The Reactions of Some Tetrahydro-β-Carbolines, of Hexahydroazepino-[3,4-*b*]indoles, and of Tetrahydrocarbazolones with Arenesulphonyl Azides

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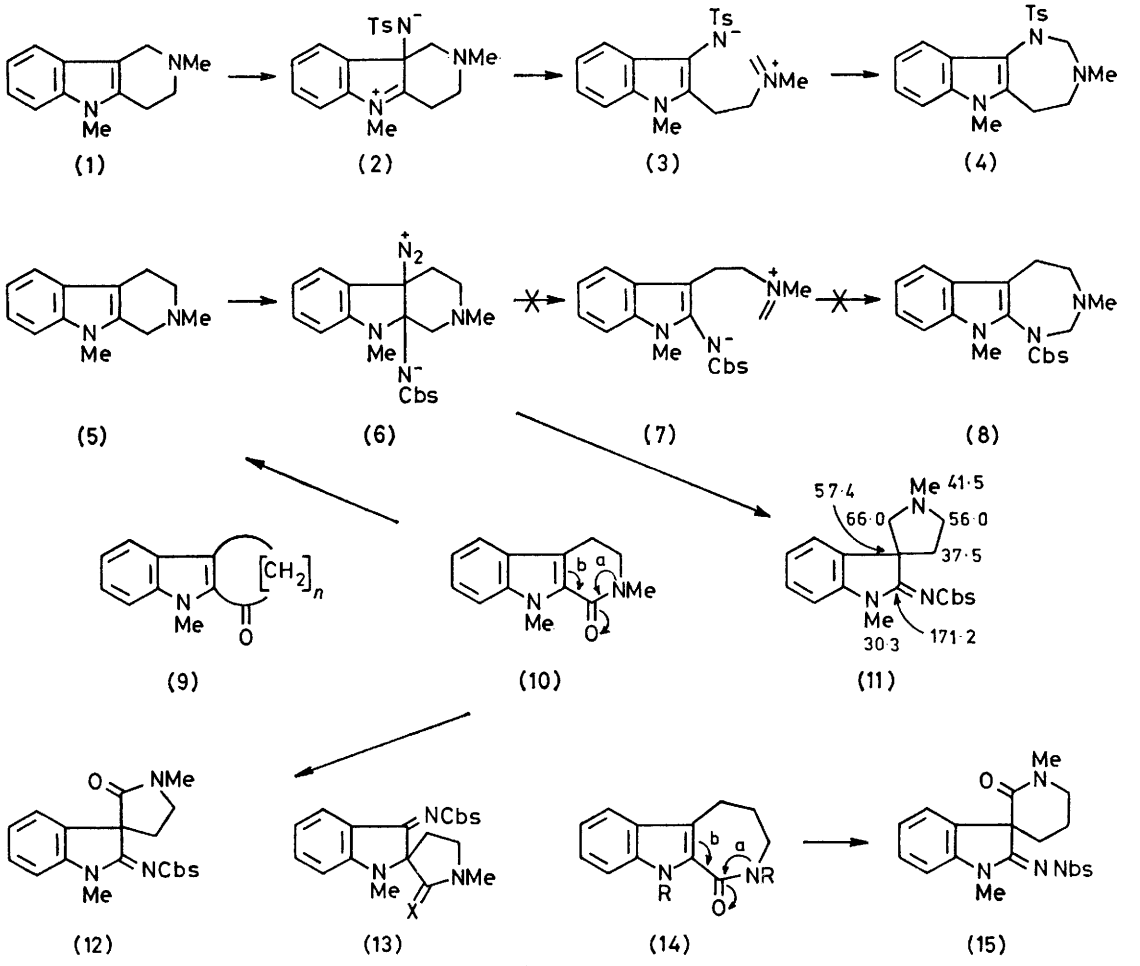
2,9-Dimethyl-1,2,3,4-tetrahydro-1-oxo-β-carboline and 2,9-dimethyl-1,2,3,4-tetrahydro-β-carboline react with arenesulphonyl azides forming indoline-3-spiropyrrolidines; 2,10-dimethyl-3,4,5,10-tetrahydroazepino[3,4-*b*]-indol-1(2*H*)-one and 2,10-dimethyl-1,2,3,4,5,10-hexahydroazepino[3,4-*b*]indole react to form indoline-3-spiropiperidines. 9-Methyl-2-oxo-tetrahydrocarbazole reacts with *p*-chlorobenzenesulphonyl azide to form 1-methyl-2-*p*-chlorophenylsulphonylimino-3′-oxoindoline-3-spirocyclopentane.

THE reaction of *N*-methyltetrahydrocarbazole with tosyl azide affords a mixture of five products.[1,2] In contrast the tetrahydro-γ-carboline (1) gave the ring-enlarged compound (4) *via* a ring-opened intermediate (3).[3] We decided to examine the reaction of the β-carboline derivative (5) to see if a similar type of ring-enlargement would occur *via* (6) and (7) to form (8). NMe group modified the reactivity of the indole 2,3-bond in compound (10) relative to that of compound (9, $n = 3$).

RESULTS AND DISCUSSION

In contrast to compound (9, $n = 3$) the amide (10) [5] reacted smoothly with *p*-chlorobenzenesulphonyl azide

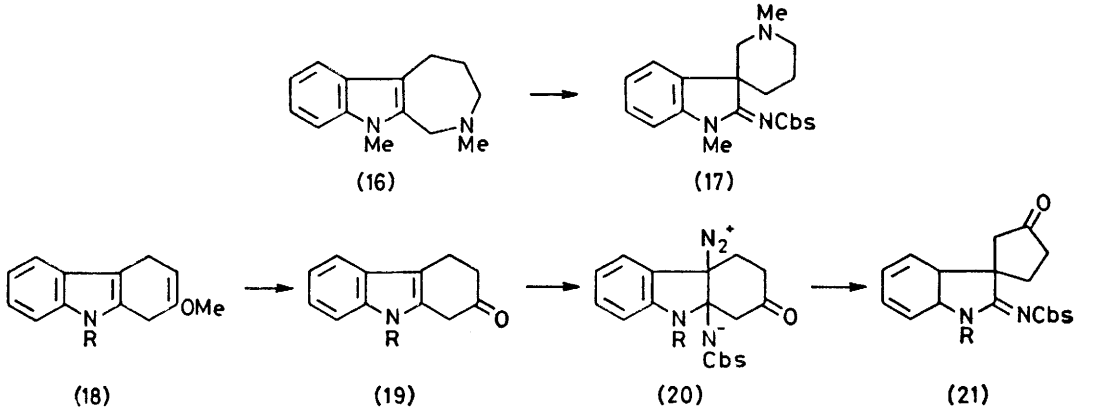


Further, we have shown that the ketones (9, $n = 3$ and 4) do not react with arenesulphonyl azides,[3,4] and we wished to examine the reactions of (10) to determine whether the 'neutralisation' of the CO group by the ($CbsN_3$). The product was assigned structure (12); the i.r. spectrum of the compound showing the presence of a C=N group and of a five-membered cyclic amide ($\nu_{max.}$ 1 700 cm^{-1}).[6] The u.v. and n.m.r. spectra showed that

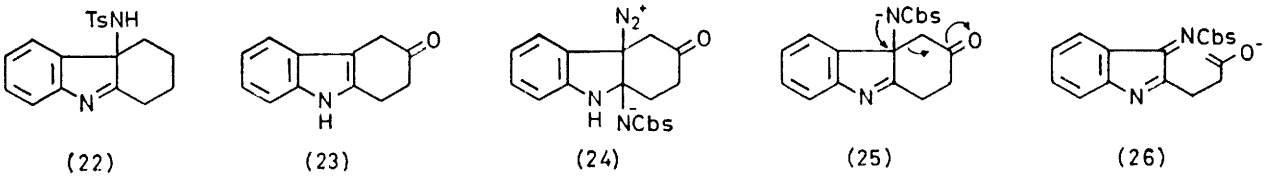
the compound did not possess the isomeric structure (13, X = O).

Compound (5) [5] reacted smoothly with $CbsN_3$ giving a 1 : 1 adduct to which we assign structure (11); the structure is supported by the absence of an NH group and the presence of C=N (i.r.), and the u.v. and n.m.r. spectra of the material eliminated structure (13, X = H_2). Confirmation of the structure is provided by the ^{13}C n.m.r. spectrum [numbers on (11) are in p.p.m. from $SiMe_4$] which showed the presence of a quaternary aliphatic carbon atom at C(3).[7] Hence it appears that the intermediate (6) does not undergo ring-opening and enlargement to form (8), but that in this case ring-contraction occurs. Similar types of ring contraction of β-carbolines have been reported.[8]

It is known [9] that azides react faster with *N*-methylhexahydrocyclohept[*b*]indole than with *N*-methyltetrahydrocarbazole, and we therefore prepared (14, R = Me) by methylation of (14, R = H) [10] in order to examine its reactions. We were surprised to observe that (14, R = Me) did not react with $CbsN_3$ under the conditions used for the reaction of (10). However (14, R = Me) reacted during 6 days with *p*-nitrobenzenesulphonyl azide ($NbsN_3$) giving the spiran (15) as the only crystalline product. It has been reported [11] that as the ring size of the ketones (9) increases steric crowding causes loss of planarity between the carbonyl group and the indole nucleus. It appears that in compound (14, R = Me) the O=C and NMe groups are no longer co-planar and the mesomeric interaction ' a ' is less effective than in (10). The C=O group and the indole 2,3-bond are, however, co-planar and interaction ' b ' is now important, reducing the reactivity of the indole 2,3-bond in (14, R = Me). Reduction of (14, R = Me) afforded (16) and this compound reacted vigorously with $CbsN_3$: the neat mixture exploded and in chloroform solution reaction was complete in 24 h at room temperature, the product being the spiran (17). In the reactions of (5) and (16) with azides the only products isolated were 1 : 1 adducts involving ring-contraction; no 1 : 2 reaction products were obtained in contrast to their carbocyclic analogues.



To complete this series the reactions of compounds containing carbonyl groups which were not conjugated with the indole nucleus were examined. 2-Methoxycarbazole was reduced to (18, R = H), hydrolysis then yielding (19, R = H).[12] This compound reacted smoothly with $CbsN_3$ yielding the ring-contracted compound (21, R = H), *via* (20, R = H). The i.r. spectrum of compound (21, R = H) contained bands at 1 600 (C=N) and 1 750 cm^{-1} (CO in five-membered ring). The reaction of (19, R = H) is in striking contrast to that of tetrahydrocarbazole which yields the indolenine (22).[1] Teuber [12] failed to methylate (19, R = H); however methylation of (18, R = H) followed by hydrolysis yielded (19, R = Me). This compound also reacted with $CbsN_3$ by ring-contraction forming (21, R = Me), no 1 : 2 products being isolated. Finally compound (23) [12] was reacted with $CbsN_3$ since ring-contraction of (24) should lead to (21, R = H). However, under a variety of conditions (23) gave polymeric material, no (21, R = H) being detected (t.l.c.). It appears that reactions of (19) and of (23) with azides follow different routes. Possibly (23) reacts in a similar manner to tetrahydrocarbazole giving (25) which then undergoes ring-opening and polymerisation *via* (26).



EXPERIMENTAL

General details and instruments used have been reported.[13] U.v. spectra were determined for solutions in

ethanol and n.m.r. spectra for solutions in $CDCl_3$ unless otherwise stated; i.r. spectra were recorded for Nujol mulls. Thin-layer chromatography was carried out on *silica* gel H.F. 254–366 plates using chloroform as eluant; column chromatography was carried out on silica.

2-p-*Chlorophenylsulphonylimino*-1,1′-*dimethyl*-2′-*oxoindoline*-3-*spiro*-3′-*pyrrolidine* (12).—2-Oxopiperidine-3-phenylhydrazone was cyclised using 70% formic acid (100 °C, 30 min) forming 1,2,3,4-tetrahydro-1-oxo-β-carboline (yield 87%), m.p. 182—183 °C (lit.,[5] 183—185 °C). Methylation (DMSO–NaH–MeI) afforded compound (10), m.p. 75—76 °C (lit.,[5] 65—66 °C); τ 2.45 (1 H, d, *J* 8 Hz, Ar), 2.6—3.0 (3 H, m, Ar), 5.91 (3 H, s, indoline NMe), 6.39 [2 H, t, *J* 7 Hz, C(3)H_2], 6.89 (3 H, s, NMe), and 7.0 [2 H, t, *J* 7 Hz, 4-H_2]. Compound (10) (0.5 g) and $CbsN_3$ (0.85 g) were mixed and kept at 50 °C for 7 days. MeOH (5 ml) was then added and the solid collected. The *amide* (12) formed prisms (from EtOH), m.p. 209—210 °C (yield 0.35 g) (Found: C, 56.3; H, 4.7; Cl, 8.4; N, 10.1; S, 8.0. $C_{19}H_{18}ClN_3O_3S$ requires C, 56.6; H, 4.5; Cl, 8.7; N, 10.4; S, 7.9%); $\lambda_{max.}$ 228, 288, and 302 nm (ε 31 300, 17 900, and 15 200); $\nu_{max.}$ 1 560 and 1 700 cm^{-1}; τ 2.03 (2 H, d, *J* 8 Hz), 2.5—3.2 (6 H, m), 6.23 [2 H, t, *J* 6 Hz, 5′-H_2], 6.72 (3 H, s, indoline NMe), 7.0 (3 H, s, NMe), and 7.5—7.9 [2 H, m, 4′-H_2]; *m/e* 403 (M^+, 16%), 347 (12%), 346 (11%), 228 (M^+ — Cbs, 100%), 185 (68%), and 171 (32%).

2-p-*Chlorophenylsulphonylimino*-1,1′-*dimethylindoline*-3-*spiro*-3′-*pyrrolidine* (11).—Compound (5) had m.p. 95—96 °C (lit.,[5] 95.5—96.5 °C); τ 2.4—3.0 (4 H, m), 6.4 [2 H, s, 1-H_2], 6.45 (NMe), 7.1—7.3 [4 H, m, 3-H_2 and 4-H_2], and 7.45 (NMe). A mixture of (5) (0.5 g) and $CbsN_3$ (0.65 g) was kept at 50 °C for 48 h. MeOH was then added and the resulting solid recrystallised (EtOH); the *pyrrolidine* (11) formed irregular plates, m.p. 150—151 °C (yield 0.75 g). (Found: C, 58.6; H, 5.2; Cl, 9.2; N, 10.7; S, 8.5. $C_{19}H_{20}ClN_3O_2S$ requires C, 58.6; H, 5.1; Cl, 9.0; N, 10.8; S, 8.4%); $\lambda_{max.}$ 225, 288, and 297sh nm (ε 34 800, 18 400, and 16 100); $\nu_{max.}$ 1 565 cm^{-1}; τ 2.03 (2 H, d, *J* 8 Hz), 2.3—3.2 (6 H, m), 6.53 (3 H, s, NMe), 6.6—7.5 (5 H, m), 7.53 (3 H, s, NMe), and 7.7—8.0 (1 H, m); *m/e* 389 (M^+, 1%), 333 (M^+ — C_3H_6N, 2%), 214 (M^+ — Cbs, 100%), 183 (15%), 171 (46%, *m** 136), and 158 (9%). Compound (11) formed a *methiodide*, needles (from EtOH), m.p. 235 °C (decomp) (Found: C, 45.5; H, 4.6; N, 7.7. $C_{20}H_{23}ClIN_3O_2S$ requires C, 45.2; H, 4.3; N, 7.9%).

1,1′-*Dimethyl*-2-p-*nitrophenylsulphonylimino*-2′-*oxoindoline*-3-*spiro*-3′-*piperidine* (15).—1-Oxotetrahydrocarbazole, m.p. 168—169 °C (lit.,[11] 168—170 °C) was converted into its oxime and the mixture of *syn*- and *anti*-isomers rearranged [10] (polyphosphoric acid) forming 3,4,5,10-tetrahydroazepino[3,4-*b*]indol-1(2*H*)-one (14; R = H), m.p. 221—223 °C (lit.,[10] 228—229 °C). Methylation (DMSO–NaH–MeI) gave 2,10-*dimethyl*-3,4,5,10-*tetrahydroazepino*[3,4-b]*indol*-1(2H)-*one* (14, R = Me), needles [from light petroleum (b.p. 60—80 °C)], m.p. 104—106 °C (Found: C, 73.7; H, 7.1; N, 12.1. $C_{14}H_{16}N_2O$ requires C, 73.7; H, 7.0; N, 12.3%); $\lambda_{max.}$ 226 and 295 nm (ε 27 400 and 16 000); $\nu_{max.}$ 1 630 cm^{-1}; τ 2.3—3.0 (4 H, m), 6.04 (3 H, s, NMe), 6.57 [2 H, t, *J* 7 Hz, 3-H_2], 6.81 (3 H, s, NMe), 7.0 [2 H, t, *J* 7 Hz, 5-H_2], and 7.6—8.0 [2 H, m, 4-H_2]. The indole (14, R = Me) (0.25 g) and $NbsN_3$ (0.35 g) were mixed and kept at 60 °C for 6 days. MeOH (2 ml) was added and the solid collected and recrystallised (EtOH) to give the *imine* (15) as prisms (0.144 g), m.p. 246—247 °C (Found: C, 55.8; H, 5.0; N, 13.0; S, 7.3. $C_{20}H_{20}N_4O_5S$ requires C, 55.9; H, 4.9; N, 13.1; S, 7.5%); $\lambda_{max.}$ 218(sh), 270, and 300(sh) (ε 27 700, 18 700, and 14 300); $\nu_{max.}$ 1 565 (C=N) and 1 650 (C=O) cm^{-1}; τ 1.5—3.1 (8 H, m, Ar), 5.9—6.5 [2 H, m, 6′-H_2], 6.63 (3 H, s, NMe), 6.93 (3 H, s, NMe), and 7.0—8.3 [4 H, m, 4′-H_2 and 5′-H_2]; *m/e* 428 (M^+, 15%), 242 (M^+ — Nbs, 100%), 200 (242 — C_2H_4N, 19%), 173 (200—C_2H_3, 31%), and 185 (242 — C_3H_7N, 32%).

2-p-*Chlorophenylsulphonylimino*-1,1′-*dimethylindoline*-3-*spiro*-3′-*piperidine* (17).—Compound (14, R = Me) was reduced ($LiAlH_4$–Et_2O, 8 h reflux). 2,10-*Dimethyl*-1,2,3,4,5,10-*hexahydroazepino*[3,4-b]*indole* (16) formed tiny prisms, m.p. 60—61 °C [from light petroleum (b.p. 60—80 °C)] (Found: C, 78.6; H, 8.5; N, 13.1. $C_{14}H_{18}N_2$ requires C, 78.5; H, 8.4; N, 13.1%); $\lambda_{max.}$ 226 and 295 nm (ε 22 000 and 13 300); τ 2.4—3.1 (4 H, m), 6.05 (2 H, s, 1-H_2), 6.35 (3 H, s, NMe), 6.8—7.2 (4 H, m, 3-H_2 and 5-H_2), 7.6 (3 H, s, NMe), and 8.0—8.3 (2 H, m, 4-H_2); *m/e* 214 (M^+, 49%), 185 (8%), 171 (100%), 170 (38%), 157 (31%), and 144 (20%). The indole (16) (0.2 g) was dissolved in chloroform (5 ml) and $CbsN_3$ (0.28 g) added. After 2 days the solvent was removed and MeOH (2 ml) added. The *spiro-compound* (17) was collected and recrystallised (EtOH) forming prisms (0.30 g), m.p. 184—186 °C (Found: C, 59.3; H, 5.5; Cl, 8.6; N, 10.2; S, 7.7. $C_{20}H_{22}ClN_3O_2S$ requires C, 59.6; H, 5.5; Cl, 8.7; N, 10.4; S, 7.9%); $\lambda_{max.}$ 225 and 282 nm (ε 24 000 and 16 000); $\nu_{max.}$ 1 560 cm^{-1}; τ 2.05 (2 H, d, *J* 8 Hz), 2.4—3.1 (6 H, m), 6.36 (3 H, s, NMe), 7.75 (3 H, s, NMe), and 6.9—8.8 (8 H, m); *m/e* 228 (M^+ — Cbs, 31%), 185 (228 — C_2H_5N, 24%), 159 (228 — C_4H_7N, 100%), and 142 (4%).

2-p-*Chlorophenylsulphonylimino*-3′-*oxoindoline*-3-*spiro*-*cyclopentane* (21, R = H).—2-Hydroxycarbazole was methylated and the methyl ether reduced (Li–NH_3) [12] forming (18, R = H), m.p. 176—178 °C (lit.,[12] 178—179 °C). Hydrolysis then afforded (19, R = H), m.p. 136—137 °C (lit.,[12] 131—133 °C); $\nu_{max.}$ 1 700 cm^{-1}. Compound (19, R = H) (1 g) was dissolved in DMSO (10 ml) and $CbsN_3$ (1.2 g) added. After 48 h water (20 ml) was added and the mixture kept at 0 °C for 24 h. The solid was collected and recrystallised from ethanol. The *ketone* (21, R = H) formed fine needles (1.5 g), m.p. 218—219 °C (Found: C, 57.7; H, 4.1; Cl, 9.1; N, 7.5; S, 8.7. $C_{18}H_{15}ClN_2O_3S$ requires C, 57.8; H, 4.0; Cl, 9.4; N, 7.5; S, 8.6%); $\lambda_{max.}$ 225, 280, and 292(sh) nm (ε 27 800, 16 100, and 11 700); $\nu_{max.}$ 1 600 (C=N), 1 750 (C=O), and 3 320 (NH) cm^{-1}; τ[$(CD_3)_2SO$] — 1.5 (1 H, s, exchanged with D_2O, NH), 2.05 (2 H, d, *J* 8 Hz), 2.2—3.0 (6 H, m), and 7.0—8.0 (6 H, m); *m/e* 374 (M^+, 60%), 346 (M^+ — CO, 13%), 319 (M^+ — C_3H_3O, 100%), 199 (M^+ — Cbs, 37%), and 171 (97%).

2-p-*Chlorophenylsulphonylimino*-1-*methyl*-3′-*oxoindoline*-3-*spirocyclopentane* (21, R = Me).—Compound (18, R = H) was methylated (DMSO–NaH–MeI), the reaction mixture diluted with water, and the product isolated by extraction with CH_2Cl_2. 2-*Methoxy*-1-*methyl*-1,4-*dihydrocarbazole* (18, R = Me) formed needles, m.p. 99—100 °C (from EtOH) (Found: C, 79.0; H, 7.2; N, 6.5. $C_{14}H_{15}NO$ requires C, 78.9; H, 7.0; N, 6.6%); $\lambda_{max.}$ 230 and 285 nm (ε 37 000 and 6 800); τ 2.4—3.0 (4 H, m), 5.0 (1 H, s br, 3-H), 6.35 (OMe), 6.39 (NMe), and 6.0—6.9 (4 H, m, 1-H_2 and 4-H_2); *m/e* 213 (M^+, 100%), 198 (70%), 182 (72%), and 168 (54%). Hydrolysis (HCl–Et_2O) [12] gave 9-*methyl*-2-*oxo*-1,2,3,4-*tetrahydrocarbazole* (19, R = Me) as prisms (from EtOH), m.p. 98—99 °C (Found: C, 78.4; H, 6.5; N, 7.2. $C_{13}H_{13}NO$ requires C, 78.4; H, 6.5; N, 7.0%); $\lambda_{max.}$ 227

and 285 nm (ε 39 600 and 9 500); $\nu_{max.}$ 1 710 cm^{-1}; τ 2.4—3.0 (4 H, m), 6.5 (5 H, NMe and 1-H_2), 6.7—7.1 (2 H, m, 3-H_2), and 7.15—7.4 (2 H, t, *J* 6 Hz, 4-H_2); *m/e* 199 (M^+, 88%), 171 (24%), 170 (49%), and 157 ($C_{11}H_{11}N$, 100%). This ketone was dissolved in DMSO and allowed to react with $CbsN_3$. After 2 days water was added and the product isolated by extraction ($CHCl_3$). The *ketone* (21, R = Me) formed prisms, m.p. 173—174 °C (from EtOH), yield 55% (Found: C, 58.8; H, 4.4; Cl, 9.1; N, 7.1; S, 8.2. $C_{19}H_{17}ClN_2O_3S$ requires C, 58.8; H, 4.4; Cl, 9.0; N, 7.2; S, 8.2%); $\lambda_{max.}$ 226, 285, and 298(sh) nm (ε 32 900, 20 700, and 16 700); $\nu_{max.}$ 1 570 (C=N) and 1 750 (C=O) cm^{-1}; τ 2.08 (2 H, d, *J* 8 Hz), 2.45—3.1 (6 H, m), 6.48 (3 H, s, NMe), and 6.3—8.0 (6 H, m); *m/e* 388 (M^+, 34%), 333 ($M^+ - C_3H_3O$, 26%), 213 (M^+ — Cbs, 100%), and 185 (60%).

6-Methoxytetrahydrocarbazole was dehydrogenated [14] and the resulting 3-methoxycarbazole reduced [12] (Li–NH_3) to the dihydro-derivative, which was then hydrolysed to the keto-compound (23), m.p. 150—151 °C (decomp.) (lit.,[12] 156 °C). This ketone was reacted with $CbsN_3$ at room temperature in $CHCl_3$, benzene, and DMSO; in all reactions polymeric materials were obtained.

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