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Nucleophilic Substitution of Bromo-*p*-benzoquinones by Dimethylamine

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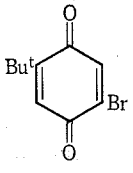
Abstract

Product analysis shows that dimethylamine, like methoxide anion, substitutes bromo-*p*-benzoquinones by an addition–elimination process, resulting in isomeric dimethylaminoquinones. Bromodimethylaminoquinones were also formed, due to incomplete elimination of hydrogen bromide. In contrast to the substitution by methoxide the product distribution is largely unaffected by changing to a dipolar aprotic solvent.

The e.s.r. spectra of 2-t-butyl-5-(*N*,*N*-dimethylamino)-1,4-benzosemiquinone and two related semiquinones have been analysed.

Introduction

Amines, like alkoxides, efficiently displace halogen and alkoxy substituents from quinones.[1] We have shown previously[2] that 2- and 3-bromo-5-t-butyl-1,4-benzoquinones when treated with methanolic alkali undergo an addition–elimination reaction to give a preponderance of the isomeric methoxyquinones, e.g. (1) → (2). We have also shown that the reaction of 2,3-dibromo-5-t-butyl-1,4-benzoquinone (3) with



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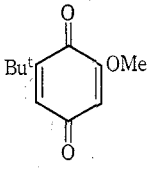

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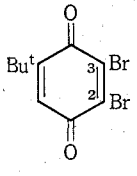

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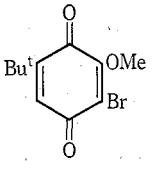

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methanolic alkali leads chiefly to 2-bromo-5-t-butyl-3-methoxy-1,4-benzoquinone (4), and that the position of substitution is reversed from C 3 to C 2 when the methanol is largely replaced by dimethyl sulphoxide. This was explained by the equilibrium being displaced towards the less hindered and therefore more readily solvated anion produced by attack at C 3 in methanol whereas in dimethyl sulphoxide, which does not effectively solvate the anion, the electronic effect of the t-butyl group directs attack to C 2.

[1] Finley, K. T., in 'The Chemistry of the Quinonoid Compounds' Part 2 (Ed. S. Patai) p. 877 (John Wiley: London 1974).

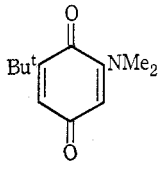
[2] Hewgill, F. R., and Mullings, L. R., *J. Chem. Soc.*, *B*, 1969, 1155.

Results presented here extend this investigation to the uncharged nucleophile dimethylamine, and include the e.s.r. spectra obtained on reduction of some of the resulting aminoquinones.

Results and Discussion

(*a*) *Substitution Reactions*

Treatment of the bromoquinone (1) with dimethylamine in ethanol gave two products, quinones (5) and (6), in the ratio 45 : 55. Similarly the bromoquinone (7) gave quinones (8) and (9) in the ratio 70 : 30. In both reactions small amounts of the hydroquinones corresponding to (6) and (9) were observed in the n.m.r. spectra of the crude reaction products; however, treatment with silver oxide converted these into the corresponding quinones, thus simplifying product analysis.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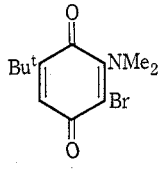
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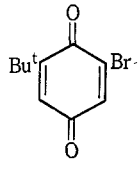
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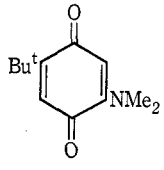
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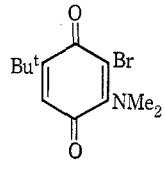
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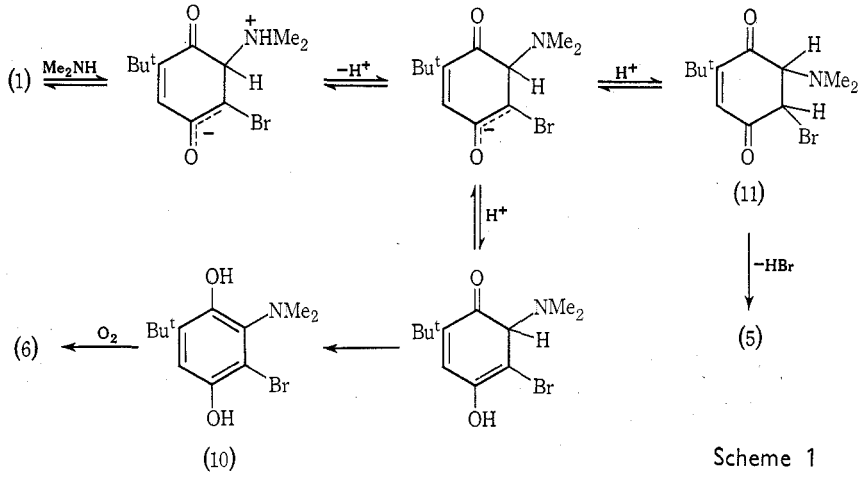
Structural assignments were made as follows. Compound (5) has already been described,[3] and clearly showed coupling of 2·5 Hz in its n.m.r. spectrum. Compound (8), whose n.m.r. spectrum showed no coupling, was hydrolysed to the known[4] 2-t-butyl-5-hydroxy-1,4-benzoquinone. Compounds (6) and (9) were hydrolysed to the bromohydroxyquinones, that from the former having previously been described.[2]

Formation of quinones (5) and (8) is clearly analogous to the transformations observed in the methanolysis of the bromoquinones, and an addition–elimination process is presumably also operating here. Isolation of the substituted bromoquinones (6) and (9), although having no counterpart in the methanolysis, is not incompatible with such a mechanism and can be accounted for by a modified sequence as shown for the reaction of (1) with dimethylamine in Scheme 1. The less basic conditions in the reaction with dimethylamine may favour formation of the hydroquinone (10), whereas in the methanolysis the prevailing route involves the diketo tautomer (11). This is in agreement with observations that alkaline conditions favour the formation of the keto tautomers of phenols.[5] The ease with which the hydroquinone (10) undergoes aerial oxidation was demonstrated when the quinone (6) was regenerated spontaneously on exposing a hydrogenated solution to air.

Nucleophilic attack by dimethylamine in dimethyl sulphoxide on the bromoquinones (1) and (7) gave the same products as were obtained in ethanol, their relative proportions being somewhat different. This is in complete contrast to the methanolysis in dimethyl sulphoxide, which strongly favours direct replacement of the bromine substituent, but can be accounted for by the differing nature of the nucleophiles.

[3] Cuntze, U., and Musso, H., *Chem. Ber.*, 1970, **103**, 62.
[4] Musso, H., and Maassen, O., *Justus Liebigs Ann. Chem.*, 1965, **689**, 93.
[5] Ershov, V. V., and Nikiforov, G. A., *Russ. Chem. Rev.*, 1966, **35**, 817; Bowman, D. F., and Hewgill, F. R., *J. Chem. Soc., C*, 1971, 1777.

Whereas the rate of nucleophilic substitution by anions is dramatically increased on changing from protic to dipolar aprotic solvents, uncharged species experience little enhancement in reactivity,[6] and thus change of solvent has little influence on the nature of the products.



Scheme 1

The dibromoquinone (3), on treatment with dimethylamine in ethanol, gave only quinones (6) and (9) in the ratio 70 : 30. This is similar to the ratio 85 : 15 obtained for the replacement at positions 3 and 2 respectively in the methanolysis reactions.[2] The same quinones in equimolar amounts were isolated from the reaction in dimethyl sulphoxide, again demonstrating a marked contrast with methanolysis in dipolar aprotic solvents.

(b) E.S.R. Spectra

Difficulty was experienced in obtaining satisfactory e.s.r. spectra by dithionite reduction of the dimethylaminoquinones under alkaline conditions. In some instances radical mixtures were observed, probably reflecting the lability of the dimethylamino group. A further complication was the lack of resolution caused by line broadening, presumably due to unresolved t-butyl splitting. Estimated splitting constants (Table 1) were verified by computer simulation.

Table 1. Hyperfine splitting constants (G) for semiquinones

1,4-Benzosemiquinone	Solvent	a_H (ring)	a_{NR}	a_N	a_{NH}	a_{Bu^t}
3-Bromo-5-t-butyl-2-(*N*,*N*-dimethylamino)	EtOH	1·51	0·49	0·49		
2-t-Butyl-5-(*N*,*N*-dimethylamino)	Me_2SO	1·80, 0·74	0·84	0·84		
	EtOH	1·20, 0·80	1·10	1·02		0·10
2-Amino-5-t-butyl	aq. EtOH	1·00, 0·36		1·35	0·37	0·12

A well resolved spectrum of considerable complexity was obtained for the semiquinone of (8) in ethanol (Fig. 1*a*). Splitting by all protons and the nitrogen atom is visible. Although computer simulation generated a spectrum (Fig. 1*b*) which closely

[6] Parker, A. J., *Quart. Rev., Chem. Soc.*, 1962, **16**, 163.

matches that of Fig. 1*a*, detailed examination reveals some minor discrepancies and hence this cannot be considered a unique solution. Nevertheless, similarities are apparent with the spectrum obtained in dimethyl sulphoxide, and certain features are also consistent with those of other aminosemiquinones.

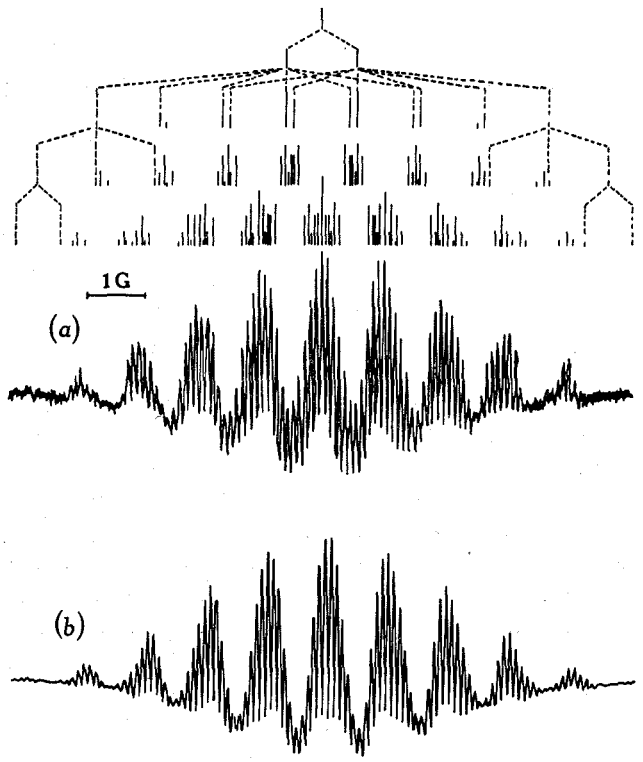


Fig. 1. (*a*) Second-derivative e.s.r. spectrum of 2-t-butyl-5-(*N*,*N*-dimethylamino)-1,4-benzosemiquinone in ethanol.
(*b*) Simulated spectrum.

As the ring proton splittings for the semiquinone of (8) are almost as large as those for the 2-alkoxy-5-t-butyl-1,4-benzosemiquinones,[2] and the nitrogen and *N*-methyl splittings are distinctly smaller than those published[7] for benzosemiquinones with less bulky *N*-alkyl substituents, we conclude, in agreement with similar observations by Huntington and Davis,[7] that there is significant resistance to the *N*,*N*-dimethylamino group becoming coplanar with the ring. This is even more noticeable in the more highly hindered 3-bromo-5-t-butyl-2-dimethylamino-1,4-benzosemiquinone derived from (9). For comparison the spectrum of 2-amino-5-t-butyl-1,4-benzosemiquinone was examined. Here the ring proton splittings are smaller and the nitrogen splitting larger as would be expected for the smaller amino group, which can now become coplanar with the ring and thus more effectively delocalize the unpaired electron.

Experimental

Melting points were determined with a Kofler hot-stage apparatus. N.m.r. spectra were obtained with a Varian A-60 spectrometer operating at 60 MHz using carbon tetrachloride solutions. E.s.r.

[7] Huntington, J. L., and Davis, D. G., *J. Magn. Resonance*, 1970, **3**, 456.

spectra were obtained with a Varian V-4500-10A spectrometer. Paramagnetic solutions were prepared by dissolving the quinone (20 mg) in the chosen solvent (6 ml) and shaking with sodium hydroxide and sodium dithionite in air. The signal was measured in a stationary system under conditions of low microwave power (attenuation 13–16 db) and low modulation amplitude.

Quinones (1), (3) and (7) were prepared as described previously,[2] as was 2-amino-5-t-butyl-1,4-benzoquinone.[8]

Reaction of 2-Bromo-5-t-butyl-1,4-benzoquinone (1) with Dimethylamine

(A) *In ethanol.*—The quinone (1) (500 mg, 2·06 mmol) in ethanol (40 ml) was treated with a solution of dimethylamine in ethanol (6% w/v, 8 ml), the initial yellow solution immediately turning dark red. After stirring for 5 min the solution was poured into water, extracted with ether, and the dried ether extracts were shaken with silver oxide (500 mg) for 5 min. After filtration and evaporation of the solvent, the resulting red oil was adsorbed on alumina. Elution with light petroleum gave *2-bromo-5-t-butyl-3-*(N,N-*dimethylamino*)-*1,4-benzoquinone* (6) (285 mg, 1·00 mmol) as a dark red oil (Found: C, 50·4; H, 5·6; N, 4·7. $C_{12}H_{16}BrNO_2$ requires C, 50·4; H, 5·6; N, 4·9%). N.m.r. δ 1·28 (Bu^t), 3·12 (NMe_2), 6·55 (olefinic H). ν_{max} (CCl_4) 1635, 1670 cm^{-1}.

Elution with benzene–light petroleum (1 : 1) gave 5-t-butyl-3-(*N,N*-dimethylamino)-1,4-benzoquinone (5) (170 mg, 0·82 mmol), m.p. 76–78° (lit.[3] 76–79°), after sublimation. N.m.r. δ 1·28 (Bu^t), 3·04 ($NMe)_2$, 5·39, 6·28 (J 2·5 Hz) (olefinic H). The absence of quinone (8) was confirmed by n.m.r.

(B) *In dimethyl sulphoxide.*—The quinone (1) in dimethyl sulphoxide (45 ml) was treated with a solution of dimethylamine in dimethyl sulphoxide (6% w/v, 10 ml). After stirring for 5 min the dark red solution was poured into water, extracted with ether, and the dried ether solution was shaken with silver oxide (600 mg) for 5 min. After filtration and evaporation of the solvent the products were identified as quinones (6) and (5) in the percentage ratio 80 : 20 (by n.m.r.).

Reaction of 3-Bromo-5-t-butyl-1,4-benzoquinone (7) with Dimethylamine

(A) *In ethanol.*—The quinone (7) (500 mg, 2·06 mmol) in ethanol (40 ml) was treated with ethanolic dimethylamine (6% w/v, 8 ml) as described above. Chromatography of the product on alumina and elution with light petroleum gave *3-bromo-5-t-butyl-2-*(N,N-*dimethylamino*)-*1,4-benzoquinone* (9) (140 mg, 0·49 mmol) as dark red prisms, m.p. 35–36°, from n-pentane (cooled in liquid air) (Found: C, 50·5; H, 5·8; N, 4·9. $C_{12}H_{16}BrNO_2$ requires C, 50·4; H, 5·6; N, 4·9%). N.m.r. δ 1·29 (Bu^t), 3·10 (NMe_2), 6·28 (olefinic H). ν_{max} (CCl_4) 1630, 1655 cm^{-1}.

Elution with benzene–light petroleum (1 : 4) gave *2-t-butyl-5-*(N,N-*dimethylamino*)-*1,4-benzoquinone* (8) (280 mg, 1·35 mmol) as dark red needles, m.p. 83–84°, from n-pentane (Found: C, 69·6; H, 8·4; N, 7·0. $C_{12}H_{17}NO_2$ requires C, 69·5; H, 8·3; N, 6·8%). N.m.r. δ 1·27 (Bu^t), 3·08 (NMe_2), 5·41, 6·24 (2 × olefinic H). ν_{max} (CCl_4) 1630, 1660 cm^{-1}. The absence of quinone (5) was confirmed by n.m.r.

(B) *In dimethyl sulphoxide.*—The quinone (7) when treated with dimethylamine in dimethyl sulphoxide as described above gave quinones (9) and (8) in the ratio 80 : 20 (by n.m.r.).

Acid Hydrolysis of N,N-*Dimethylaminoquinones*

(A) *2-t-Butyl-5-*(N,N-*dimethylamino*)-*1,4-benzoquinone* (*8*).—The quinone (8) (40 mg) was warmed in 10% sulphuric acid (20 ml) at 70° for 10 min. Extraction of the cooled solution with ether, evaporation of the washed and dried extract, sublimation of the residue, and recrystallization of the sublimate from light petroleum gave 2-t-butyl-5-hydroxy-1,4-benzoquinone (15 mg), m.p. 105–107° (lit.[4] 107·5–109°).

(B) *2-Bromo-5-t-butyl-3-*(N,N-*dimethylamino*)-*1,4-benzoquinone* (*6*).—Hydrolysis of 70 mg as described above gave a precipitate of 2-bromo-5-t-butyl-3-hydroxy-1,4-benzoquinone (50 mg), m.p. and mixed m.p. 214–217°.

(C) *3-Bromo-5-t-butyl-2-*(N,N-*dimethylamino*)-*1,4-benzoquinone* (*9*).—Hydrolysis of 90 mg as described above gave a precipitate of *3-bromo-5-t-butyl-2-hydroxy-1,4-benzoquinone* (65 mg) as yellow plates, m.p. 238·5–239·5°, from benzene–light petroleum (Found: C, 46·5; H, 4·3. $C_{10}H_{11}BrO_3$ requires C, 46·4; H, 4·3%). N.m.r. δ 1·33 (Bu^t), 6·58 (olefinic H). ν_{max} (CCl_4) 3400, 1655 cm^{-1}.

[8] Haynes, R. K., and Hewgill, F. R., *J. Chem. Soc., Perkin Trans. 1*, 1972, 396.

2-Bromo-5-t-butyl-3-(N,N-*dimethylamino*)*hydroquinone*

Quinone (6) (120 mg) was hydrogenated in ethanol over palladium charcoal until 1 mol. equiv. of hydrogen had been absorbed. The filtered solution, which quickly turned red on exposure to air, was evaporated under reduced pressure giving the hydroquinone (10) as a gum which could not be crystallized. N.m.r. ($CDCl_3$) δ 1·36 (Bu^t), 2·86 (NMe_2), 6·3–6·5 (2 × OH), 6·84 (aromatic H).

The hydroquinone was dissolved in acetic anhydride (8 ml) containing anhydrous sodium acetate (300 mg) and after 20 min the solution was poured into water. Extraction with ether and chromatography of the extract on alumina gave *2-bromo-5-t-butyl-3-*(N,N-*dimethylamino*)*-4-hydroxyphenyl acetate* (65 mg) as prisms, m.p. 111–112°, from light petroleum (Found: C, 51·1; H, 6·3; N, 3·9. $C_{14}H_{20}BrNO_3$ requires C, 50·9; H, 6·1; N, 4·2%). N.m.r. δ 1·37 (Bu^t), 2·22 (OAc), 2·88 (NMe_2), 6·37 (aromatic H), 8·28 (OH).

Reaction of 2,3-Dibromo-5-t-butyl-1,4-benzoquinone (3) with Dimethylamine

(A) *In ethanol.*—The quinone (3) (470 mg, 1·46 mmol) was treated with dimethylamine as described for the monobromoquinone. Chromatography of the product on alumina and elution with light petroleum gave 3-bromo-5-t-butyl-2-(*N,N*-dimethylamino)-1,4-benzoquinone (9) (120 mg, 0·42 mmol), m.p. and mixed m.p. 35–36°. Further elution with light petroleum gave 2-bromo-5-t-butyl-3-(*N,N*-dimethylamino)-1,4-benzoquinone (6) (n.m.r. and i.r. comparison) (280 mg, 0·98 mmol).

(B) *In dimethyl sulphoxide.*—Treatment of quinone (3) as described for the monobromoquinones gave approximately equal quantities of quinones (9) and (6) (by n.m.r.).

Acknowledgments

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