1,3-Dipolar Character of Six-membered Aromatic Rings. Part XXV.[1] 5-Aryl-1-methyl-3-oxidopyridiniums

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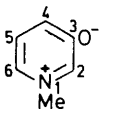
The title betaines react at the 2- and 6-positions with 2π addends and at the 2- and 4-positions with 4π addends. Adducts from the 2π addends are transformed into aryl-substituted tropones *via* methylation and Hofmann elimination.

1-METHYL-3-OXIDOPYRIDINIUM (1) shows 1,3-dipolar reactivity across the 2- and 6-positions,[2,3] and gives cycloadducts with electron-deficient olefins, convertible conveniently into tropones and tropolones.[3,4] We have now extended our investigations to 5-aryl-1-methyl-3-oxidopyridiniums (7).



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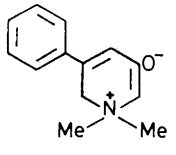

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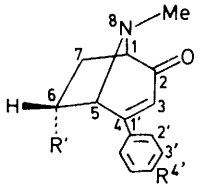
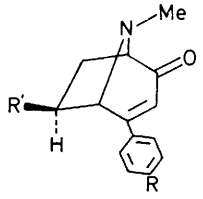
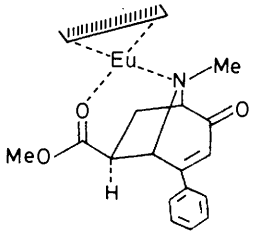


(9) R'=CN, R=H
(10) R'=CO_2Me, R=H
(11) R'=Ph, R=H
(12) R'=CN, R=OMe



(13) R'=CN, R=H
(14) R'=CO_2Me, R=H
(15) R'=Ph, R=H
(16) R'=CN, R=OMe



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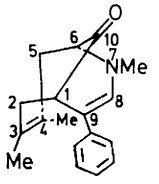


(18)

5-Aryl-3-hydroxy-1-methylpyridinium bromides (6) were prepared by a modification (Scheme) of the method of Heffe.[5] The intermediate *N*-acetonyl-*NN*-dimethyl-*N*-phenacylammonium bromides (4) were obtained by treating the appropriate phenacyl bromide (3) with 1-dimethylaminoacetone. The structures of these salts were readily determined by n.m.r. (see Experimental section); in all cases the methylene protons show fast exchange with D_2O. Aldol condensation of the *N*-acetonyl-*NN*-dimethyl-*N*-phenacylammonium bromides (4) followed by treatment with hydrogen bromide yielded the corresponding cyclic 5-aryl-1,2,3,6-tetrahydro-1,1-dimethyl-3-oxopyridinium bromides (5), which were readily oxidised to the corresponding 5-aryl-3-hydroxy-1-methylpyridinium bromides (6) by pyridinium bromide perbromide.[6] In the case of 1,2,3,6-tetrahydro-1,1-dimethyl-3-oxo-5-phenylpyridinium bromide (5A) itself, the intermediate 1,6-dihydro-1,1-dimethyl-3-oxido-5-phenylpyridinium (8) was isolated.

Treatment of the 5-aryl-3-hydroxy-1-methylpyridinium bromides (6) with Amberlite IRA-401 (OH^-) ion-exchange resin gives the corresponding betaines (7), with n.m.r. spectra showing upfield shifts of ring protons characteristic [2] of the conversion of a halide into a betaine (Table 1).† The betaines (7) were obtained as stable anhydrous crystalline solids (*cf.* 1-methyl-3-oxidopyridinium [2]).

1-Methyl-3-oxido-5-phenylpyridinium (7A) with methyl acrylate, acrylonitrile, and styrene, and 5-(4-methoxyphenyl)-1-methyl-3-oxidopyridinium (7B) with acrylonitrile gave the expected cycloadducts. Unlike the cycloadducts obtained from 1-methyl-3-oxidopyridinium (1),[2] the mixtures of *endo*-[(9)—(12)] and *exo*-isomers [(13)—(16)] were readily separated in good yields. Their structures were confirmed by i.r., mass, and n.m.r. spectra. The increased reactivity of 5-aryl-1-methyl-3-oxidopyridinium betaines is witnessed by the formation of cycloadducts with the relatively unreactive dipolarophile,[7] styrene (contrast unreactivity of 1-methyl-3-oxidopyridinium).

The rules [8] formulated for the use of n.m.r. spectra for other cycloadducts in this series can be applied for diagnostic purposes. In the cycloadducts (9)—(16) (Table 2) † H-3 forms a doublet due to long-range W-type coupling with the bridgehead proton, H-1. The splitting pattern of the bridgehead proton H-5 characterises the stereochemistry of the cycloadducts, since $J_{5,6\text{-}endo}$ is negligibly small whereas $J_{5,6\text{-}exo}$ is relatively large (6—8 Hz). In the present compounds, the absence of a proton at C-4 greatly simplifies the H-5 signal. Thus H-5 gives

† These data are given in Supplementary Publication No. SUP 21830 (6 pp.). For details of Supplementary Publications see Notice to Authors No. 7 in *J.C.S. Perkin I*, 1975, Index issue. Items less than 10 pp. are supplied as full-size copies.

[1] Part XXIV, N. Dennis, B. Ibrahim, and A. R. Katritzky, *Org. Mass Spectrometry*, 1976, **11**, 814.

[2] A. R. Katritzky and Y. Takeuchi, *J. Chem. Soc.* (*C*), 1971, 874.

[3] A. R. Katritzky and Y. Takeuchi, *J. Amer. Chem. Soc.*, 1970, **92**, 4134.

[4] A. R. Katritzky and Y. Takeuchi, *J. Chem. Soc.* (*C*), 1971, 878.

[5] W. Heffe, personal communication.

[6] L. F. Fieser and M. Fieser, ' Reagents for Organic Synthesis,' Wiley, New York, 1967, p. 967.

[7] R. Huisgen, R. Grashey, and J. Sauer in ' The Chemistry of Alkenes,' in the series ' The Chemistry of Functional Groups,' ed. S. Patai, Interscience, London, 1964, p. 865.

[8] N. Dennis, A. R. Katritzky, T. Matsuo, S. K. Parton, and Y. Takeuchi, *J.C.S. Perkin I*, 1974, 746.

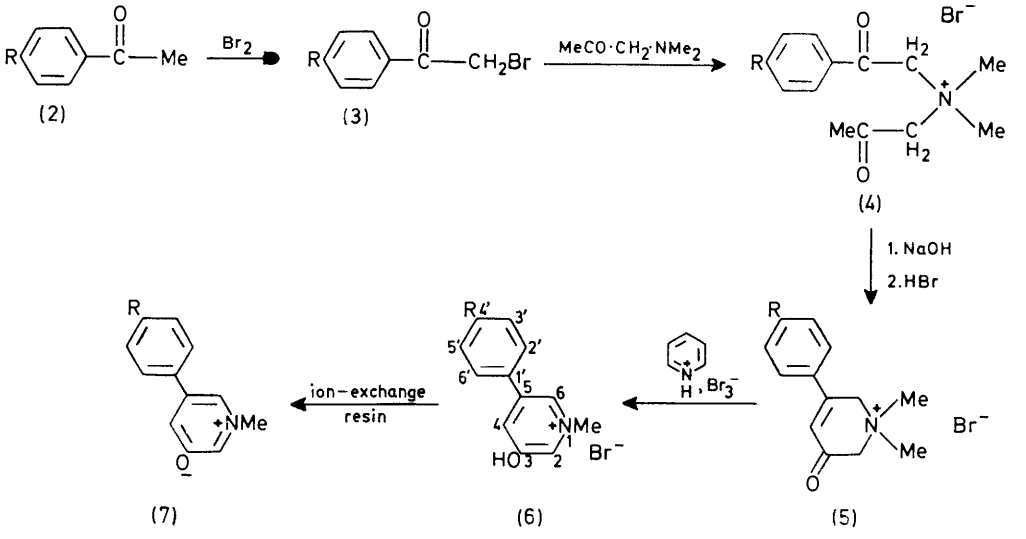
rise to a singlet for the *exo*-isomers and a doublet ($J_{5,6\text{-}exo}$ 6.0—6.5 Hz) for the *endo*-isomers.

All assignments were confirmed by double irradiation of each ring proton, *e.g.* irradiation at the frequency of H-1 caused the H-3 doublet to collapse to a singlet, and the H-7-*exo* octet to collapse to a quartet. The cycloadducts (9)—(16) showed the *N*-methyl signal and characteristic patterns for the 4-aryl group protons (Table 2).†

Further support for the n.m.r. assignments for the cycloadducts (9), (10), (13), and (14) was obtained by the use of the lanthanide shift reagent, tris-(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyloctane-4,6-dionato)europium(III) [Eu(fod)$_3$].[9,10] In the cases of the *endo*-adducts (9) and (10) and the *exo*-adduct (13), plots of downfield shift ($\delta\Delta$) *vs.* weight ratio of Eu(fod)$_3$ to substrate [see Figure 1; *endo*-methoxycarbonyl cycloadduct (10) as typical example] * show that H-1 and H-3 are

Reported pericyclic additions to 1-methyl-3-oxidopyridinium betaines have previously been of the type [$_{\pi}2 + _{\pi}4$]. However, 1-methyl-3-oxido-5-phenylpyridinium (7A) reacted with the 4π component, 2,3-dimethyl 1,3-butadiene to yield 3,4,7-trimethyl-9-phenyl-7-azabicyclo[4.3.1]deca-3,8-dien-10-one (18). Such [$_{\pi}4 + _{\pi}6$] pericyclic addition reactions are well known for 1-aryl-3-oxidopyridinium betaines.[15] The cycloadduct (18) was characterised by a saturated ketone absorption ($\nu_{max.}$ 1 725 cm^{-1}) in the i.r. and a parent molecular ion at *m/e* 267 in the mass spectrum.

The cycloadducts (9), (10), (12)—(14), and (16) reacted smoothly with methyl iodide to produce the corresponding methiodides (19)—(24). We have previously [3,4] described the ready synthesis of 2-dimethylaminotropones and the corresponding tropolones from 8-azabicyclo[3.2.1]oct-3-en-2-one methiodides by Hofmann elimination. Treatment of the quaternary salts



A: R=H B;R=OMe C;R=NO$_2$

SCHEME

influenced much more than H-5 and *N*-methyl; thus the shift reagent complexes with the ketonic carbonyl group.[11,12] Although amino is often [13,14] a stronger complexing group than oxo, here steric crowding by the *N*-methyl group evidently lowers the donor strength of the N atom. However, in the case of the *exo*-methoxycarbonyl adduct (14) plots of downfield shift ($\delta\Delta$) *vs.* weight ratio of Eu(fod)$_3$ to substrate (see Figure 1) † show a reversed order of lanthanide-induced shift, *i.e.* *N*-methyl > H-5 > H-1 > H-3. In this case the lanthanide is complexed by chelate formation (17), favoured by the unique arrangement of the N atom and the *exo*-carboxylate group.

(19) and (22) with silver oxide gave 4-cyano-2-dimethylamino-6-phenyltropone (25), m.p. 95—96 °C. The ^{1}H n.m.r. spectrum showed the NMe$_2$ signal and the absence of aliphatic ring protons, the i.r. spectrum included ν(C≡N) (2 230 cm^{-1}) and ν(C=O) (1 575 cm^{-1}) bands, and the mass spectrum had the molecular ion at *m/e* 250. Acidification of the aqueous solution after compound (25) had been removed gave 4-cyano-6-phenyltropolone (27), identified by elemental analysis, and i.r. and mass spectra. Attempted Hofmann elimination with sodium hydrogen carbonate yielded a red crystalline compound, m.p. 138—139 °C, of unidentified structure.

Similarly, on treatment with silver oxide, the methio-

* See footnote p. 2329.

[9] R. von Ammon and R. D. Fischer, *Angew. Chem. Internat. Edn.*, 1972, **11**, 675.

[10] R. E. Rondeau and R. E. Sievers, *J. Amer. Chem. Soc.*, 1971, **93**, 1522.

[11] P. Bélanger, C. Freppel, D. Tizané, and J. C. Richer, *Chem. Comm.*, 1971, 266.

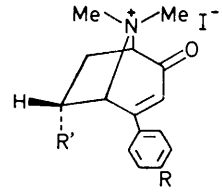
[12] Z. W. Wolkowski, *Tetrahedron Letters*, 1971, 821.

[13] A. F. Cockerill, G. L. O. Davies, R. C. Harden, and D. M. Rackham, *Chem. Rev.*, 1973, **73**, 553.

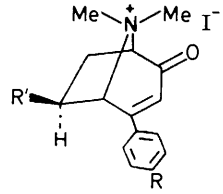
[14] J. K. M. Sanders and D. H. Williams, *J. Amer. Chem. Soc.*, 1971, **93**, 641.

[15] N. Dennis, B. Ibrahim, and A. R. Katritzky, *J.C.S. Chem. Comm.*, 1974, 500.

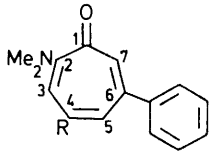
dides (20) and (23) gave 2-dimethylamino-4-methoxycarbonyl-6-phenyltropone (26), m.p. 138—139 °C. The structure was confirmed by n.m.r. (Table 3) * (NMe_2 and



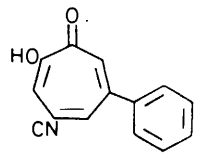
(19) R=H,R'=CN
(20) R=H,R'=CO_2Me
(21) R=OMe,R'=CN



(22) R=H,R'=CN
(23) R=H,R'=CO_2Me
(24) R=OMe,R'=CN



(25) R=CN
(26) R=CO_2Me



(27)

CO_2Me signals and the absence of aliphatic protons), the i.r. spectrum, and the molecular ion at *m/e* 283. The n.m.r. assignments of the ring protons (H-3, H-5, and H-7) of the tropones were confirmed by spin–spin decoupling; *e.g.* irradiation at the frequency of H-3 caused collapse of the multiplet for H-5 to a doublet. Further support was obtained by the addition of the lanthanide shift reagent tris-(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyloctane-4,6-dionato)praeseodymium(III) [Pr(fod)$_3$].[10] Plots of upfield shifts ($\delta\Delta$) *vs.* weight ratio of Pr(fod)$_3$ to substrate for the cyanotropone (25) (Figure 2) † and for the methoxycarbonyltropone (26) (Figure 2) † show that H-7 is influenced much more than H-3 and H-5; the shift reagent complexes with the ketonic carbonyl group, in agreement with reported [16] results with Eu(dpm)$_3$.

EXPERIMENTAL

M.p.s were determined with a Reichert apparatus. Spectra were recorded with Perkin-Elmer IR models 237 and 257, Perkin-Elmer R-12 60 MHz and Varian HA-100 n.m.r. spectrometers, a Hitachi–Perkin-Elmer RMU-6E mass spectrometer, and a Unicam SP 800A u.v. spectrophotometer.

N-Acetonyl-NN-dimethyl-N-phenacylammonium Bromide (4A).—Phenacyl bromide (10 g, 0.05 mol) in sodium-dried Et_2O (50 ml) was added dropwise, with stirring, to 1-dimethylaminoacetone [b.p. 43 °C at 30 mmHg; lit.,[17] 35—36 °C at 25 mmHg] (5.1 g, 0.05 mol) in sodium-dried Et_2O (130 ml), at 0 °C, during 15 min. The mixture was stirred, for 7 h, kept for 2 days, and filtered. The bromide (4A) crystallised from EtOH–Et_2O as prisms (7.5 g, 50%), m.p. 148—150 °C (lit.,[5] 155 °C) (Found: C, 52.0; H, 6.0; N, 4.8. Calc. for $C_{13}H_{18}BrNO_2$: C, 52.0; H, 6.0; N, 4.7%): $\nu_{max.}$ (Nujol) 1 725 (aliphatic ketone, C=O), 1 690 (arom. ketone, C=O), 1 595 and 1 580 (C=C), 765, and 680 cm^{-1}; $\delta(D_2O)$ 2.32 (3 H, s, Ac), 3.56 (6 H, s, NMe_2), 5.02 (2 H, s, N·CH_2Ac), 5.48 (2 H, s, BzCH_2·N), and 7.80 (5 H, m, arom.); δ (CF_3·CO_2H) 2.40 (3 H, s, Ac), 3.68 (6 H, s, NMe_2), 5.11 (2 H, s, N·CH_2Ac), 5.51 (2 H, s, BzCH_2·N), and 7.81 (5 H, m, arom.).

1,2,3,6-*Tetrahydro*-1,1-*dimethyl*-3-*oxo*-5-*phenylpyridinium Bromide* (5A).—Compound (4A) (4.0 g, 0.013 mol) was treated with 2N-NaOH (10 ml) at 0 °C. Cooling (to −10 °C) caused deposition of needles of 1,6-*dihydro*-1,1-*dimethyl*-3-*oxido*-5-*phenylpyridinium* (8); $\nu_{max.}$ (Nujol) 3 300, 1 615, and 1 540 cm^{-1}. After 24 h at 0 °C the deep blue solution was neutralised with 48% HBr. The deposited bromide crystallised from EtOH–Et_2O as pale yellow prisms (2.32 g, 62%), m.p. 199—200 °C (lit.,[5] 204 °C) (Found: C, 55.2; H, 5.4; N, 5.2. Calc. for $C_{13}H_{16}BrNO$: C, 55.3; H, 5.7; N, 5.0%); $\nu_{max.}$ (Nujol) 1 660 ($\alpha\beta$-unsat. ketone, C=O), 1 600, 1 590, 1 570, 760, and 675 cm^{-1}; $\lambda_{max.}$ (EtOH) 239 (log ε 3.9) and 334 nm (4.3).

3-*Hydroxy*-1-*methyl*-5-*phenylpyridinium Bromide* (6A).—Bromine (2.0 ml, 6.2 g, 0.04 mol) was added dropwise to a stirred, cooled (0 °C) solution of pyridinium bromide (6.4 g, 0.04 mol) and 1,2,3,6-tetrahydro-1,1-dimethyl-3-oxo-5-phenylpyridinium bromide (11.3 g, 0.04 mol) in MeOH (50 ml). Solvent (40 ml) was distilled off, and the residue heated at 200—205 °C for 15 min. After cooling, MeOH (30 ml) was added and the mixture heated under reflux until the residue dissolved. The salt (6A) slowly crystallised as cream needles (4.7 g, 44%), m.p. 222—224 °C (lit.,[5] 229—230 °C) (Found: C, 54.2; H, 4.5; N, 5.6. Calc. for $C_{12}H_{12}BrNO$: C, 54.2; H, 4.6; N, 5.3%); $\nu_{max.}$ (Nujol) 2 620 (OH), 1 610, 1 595, 1 575, 760, and 690 cm^{-1}; $\lambda_{max.}$ (EtOH) 347 (log ε 3.6), 310 (3.9), 235 (4.4), and 208 nm (4.4); *m/e* 185 (betaine).

1-*Methyl*-3-*oxido*-5-*phenylpyridinium* (7A).—3-Hydroxy-1-methyl-5-phenylpyridinium bromide (6.7 g, 0.025 mol) in distilled water (700 ml) and EtOH (95%, 250 ml) was passed through Amberlite IRA-401 (OH^-) ion-exchange resin followed by distilled water until the eluate was neutral. The combined eluate was evaporated to dryness [50 °C at 15 mmHg]. On adding tetrahydrofuran (THF) to the resultant pale brown oil, *compound* (7A) was precipitated. Recrystallisation from $CHCl_3$–Et_2O yielded needles (4.3 g 81%), m.p. 39—40 °C (Found: C, 67.9; H, 6.2; N, 6.8. $C_{12}H_{11}NO,1.5H_2O$ requires C, 67.9; H, 6.6; N, 6.6%); $\nu_{max.}$ ($CHBr_3$) 3 320 (H_2O), 1 575 (C=C), 1 660, 1 490, 1 425, 1 375, 1 275, 1 240, 1 180, 1 070, 1 040, 965, 870, 760, and 690 cm^{-1}; $\lambda_{max.}$ (MeCN) 360 (log ε 3.56), 283 (3.94), 259 (4.04), and 226 nm (4.18).

Reactions of Compound (7A).— (i) *With acrylonitrile.* Compound (7A) (3.8 g, 0.020 mol), acrylonitrile (40.3 g, 0.76 mol), and hydroquinone (0.20 g) were heated under reflux in dry ($LiAlH_4$) THF (50 ml) for 90 min, then the mixture was evaporated (80 °C at 20 mmHg). The brown oil (4.8 g) was chromatographed [aluminium oxide, grade I; CH_2Cl_2–light petroleum (b.p. 40—60 °C) (1 : 1)] to give a yellow solid (4.6 g). Thick-layer chromatography [Kieselgel PF 254; $CHCl_3$–EtOAc (2 : 1)] separated the isomeric cycloadducts. The higher R_F fraction (2.4 g, 50%) crystallised from THF–light petroleum (b.p. 60—80 °C) to give 8-*methyl*-2-*oxo*-4-*phenyl*-8-*azabicyclo*[3.2.1]*oct*-3-*ene*-6-exo-*carbonitrile* (13), as yellow plates, m.p. 99—101 °C (Found: C, 75.3; H, 5.8; N, 12.0. $C_{15}H_{14}N_2O$ requires C, 75.6;

* See footnote p. 2329.

[16] H. Tanida, T. Tsushima, and Y. Terui, *Tetrahedron Letters*, 1972, 399.

[17] H. E. Zaugg and B. W. Horrom, *J. Amer. Chem. Soc.*, 1950, **72**, 3004.

H, 5.9; N, 11.8%); $\nu_{max.}$ (Nujol) 1 605 (C=C), 1 665, 1 675 (αβ-unsat. ketone C=O), and 2 240 cm^{-1} (C≡N); $\lambda_{max.}$ (EtOH) 225 (log ε 3.9) and 289 nm (4.2); *m/e* 238. The lower R_F fraction consisted of two compounds (t.l.c.) Repeated crystallisations gave a small quantity of unchanged betaine (7A). The mother liquors were combined and evaporated to give a yellow residue, which was chromatographed (aluminium oxide, grade I; EtOAc), to give 8-*methyl*-2-*oxo*-4-*phenyl*-8-*azabicyclo*[3.2.1]*oct*-3-*ene*-6-endo-*carbonitrile* (9) (0.31 g, 6.4%) as a yellow oil characterised by its spectra: $\nu_{max.}$ (Nujol) 1 605 (C=C), 1 675, 1 680 (αβ-unsat. ketone, C=O), and 2 245 cm^{-1} (C≡N); *m/e* 238.

(ii) *With methyl acrylate.* Compound (7A) (2.95 g, 0.014 mol) and methyl acrylate (19.1 g, 0.22 mol) were heated under reflux in dry ($LiAlH_4$) THF (40 ml) with hydroquinone (0.2 g) for 30 h. The black deposit was removed, and the solution was evaporated at 20 mmHg. The residue was dissolved in 2N-HCl (80 ml) and the solution washed with Et_2O (4 × 30 ml), basified (Na_2CO_3), and extracted with Et_2O (4 × 50 ml). The extract was dried ($MgSO_4$) and evaporated to leave a green mass (3.5 g), which was chromatographed [aluminium oxide, grade I; CH_2Cl_2–light petroleum (b.p. 40—60 °C) (1 : 1)]. The eluate was evaporated and the residue treated with Et_2O (30 ml) to give *methyl* 8-*methyl*-2-*oxo*-4-*phenyl*-8-*azabicyclo*[3.2.1]*oct*-3-*ene*-6-endo-*carboxylate* (10) (0.464 g, 12%), which crystallised from light petroleum (b.p. 40—60 °C) as yellow plates, m.p. 128—129 °C (Found: C, 70.5; H, 6.3; N, 5.2. $C_{16}H_{17}NO_3$ requires C, 70.8; H, 6.3; N, 5.2%); $\nu_{max.}$ (Nujol) 1 600 (C=C), 1 670 (αβ-unsat. ketone C=O), 1 725, and 1 730 cm^{-1} (ester, C=O); $\lambda_{max.}$ (EtOH) 225 (log ε 3.9) and 287 nm (4.2); *m/e* 271.

The ethereal solution was evaporated to yield a yellow oil (2.81 g). Thick layer chromatography [Kieselgel PF 254; $CHCl_3$–EtOAc (1 : 1)] yielded three main fractions. The highest R_F fraction was repeatedly crystallised from $CHCl_3$ to give a brown powder, which was chromatographed (aluminium oxide, grade I; EtOAc) to give yellow prisms (0.064 g, 10%) still showing a broad absorption band at $\nu_{max.}$ (Nujol) 3 380—3 300 cm^{-1}. Further chromatography [aluminium oxide, grade I; Et_2O–EtOAc (4 : 1)] gave *methyl* 8-*methyl*-2-*oxo*-4-*phenyl*-8-*azabicyclo*[3.2.1]*oct*-3-*ene*-6-exo-*carboxylate* (14) as yellow plates, m.p. 63—67 °C [from light petroleum (b.p. 40—60 °C)] (Found: C, 71.2; H, 6.5; N, 5.0. $C_{16}H_{17}NO_3$ requires C, 70.8; H, 6.3; N, 5.2%); $\nu_{max.}$ (Nujol) 1 600 (C=C), 1 680 (αβ-unsat. ketone, C=O), and 1 740 cm^{-1} (ester, C=O); $\lambda_{max.}$ (EtOH) 225 (log ε 3.9) and 290 nm (41); *m/e* 271. From the medium R_F fraction, a further quantity (0.180 g, 27%) of the *endo*-cycloadduct (10) was obtained. The lowest R_F fraction, a white solid, was identified as unchanged betaine (7A).

(iii) *With styrene.* Compound (7A) (3.8 g, 0.02 mol) and styrene (27.2 g, 0.26 mol) in dry ($LiAlH_4$) THF (25 ml) containing hydroquinone (0.2 g), were heated under reflux for 2 days. Evaporation at 20 mmHg yielded a brown oil which was chromatographed [aluminium oxide, grade I; first run PhMe to remove unchanged styrene; second run CH_2Cl_2–light petroleum (b.p. 40—60 °C) (1 : 1)]. The eluate was evaporated and the residue (two components by t.l.c.) (2.4 g) separated by preparative t.l.c. on silica gel (0.78 g) [Kieselgel PF 254; light petroleum (b.p. 40—60 °C)–EtOAc (9 : 1)]. 8-*Methyl*-4,6-exo-*diphenyl*-8-*azabicyclo*-[3.2.1]*oct*-3-*en*-2-*one* (15) formed a yellow oil (0.193 g, 11%) (Found: C, 82.3; H, 6.9; N, 4.4. $C_{20}H_{19}NO$ requires C, 83.0; H, 6.6; N, 4.8%); $\nu_{max.}$ ($CHBr_3$) 1 675 (αβ-unsat. ketone, C=O), 1 600 (C=C), and 1 570 cm^{-1} (C=C); $\lambda_{max.}$ (EtOH) 210 (log ε 4.3), 222 (4.1), 285 (4.1), and 345 nm (3.3). 8-*Methyl*-4,6-endo-*diphenyl*-8-*azabicyclo*[3.2.1]*oct*-3-*en*-2-*one* (11) formed a yellow oil (0.315 g, 17%) (Found: C, 80.8; H, 6.7; N, 4.4. $C_{20}H_{19}NO$ requires C, 83.0; H, 6.6; N, 4.8%); $\nu_{max.}$ (Nujol) 1 675 (αβ-unsat. ketone, C=O), 1 600 (C=C), and 1570 cm^{-1} (C=C); $\lambda_{max.}$ (EtOH) 210 (log ε 4.3), 222 (4.2), 285 (4.2), and 345 nm (3.5).

(iv) *With 2,3-dimethylbuta-1,3-diene.* Compound (7A) (1.9 g, 0.01 mol), 2,3-dimethylbuta-1,3-diene (3.7 g, 0.04 mol), and hydroquinone (0.2 g) in dry ($LiAlH_4$) THF (25 ml) were heated at 40—45 °C for 2 days. The mixture was evaporated at 20 mmHg and the residue chromatographed [aluminium oxide, grade I; CH_2Cl_2–light petroleum (b.p. 40—60 °C) (1 : 1)] to give a brown oil (1.09 g). Further thick layer chromatography [Kieselgel PF 254; $CHCl_3$–EtOAc (6 : 1)] gave 3,4,7-*trimethyl*-9-*phenyl*-7-*azabicyclo*-[4.3.1]*deca*-3,8-*dien*-10-*one* (18) (0.74 g, 28%) as yellow prisms [from $CHCl_3$–light petroleum (b.p. 40—60 °C)], m.p. 130—132 °C (Found: C, 81.2; H, 8.1; N, 5.5. $C_{18}H_{21}NO$ requires C, 80.9; H, 7.9; N, 5.2%); $\nu_{max.}$ (Nujol) 1 725, 1 670, 1 600, 1 490, 1 450, 1 380, 1 280, 1 260, 1 075, 1 040, 920, 760, 690, and 650 cm^{-1}; $\lambda_{max.}$ (EtOH) 269sh (log ε 3.0) and 215 nm (3.7); *m/e* 267.

Quaternisation of a Mixture of 8-*Methyl*-2-*oxo*-4-*phenyl*-8-*azabicyclo*[3.2.1]*oct*-3-*ene*-6-endo- *and* -6-exo-*carbonitrile* [(9) *and* (13)].—The mixed cycloadducts (9) and (13) (0.515 g, 2.2 × 10^{-3} mol) in EtOAc (25 ml) with MeI (10 ml) at 20 °C for 4 days gave the *quaternary salts* (19) and (22), as a yellow solid (0.526 g, 64%), m.p. 168—170 °C (from EtOH) (Found: C, 50.1; H, 4.7; N, 7.6. $C_{16}H_{17}IN_2O$ requires C, 50.5; H, 4.5; N, 7.4%).

Quaternisation of Methyl 8-*Methyl*-2-*oxo*-4-*phenyl*-8-*azabicyclo*[3.2.1]*oct*-3-*ene*-6-endo-*carboxylate* (10).—Compound (10) (0.136 g, 5.0 × 10^{-4} mol) in EtOAc (20 ml) with MeI (10 ml) at 20 °C for 3 days gave the *quaternary salt* (20; R = *endo*-MeO_2C) (0.186 g, 90%) as needles (from EtOH), m.p. 154—156 °C (Found: C, 49.8; H, 5.2; N, 3.5. $C_{17}H_{20}INO_3$ requires C, 49.4; H, 4.9; N, 3.4%); $\nu_{max.}$ (Nujol) 1 735 (ester, C=O), 1 675 (αβ-unsat. ketone, C=O), 1 600, 1 570 (C=C), and 1 260 cm^{-1} (C–O).

Quaternisation of a Mixture of Methyl 8-*Methyl*-2-*oxo*-4-*phenyl*-8-*azabicyclo*[3.2.1]*oct*-3-*ene*-6-endo-*and*-6-exo-*carboxylate* [(10) *and* (14)].—The cycloadducts (10) and (14) (1.5 g, 5.5 × 10^{-3} mol) in EtOAc (25 ml) with MeI (12 ml) at 20 °C for 3 days gave the *quaternary salts* (20) and (23) as yellow needles (1.9 g, 84%), m.p. 148—150 °C (EtOH) (Found: C, 49.0; H, 5.2; N, 3.4. $C_{17}H_{20}INO_3$ requires C, 49.4; H, 4.9; N, 3.4%).

Treatment of the Methiodides (19) *and* (22) *with Base.*—(i) *With silver oxide.* The quaternary salts (19) and (22) (1.07 g, 2.9 × 10^{-3} mol) in distilled water (20 ml) were stirred with silver oxide (0.7 g) for 10 min at 20 °C. The solid was filtered off and the filtrate extracted with Et_2O (40 ml). The dried ($MgSO_4$) extracts were evaporated to afford 4-*cyano*-2-*dimethylamino*-6-*phenyltropone* (25), which after thick-layer chromatography [Kieselgel PF 254; first run $CHCl_3$–EtOAc (4 : 1); second run $CHCl_3$–EtOAc (1 : 2)] crystallised from Et_2O as yellow-brown needles (0.12 g, 37%), m.p. 95—96 °C (Found: C, 76.5; H, 5.8; N, 11.2. $C_{16}H_{14}N_2O$ requires C, 76.8; H, 5.6; N, 11.2%); $\nu_{max.}$ (KBr) 2 230 (C≡N), 1 670, 1 605, 1 575 (C=O), and 1 560 cm^{-1}; $\lambda_{max.}$ (MeCN) 280 (log ε 4.2) and 362 nm (3.3); *m/e* 250.

The aqueous layer was acidified with 2N-HCl and

extracted with Et_2O (3 × 20 ml). The dried ($MgSO_4$) extracts were evaporated. The residue (0.033 g, 11%) was repeatedly crystallised from EtOH to give yellow-brown needles of 4-*cyano*-6-*phenyltropolone* (27), m.p. 158—159 °C (Found: C, 75.0; H, 4.5; N, 6.0. $C_{14}H_9NO_2$ requires C, 75.3; H, 4.1; N, 6.3%); $\nu_{max.}$ (Nujol) 3 200 (O–H), 2 230 (C≡N), 1 600, 1 580, and 1 550 cm^{-1}; *m/e* 223.

(ii) *With sodium hydrogen carbonate.* The mixture of (19) and (22) (0.750 g, 2.0×10^{-3} mol) and $NaHCO_3$ (1.5 g) in water (100 ml) were stirred at 20 °C for 2 h and the filtrate was extracted with Et_2O (4 × 40 ml). The dried ($MgSO_4$) extracts were evaporated; the red residue, after chromatography [Kieselgel PF 254; $CHCl_3$–EtOAc (4 : 1)], crystallised from Et_2O–light petroleum (b.p. 40—60 °C) as red prisms (0.135 g, 55%), m.p. 138—139 °C (Found: C, 74.3; H, 5.7; N, 8.9. Calc. for $C_{16}H_{14}N_2O$: C, 76.8; H, 5.6; N, 11.2%); $\nu_{max.}$ (Nujol) 3 260, 2 230, 1 585, and 1 570 cm^{-1}; $\lambda_{max.}$ (MeCN) 280 (log ε 3.8) and 362 nm (3.3); *m/e* 250.

2-*Dimethylamino*-4-*methoxycarbonyl*-6-*phenyltropone*.—The mixed methiodides (20) and (23) (0.91 g, 2.2×10^{-3} mol) in water (20 ml) were stirred for 10 min with silver oxide (0.7 g) at 20 °C. The filtrate was extracted with Et_2O (3 × 40 ml) and the extract dried ($MgSO_4$) and evaporated. The residue, after thick-layer chromatography [Kieselgel PF 254; $CHCl_3$–EtOAc (4 : 1)], gave the *tropone* (26) (0.26 g, 42%), which crystallised from EtOH as orange-red needles, m.p. 138—139 °C (Found: C, 72.0; H, 6.3; N, 4.8. $C_{17}H_{17}NO_3$ requires C, 72.1; H, 6.1; N, 4.9%); $\nu_{max.}$ (KBr) 1 705 (ester, C=O), 1 605, 1 575 (ketone, C=O), 1 560, and 1 250 cm^{-1}; $\lambda_{max.}$ (MeCN) 360 (log ε 3.3) and 277 nm (3.8); *m/e* 283.

N-*Acetonyl*-N-(4-*methoxyphenacyl*)-NN-*dimethylammonium Bromide* (4B).—*p*-Methoxyphenacyl bromide (37.7 g, 0.166 mol) (m.p. 68—70 °C; lit.,[18] 73—74 °C) in dry Et_2O (200 ml) and dry (NaOH; molecular sieves) dioxan (100 ml) was added, dropwise, with stirring, during 30 min, to 1-dimethylaminoacetone (16.7 g, 0.166 mol) in sodium-dried Et_2O (700 ml), at 0 °C. The mixture was stirred for 7 h at 0 °C and kept at 20 °C for 2 days. *Compound* (4B) was filtered off and washed with Et_2O; it crystallised from MeOH–Et_2O as yellow prisms (43.4 g, 79%), m.p. 145—146 °C (Found: C, 50.6; H, 6.3; N, 3.9. $C_{14}H_{20}BrNO_3$ requires C, 50.9; H, 6.1; N, 4.2%); $\nu_{max.}$ (Nujol) 1 740 (alkyl C=O), 1 675 (aryl C=O), 1 600, 1 570, 1 510, 1 260 (C–O), 1 010 (C–O), 845, and 810 cm^{-1}; δ (D_2O) 2.41 (3 H, s, Ac), 3.61 (6 H, s, NMe_2), 3.97 (3 H, s, MeO), 5.07 (2 H, s, N·CH_2Ac), 5.47 (2 H, s, *p*-MeO·C_6H_4·CO·CH_2·N), 7.10 (2 H, d, H-3′), and 8.00 (2 H, d, H-2′, $J_{2',3'}$ 9 Hz).

1,2,3,6-*Tetrahydro*-5-(4-*methoxyphenyl*)-1,1-*dimethyl*-3-*oxopyridinium Bromide* (5B).—*N*-Acetonyl-*N*-(4-methoxyphenacyl)-*NN*-dimethylammonium bromide (4.1 g, 0.012 mol) in 2N-NaOH (9 ml) was kept for 5 h at 15—20 °C, cooled (ice bath), then neutralised with 48% HBr. *Compound* (5B) (3.5 g, 90%) crystallised from EtOH as yellow needles, m.p. 183—185 °C (Found: C, 53.7; H, 6.0; N, 4.6. $C_{14}H_{18}BrNO_2$ requires C, 53.9; H, 5.8; N, 4.5%); $\nu_{max.}$ (Nujol) 1 665 (C=O), 1 610, 1 600, 1 570, 1 515, 1 245 (C–O), 1 020, and 815 cm^{-1}; $\lambda_{max.}$ (EtOH) 239 (log ε 4.0) and 329 nm (4.4).

3-*Hydroxy*-5-(4-*methoxyphenyl*)-1-*methylpyridinium Bromide* (6B).—Pyridinium bromide (5.1 g, 0.03 mol) and 1,2,3,6-tetrahydro-5-(4-methoxyphenyl)-1,1-dimethyl-3-oxopyridinium bromide (10 g, 0.03 mol) in MeOH (40 ml) were treated with bromine (1.6 ml, 5.0 g, 0.03 mol) as for compound (6A). *Compound* (6B) (2.5 g, 27%) crystallised from MeCN as prisms, m.p. 197—198 °C (Found: C, 53.1; H, 4.7; N, 5.5. $C_{13}H_{14}BrNO_2$ requires C, 52.7; H, 4.8; N, 5.5%); $\nu_{max.}$ (Nujol) 2 700 (O–H), 1 610 (C=C), 1 585, 1 570, 1 270 (C–O), and 825 cm^{-1}; $\lambda_{max.}$ (EtOH) 210 (log ε 4.4), 235 (4.1), 262 (4.3), 290 (3.9), and 335 nm (3.9); *m/e* 215 (betaine).

5-(4-*Methoxyphenyl*)-1-*methyl*-3-*oxidopyridinium* (7B).—3-Hydroxy-5-(4-methoxyphenyl)-1-methylpyridinium bromide (1.0 g, 3.4 × 10^{-3} mol) in water (150 ml) and EtOH (95%; 50 ml) was passed through an Amberlite IRA-401 (OH^-) column (15 g) followed by water until the eluate was neutral. The combined eluate was evaporated at 20 mmHg to constant weight. THF (25 ml) was added to give *compound* (7B), which crystallised from $CHCl_3$–light petroleum (b.p. 40—60 °C) as needles (0.44 g, 60%), m.p. 182—184 °C (Found: C, 72.9; H, 6.1; N, 6.3. $C_{13}H_{13}NO_2$ requires C, 72.5; H, 6.1; N, 6.5%); $\nu_{max.}$ ($CHBr_3$) 3 350 (O–H), 1 660, 1 610, 1 575 (C=C), 1 510, 1 490, 1 410, 1 370, 1 290, 1 240 (C–O–C), 1 180, 1 040, 1 035 (C–O–C), and 840 cm^{-1}; $\lambda_{max.}$ (MeCN) 207 (log ε 3.9), 220 (3.7), 250 (3.7), 271 (3.8), and 360 nm (3.4).

Reaction of Compound (7B) *with Acrylonitrile*.—Compound (7B) (1.7 g, 7.9 × 10^{-3} mol) and acrylonitrile (24 g, 0.46 mol) were heated under reflux in dry ($LiAlH_4$) THF (30 ml) with hydroquinone (0.2 g). After 2 days, the mixture was evaporated at 20 mmHg and the residue chromatographed [aluminium oxide, grade I; CH_2Cl_2–light petroleum (b.p. 40—60 °C) (1 : 1)]. The eluate [a yellow oil (1.98 g)] was separated by thick-layer chromatography [Kieselgel PF 254; $CHCl_3$–EtOAc (2 : 1)] into two major fractions. The higher R_F fraction (0.103 g, 15%) crystallised from $CHCl_3$–light petroleum (b.p. 40—60 °C) to give 4-(4-*methoxyphenyl*)-8-*methyl*-2-*oxo*-8-*azabicyclo*[3.2.1]*oct*-3-*ene*-6-exo-*carbonitrile* (16), as yellow prisms, m.p. 103—105 °C (Found: C, 71.2; H, 5.9; N, 9.5. $C_{16}H_{16}N_2O_2$ requires C, 71.6; H, 6.0; N, 10.4%); $\nu_{max.}$ (Nujol) 2 240 (C≡N), 1 660 (αβ-unsat. ketone C=O), 1 600, 1 585, 1 565, and 1 270 cm^{-1} (C–O); $\lambda_{max.}$ (EtOH) 235 (log ε 3.7) and 325 nm (4.0); *m/e* 268. The *picrate* crystallised from EtOH as yellow prisms, m.p. 204—207 °C (Found: C, 52.7; H, 4.2; N, 13.9. $C_{22}H_{19}N_5O_9$ requires C, 53.1; H, 3.9; N, 14.1%).

The lower R_F fraction (0.0367 g, 5.1%) was obtained as a yellow oil, identified as 4-(4-*methoxyphenyl*)-8-*methyl*-2-*oxo*-8-*azabicyclo*[3.2.1]*oct*-3-*ene*-6-endo-*carbonitrile* (12), $\nu_{max.}$ ($CHBr_3$) 2 240 (C≡N), 1 660 (αβ-unsat. ketone, C=O), 1 605, 1 590, 1 565, and 1 260 cm^{-1} (C–O); $\lambda_{max.}$ (EtOH) 235 (log ε 3.7) and 325 nm (4.1). The *picrate* crystallised from EtOH as yellow prisms, m.p. 214—216 °C (Found: C, 53.0; H, 4.2; N, 13.8. $C_{22}H_{19}N_5O_9$ requires C, 53.1; H, 3.9; N, 14.1%).

Quaternisation of 4-(4-*Methoxyphenyl*)-8-*methyl*-2-*oxo*-8-*azabicyclo*[3.2.1]-*oct*-3-*ene*-6-exo-*carbonitrile* (16).—Compound (16) (0.034 g, 1.3 × 10^{-4} mol) in EtOAc (10 ml) with MeI (5 ml) at 20 °C for 2 days gave the *quaternary salt* (24) as prisms (0.035 g, 66%), m.p. 194—196 °C (from EtOH) (Found: C, 49.7; H, 4.5; N, 6.9. $C_{17}H_{19}IN_2O_2$ requires C, 49.8; H, 4.7; N, 6.8%); $\nu_{max.}$ (Nujol) 2 240 (C≡N), 1 690 (αβ-unsat. ketone. C=O), 1 600 (C=C), 1 570, and 1 240 cm^{-1} (C–O).

N-*Acetonyl*-NN-*dimethyl*-N-(4-*nitrophenacyl*)*ammonium Bromide* (4C).—*p*-Nitrophenacyl bromide (44.3 g, 0.18 mol) (m.p. 97—99 °C; lit.,[18] 98—99 °C) in sodium dried Et_2O (600 ml) and dry (NaOH; molecular sieves) dioxan (300 ml

[18] M. I. Shevchuk and A. V. Dombrovskii, *J. Gen. Chem., U.S.S.R.*, 1963, **33**, 1118.

was added, dropwise, with stirring to 1-dimethylaminoacetone (18.3 g, 0.18 mol) in dry Et_2O (200 ml) at 0 °C, during 1 h. The mixture was stirred for 7 h at 0 °C, and kept at 20 °C for 2 days. *Compound* (4C) (46.7 g, 75%) was washed with Et_2O; it crystallised from EtOH–Et_2O as yellow prisms, m.p. 163—165 °C (Found: C, 45.1; H, 4.8; N, 7.7. $C_{13}H_{17}BrN_2O_4$ requires C, 45.2; H, 5.0; N, 8.1%); $\nu_{max.}$ (Nujol) 1 735 (alkyl C=O), 1 690 (aryl C=O), 1 600 (C=C), 1 520 (antisym. NO_2), 1 345 (sym. NO_2), 850, and 740 cm^{-1}; δ (D_2O) 2.38 (3 H, s, Ac), 3.62 (6 H, s, NMe_2), 5.08 (2 H, s, N·CH_2Ac), 5.60 (2 H, s, *p*-NO_2·C_6H_4·CO·CH_2·N), 8.20 (2 H, d, H-2′), and 8.42 (2 H, d, H-3′, $J_{2',3'}$ 9 Hz).

1,2,3,6-*Tetrahydro*-1,1-*dimethyl*-5-(4-*nitrophenyl*)-3-*oxopyridinium Bromide* (5C).—2N-NaOH (5 ml) was added to compound (4C) (2.3 g, 0.007 mol) at −40 °C and the mixture stirred for 24 h. Neutralisation with 48% HBr and evaporation at 20 mmHg gave *compound* (5C), which crystallised from EtOH as yellow prisms (0.75 g, 33%), m.p. 195—197 °C (Found: C, 46.0; H, 5.1; Br, 24.3; N, 8.8. $C_{13}H_{15}BrN_2O_3$ requires C, 47.7; H, 4.7; Br. 24.4; N, 8.6%); $\nu_{max.}$ (Nujol) 1 680 (αβ-unsat. ketone, C=O), 1 610, 1 595, 1 580, 1 515 (antisym. NO_2), 840, and 740 cm^{-1}; $\lambda_{max.}$ (EtOH) 217 (log ε 4.0) and 294 nm (4.3).

3-*Hydroxy*-1-*methyl*-5-(4-*nitrophenyl*)*pyridinium Bromide* (6C).—Pyridinium bromide (3.2 g, 0.02 mol) and 1,2,3,6-tetrahydro-1,1-dimethyl-5-(4-nitrophenyl)-3-oxopyridinium bromide (6.54 g, 0.02 mol) in MeOH (35 ml) were treated with bromine (1.0 ml, 3.1 g, 0.02 mol) as for compound (6A). The precipitate was filtered off and crystallised from EtOH to give *compound* (6C) as light yellow plates, m.p. 266—268 °C (Found: C, 46.1; H, 3.8; N, 8.9. $C_{12}H_{11}BrN_2O_3$ requires C, 46.3; H, 3.6; N, 9.0%); $\nu_{max.}$ (Nujol) 2 700 (O–H), 1 610, 1 600, 1 585, 1 520 (antisym. NO_2), 1 345 (sym. NO_2), 840, and 735 cm^{-1}; $\lambda_{max.}$ (EtOH) 213 (log ε 4.3), 260 (4.2), 281 (4.3), 308 (4.2), and 350 nm (3.6); *m/e* 230 (betaine).

1-*Methyl*-5-(4-*nitrophenyl*)-3-*oxidopyridinium* (7C).—3-Hydroxy-1-methyl-5-(4-nitrophenyl)-pyridinium bromide (0.8 g, 2.6×10^{-3} mol) in water (200 ml) and EtOH 95% (50 ml) was filtered through an Amberlite IRA-401 (OH^-) column (15 g) followed by water until the eluate was neutral. The combined eluate was evaporated at 20 mmHg to give *compound* (7C) (0.38 g, 64%), which crystallised (charcoal) from EtOH as yellow prisms, m.p. 215—221 °C (Found: C, 61.8; H, 4.6; N, 11.6. $C_{12}H_{10}N_2O_3$ requires C, 62.6; H, 4.4; N, 12.2%); $\nu_{max.}$ ($CHBr_3$) 1 600, 1 605, 1 580 (C=C), 1 560, 1 520 (antisym. NO_2) 1 500, 1 430, 1 405, 1 345 (sym. NO_2), 1 265, 1 070, 1 040, 840, and 750 cm^{-1}; $\lambda_{max.}$ (MeCN) 215 (log ε 4.1), 242 (3.9), 277 (4.1), 290 (4.0), and 372 nm (3.6).

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