Synthesis of 4-(*N,N*-Dimethylaminoethyl)-1,2,3,4-tetrahydrocarbazole: Molecular Structure and Reactivity of the 1,2-Dihydrocarbazol-4(3H)-one and Derivatives

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The synthesis and reactivity of 1,2-dihydrocarbazol-4(3*H*)-one, (**1**), is reported. An *X*-ray molecular structure study of (**1**) provided information on the inactivity of its carbonyl group with potentially anionic reagents. 4(2-Dimethylaminoethyl)-1,2,3,4-tetrahydrocarbazole has been synthesized from 1,2,3,4-tetrahydrocarbazol-4-ylidenemethyl acetate by reduction of the exocyclic double bond, followed by transamination and reduction.

4-Alkylidene-1,2,3,4-tetrahydrocarbazoles can be prepared by Wittig reaction between a suitable ylide and the 1,2-dihydrocarbazol-4(3*H*)-one. Thus, the synthesis of this carbazol-4-one, has been outlined as a functionalized intermediate. We have investigated the reactivity of this carbonyl group with such nitrogen-nucleophiles as amines or potential carbanions as Wittig ylides, to form the 4-(*N,N*-dimethylaminoalkyl)-1,2,3,4-tetrahydrocarbazole derivatives which are potentially antidepressant drugs.[1]

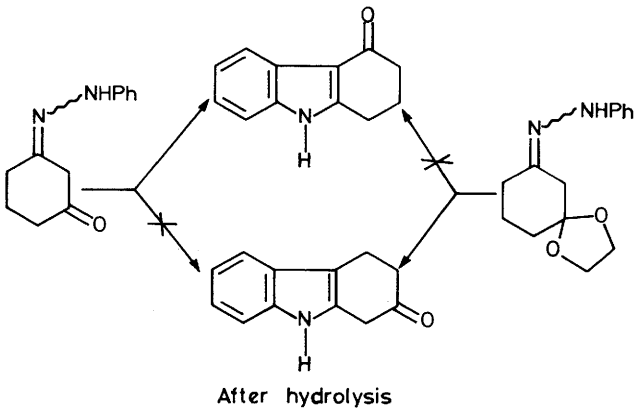
Results and Discussion

1,2-Dihydrocarbazol-4(3*H*)-one (**1**) has been synthesized by a Fischer reaction between phenylhydrazine and cyclohexane-1,3-dione in acetic acid (10%). With a 1:1 molar ratio of the reagents the monophenylhydrazone alone is obtained, the second carbonyl group not undergoing reaction presumably because of displacement of the tautomeric equilibrium to the enolic form; evidence in favour of this explanation was provided by ^{1}H n.m.r. and i.r. spectral results for the phenylhydrazone, both in solution and in the solid state.

In effect, we have compared the tautomeric equilibrium of this monophenylhydrazone with its cyclohexane-1,3-dione, recently reported,[2] in various solvents in the presence of an acid catalyst. From an analysis of the i.r. and n.m.r. spectral results, the cyclohexane-1,3-dione monophenylhydrazone upon dissolution in polar solvents, shows a complete displacement of the equilibrium to the enolic form; the latter exhibits geometrical *syn-anti* type association of the enolic hydroxy group and the C=N bond. Moreover, two crystalline forms of the monophenylhydrazone having different m.p.s were isolated; these corresponded with *syn-* and *anti-* C=N isomers respectively.

In contrast, reaction of phenylhydrazine and cyclohexane-1,3-dione (1:1 molar ratio) in benzene as solvent in the absence of an acid catalyst give a mixture of the mono- and bis-phenylhydrazones together with free cyclohexane-1,3-dione; this indicated that the keto form predominates in the tautomeric equilibrium, the reverse situation to that observed in the presence of an acid catalyst.

Finally, Fischer reaction of the pure monophenylhydrazone of the cyclohexane-1,3-dione was carried out in presence of sulphuric acid (20%) as catalyst, yielding 51% of the carbazol-4-one (**1**). The regioselectivity taking place in this reaction probably results from the presence of the carbonyl group which enables formation of the conjugate enehydrazinone as intermediate, following an earlier proposed mechanism.[3] In effect, thermal reaction of the phenylhydrazone of the cyclohexane-1,3-dione ethylene glycol monoacetal, in ethylene glycol, gives the 1,2,3,4-tetrahydrocarbazole 2-ethylene glycol acetal, as the main product, (see Scheme 1 and see Experimental section).

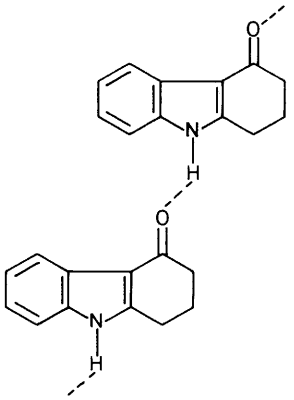


Scheme 1.

Central to this synthetic method, is the reaction of (**1**) with nucleophiles such as hydrazine, phenylhydrazine, hydroxylamine, and the potentially anionic Wittig ylides, to form tetrahydrocarbazoles containing a C–N or C–C side chain at the 4-position. However, all the attempts carried out under a variety of reaction conditions, were unsuccessful. A similar benzylic type carbonyl substituent at the 3-position of the indole nucleus (*e.g.* 3-formylindole) reacts normally with the same nucleophiles.[4]

The synthesis and structural analysis of (**1**) on the basis of i.r. results was reported earlier;[5] and an *X*-ray study was, therefore, undertaken in order to understand its inactivity.

Crystal Structure Analysis of Compound (**1**).—The molecular structure of (**1**), analysed by *X*-ray diffraction, was shown to consist of strongly associated molecular aggregates with intermolecular nitrogen–hydrogen–oxygen bridges between the NH of the indole and the carbonyl groups in an *anti-* form (see Scheme 2). Figure 1 shows the final *X*-ray model with the atomic numbering. Atomic parameters are given in Table 1 and bond lengths and angles are shown in Tables 2 and 3. Some bond



Scheme 2.

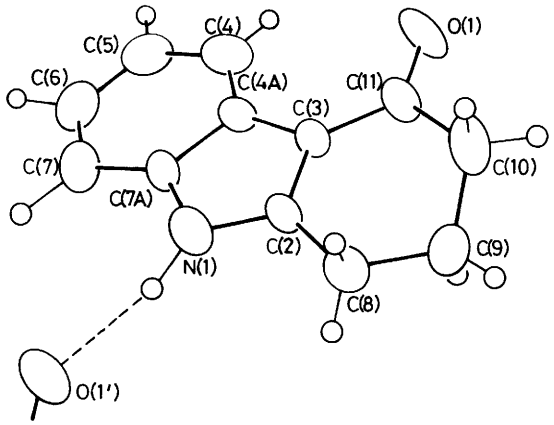


Figure 1. Final *X*-ray model showing the atomic numbering.

Table 1. Atomic parameters

Atom	*x/a*	*y/b*	*z/c*
O(1)	0.370 8(1)	0.201 5(1)	0.607 9(—)
N(1)	0.235 8(2)	0.506 1(2)	0.934 0(3)
C(2)	0.218 1(2)	0.460 2(2)	0.790 0(3)
C(3)	0.305 0(2)	0.363 7(2)	0.767 3(3)
C(4)	0.489 6(2)	0.276 2(2)	0.953 3(4)
C(4A)	0.383 2(2)	0.350 9(2)	0.906 4(3)
C(5)	0.543 1(2)	0.291 4(2)	0.098 7(4)
C(6)	0.494 5(3)	0.380 3(2)	0.198 8(4)
C(7)	0.390 0(2)	0.457 4(2)	0.154 9(3)
C(7A)	0.337 5(2)	0.440 9(2)	0.008 1(3)
C(8)	0.122 2(3)	0.507 7(2)	0.674 3(3)
C(9)	0.170 1(3)	0.470 2(2)	0.514 2(4)
C(10)	0.201 8(2)	0.335 2(2)	0.506 2(3)
C(11)	0.301 0(2)	0.293 8(2)	0.628 4(3)

lengths are noteworthy because they are either shorter or longer than expected. In effect, the charge releasing nature of N(1) is suggested by the bond lengths for N(1)–C(2) and N(1)–C(7A) of 1.357(4) and 1.397(3) Å (1.36 and 1.38 Å found in indole-3-carbaldehyde[6a] and indole-3-yl ketone derivatives.[6b] Polarization of the carbonyl C(11) = O group, indicated by bond lengthening of 1.242(2) Å, affected the C(3)–C(11) bond which suffers an important bond shortening 1.427(4) (1.43 found for indole-3-carbaldehyde[6a] and 1.44 and 1.45 for the indole-3-yl ketones[6b]), as compared with the benzylic type bond distance for C(2)–C(8) of 1.479(4) Å. The torsional angles are listed in Table 4. Analysis of the conformational parameters,[7] indicates that the cycloalkane ring adopts an envelope conformation, with the C(9) atom at the flap (see Table 5).

Table 2. Bond lengths (Å) (standard deviations in parentheses)

N(1)–H(1)	0.99(3)	C(6)–C(7)	1.395(4)
N(1)–C(2)	1.357(4)	C(7)–H(7)	1.13(3)
N(1)–C(7A)	1.391(3)	C(7)–C(7A)	1.386(4)
C(2)–C(3)	1.383(3)	C(8)–H(81)	0.91(3)
C(2)–C(8)	1.479(4)	C(8)–H(82)	1.08(3)
C(3)–C(4A)	1.441(3)	C(8)–C(9)	1.523(4)
C(3)–C(11)	1.427(4)	C(9)–H(91)	0.92(3)
C(4)–H(4)	0.93(3)	C(9)–H(92)	0.93(3)
C(4)–C(4A)	1.401(3)	C(9)–C(10)	1.519(4)
C(4)–C(5)	1.377(4)	C(10)–H(101)	1.03(3)
C(4A)–C(7A)	1.400(3)	C(10)–H(102)	0.98(3)
C(5)–H(5)	1.00(3)	C(10)–C(11)	1.517(4)
C(5)–C(6)	1.393(4)	C(11)–O(1)	1.242(2)
C(6)–H(6)	1.07(3)		

Hydrogen bond

X–H···Y	X···Y	X–H	H···Y	<X–H···Y
N(1)–H(1)···O(1)[I]	2.830(4) Å	0.99(3) Å	1.87(3) Å	162(2)°

Symmetry operation
I 0.5 − *x*, 0.5 + *y*, 0.5 + *z*

Table 3. Bond angles (°) (standard deviations in parentheses)

C(2)–N(1)–C(7A)	109.1(2)	C(4A)–C(7A)–C(7)	123.1(2)
H(1)–N(1)–C(7A)	124.0(1)	N(1)–C(7A)–C(7)	128.9(2)
H(1)–N(1)–C(2)	126.0(2)	N(1)–C(7A)–C(4A)	108.0(2)
N(1)–C(2)–C(8)	125.1(2)	C(2)–C(8)–C(9)	108.6(2)
N(1)–C(2)–C(3)	109.5(2)	H(82)–C(8)–C(2)	110.0(2)
C(3)–C(2)–C(8)	125.4(2)	H(81)–C(8)–C(2)	108.0(2)
C(2)–C(3)–C(11)	121.0	H(82)–C(8)–C(9)	108.0(2)
C(2)–C(3)–C(4A)	107.1	H(81)–C(8)–C(9)	108.0(2)
C(4A)–C(3)–C(11)	131.8(2)	H(81)–C(8)–H(82)	114.0(2)
C(4A)–C(4)–C(5)	119.1(2)	C(8)–C(9)–C(10)	111.8(2)
H(4)–C(4)–C(5)	117.0(2)	H(92)–C(9)–C(8)	110.0(2)
H(4)–C(4)–C(4A)	124.0(2)	H(91)–C(9)–C(8)	108.0(2)
C(3)–C(4A)–C(4)	135.1(2)	H(92)–C(9)–C(10)	109.0(2)
C(4)–C(4A)–C(7A)	118.5(2)	H(91)–C(9)–C(10)	107.0(2)
C(3)–C(4A)–C(7A)	106.4(2)	H(91)–C(9)–H(92)	111.0(3)
C(4)–C(5)–C(6)	121.3(2)	C(9)–C(10)–C(11)	113.4(2)
H(5)–C(5)–C(4)	117.0(2)	H(102)–C(10)–C(9)	111.0(2)
H(5)–C(5)–C(6)	122.0(2)	H(101)–C(10)–C(9)	111.0(1)
C(5)–C(6)–C(7)	121.0(3)	H(102)–C(10)–C(11)	104.0(2)
H(6)–C(6)–C(5)	121.0(1)	H(101)–C(10)–C(11)	109.0(1)
H(6)–C(6)–C(7)	118.0(1)	H(101)–C(10)–H(102)	109.0(2)
C(6)–C(7)–C(7A)	116.9(2)	C(3)–C(11)–C(10)	116.4(2)
H(7)–C(7)–C(6)	121.0(2)	O(1)–C(11)–C(10)	120.6(2)
H(7)–C(7)–C(7A)	122.0(1)	O(1)–C(11)–C(3)	122.9(2)

On this structural basis, to avoid tautomeric equilibriation between the keto-enol structures in carbazol-4-one (**1**), it was treated in two ways: (*a*) a sample was slowly dissolved (low solubility) in chloroform. The i.r. spectrum of (**1**) in chloroform solution shows two main absorption bands at 3 455 and 1 647 cm^{-1} (1 605 in KBr[5]) for the NH and CO groups respectively. Moreover, these frequencies remain constant upon dilution of the solution, an indication that hydrogen bonding is absent and that no association is taking place (C=O absorption at 1 647 is practically the same as that found for the *N*-methyl derivative; in the ^{13}C n.m.r. spectra the C=O absorption occurs at δ 194.1, *vs.* 193.6 p.p.m. for the *N*-methyl derivative); (*b*) the NH bridge was blocked by methylation or tosylation respectively. In contrast with the NH compound, *N*-methyl- and *N*-tosyl-1,2-dihydrocarbazol-4(3*H*)-one show strong absorption bands in their i.r. spectrum for the carbonyl group at 1 640 and 1 670 cm^{-1}, for KBr mulls, and 1 635 and 1 665 cm^{-1} in $CHCl_3$, respectively. In each compound, the carbonyl group is polarized, the i.r.

Table 4. Torsional angles (°) (e.s.d.'s in parentheses)

C(2)–N(1)–C(7A)–C(4A)	−0.6(3)
C(2)–N(1)–C(7A)–C(7)	179.0(2)
C(7A)–N(1)–C(2)–C(8)	−178.0(2)
C(7A)–N(1)–C(2)–C(3)	1.0(3)
N(1)–C(2)–C(8)–C(9)	156.9(2)
N(1)–C(2)–C(3)–C(4A)	−1.1(3)
N(1)–C(2)–C(3)–C(11)	175.9(2)
C(3)–C(2)–C8–C(9)	−21.9(3)
C(8)–C(2)–C(3)–C(11)	−5.1(3)
C(8)–C(2)–C(3)–C(4A)	178.0(2)
C(2)–C(3)–C(11)–O(1)	−174.9(2)
C(4A)–C(3)–C(11)–O(1)	1.2(4)
C(2)–C(3)–C(11)–C(10)	2.9(3)
C(2)–C(3)–C(4A)–C(7A)	0.7(2)
C(2)–C(3)–C(4A)–C(4)	−176.5(3)
C(4A)–C(3)–C(11)–C(10)	178.9(2)
C(11)–C(3)–C(4A)–C(4)	7.0(4)
C(11)–C(3)–C(4A)–C(7A)	−175.8(2)
C(5)–C(4)–C(4A)–C(3)	178.7(3)
C(4A)–C(4)–C(5)–C(6)	−0.8(4)
C(5)–C(4)–C(4A)–C(7A)	1.8(4)
C(3)–C(4A)–C(7A)–N(1)	−0.1(2)
C(4)–C(4A)–C(7A)–N(1)	177.6(2)
C(4)–C(4A)–C(7A)–C(7)	−1.9(3)
C(3)–C(4A)–C(7A)–C(7)	−179.7(2)
C(4)–C(5)–C(6)–C(7)	−0.1(4)
C(5)–C(6)–C(7)–C(7A)	0.0(4)
C(6)–C(7)–C(7A)–C(4A)	1.0(4)
C(6)–C(7)–C(7A)–N(1)	−178.5(2)
C(2)–C(8)–C(9)–C(10)	50.0(3)
C(8)–C(9)–C(10)–C(11)	−54.4(3)
C(9)–C(10)–C(11)–C(3)	26.7(3)
C(9)–C(10)–C(11)–O(1)	−155.4(2)

Table 5. Atomic deviations from l.s. (A) plane* (Atoms marked with asterisks are not included in the calculations. E.s.d.'s are in parentheses)

Plane 1		Plane 2	
C(4)	0.014(2)	C(10)	−0.012(3)
C(5)	0.017(3)	C(11)	0.008(2)
C(6)	0.004(3)	C(2)	−0.008(2)
C(7)	−0.010(3)	C(8)	0.013(3)
C(7A)	−0.011(2)	*C(3)	0.040(2)
C(4A)	−0.020(2)	*C(9)	0.630(3)
C(2)	0.019(2)		
C(3)	−0.011(2)		
N(1)	0.005(2)		

Angle between planes 1/2 = 3.25(6)°

* M. Nardelli, A. Musatti, P. Domiano, and G. Andreetti, 1965, **35**, 807.

frequency increasing with the presence of electron-withdrawing substituent. However, the carbazol-4-one (**1**), in chloroform solution as for the *N*-blocked derivatives is not reactive towards Wittig reagents. Moreover, nucleophilic reagents such as the nitroalkane carbanions, generated *in situ* with ammonium acetate, which react well with 3-formylindole,[4] does not give the corresponding carbazolone condensation product.

Acetalization of (**1**) was attempted with ethylene glycol in benzene to remove water azeotropically but there was reaction of product even after 100 h.

However, recently it was reported that 1-ethyl-1,2-dihydro-β-carbolin-4(3*H*)—one is transformed[8] into a 4-amino derivative when heated with hydrazine, probably *via* a hydrazone intermediate. No such reaction occurred with compound (**1**) in THF or in chloroform at reflux temperature. Accordingly

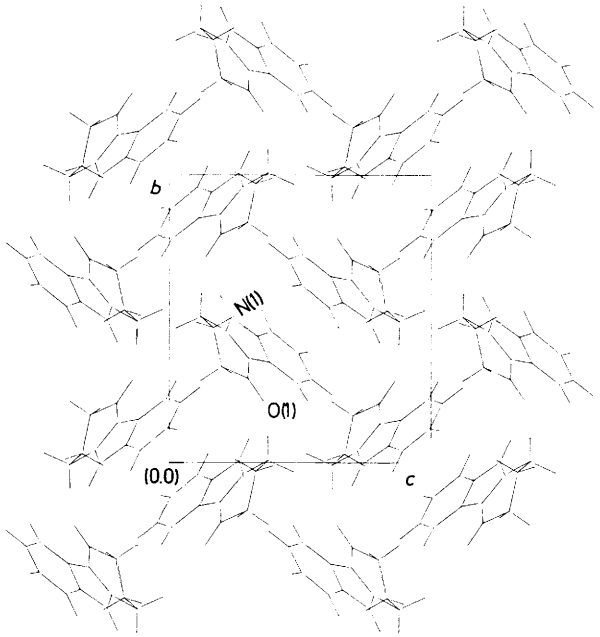


Figure 2. Molecular packing of compound (**1**) and envelope conformation of the cyclohexenone fragment

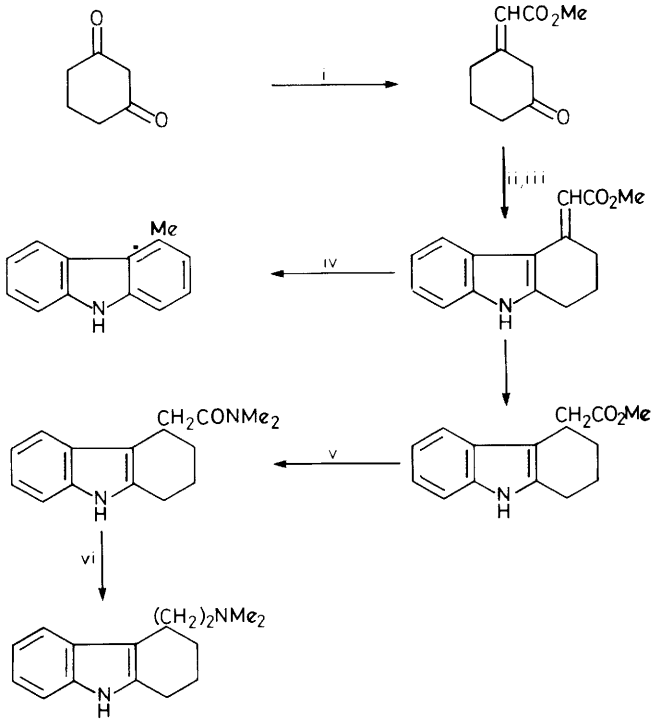
from the structural data, we interpret the inactivity of the carbonyl group in (**1**), as due to the rigid and stable envelope conformation of the specially conjugated cyclohexenone ring.

Finally, the preparation of the 4-(2-dimethylaminoethyl)-1,2,3,4-tetrahydrocarbazole was carried out by Fischer reaction of the phenylhydrazone of the 1-oxo-3-cyclohexylidenemethyl acetate. In this reaction, only the 1,2,3,4-tetrahydrocarbazol-4-ylidenemethyl acetate isomer was detected although 4-methylcarbazole and methyl carbazol-4-yl-acetate were found as side-products in variable amounts, depending on the catalyst used and the reaction conditions. Thus, the regioselectivity in the Fischer reaction of 1-oxo-3-cyclohexylidenemethyl acetate phenylhydrazone can be understood in terms of stabilization of the intermediate enehydrazine by conjugation with the exocyclic double bond,[3] such as occurs in the Fischer reaction of the cyclohexane-1,3-dione phenylhydrazone.

Hydrolysis of methyl carbazol-4-ylacetate with (10%) ethanolic potassium hydroxide (or aqueous sulphuric acid) give as the main product 4-methylcarbazole, which is generated by decarboxylation, isomerization, and aromatization. To avoid this transformation, the exocyclic double bond was hydrogenated using platinum oxide in methanol–acetic acid (40 p.s.i. and 50 °C) to give methyl 1,2,3,4-tetrahydrocarbazol-4-ylacetate in 88% yield. The latter was transformed first to the 4-(dimethylcarbamoylmethyl) derivative by transamination with methanolic dimethylamine at room temperature during 6 days, and finally to the corresponding 4-(2-dimethylaminoethyl) compound by reduction with lithium aluminium hydride in good yields (see Scheme 3).

Experimental

M.p.s were measured on a hot-stage microscope and are uncorrected. The i.r. spectra were recorded on a Pye-Unicam SP1100 spectrophotometer and the n.m.r. spectra were obtained with a Bruker WH-200-SY instrument. Mass spectra were obtained in a Hewlett-Packard 5985 g.c.-m.s. system. Elemental analyses were performed with a Perkin-Elmer 240



Scheme 3. *Reagents:* i, $Ph_3P = CHCO_2Me$; ii, $PhNHNH_2$; iii, H^+; iv, hydrolysis; v, Me_2NH; vi, $LiAlH_4$

elemental analyser. 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**).—This compound was synthesized by a Fischer reaction of cyclohexane-1,3-dione phenylhydrazone. A solution of phenylhydrazine (0.6 g, 5.5 mmol) in 10% aqueous acetic acid (25 ml) was added to a solution of cyclohexane-1,3-dione (0.6 g, 5.3 mmol) in 10% aqueous acetic acid (25 ml). The mixture was warmed to 50—60 °C during 20 min and then allowed to cool when a yellow-brown solid was precipitated. This was filtered off and recrystallized from aqueous methanol to give the phenylhydrazone as a pale-yellow solid (1.01 g). Two crystalline forms were observed under a microscope (m.p.s 177—178 and 185—187 °C), the microanalyses of which were identical; these corresponded to the *syn* and *anti* isomers, respectively. A repeat experiment in benzene gave a mixture of the mono- and bis-phenylhydrazones (80:20) together with unchanged cyclohexane-1,3-dione: $\nu_{max.}$(Nujol) 3 260 (NH), 3 500—2 500 br (C=C–OH), 1 605 (C=N), 1 550 (C=C), 1 200 (=C–OH), and 740 and 690 cm^{-1} (Ar, mono-substituted); δ_H(200 MHz; $CDCl_3$–MeOD) 7.30 (2 H, m, ArH), 6.81 (3 H, m, ArH), 5.53 (1 H, s, HC=C), and 2.42 [6 H, m, $(CH_2)_n$].

Fischer Reaction of Cyclohexane-1,3-*dione Phenylhydrazone.*—Cyclohexane-1,3-dione (1 g, 5.0 mmol) phenylhydrazone was dispersed in aqueous sulphuric acid (20%); 20 ml, and the mixture was warmed at 110 °C during 3 h. It was then poured into water–ice (50 ml) and to give a yellow solid which was filtered off and recrystallized from aqueous ethanol to afford the carbazol-4-one (**1**) as a white solid (51%), m.p. 221—223 °C (Found: C, 77.5; H, 6.1; N, 7.9. $C_{12}H_{11}NO$ requires C, 77.81; H, 5.99; N, 7.56; $\nu_{max.}$(KBr) 3 400—2 100br (NH), 1 605 (C=O), and 750 cm^{-1} (Ar); $\nu_{max.}$($CHCl_3$) 3 455br (NH), 1 647 (C=O), and 750 cm^{-1} (Ar); δ_H($CDCl_3$) 8.55 (br s, 1 H, NH), 8.22 (1 H, m, 5-H), 7.3 (3 H, m, 6-H, 7-H, 8-H), 2.98 (2 H, t *J* 6.18 Hz, 1-CH_2), 2.60 (2 H, t *J* 6.35 Hz, 3-CH_3), 2.25 (2 H, 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), and 51 (11).

Ethylene Glycol Acetalization of 1,2-*Dihydrocarbazol*-3(4H)-*one.*—(a). *Preparation of cyclohexane*-1,3-*dione ethylene glycol monoacetal.* The optimum yield was obtained by means of the following procedure. A solution of ethylene glycol (3.2 g, 0.05 mol) in benzene (40 ml), and sulphuric acid (10%; 0.5 ml) was kept under reflux with azeotropic removal of water during 16 h. Evaporation of the benzene gave a residual oil which was chromatographed on a silica gel column with ethyl acetate–chloroform (4:1) as eluant to afford cyclohexane-1,3-dione mono- and di-acetal in 72 and 28% yields as a yellow oil and a colourless solid respectively.

(b) *Preparation of cyclohexane*-1,3-*dione ethylene glycol monoacetal phenylhydrazone.* A solution of cycohexane-1,3-dione ethylene glycol monoacetal (0.8 g, 5.1×10^{-3} mol) and phenylhydrazine (0.553 g, 5.1×10^{-3} mol) in anhydrous benzene (10 ml) was kept under reflux with azeotropic removal of water during 4 h. Solvent was then removed to give the phenylhydrazone as a red-brown oil; this was redissolved in ethylene glycol and the solution warmed at 180 °C, overnight. The mixture was poured into water and extracted with dichloromethane and the residue on removal of solvent chromatographed on a gel silica column with ethyl acetate–dichloromethane (2:1) as eluant to give the carbazole and the carbazol-2-one ethylene glycol acetal as the main products. Carbazole was obtained as a white solid (10%); picrate, m.p. 182 °C (compared with an authentic sample); *m*/*z* (70 eV) 167 (M^+, 100). The carbazol-2-one ethylene glycol acetal, was the main product (30%), obtained as a white solid, m.p. 138—140 °C (Found: C, 73.6; H, 6.3; N, 5.85. $C_{14}H_{15}NO_2$ requires C, 73.34; H, 6.59; N, 6.11%); $\nu_{max.}$(KBr) 3 420 (NH), 1 110, 1 050, and 1 020 (C–O–C–O–C), and 750 cm^{-1} (Ar *ortho* disubst.); δ_H(200 MHz; $CDCl_3$) 7.70 (1 H, br, NH), 7.58 (1 H, m, 5-H), 7.07 (3 H, m, ArH), 4.02 [4 H, m, $O(CH_2)_2O$], 2.95 (2 H, t, *J* 6.50 Hz, 4-CH_2), 2.80 (2 H, s, br, 1-CH_2), and 2.02 (2 H, t, *J* 6.50 Hz, 3-CH_2); *m*/*z* (70 eV) 229 (M^+, 25); 156 (19), 144 (13), 143 (100), 128 (11), and 115 (8).

Crystal Structure Analysis.—Crystals of compound (**1**), $C_{12}H_{11}NO$, M_w = 185.22, were colourless and prismatic orthorhombic, space group $Pna2_1$ (No. 33) with a = 9.958(1), b = 10.990(1), c = 8.659(1) Å, V = 947.7(2) Å^3, Z = 4. μ = 6.23 cm^{-1}, D_c = 1.30 g cm^{-3}, $F(000)$ = 392. Crystals for *X*-ray diffraction study were obtained by slow evaporation of a diluted ethanolic solution of (**1**). A single crystal of dimensions 0.2 × 0.3 × 0.3 mm was used for data collection on a PW1100 diffractometer, employing graphite monochromated Cu-K_α radiation.

Intensity measurements, structure determination, refinement. The intensity for 1036 independent reflections up to $\theta < 68°$ were recorded using an $\omega/2\theta$ scan mode technique. Standard reflections measured every 90 min showed no crystal decomposition. 897 Reflections were considered as observed with the criterion $I > 2\sigma(I)$ and used in subsequent calculations. The data were corrected for Lorentz and polarization factors but no absorption correction was applied. The structure was solved by direct methods, MULTAN[8] and Fourier synthesis. Refinement was done by full-matrix least-squares analysis with anisotropic, for C, N, O, temperature factors. All H atoms were found in a difference synthesis and included in subsequent refinements as an isotropic contribution. A convenient weighting scheme[10] was used to prevent bias on $\langle w\Delta^2F\rangle$ *vs.* $\langle F_0\rangle$ and *vs.* $\langle \sin\theta/\lambda\rangle$. Final full matrix anisotropic weighted refinement (isotropic for H atoms) gave the discrepance indices R = 0.026 and R_w = 0.028. Scattering factors for neutral atoms were taken from the

literature.[11] Most calculations were performed using the XRAY 70 System.[12] Thermal paramaters are available on request from the C.C.D.C.*

Synthesis of 4-(2-*Dimethylaminoethyl*)-1,2,3,4-*tetrahydrocarbazole.*—(a) *Preparation of* 1,2,3,4-*tetrahydrocarbazol*-4-*ylidene methyl acetate:* 1-*Oxo*-3-*cyclohexylidenemethyl acetate.* To a stirred and rigorously dried solution of cyclohexane-1,3-dione (4.27 g, 3.8 mmol) in chloroform (100 ml), at the reflux and under an argon atmosphere was added a solution of methoxycarbonylmethylenetriphenylphosphorane (12.74 g, 3.8 mmol). After complete addition the intense red solution was stirred at 75 °C during 80 h. Solvent was removed under reduced pressure and the crude product was chromatographed on silica gel column using ethyl acetate–chloroform (4:1) as eluant to give 1-oxo-3-cyclohexylidenemethyl acetate as a yellow liquid (56%), b.p. 120—123 °C/0.1 mmHg (Found: C, 64.75; H, 7.3. $C_8H_{12}O_3$ requires C, 64.27; H, 7.19%); $\nu_{max.}$(film) 1 740 (C=O, ester), 1 680 C=O, ketone), and 1 630 cm^{-1} (C=C, conjugated); δ_H(200 MHz; $CDCl_3$) 5.83 (1 H, m, HC=C), 3.61 (3 H, s, CH_3–O), 3.14 (2 H, m, $COCH_2C$=C), 2.29 (4 H, m, C=CCH_2CCH_2CO), and 1.90 (2 H, m, C=$CCCH_2C$–CO).

(b) *Preparation of methoxycarbonylmethylenetriphenylphosphorane.* A solution of triphenylphosphine (7.8 g, 0.03 mol) and methyl bromoacetate (4.6 g, 0.03 mol) of anhydrous benzene (125 ml) was stirred under reflux during 3 h. The phosphonium salt was filtered off, washed with hexane, and dried *in vacuo.* To a solution of this salt in water–ice (250 ml) was added, with stirring, aqueous sodium hydroxide (2%; 250 ml) using phenolphthalein as indicator. The phosphorus ylide was precipitated as a pink solid which was filtered off *in vacuo*, washed with water to provide a white solid, and dissolved in benzene. The organic layer was purified by heating under reflux to complete azeotropic removal of residual water after which it was distilled. The methoxycarbonylmethylenetriphenylphosphorane was obtained as a white crystalline solid after recrystallization from ethyl acetate–hexane, m.p. 161—163 °C (75% yield on the starting bromoacetate).

Preparation of the 1-*oxo*-3-*cyclohexylidenemethyl acetate phenylhydrazone.* A mixture of 1-oxo-3-cyclohexylidenemethyl acetate (3.00 g, 17.8 mmol) and phenylhydrazine (1.93 g, 17.8 mmol) in benzene (160 ml), was warmed at reflux temperature in a Dean-Stark system to remove water azeotropically. After 4 h, benzene was removed under reduced pressure to give a near quantitative yield of the phenylhydrazone, as a yellow-red oil.

Fischer reaction of 1-*oxo*-3-*cyclohexylidenemethyl acetate phenylhydrazone.* 1-Oxo-3-cyclohexylidenemethyl acetate phenylhydrazone (4.59 g, 17.8 mmol) was dissolved in anhydrous tetrahydrofuran (200 ml) under an argon atmosphere and the mixture was kept at 85 °C. It was then added to boron trifluoride–diethyl ether (5.05 g, 35.6 mmol). After 5 h further boron trifluoride (2.0 g) was added and above conditions maintained during 20 h. Finally, the reaction mixture was treated with saturated aqueous sodium acetate and extracted with dichloromethane. Evaporation of the extract gave a brown oil which was chromatographed on a silica gel column with toluene–ethyl acetate (1:1) as eluant, to give the 1,2,3,4-tetrahydrocarbazol-4-ylidenemethyl acetate as a yellow solid (49%), m.p. 188—190 °C. Moreover, two minor products were obtained and identified: 4-methylcarbazole as a white solid (3%), m.p. 127—129 °C, and methyl carbazol-4-ylacetate as a slightly yellow solid (5%), m.p. 146—148 °C.

Catalysis of the Fischer reaction by acetic acid (96%) instead of the boron trifluoride, under the above reaction conditions, gave the same products: 1,2,3,4-tetrahydrocarbazol-4-ylidenemethyl acetate (32%), 4-methylcarbazole (10%), and methyl carbazole-4-ylacetate (12%).

When the Fischer reaction was carried out with ethylene glycol as solvent at 180 °C, a complex mixture of carbazole aromatization products were obtained.

1,2,3,4-Tetrahydrocarbazol-4-ylidenemethyl acetate (Found: C, 74.9; H, 6.15; N, 5.95. $C_{15}H_{15}NO_2$ requires C, 74.67; H, 6.27; N, 5.81); $\nu_{max.}$(KBr) 3 320 (NH), 1 690 (C=O, conjugated ester), and 1 600 cm^{-1} (C=C, conjugated); δ_H(200 MHz; $CDCl_3$) 8.3 (1 H, br s, NH), 7.9 (1 H, m, 5-H), 7.2 (3 H, m, Ar), 6.38 (1 H, m, HC=C), 3.73 (3 H, s, CH_3O), 3.25 (2 H, m, 3-CH_2), 2.83 (2 H, t, *J* 6.3 Hz, 1-CH_2), and 2.00 (2 H, q, *J* 6.3 Hz, 2-CH_2); *m/z* (70 eV) 241 (M^+, 100), 211 (19), 210 (98), 209 (31), 183 (46), 182 (28), 181 (22), 180 (56), 168 (31), 167 (37), 154 (25), 130 (20), 127 (18), 105 (10), 90 (23), and 77 (23).

4-Methylcarbazole (Found: C, 85.8; H, 6.15; N, 7.5. $C_{13}H_{11}N$ requires C, 86.15; H, 6.12; N, 7.73); $\nu_{max.}$(KBr) 3 420 (NH), and 730, 750, and 760 cm^{-1} (ArH); δ_H(200 MHz; $CDCl_3$) 7.5 (8 H, br m, Ar) and 2.8 (3 H, s, CH_3); *m/z* (70 eV) 181 (M^+, 100), 180 (98), 152 (18), 127 (5), 91(5), and 77 (6).

Methyl carbazol-4-ylacetate (Found: C, 74.95; H, 5.5; N, 5.8. $C_{15}H_{13}NO_2$ requires C, 75.30; H, 5.48; N, 5.85); $\nu_{max.}$(KBr) 3 440 (NH), 1 730 (C=O), and 760 and 730 cm^{-1} (ArH); δ_H(200 MHz; $CDCl_3$) 7.54 (8 H, m, Ar), 3.81 (2 H, s, CH_2CO), and 3.73 (3 H, s, CH_3O); *m/z* (70 eV) 239 (M^+, 70), 180 (100), 178 (10), 152 (14), and 77 (6).

Hydrolysis of the 1,2,3,4-*Tetrahydrocarbazol*-4-*ylidenemethyl Acetate.*—Hydrolysis of the ester was conducted with 10% aqueous ethanolic potassium hydroxide, at 75 °C or with 5% aqueous sulphuric acid at 75 °C. In both cases, the main reaction product was the 4-methylcarbazole, in 67 or 78% yield respectively.

Synthesis and Hydrolysis of Methyl 1,2,3,4-*Tetrahydrocarbazol*-4-*ylacetate.*—A mixture of 1,2,3,4-tetrahydrocarbazol-4-ylidenemethyl acetate (0.24 g, 1 mmol), dissolved in methanol (30 ml), glacial acetic acid (1 ml), and platinum oxide (10 mg), were hydrogenated at 50 °C and 40 p.s.i., during 48 h. Removal of the solvent left a brown oil which was chromatographed on a silica gel column using ethyl acetate–heptane (1:2) as eluant to give the title ester as a yellow oil (88%).

Hydrolysis of this ester with 10% aqueous potassium hydroxide was effected in water–ethanol (9:1) at 70 °C during 5 h. Neutralization with 10% sulphuric acid gave the 1,2,3,4-tetrahydrocarbazol-4-ylacetic acid as a white crystalline solid, m.p. 136—138 °C, in practically quantitative yield (Found: C, 74.25; H, 7.3; N, 5.85. $C_{15}H_{17}NO_2$ requires C, 74.05; H, 7.04; N, 5.76%) $\nu_{max.}$(film) 3 420 (NH), 1 725 (C=O), and 750 cm^{-1} (ArH); δ_H(200 MHz; $CDCl_3$) 7.8 (1 H, br s, NH), 7.3 (4 H, m, Ar), 3.73 (3 H, s, CH_3O), 3.00 (1 H, dd, *J* 3.92, 15.17 Hz, HCCO), 2.71 (3 H, m, 4-H, 1-CH_2), 2.42 (1 H, dd, *J* 10.70, 15.17 Hz, HCCO), 1.90 (4 H, br m, 2-CH_2, 3-CH_2); *m/z* (70 eV) 243 (M^+, 15%), 171 (13), 170 (100), 168 (17), 154 (7), 128 (5), and 77 (4).

Preparation of 4-(*Dimethylcarbamoylmethyl*)-1,2,3,4-*tetrahydrocarbazole.*—A solution of 1,2,3,4-tetrahydrocarbazol-4-ylacetic acid (0.24 g, 1.0 mmol) in anhydrous methanol (20 ml) previously saturated with gaseous dimethylamine, at 0 °C, was kept at room temperature during 6 days. The solvent was then removed and the residual oil chromatographed on a silica gel column using ethyl acetate–heptane (1:2) as eluant to give the title compound as a yellow oil in 86% yield; $\nu_{max.}$(film) 1 650 (C=O, amide) and 745 cm^{-1} (ArH); δ_H(200 MHz; $CDCl_3$) 7.9 (1 H, br s, NH), 2.91 (1 H, s, HCCO), 2.89 (3 H, s CH_3NCO), 2.82 (3 H, s, CH_3NCO), 2.78 (3 H, m, 4-H, 1-CH_2, 1-CH_2), 2.39 (1 H,

* See 'Instructions for Authors (1989),' *J. Chem. Soc., Perkin Trans. 1*, 1989, Issue 1.

dd, *J* 9.63, 15.32 Hz, HCCO), and 1.9 (4 H, br m, 2-CH_2, 3-CH_2); *m/z* (70 eV) 256 (M^+, 21%), 170 (100), 168 (20), 167 (12), 155 (9), 154 (12), 128 (7), and 77 (5).

Preparation of 4-(2-*Dimethylaminoethyl*)-1,2,3,4-*tetrahydrocarbazole.*—To a suspension of lithium aluminium hydride (50 mg, 1.32 mmol) in anhydrous tetrahydrofuran (5 ml), protected from moisture under an argon atmosphere, was added a solution of 4-(dimethylcarbamoylmethyl)-1,2,3,4-tetrahydrocarbazole (128 mg, 0.5 mmol) in anhydrous tetrahydrofuran (5 ml); the mixture was then stirred at room temperature for 3 h. The subsequent hydrolysis was effected with tetrahydrofuran–water (2:1) after which the THF layer was separated, dried (Na_2SO_4), filtered, and evaporated to give the 4-(2-dimethylaminoethyl)-1,2,3,4-tetrahydrocarbazole as a crystalline white solid, m.p. 158—160 °C, in 87% yield (Found: C, 78.8; H, 8.9; N, 11.65. $C_{16}H_{22}N_2$ requires C, 79.29; H, 9.15; N, 11.56%); δ_H(200 MHz; $CDCl_3$) 8.0 (1 H, br s, NH), 7.2 (4 H, m, Ar), 2.8 (5 H, br m, CH_2N, 1-CH_2, 4-H), 1.9 (6 H, br m, 2-CH_2, 3-CH_2, 4-CH_2), and 2.26 [6 H, s, $(CH_3)_2N$].

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