

Some Piperidinomethyl Quinols and Quinones

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Abstract

Tris- and tetrakis-piperidinomethylquinols have been synthesized by the Mannich procedure. The corresponding quinones, along with those of related compounds, have been obtained as nitrate salts by oxidation with oxides of nitrogen.

Reaction between methyl-substituted 1,4-benzoquinones and amines may involve attack at the methyl group.^{1,2} Thus duroquinone (1) and piperidine at room temperature gave successively bis-, tris-, and tetrakis-piperidinomethylquinols (2), (3), (4) respectively. This process differed from normal nuclear amination of benzoquinones in that more than two amino groups could be introduced and in the fact that quinonoid products were never isolated, the quinol form being favoured by intramolecular hydrogen-bonding. Quinones must nevertheless have been present as intermediates to enable each amination step to proceed and the overall process involved uptake of oxygen.

This communication describes the completion of two aspects of this study. Compound (2) had been synthesized independently by a Mannich reaction;¹ the monopiperidino analogue (5), which could not be isolated from the amination, was synthesized in the same way.² Synthetic confirmation of the remaining members of the series, (3) and (4), was not achieved at the time because the conventional Mannich procedure in boiling ethanol does not go beyond disubstitution of quinol systems.

Treatment of toluquinol with formaldehyde and piperidine in a sealed tube at 120° has now been shown to effect conversion into (3); hydroquinone similarly gave (4). Attempts to moderate this last reaction so as to obtain tris(piperidinomethyl)quinol were unsuccessful. Depending on the severity of the conditions it gave either (4) or the bispiperidino derivative (6)³ or mixtures of the two. Greater selectivity has been achieved in analogous reactions involving the weaker base morpholine.⁴

The most promising approach to the quinones of this series was through oxidation with liquid oxides of nitrogen.⁵ In this way the quinol (2) was converted into the

¹ Cameron, D. W., Scott, P. M., and Lord Todd, A., *J. Chem. Soc.*, 1964, 42.

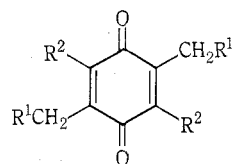
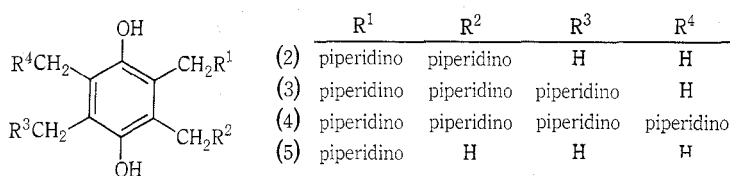
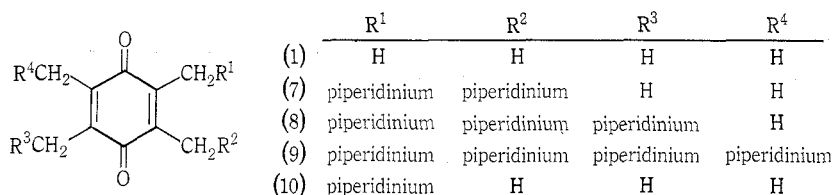
² Cameron, D. W., Giles, R. G. F., and Titman, R. B., *J. Chem. Soc. C*, 1969, 1245.

³ Bogolyubskii, V. A., *Zh. Obshch. Khim.*, 1960, 30, 3589.

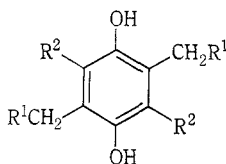
⁴ Burke, W. J., Bishop, J. L., and Warburton, J. A., *J. Org. Chem.*, 1962, 27, 4003.

⁵ Brook, A. G., *J. Chem. Soc.*, 1952, 5040.

cation (7) as its dinitrate salt.¹ In order to extend the range of systems available for study as high-potential quinones, the oxidation process has been shown to be capable of extrapolation. The cations (8), (9) and (10) were thus obtained as tri-, tetra-, and mono-nitrate salts respectively. Analogous salts of (11) and (12) were also prepared from the corresponding quinols (6),³ (13).¹ In the conversion (6) → (11) it is interesting to note that there was no evidence of nitration of the benzenoid ring.



	R ¹	R ²
(11)	piperidinium	H
(12)	piperidinium	Me



	R ¹	R ²
(6)	piperidino	H
(13)	piperidino	Me

Structures (8)–(12) were supported by spectroscopic evidence. In p.m.r. spectra the methylene protons of the 2',6'-positions of the piperidine rings showed separate equatorial and axial resonances in every case. For the non-protonated quinols (3)–(6), (13), where inversion of nitrogen can occur, single broad methylene resonances were observed.

The tetranitrate of cation (9) was the least stable of the quinones. On being dissolved in water or after being boiled in methanol it appeared to undergo reduction, presumably by abstraction of hydrogen from the solvent. The free base was less stable still. On being precipitated from the tetranitrate by addition of bicarbonate it was obtained as an orange yellow solid (λ_{max} 1640 cm^{-1}). Attempted recrystallization from methanol caused rapid reduction to (4). These superficial experiments suggest that, while the piperidinomethyl quinones could well be interesting oxidizing agents, handling them will require milder methods than have been developed so far.

Experimental

Unless otherwise stated i.r. spectra were measured as KBr discs and p.m.r. spectra in D_2O ; chemical shifts are quoted on the δ scale with sulphuric acid as external reference.

Tetrakis(piperidinomethyl)quinol

Piperidine (11 cm³) was added slowly and with cooling to a Carius tube containing a mixture of hydroquinone (1 g) and formalin (9 cm³) under nitrogen. After sealing, the tube was heated at 120° for 65 h. The solid product (3.3 g) obtained upon cooling was filtered off and recrystallized to give the tetrakis compound (4), m.p. 245° (dec.), undepressed in admixture with authentic material (lit.¹ 240° (dec.)) and having identical u.v. and i.r. spectra.

Methyl(trispiperidinomethyl)quinol

Toluquinol (1 g), formalin (3 cm³), piperidine (1 cm³) and dioxan (10 cm³) were heated in a Carius tube at 125° for 65 h. This gave the tris compound (3) (2.2 g), colourless needles, m.p. 163–164° from ethanol. It was undepressed in admixture with authentic material (lit.¹ 163.5–164.5°) and had identical i.r. and p.m.r. spectra.

2,5-Bis(piperidinomethyl)quinol

Hydroquinone (1 g), formalin (2.2 cm³), piperidine (2.7 cm³) and dioxan (7.5 cm³) were made to react at 100° for 48 h as above. The product (1.6 g) was recrystallized from chloroform–ethanol to give 2,5-bis(piperidinomethyl)quinol (6) as colourless crystals, m.p. 190–191° (lit.³ 190°).

The same quantities of reactants were boiled under nitrogen for 18 h. This yielded the same product (6) (2.5 g), m.p. and m.m.p. 190–191°.

Oxidation of Quinols

Liquid oxides of nitrogen were prepared according to the literature.⁵

Apart from (i) below the quinol was added to dry carbon tetrachloride (20 cm³) and liquid oxides of nitrogen added with stirring. After a further 5–7 min at room temperature the product was filtered off, triturated if necessary with methanol or ethanol and recrystallized from dry methanol.

(i) Trimethyl(piperidinomethyl)quinol² (0.1 g) was treated with oxides of nitrogen (0.3 cm³). Solvent was evaporated and the resultant yellow oil triturated with methanol to give 1-(3,5,6-trimethyl-1,4-benzoquinone-2-ylmethyl)piperidinium nitrate (10) (0.08 g), yellow crystals from dry methanol, m.p. 160–165° (dec.) (Found: C, 57.6; H, 7.3; N, 8.8. C₁₅H₂₂N₂O₅ requires C, 58.0; H, 7.1; N, 9.0%). λ_{\max} (log ϵ) (H₂O) 261 (4.21), 350 (2.51) nm. ν_{\max} 1645 cm⁻¹. P.m.r. 1.79 (pip-CH₂), 1.97, 2.10 (3 × CH₃), 3.03, 3.49 (pip-CH₂N⁺), 4.13 (quin-CH₂N⁺).

(ii) 2,5-Bis(piperidinomethyl)quinol³ (0.9 g) with oxides of nitrogen (0.5 cm³) gave 1,1'-[(1,4-benzoquinone-2,5-diyl)dimethyl]bis(piperidinium dinitrate) (11) (0.85 g), m.p. 180–185° (dec.) (Found: C, 50.5; H, 6.4; N, 12.9. C₁₈H₂₈N₄O₈ requires C, 50.5; H, 6.6; N, 13.1%). λ_{\max} (log ϵ) (H₂O) 250 (4.25), 306 (2.91) nm. ν_{\max} 1656 cm⁻¹. P.m.r. (ref. ext. SiMe₄) 2.30 (pip-CH₂), 3.47, 3.91 (pip-CH₂N⁺), 4.59 (quin-CH₂N⁺), 7.62 (quin H).

(iii) 2,5-Dimethyl-3,6-bis(piperidinomethyl)quinol¹ (0.24 g) treated as in (ii) gave 1,1'-[(3,6-dimethyl-1,4-benzoquinone-2,5-diyl)dimethyl]bis(piperidinium dinitrate) (12) (0.31 g), yellow crystals, m.p. 220–225° (dec.) (Found: C, 52.8; H, 7.2. C₂₀H₃₂N₄O₈ requires C, 52.6; H, 7.1%). λ_{\max} (log ϵ) (H₂O) 262 (4.29), 320 (2.62) nm. ν_{\max} 1656 cm⁻¹. P.m.r. (CF₃CO₂H, ref. int. Me₄N⁺I⁻) 2.01 (pip-CH₂), 2.25 (CH₃), 3.14, 3.70 (pip-CH₂N⁺), 4.30 (d, *J* 6 Hz, quin-CH₂N⁺), 7.17 (+NH).

(iv) Methyl(trispiperidinomethyl)quinol¹ (0.1 g) with nitrogen oxides (0.75 g) gave 1,1',1''-[(6-methyl-1,4-benzoquinone-2,3,5-triyl)trimethyl]trispiperidinium trinitrate (8) (0.08 g), yellow crystals, m.p. 130–135° (dec.) (Found: C, 49.3; H, 7.5; N, 13.4. C₂₅H₄₂N₆O₁₁·CH₃OH requires C, 49.2; H, 7.3; N, 13.2%). λ_{\max} (log ϵ) H₂O 257 (4.02), 328 (3.11) nm. ν_{\max} 1660 cm⁻¹. P.m.r. 2.00 (pip-CH₂), 2.41 (CH₃), 3.28, 3.66 (pip-CH₂N⁺), 4.41, 4.53 (1:2) (quin-CH₂N⁺).

(v) Tetrakis(piperidinomethyl)quinol¹ (0.1 g) with nitrogen oxides (1 cm³) gave, after crystallizing as rapidly as possible, 1,1',1'',1'''-[(1,4-benzoquinone-2,3,5,6-tetrayl)tetramethyl]tetra(piperidinium tetranitrate) (9) (0.14 g), yellow plates, m.p. 165–170° (dec.) (Found: C, 47.9; H, 7.1. C₃₀H₅₂N₈O₁₄ requires C, 48.1; H, 7.0%). λ_{\max} (log ϵ) (EtOH) 254sh (3.72), 313 (3.56), 384sh (2.88) nm. ν_{\max} 1665 cm⁻¹. P.m.r. 1.98 (pip-CH₂), 3.27, 3.67 (pip-CH₂N⁺), 4.57 (quin-CH₂N⁺).