

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

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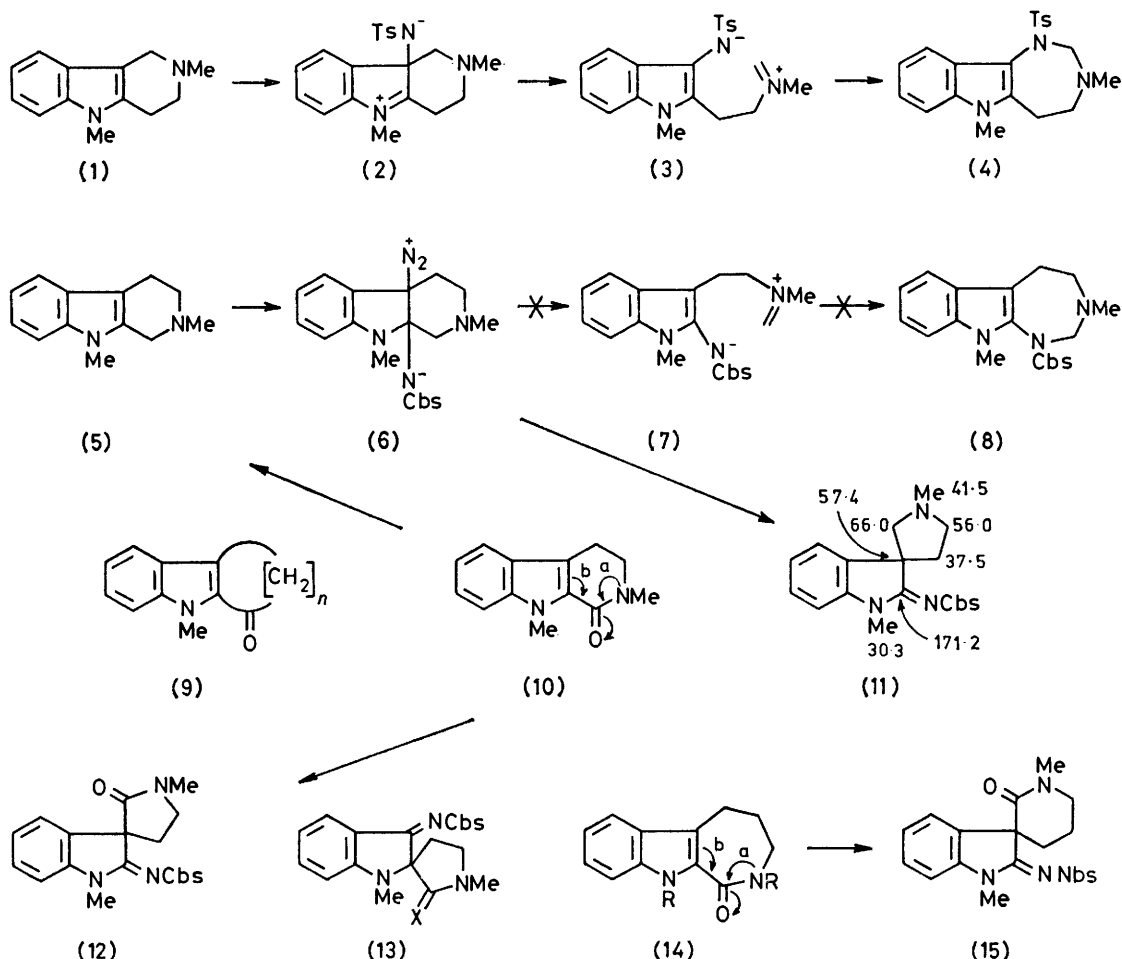
2,9-Dimethyl-1,2,3,4-tetrahydro-1-oxo- β -carboline and 2,9-dimethyl-1,2,3,4-tetrahydro- β -carboline react with arenesulphonyl azides forming indoline-3-spiropyrrolidines; 2,10-dimethyl-3,4,5,10-tetrahydroazepino[3,4-*b*]indol-1(2*H*)-one and 2,10-dimethyl-1,2,3,4,5,10-hexahydroazepino[3,4-*b*]indole 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).

*N*Me 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



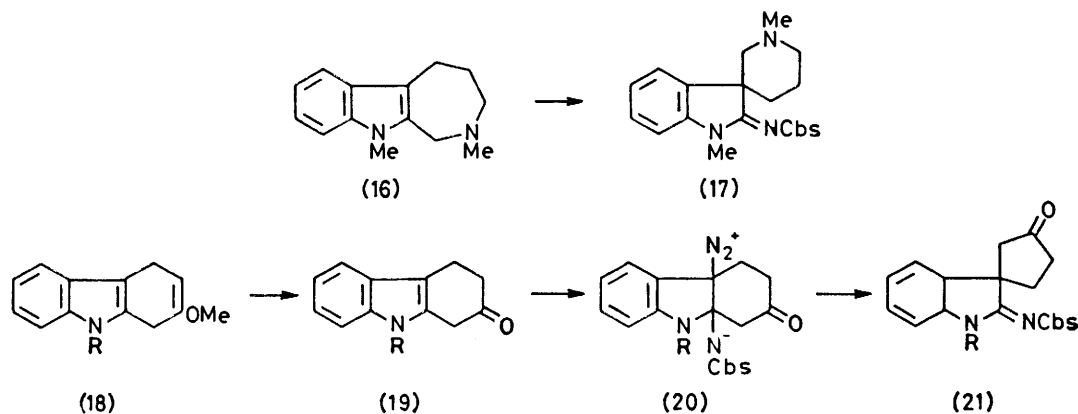
Further, we have shown that the ketones (9, *n* = 3 and 4) do not react with arenesulphonyl azides,^{3,4} and we wished to examine the reactions of (10) to determine whether the 'neutralisation' of the CO group by the

(CbsN₃). 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 (ν_{max} . 1700 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 CbsN₃ 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 =

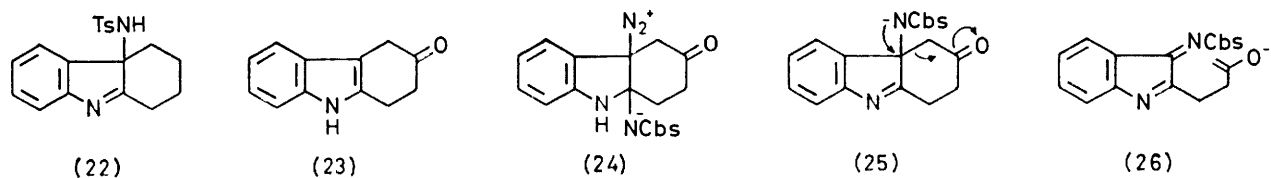
pound reacted vigorously with CbsN₃: the neat mixture exploded and in chloroform solution reaction was complete in 24 h at room temperature, the product being the spiran (17). In the reactions of (5) and (16) with azides the only products isolated were 1:1 adducts involving ring-contraction; no 1:2 reaction products were obtained in contrast to their carbocyclic analogues.



H₂). Confirmation of the structure is provided by the ¹³C n.m.r. spectrum [numbers on (11) are in p.p.m. from SiMe₄] 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 known⁹ that azides react faster with *N*-methylhexahydrocyclohept[b]indole than with *N*-

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 CbsN₃ 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



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 CbsN₃ under the conditions used for the reaction of (10). However (14, R = Me) reacted during 6 days with *p*-nitrobenzenesulphonyl azide (NbsN₃) giving the spiran (15) as the only crystalline product. It has been reported¹¹ 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 com-

that of tetrahydrocarbazole which yields the indolenine (22).¹ Teuber¹² failed to methylate (19, R = H); however methylation of (18, R = H) followed by hydrolysis yielded (19, R = Me). This compound also reacted with CbsN₃ by ring-contraction forming (21, R = Me), no 1:2 products being isolated. Finally compound (23)¹² was reacted with CbsN₃ 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'-oxo-indoline-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)H₂], 6.89 (3 H, s, NMe), and 7.0 [2 H, t, J 7 Hz, 4-H₂]. Compound (10) (0.5 g) and CbsN₃ (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. C₁₉H₁₈ClN₃O₃S requires C, 56.6; H, 4.5; Cl, 8.7; N, 10.4; S, 7.9%); λ_{max} 228, 288, and 302 nm (ϵ 31 300, 17 900, and 15 200); ν_{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'-H₂], 6.72 (3 H, s, indoline NMe), 7.0 (3 H, s, NMe), and 7.5—7.9 [2 H, m, 4'-H₂]; 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-H₂], 6.45 (NMe), 7.1—7.3 [4 H, m, 3-H₂ and 4-H₂], and 7.45 (NMe). A mixture of (5) (0.5 g) and CbsN₃ (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. C₁₉H₂₀ClN₃O₃S requires C, 58.6; H, 5.1; Cl, 9.0; N, 10.8; S, 8.4%); λ_{max} 225, 288, and 297sh nm (ϵ 34 800, 18 400, and 16 100); ν_{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^+ - C₃H₆N, 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. C₂₀H₂₃ClIN₃O₃S requires C, 45.2; H, 4.3; N, 7.9%).

1,1'-Dimethyl-2-p-nitrophenylsulphonylimino-2'-oxo-indoline-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 rearranged¹⁰ (polyphosphoric acid) forming 3,4,5,10-tetrahydroazepino[3,4-*b*]indol-1(2H)-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. C₁₄H₁₆N₂O requires C, 73.7; H, 7.0; N, 12.3%); λ_{max} 226 and 295 nm (ϵ 27 400 and 16 000); ν_{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-H₂], 6.81 (3 H, s, NMe), 7.0 [2 H, t, J 7 Hz, 5-H₂], and 7.6—8.0 [2 H, m, 4-H₂]. The indole (14, R = Me) (0.25 g) and NbsN₃ (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. C₂₀H₂₀N₄O₅S requires C, 55.9; H, 4.9; N, 13.1; S, 7.5%); λ_{max} 218(sh), 270, and 300(sh) (ϵ 27 700, 18 700, and 14 300); ν_{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'-H₂], 6.63 (3 H, s, NMe), 6.93 (3 H, s, NMe), and 7.0—8.3 [4 H, m, 4'-H₂ and 5'-H₂]; m/e 428 (M^+ , 15%), 242 (M^+ - Nbs, 100%), 200 (242 - C₂H₄N, 19%), 173 (200 - C₂H₃, 31%), and 185 (242 - C₃H₇N, 32%).

2-p-Chlorophenylsulphonylimino-1,1'-dimethylindoline-3-spiro-3'-piperidine (17).—Compound (14, R = Me) was reduced (LiAlH₄-Et₂O, 8 h reflux). 2,10-Dimethyl-1,2,3,4,5,10-hexahydroazepino[3,4-*b*]indole (16) formed thin prisms, m.p. 60—61 °C [from light petroleum (b.p. 60—80 °C)] (Found: C, 78.6; H, 8.5; N, 13.1. C₁₄H₁₈N₂ requires C, 78.5; H, 8.4; N, 13.1%); λ_{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-H₂), 6.35 (3 H, s, NMe), 6.8—7.2 (4 H, m, 3-H₂ and 5-H₂), 7.6 (3 H, s, NMe), and 8.0—8.3 (2 H, m, 4-H₂); 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 CbsN₃ (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. C₂₀H₂₂ClN₃O₃S requires C, 59.6; H, 5.5; Cl, 8.7; N, 10.4; S, 7.9%); λ_{max} 225 and 282 nm (ϵ 24 000 and 16 000); ν_{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 - C₂H₅N, 24%), 159 (228 - C₄H₇N, 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-NH₃)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); ν_{max} 1 700 cm⁻¹. Compound (19, R = H) (1 g) was dissolved in DMSO (10 ml) and CbsN₃ (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. C₁₈H₁₅ClN₂O₃S requires C, 57.8; H, 4.0; Cl, 9.4; N, 7.5; S, 8.6%); λ_{max} 225, 280, and 292(sh) nm (ϵ 27 800, 16 100, and 11 700); ν_{max} 1 600 (C=N), 1 750 (C=O), and 3 320 (NH) cm⁻¹; τ [(CD₃)₂SO] - 1.5 (1 H, s, exchanged with D₂O, 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^+ - C₃H₃O, 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 CH₂Cl₂. 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. C₁₄H₁₅NO requires C, 78.9; H, 7.0; N, 6.6%); λ_{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-H₂ and 4-H₂); m/e 213 (M^+ , 100%), 198 (70%), 182 (72%), and 168 (54%). Hydrolysis (HCl-Et₂O)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. C₁₃H₁₃NO requires C, 78.4; H, 6.5; N, 7.0%); λ_{max} 227

and 285 nm (ϵ 39 600 and 9 500); ν_{\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 ($\text{C}_{11}\text{H}_{11}\text{N}$, 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. $\text{C}_{19}\text{H}_{17}\text{ClN}_2\text{O}_3\text{S}$ requires C, 58.8; H, 4.4; Cl, 9.0; N, 7.2; S, 8.2%); λ_{\max} 226, 285, and 298(sh) nm (ϵ 32 900, 20 700, and 16 700); ν_{\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 ($M^+ - \text{C}_3\text{H}_3\text{O}$, 26%), 213 ($M^+ - \text{Cbs}$, 100%), and 185 (60%).

6-Methoxytetrahydrocarbazole was dehydrogenated¹⁴ and the resulting 3-methoxycarbazole reduced¹² (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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