2,3-Dichloro-5,6-Dicyanobenzoquinone (DDQ). A New Preparation

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The first synthesis of 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) was described by Thiele and Günther[1] in 1906. However, no interest was shown in the compound until Linstead and co-workers[2] discovered its extraordinary potency as a dehydrogenating agent. Its oxidation potential is greater than that of any other known quinone.[2,3]

The broad utility of DDQ in the steroid field was first demonstrated by the British Drug Houses group. Since that time a number of drug companies, notably Syntex S.A. and E. Merck A.G., have studied its reactions in the steroid field. It now appears to be a reagent *par excellence* for converting Δ^4- and $\Delta^{4,6}$-steroidal 3-ketones into the corresponding $\Delta^{1,4}$ and $\Delta^{1,4,6}$ ketones, though this reaction by no means defines the scope of its usefulness. Recent reviews[4,5] clearly indicate that its unique properties are encouraging wider interest.

Thiele's original preparation of DDQ from 2,3-dicyanohydroquinone involved five steps.[1] Oxidation of 2,3-dicyanohydroquinone with nitric acid fumes gave 2,3-dicyanobenzoquinone which, with anhydrous hydrogen chloride, gave 2-chloro-5,6-dicyanohydroquinone. Repetition of these two steps yielded 2,3-dichloro-5,6-dicyanohydroquinone which was oxidized with nitric acid fumes to DDQ. This procedure was improved by Brook[6] who employed nitrogen tetroxide instead of nitric acid fumes. Later Mitchell[7] eliminated four steps of the original procedure when he found that chlorination of 2,3-dicyanohydroquinone in acetic acid gave 2,3-dichloro-5,6-dicyanohydroquinone. This compound was then oxidized to DDQ with lead dioxide in aqueous ethanol containing hydrochloric acid. However, while a more convenient synthesis, the over-all yield reported by Mitchell was only 36.5%, compared with the 70% yield obtained by Linstead, *et al.*,[2] using the five-step procedure.

We now wish to report a simple one-step procedure for converting 2,3-dicyanohydroquinone into DDQ in 90% yield. It is reported[4,8] that DDQ decomposes in water, and, while true, these statements have tended to obscure the fact that DDQ is stable in aqueous mineral acid. Herein lies one basis of the present process. We also found that 2,3-dicyanobenzoquinone and 2-chloro-5,6-dicyanobenzoquinone would rapidly add hydrogen chloride from aqueous solution. Thus, when 2,3-dicyanohydroquinone was suspended in 1:1 hydrochloric acid and the mixture was treated with a suitable oxidizing agent, pure DDQ was obtained in 90% yield.

Attempts to extend this procedure to other strong acid systems have failed. Hydrogen bromide adds only slowly to 2,3-dicyanobenzoquinone, and several other acids, among them hydrogen fluoride and trifluoroacetic acid, failed to add under the conditions employed. A large number of oxidizing agents have been used successfully, for example, nitric acid, nitric acid and air or oxygen, nitrogen tetroxide, bromic acid, chromic acid, and permanganic acid. Finally, since the 2,3-dichloro-5,6-dicyanohydroquinone recovered from DDQ oxidations can be readily reconverted to the quinone using the new process, it is obvious that DDQ now becomes a relatively economical dehydrogenating agent.

Experimental

A slurry of 2,3-dicyanohydroquinone (5 g., 0.031 mole) in water (35 g.) and concentrated hydrochloric acid (35 ml.) was treated over 45 min. with concentrated nitric acid (9.4 g. of 70%, 0.15 mole) at a temperature of 35 ± 3°. The mixture, which foamed initially, turned yellow. After all the nitric acid had been added, the yellow suspension was stirred for 1 hr., filtered, washed with carbon tetrachloride, and dried, yield 6.4 g. (90%), m.p. 212–213° (lit.[7] m.p. 213–215°). The infrared spectrum and elemental analysis were consistent with expectation. Reduction of DDQ with aqueous sodium bisulfite gave 2,3-dichloro-5,6-dicyanohydroquinone, mol. wt. 229.3 (calcd. 229).

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[1] J. Thiele and F. Günther, *Ann.* **349**, 45 (1906).

[2] E. A. Braude, A. G. Brook, and R. P. Linstead, *J. Chem. Soc.*, 3569 (1954).

[3] M. E. Peover, *ibid.*, 4540 (1962).

[4] L. M. Jackman, *Advan. Org. Chem.*, **2**, 329 (1960).

[5] "DDQ— Its Reactions and Uses," Arapahoe Chemicals, Inc., Boulder, Colo., 1964.

[6] A. G. Brook, *J. Chem. Soc.*, 5040 (1952).

[7] P. W. D. Mitchell, *Can. J. Chem.*, **41**, 550 (1963).

[8] L. Anderseh, *Finska Kemistsamfundets Medd.*, **70**, 31 (1961); *Chem. Abstr.*, **56**, 5383 (1962).

Carbon–Carbon Alkylations of Enamines with Mannich Bases

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Carbon–carbon bond formation by amine replacement has been the subject of extensive studies.[1] In comparison to the large number of reports on alkylation of substances which readily form anions, such as nitroalkanes, β-dicarbonyl compounds, etc., relatively few examples of the application of this method to the alkylations of simple ketones have been described. These have been carried out in the presence of a strong base, usually with a quaternary Mannich amine as the alkylating agent.[2] A useful modification has been reported by Gill, *et al.*,[3] who have effected β-acylethylations by thermal decomposition of a Mannich base in an excess of a suitable ketone.

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[1] For pertinent reviews, see (a) J. H. Brewster and E. L. Eliel, *Org. Reactions*, **7**, 99 (1953); (b) H. Hellmann and G. Opitz, "α-Aminoalkylierung," Verlag Chemie, Weinheim, 1960; (c) F. Möller (Houben–Weyl), "Methoden der Organischen Chemie," 4th Ed., Vol. 11, part 1, Georg Thieme Verlag, Stuttgart, 1957, p. 259; part 2, 1958, p. 207.

[2] (a) E. C. du Feu, F. J. McQuillin, and R. Robinson, *J. Chem. Soc.*, **53** (1937); (b) R. Robinson and F. Weygand, *ibid.*, 386 (1941); (c) F. D. Gunstone and R. M. Heggie, *ibid.*, 1437 (1952).

[3] N. S. Gill, K. B. James, F. Lions, and K. T. Potts, *J. Am. Chem. Soc.*, **74**, 4923 (1952).