	
Radiation,	graphite monochromator, CuKα, λ = 1.5418	
Max crystal dimensions, mm,		
0.2 × 0.3 × 0.3		0.2 × 0.25 × 0.2
Scan width,	1.5	
Standard reflections,	90 measurements	
Decay of standards,	no intensity variation	
Reflections measured, 1811, 1371		
observed, with $I > 4\sigma(I)$		3002, 2757 observed, with $I > 2\sigma(I)$
2θ range, deg	$2 < \theta < 68$	
Range of *h*, *k*, *l*;	9, 19, ±8	14, 10, ±18
Corrections applied,	Lorenzt and polarization	
computer and programs,	VAX6410, MULTAN80[4], XRay76[5], PARST	
Source of Struture factors used,	International Tables for X-Ray Crystallography.[6]	
Structure solution,	direct methods, Least-squares in a block	
Treatment of hydrogen atoms,	difference synthesis, fixed as isotropic	
Weights, w-scheme,[7]	empirical as to give no trends in $\langle w\Delta F^2 \rangle$ versus $\langle \|F_o\| \rangle$ and $\langle \sin\theta/\lambda \rangle$,	
$R = \Sigma[\|F_o\| - \|F_c\|]/\Sigma\|F_o\|$, *R*w, 0.083; 0.105		0.045; 0.045



Scheme 1

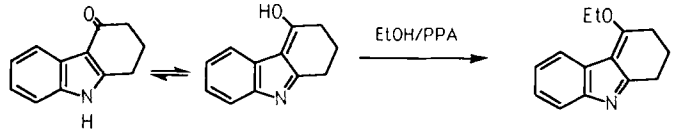
Structural analysis of **1**, **2**, **3** and **4** was carried out by ir and ^1H and ^{13}C-nmr and finally an X-ray study was carried out for **2** and **3** to understand the behavior of the carbonyl group in these compounds and the relation with **1** previously analysed.[2]

On the basis of the structural information obtained for **1**, to avoid the N-H···O=C bridged structure in the 4-oxocarbazole **1**, which can be related with the chemical inactivity of the compound, this was treated in two ways: a) a sample was slowly dissolved (low solubility) in chloroform. The ir spectrum of **1** in chloroform solution shows an absorption stretching band for the CO group at 1647 cm^{-1} (1605 in KBr[9]). Moreover, this frequency remains constant with the dilution, indicating the absence of hydrogen bridged structure (or no associate C=O group in chloroform) b) the N-hydrogen-oxygen bridge was blocked by methylation or tosylation forming **2** or **3**, respectively. In contrast to the NH, N-methyl- and N-tosyl-1,2-dihydrocarbazol-4(3H)-ones, show strong absorption bands in the ir spectrum for the carbonyl group at 1635 and 1665 cm^{-1} in $CHCl_3$, and 1640 and 1670 cm^{-1}, in KBr mulls, respectively.



Oxime	%	mp (°C)	Azepinone	(%)	mp (°C)
5 R_2=H, R_1=H,	96	203-5	**9** R_2=H, R_1=H	55	214-6
6 R_2=H, R_1=Me,	100	228-9	**10** R_2=H, R_1=Me	63	266-9
7 R_2=H, R_1=Ts,	100	145-7	**11** R_2=H, R_1=Ts	79	265-8
8 R_2=Me, R_1=H,	90	215-7	**12** R_2=Me, R_1=H	49	265-9

Scheme 2



13

Scheme 3

Compound **4**, shows two absorption bands for the C=O group at 1615 and 1640 in KBr mulls and 1640 cm^{-1} in $CHCl_3$. In the ^{13}C-nmr spectrum the C=O signal appears at 194.1 for **1** in chloroform vs 193.6 ppm for N-methyl and 195.0 for N-tosyl derivative. Thus, in chloroform solution, the NH derivatives **1** and **4** appears as the carbonyl tautomer. The 4-oxocarbazoles **1** and **4**, in chloroform solution, and the N-blocked derivatives **2** and **3** are inactive with Wittig reagents.

An interesting point was the formation of C-N bonds on 4-position of the tetrahydrocarbazole ring. Nucleophilic reaction of the hydroxylamine with the compounds **1** and **4** in chloroform (avoiding the N-H···O=C bridge) was unsuccessful, but in methanol-water (2 : 1) (protic solvents), oximation occurs in practically quantitative yield. Kinetics of this reaction were faster for the tosyl derivative **3**. Reactivity of these carbonyl compounds with hydroxylamine to give the oximes can be related with the evolution of the hydroxyl intermediate, formed by attack of the nucleophile, to the oxime which also exhibits an extent conjugation as the parent carbonyl compounds.

Beckmann rearrangement of the oximes **5-9** has been carried out in polyphosphoric acid at 150°C in short times in moderate-good yields, Scheme 2. Kinetic of the reaction was faster for the oxime **7** which have the more withdrawing substituent on the nitrogen. Moreover, evidence for the enolic form in the equilibrium of **1** was obtained by etherification of the enolic form, which has been possible using ethanol in polyphosphoric acid. The 4-ethoxycyclohexano[b]indole **13**, was isolated as a yellow oil (Scheme 3).

Crystal structure analysis of the tetrahydrocarbazolones 2 and 3

Figures 1 and 2 show the final X-ray model with the atomic numbering for compounds **2** and **3**, respectively. Atomic parameters for **2** and **3** are given in Tables 2 and 3, respectively. Bond lengths and angles for **2** and **3** are shown in Table 4. There are some bond lengths which are noticeable because of the shortening or lengthening for **2** and **3** which must be compared with **1**. In effect, for **1** and **2** the charge releasing around of the N(1) atom is suggested by the N(1)-C(2), 1.357(4) and 1.361(7) while for **3** is 1.404(3) and by the N(1)-C(7A), 1.391(3), 1.389(7) while **3** is 1.421(3)Å (1.36 and 1.38Å, respectively, found in indole-3-aldehyde[10a] and indole-3-yl-ketones derivatives[10b]). Polarization of the carbonyl C(11)=O(1) was observed by the bond lengthening in all the cases, 1.242(2), 1.231(7) and 1.220(4) for **1**, **2**, and **3**, respectively affecting to the C(3)-C(11) which suffers an important bond shortening, 1.427(4), 1.444(8), and 1.457(4), respectively (1.43

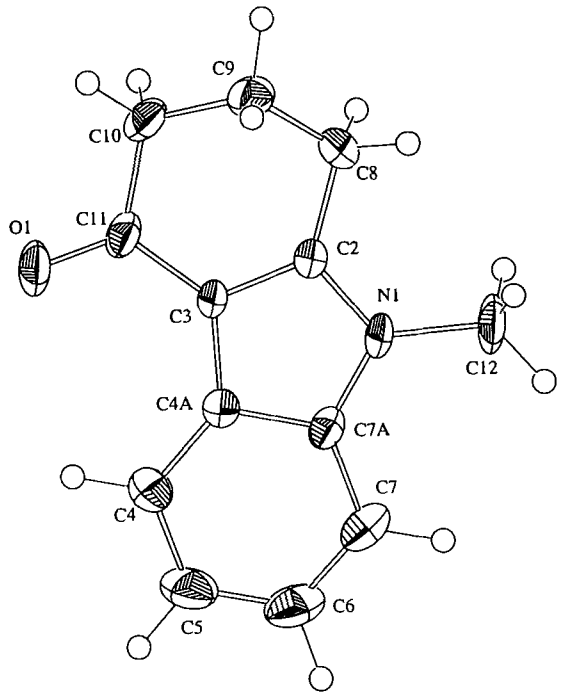


Fig. 1. Final X-ray model showing the atomic numbering for compound **2**.

found for indole-3-aldehyde[10a] and 1.44 and 1.45 for the indole-3-yl-ketones[10b]), as deduced by contrast with the benzylic type bond distance C(2)–C(8) of 1.479(4), 1.487(7), and 1.485(3). Thus, conjugation of the carbonyl C(11)=O(1) with the pyrrole part of the indole ring C(3)–C(11), C(2)–C(3) and N(1)–C(2) is deduced by the following bond lengths values although the tosyl group in **3** affects to the N(1) charge releasing as observed in N(1)–C(2), and C(2)–C(3), 1.383, 1.384, and 1.357(3) Å, respectively.

An expected approximate tetrahedral configuration around of S(1) atom is observed for the tosyl group in compound **3**, (Table 4). Moreover, the benzene ring is planar within the error limits and bond lengths and angles show normal values (Table 4).

In all these compounds, the indole ring is planar within experimental error limits. For **1**, the angle formed between planes 1 (indole-cyclohexenone) and 2 is 3.25(6)° and the conformational parameters following Cremer and Pople[11] indicates that the cyclohexenone ring adopts an envelope conformation with the C(9) atom at the flap. For **2**, the angle between planes of indole and cyclohexenone rings is 2.8°(2) and the conformational parameters indicates an envelope conformation with the C(9) atom down the mean plane. For **3**, the angle between planes 1 and 2 is 2.51(8)° and the conformational parameters[11] indicates an envelope conformation with the C(9) atom down the mean plane. Analysis of the X-ray bond distance C=O, (1.242(2), 1.231(7), and 1.220(4)A in **1**, **2**, and **3**, respectively, indicates that the carbonyl group in these structures is polarized and taking into account the electronic character of the N-substituent, this bond distance decreases when increases the withdrawing character of the substituent. The ir frequency of the carbonyl group in compounds **1** (or **4**), **2**, and **3**, increases in this order so in solution as in the solid state, indicating the same effect of the N-substituent.

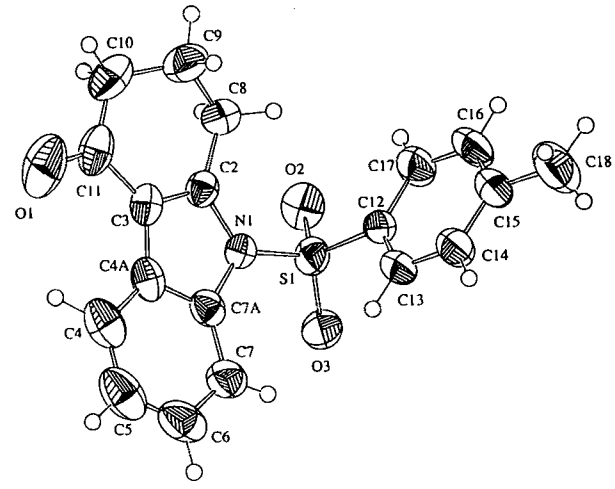


Fig. 2. Final X-ray model showing the atomic numbering for compound **3**.

Table 2. Atomic parameters for $C_{13}H_{13}NO$, **2**: Thermal parameters as: $U_{eq} = (1/3) \cdot \Sigma[U_{ij} \cdot a_{ij}^* \cdot a_i \cdot a_j \cdot \cos(a_i, a_j)] \cdot 10^3$ $U = 0.063$ for H atoms

Atom	*x/a*	*y/b*	*z/c*	U_{eq}
O(1)	1.1684(4)	0.3070(2)	0.8908(6)	46(2)
N(1)	0.6533(5)	0.2280(3)	0.8313(6)	30(2)
C(2)	0.8021(6)	0.1998(3)	0.8468(7)	27(2)
C(3)	0.9050(6)	0.2638(3)	0.8574(7)	27(2)
C(4)	0.8463(7)	0.4188(3)	0.8468(9)	39(2)
C(4A)	0.8127(6)	0.3363(3)	0.8461(7)	29(2)
C(5)	0.7218(8)	0.4726(4)	0.8329(10)	52(3)
C(6)	0.5688(8)	0.4464(4)	0.8200(10)	51(3)
C(7)	0.5321(7)	0.3655(4)	0.8192(9)	41(2)
C(7A)	0.6558(6)	0.3114(3)	0.8312(8)	30(2)
C(8)	0.8446(7)	0.1132(3)	0.8508(9)	37(2)
C(9)	1.0325(7)	0.1048(3)	0.9436(9)	39(2)
C(10)	1.1191(6)	0.1654(4)	0.8628(9)	39(2)
C(11)	1.0712(6)	0.2517(3)	0.8734(8)	32(2)
C(12)	0.5107(7)	0.1795(4)	0.8157(9)	46(3)

Table 3. Atomic parameters for $C_{19}H_{17}NO_3S$, **3**: Thermal parameters as: $U_{eq} = (1/3) \cdot \Sigma[U_{ij} \cdot a_i^* \cdot a_j^* \cdot a_i \cdot a_j \cdot \cos(a_i, a_j) \cdot 10^4$ $U = \exp[-8 \cdot \pi^2 \cdot U \cdot (\sin\theta/\lambda)^2] \cdot 10^3$

Atom	*x/a*	*y/b*	*z/c*	U_{eq}	Atom	*x/a*	*y/b*	*z/c*	U_{eq}
S(1)	0.70991(5)	0.18964(7)	0.08125(4)	518(2)	C(7A)	0.9458(2)	0.1506(3)	0.1354(1)	485(3)
O(1)	1.0953(2)	−0.2701(3)	0.0821(2)	1065(11)	C(8)	0.7466(2)	−0.1544(3)	0.0312(2)	598(10)
O(2)	0.6373(2)	0.1395(2)	0.0016(1)	672(7)	C(9)	0.7865(3)	−0.3155(3)	0.0448(2)	754(13)
O(3)	0.7406(2)	0.3434(2)	0.0932(1)	703(8)	C(10)	0.9001(3)	−0.3445(4)	0.0265(2)	783(13)
N(1)	0.8339(2)	0.0962(2)	0.0958(1)	455(6)	C(11)	0.9935(2)	−0.2389(3)	0.0690(2)	650(10)
C(2)	0.8436(2)	−0.0531(2)	0.0706(1)	443(7)	C(12)	0.6518(2)	0.1293(3)	0.1655(2)	459(7)
C(3)	0.9566(2)	−0.0912(3)	0.0901(1)	485(8)	C(13)	0.7079(2)	0.1659(3)	0.2495(2)	555(9)
C(4)	1.1416(2)	0.0568(4)	0.1646(2)	704(11)	C(14)	0.6588(2)	0.1274(3)	0.3158(2)	625(10)
C(4A)	1.0231(2)	0.0350(3)	0.1311(1)	513(8)	C(15)	0.5545(2)	0.0534(3)	0.2994(2)	649(10)
C(5)	1.1774(3)	0.1919(5)	0.2024(2)	851(14)	C(16)	0.5011(2)	0.0152(4)	0.2152(2)	756(12)
C(6)	1.0998(3)	0.3047(5)	0.2075(2)	810(13)	C(17)	0.4590(2)	0.0524(3)	0.1479(2)	642(10)
C(7)	0.9819(3)	0.2877(3)	0.1743(2)	660(11)	C(18)	0.4993(4)	0.0159(6)	0.3709(3)	1042(22)

Accordingly with the structural data, we interpret the inactivity of the C=O group in **1**, **2**, and **3** as due to the rigid and stable envelope conformation with C(9) at the flap, exhibed by the three compounds with the specially conjugated cyclohexenone ring. In this way was prepared **4** which have two methyl substituents on this namely C(9) carbon atom. The inactivity of this compound seems to indicate that the envelope structure is also stable for the geminal methyl substitution on 2-position of the tetrahydrocarbazolone ring.

Table 4.

	1*	2	3		1*	2	3
N(1)-C(7A)	1.391(3)	1.389(7)	1.421(3)	C(2)-C(8)	1.479(4)	1.487(7)	1.485(3)
N(1)-C(2)	1.357(4)	1.361(7)	1.404(3)	C(8)-C(9)	1.523(4)	1.533(8)	1.513(4)
C(2)-C(3)	1.383(3)	1.384(7)	1.357(3)	C(9)-C(10)	1.519(4)	1.534(10)	1.487(5)
C(3)-C(11)	1.427(4)	1.444(8)	1.457(4)	C(10)-C(11)	1.517(4)	1.511(8)	1.493(4)
C(3)-C(4a)	1.441(3)	1.443(7)	1.441(3)	C(11)-O(1)	1.242(2)	1.231(7)	1.220(4)
C(4a)-C(7a)	1.400(3)	1.413(8)	1.400(4)	C(4a)-C(4)	1.401(3)	1.405(8)	1.403(3)
C(4)-C(5)	1.377(4)	1.394(9)	1.370(5)	S(1)-O(2)			1.429(2)
C(5)-C(6)	1.393(4)	1.392(11)	1.387(6)	S(1)-O(3)			1.421(2)
C(6)-C(7)	1.395(4)	1.384(9)	1.391(4)	S(1)-C(12)			1.752(3)
C(7)-C(7a)	1.386(4)	1.394(8)	1.392(4)	N(1)-H(1)	0.99(3)	—	—
C(12)-C(13)	—	—	1.389(3)	N(1)-C(12)	—	1.464(8)	—
C(12)-C(17)	—	—	1.378(3)	N(1)-S(1)	—	—	1.671(2)
C(13)-C(14)	—	—	1.382(4)				
C(14)-C(15)	—	—	1.381(4)				
C(15)-C(16)	—	—	1.387(4)				
C(15)-C(18)	—	—	1.498(6)				
C(16)-C(17)	—	—	1.384(5)				

	2	3		2	3
C(2)-N(1)-C(7A)	109.3(4)	108.4(2)	N(1)-C(7A)-C(4A)	108.0(5)	106.9(2)
N(1)-C(2)-C(8)	124.4(5)	126.0(2)	C(3)-C(11)-C(10)	115.3(5)	116.1(3)
N(1)-C(2)-C(3)	109.5(5)	108.6(2)	O(1)-C(11)-C(10)	121.2(5)	122.8(3)
C(3)-C(2)-C(8)	126.1(5)	125.4(2)	O(1)-C(11)-C(3)	123.6(5)	121.0(3)
C(2)-C(3)-C(11)	121.7(5)	121.1(2)	C(2)-C(8)-C(9)	112.6(5)	114.2(3)
C(4A)-C(3)-C(11)	131.1(5)	130.3(2)	C(9)-C(10)-C(11)	114.1(5)	104.9(3)
C(3)-C(4A)-C(4)	134.8(6)	132.6(3)	N(1)-S(1)-O(3)	—	105.7(1)
C(4)-C(4A)-C(7A)	119.2(5)	120.0(2)	N(1)-S(1)-O(2)	—	107.0(1)
C(3)-C(4A)-C(7A)	106.0(4)	107.4(2)	N(1)-S(1)-C(12)	—	104.5(1)
C(4A)-C(7A)-C(7)	122.6(5)	122.2(2)	S(1)-N(1)-C(7A)	—	127.1(2)
N(1)-C(7A)-C(7)	129.4(5)	130.9(2)	S(1)-N(1)-C(2)	—	124.5(2)

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