A New Route to Cycloheptatrienylideneammonium Salts; Restricted Rotation about the C=N Bond

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Reactions of 3- and 4-dimethylaminocycloheptatrienone with methyl fluorosulphate and the reaction of the 3-derivative with methyl iodide result in predominant *O*-methylation. The *N*-methyl groups of the 4-methoxy-salt (4) are magnetically non-equivalent at room temperature, but the corresponding methyl groups of the 2- and 3-isomers are indistinguishable, even at −80 °C.

KNOWN routes to cycloheptatrienylideneammonium salts include bromination–dehydrobromination of aminocycloheptatrienes,[1] hydride ion abstraction from cycloheptatrienylamines by the cycloheptatrienylium cation,[2] displacement of chloride ion from chlorocycloheptatrienylium salts by amines,[3] and, although with less generality, methylation of cycloheptatrienone anils.[3]

We report here that the three isomeric methoxy-substituted *NN*-dimethylcycloheptatrienylideneammonium salts can be prepared by methylation of dimethylaminocycloheptatrienones and exhibit differing barriers to rotation about the C:N bond.

Treatment of 3-dimethylaminocycloheptatrienone [4] (1) with methyl fluorosulphate in benzene led to the yellow crystalline material salt (2a), isolated in high yield. The structure is supported by the ^{1}H n.m.r. spectrum (CD_3OD) which at ordinary probe temperature shows a complex multiplet between δ 7.8 and 7.4 (4 H) attributable to the four adjacent protons on the ring, a broad singlet at δ 6.8 (1 H) attributable to the other ring proton, a singlet at δ 3.58 (6 H) attributable to the dimethyliminium group, and a methoxy-singlet at δ 4.08 (3 H).

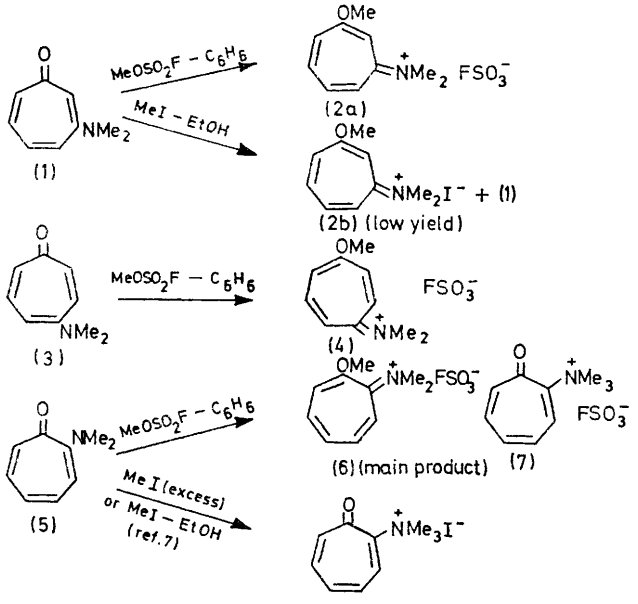
The only material isolated, in low yield, apart from unchanged ketone (1) on treatment of (1) with methyl iodide, was a crystalline compound exhibiting a u.v. absorption spectrum [$\lambda_{max.}$ (EtOH) 328 and 265 nm] identical with that of the salt (2) and a ^{1}H n.m.r. spectrum (see Experimental section) clearly indicating the 3-methoxy-*NN*-dimethylcycloheptatrienylideneammonium iodide structure (2b).

Treatment of the ketone (1) with dimethyl sulphate led only to a product which, although not isolated pure, exhibited a u.v. spectrum similar to that of (2), suggesting a cycloheptatrienylideneammonium structure.

[1] C. Jutz, *Chem. Ber.*, 1964, **97**, 2050.
[2] N. L. Bould and Yong Sung Rim, *J. Amer. Chem. Soc.*, 1967, **89**, 6763; H. J. Dauben and F. D. Roades, *ibid.*, p. 6766.
[3] E. Haug and B. Föhlish, *Z. Naturforsch.*, 1969, **24b**, 1353.
[4] B. Ricciarelli, R. Cabrino, F. Del Cima, C. A. Veracini, and F. Pietra, *J.C.S. Chem. Comm.*, 1974, 723.

The product of *N*-methylation of (1) would have been expected [5] to show a spectrum similar to that of cycloheptatrienone [$\lambda_{max.}$ (EtOH) 308 nm].

4-Dimethylaminocycloheptatrienone (3), was synthesized from 4-tosyloxycycloheptatrienone (obtained by tosylation of 4-hydroxycycloheptatrienone [6]) and dimethylamine in methanol. The behaviour of (3)



SCHEME

towards methylating agents was similar to that of (1). Thus, treatment of (3) with methyl fluorosulphate in benzene gave the crystalline yellow salt (4), isolated as a monohydrate in high yield. U.v. absorptions at 375 and 255 nm rule out the possibility of *N*-methylation, as before.

The ^{1}H n.m.r. spectrum (CD_3OD) of (4) at normal probe temperature shows two singlets at δ 3.549 and 3.591, attributable to the two non-equivalent *N*-methyl groups, a methoxy-singlet at δ 4.04 (3 H), a complex series of signals between δ 7.1 and 8.1 (5 H) attributable to the ring protons, and a water (or HDO) signal at δ 4.8. The two *N*-methyl singlets coalesce at 49 °C, *i.e.* the activation energy for rotation around the C:N bond is *ca.* 18 kcal mol^{-1}.

O-Methylation of both compounds (1) and (3) under a variety of conditions [for (1)] was surprising because 2-dimethylaminocycloheptatrienone [7a] and its 6-methyl derivative [7b] are cleanly *N*-methylated by methyl iodide.

[5] G. Biggi, F. Del Cima, and F. Pietra, *J. Amer. Chem. Soc.*, 1972, **94**, 4700.

[6] The synthesis of 4-hydroxytropone was carried out first according to J. Meinwald and O. L. Chapman (*J. Amer. Chem. Soc.*, 1956, **78**, 4816) from teloidinone methobromide with some modifications as described in the Experimental section. Then 4-hydroxytropone was prepared according to J. Meinwald and O. L. Chapman (*J. Amer. Chem. Soc.*, 1958, **80**, 633) from 6β,7β-dimethoxytropinone methobromide. The latter was synthesized in a better yield than described in the literature, by combination of the described methods, with some modifications: J. C. Sheehan and B. M. Bloom, *J. Amer. Chem. Soc.*, 1952, **74**, 3825; K. Zeile and A. Heusner, *Ber.*, 1954, **87**, 439.

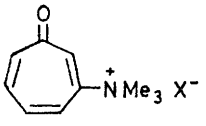
We have therefore attempted methylation of 2-dimethylaminocycloheptatrienone (5) with methyl fluorosulphate under the conditions used for methylation of (1) and (3). We succeeded in isolating, by fractional crystallization, a main product identified as the cycloheptatrienylideneammonium salt (6) (difficulty in removing slight impurities prevented the formation of good crystals) and a little of the quaternary ammonium salt (7).

Structure (7) is supported by the u.v. absorption spectrum [$\lambda_{max.}$ (EtOH) 305 nm], which is almost identical with that of cycloheptatrienone and by the observation that, as expected for a 2-(trialkylammonio)cycloheptatrienone,[5] its reaction with piperidine in ethanol led to 2-piperidinocycloheptatrienone in quantitative yield. No 2-piperidinocycloheptatrienone was formed on treatment of (6) with piperidine.

Structure (6) is supported by the u.v. absorption spectrum [$\lambda_{max.}$ (EtOH) 376 and 255 nm] and by the ^{1}H n.m.r. spectrum (CD_3OD) which shows, at normal probe temperature, a singlet at δ 3.58 (6 H) attributable to the dimethyliminium group, a methoxy-singlet at δ 4.08, and a multiplet between δ 7.2 and 7.8 attributable to the ring protons.

The different behaviour of (5) towards methyl fluorosulphate and methyl iodide (see Scheme) suggests that the quaternary ammonium salt is thermodynamically preferred with respect to the iminium salt, so that the former is the end product in the reversible (because of the nucleophilicity of iodide ion) reaction with methyl iodide.

More difficult is to understand why compound (1) is *O*-methylated by methyl iodide. Perhaps this is because the product (2) is thermodynamically preferred to the corresponding hypothetical quaternary ammonium salt



(8)

(8); free conjugation of nitrogen with the ring in (2) may be hampered with (6) for steric reasons.

Of the three isomeric methoxy-substituted cycloheptatrienylideneammonium salts (2a), (4), and (6), only the 4-methoxy-salt (4) shows non-equivalence of the two *N*-methyl groups. However, the energy barrier for rotation around the C:N bond in (4) is lower than in ordinary iminium salts, thus implying a large cycloheptatrienylium ion contribution to structure (4), as already found for 3-t-butyl-substituted *N*-aryl-*N*-alkylcycloheptatrienylideneammonium salts.[8]

With both the 2- and the 3-methoxy-salts (6) and (2a), ^{1}H n.m.r. investigations in CD_3OD down to −80 °C failed to reveal even line broadening of the NMe_2 signal.

[7] (*a*) T. Nozoe, S. Seto, H. Takeda, S. Morosawa, and K. Matsumoto, *Sci. Reports Tohoku Univ.*, I, 1952, **36**, 126; (*b*) P. Akroyd, R. D. Haworth, and P. R. Jefferies, *J. Chem. Soc.*, 1954, 286.

[8] A. Krebs, *Tetrahedron Letters*, 1971, 1901.

Solubility problems prevented investigation at even lower temperatures. It may be that with both (2a) and (6) accidental isochrony is responsible for this behaviour. This would also be in accord with the occurrence of the NMe_2 signals at the same field in the spectra of the three isomeric salts (2a), (4), and (6).

EXPERIMENTAL

M.p.s were taken with a Kofler hot-stage apparatus. ^1H N.m.r., u.v., and i.r. spectra were recorded with, respectively, JEOL PS 100, Unicam SP 800, and Perkin-Elmer 337 spectrometers. ^1H N.m.r. data are given with respect to Me_4Si as internal standard.

Methylation of 3-*Dimethylaminocycloheptatrienone*.—(a) *With methyl fluorosulphate*. To a stirred solution of 3-dimethylaminocycloheptatrienone [4] (0.225 g, 1.5 mmol) in dried benzene (10 ml) at room temperature under nitrogen, was added methyl fluorosulphate (0.15 ml, 1.9 mmol); yellow crystals were immediately precipitated. Filtration under nitrogen led to 3-*methoxy*-NN-*dimethylcycloheptatrienylideneammonium fluorosulphate* (2a), m.p. 133—143°, in almost quantitative yield. Recrystallization from methanol raised the m.p. to 149—151° (Found: C, 45.7; H, 5.7; N, 5.2; S, 12.3. $C_{10}H_{14}NO_4FS$ requires C, 45.6; H, 5.4; N, 5.3; S, 12.2%), $\lambda_{max.}$ (EtOH) 328 and 265 nm; $\nu_{max.}$ (Nujol) 3 060, 3 030, 1 640, 1 560, 1 380, 1 285, 1 225, 1 210, 1 162, 1 065, 975, 895, 847, 797, 708, and 580 nm (for ^1H n.m.r. data see text).

(b) *With methyl iodide*. To a solution of the ketone (1) (0.160 g, 1.07 mmol) in ethanol (1.5 ml) was added methyl iodide (0.5 ml). The mixture was heated at 78 °C for 2 h in a sealed glass ampoule. Evaporation, fractional crystallization, and layer chromatography on silica gel [eluant benzene–ethanol (70 : 30)] led to much unchanged (1), R_F 0.4, and a little of the salt (2b), R_F 0 [$\lambda_{max.}$ and ^1H n.m.r. spectra identical with those of (2a)].

(c) *With dimethyl sulphate*. To a solution of the ketone (1) (0.008 g) in deuterium oxide (0.4 ml) was added dimethyl sulphate, (0.005 ml). The mixture was sealed in a n.m.r. tube and heated at 100 °C with ^1H n.m.r. monitoring. After 2 h the spectrum was that expected for (2). The u.v. spectrum was also identical with that of (2).

4-*Hydroxycycloheptatrienone*.—We merely describe our modifications to reported procedures.[6]

Hydrolysis of teloidinone methobromide (cf. *Meinwald and Chapman* [6]). In our hands, concentration of the mixture after precipitation of barium carbonate failed to give the desired material, leading instead to unidentified material. The mother liquor was concentrated, then methanol was added, and the mixture was chromatographed on a silica gel layer [eluant benzene–ethanol (80 : 20)]. Pure 4-hydroxycycloheptatrienone was collected in 20% yield from the band at R_F 0.37.

6β,7β-*Dimethoxytropinone methiodide*. The synthesis of 2,5-dihydro-2,5-dimethoxyfuran was carried out as indicated by Sheehan and Bloom [6] for the synthesis of the diethoxy-analogue, with methanol in the place of ethanol. pH Control during the methylation of 2,5-dimethoxy-3,4-dihydroxytetrahydrofuran with dimethyl sulphate (Zeile and Heusner [6]) was effected by means of a glass electrode because the dark mixture prevented the use of indicators. This raised the yield from the reported 69 [6] to 95%.

4-*Tosyloxycycloheptatrienone*.—To a solution of 4-hydroxycycloheptatrienone (0.10 g, 0.82 mmol) in dried pyridine (1.7 ml) was added, under nitrogen at room temperature with stirring, toluene-*p*-sulphonyl chloride (0.183 g, 0.96 mmol). After 20 h, water (25 ml) was added. Then one third of the solvent was evaporated off, and a dark solid was precipitated. The solution was removed by suction and the solid residue was chromatographed on silica gel [eluant benzene–ethanol (75 : 25)]. Extraction of the band at R_F 0.8 led to 4-*tosyloxycycloheptatrienone* (0.07 g, 30%), m.p. 83—85° (Found: C, 61.0; H, 4.3. $C_{14}H_{12}O_4S$ requires C, 61.0; H, 4.35%), $\lambda_{max.}$ (EtOH) 313 (log ε 3.78), and 303 nm (3.81), δ ($CDCl_3$) 7.7 (4 H, AB system), 7.0 (5 H, m), and 2.5 (3 H, s).

4-*Dimethylaminocycloheptatrienone* (3).—To a solution of 4-tosyloxycycloheptatrienone (0.04 g, 0.14 mmol) in methanol (2.5 ml) was added, at room temperature, dimethylamine (0.5 ml). The mixture became yellow immediately and after 30 min was evaporated under vacuum. The oily residue was chromatographed on a silica gel layer [eluant benzene–methanol (90 : 10)]. The yellow band at R_F 0.4 gave the *amine* (3) (0.021 g, 97%), m.p. 78—79° (Found: C, 72.0; H, 7.3. Calc. for $C_9H_{11}NO$: C, 72.5; H, 7.4%), $\lambda_{max.}$ (EtOH) 375 nm (log ε 4.08), δ ($CDCl_4$) 7.0 (3 H, m), 6.5 (1 H, d), 5.95 (1 H, d), and 3.0 (3 H, s).

Methylation of 4-*Dimethylaminocycloheptatrienone*.—The reaction was carried out as in the case of (2a) with 0.015 g (0.1 mmol) of the ketone (3). Filtration under nitrogen gave 4-*methoxy*-NN-*dimethylcycloheptatrienylideneammonium fluorosulphate* (4) as yellow crystals, m.p. 122° (0.018 g, 64%). Recrystallization from chloroform–ether led to yellow needles, m.p. 127—128° (Found: C, 42.2; H, 4.8; N, 4.7. $C_{10}H_{14}FNO_4S,H_2O$ requires C, 42.7; H, 5.7; N, 4.9%), $\lambda_{max.}$ (EtOH) 375 and 255 nm (for ^1H n.m.r. data see text).

Methylation of 2-*Dimethylaminocycloheptatrienone*.—The reaction was carried out as in the above case with 0.028 g (0.19 mmol) of the ketone (5). Filtration under nitrogen gave a yellow crystalline mass, which was washed with benzene and then recrystallized from chloroform–ether; overnight a few crystals of the salt (7) separated, m.p. 133°, $\lambda_{max.}$ (EtOH) 305 nm. Concentration of the mother liquor under vacuum led to a semisolid identified as the salt (6) [$\lambda_{max.}$ (EtOH) 376 and 255 nm]; for ^1H n.m.r. data see text.

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