The Oxidation of 4,5-Diphenyl-2-imidazolone

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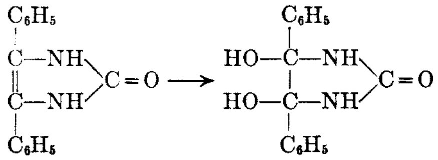
The sole practical method reported[1] for the oxidation of 4,5-diphenyl-2-imidazolone (I) to 4,5-diphenyl - 4,5 - dihydroxy - 2 - imidazolone (II) utilizes concentrated nitric acid as the oxidant.



I II

Numerous failures to duplicate this method indicated the lack of specific detail in the description of the synthetic method. It is essential that the nitric acid be cooled to 0° before addition to a slurry of I in glacial acetic acid at the same temperature. Addition of the acid at room temperature results in benzil or N,N′-dibenzoyl urea as the sole products isolable.

Cursory attempts to hydroxylate I using several catalyzed hydrogen peroxide reagents or performic acid resulted only in N,N′-dibenzoyl urea, benzil, or benzoic acid.

In view that the rather unusual nitric acid hydroxylation method may be applicable to other carbon-carbon double bonds with adjacent amide linkages where the customary hydroxylating reagents may fail it is deemed desirable to report the clarified reaction procedure.

EXPERIMENTAL[2]

4,5-Diphenyl-4,5-dihydroxy-2-imidazolone. A suspension of I[3] (2 g.) in 30 ml. of glacial acetic acid was chilled to a thick slurry with rapid stirring in an ice-bath at 0°. Concentrated nitric acid (2 ml.) was chilled to the same temperature and then was added dropwise to the slurry. As soon as a clear green solution formed 50 ml. of water was added in small portions and the mixture was stirred rapidly for 30 minutes. A fine precipitate formed which was filtered, dried, and then stirred twice with 30-ml. portions of a 1:3 ethanol–ether mixture to remove impurities. The yield was 0.99 g. (43%) of very small white crystals of II. After recrystallization from ethanol the white crystals turned yellow at 155° and partially fused with decomposition at 158–161° when heated at 6° per minute.[4] The product showed hydroxyl absorption at 2.95 μ in the infrared and rearranged to 5,5-diphenyl hydantoin upon refluxing for two hours with ethanolic potassium hydroxide.

Anal. Calc'd for $C_{15}H_{14}N_2O_3$: C, 66.65; H, 5.22; H, 10.36. Found: C, 66.79; H, 5.21; N, 10.22.

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[1] Biltz, *Ann.*, **368**, 173 (1907).

[2] M.p. is uncorrected and was obtained on a Fisher-Johns melting-point block. The microanalysis was performed by Schwarzkopf Microanalytical Laboratory, Woodside, New York.

[3] Corson and Freeborn, *Org. Syntheses*, **Coll. Vol. 2**, 231 (1950).

[4] Slow heating, *i.e.* 1–2° per minute resulted in yellowing at 155°, but no apparent fusion occurred.

Magnesium Bromide Catalysis in the Lithium Borohydride Reduction of Substituted Styrene Oxides

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Previous studies[1,2] on the reduction of substituted sytrene oxides with lithium borohydride demonstrated that electron-donating substituents favor the reaction at the benzyl carbon atom with formation of primary alcohols, and electron withdrawing substituents usually favor the formation secondary alcohols. A plot of log % primary alcohol *vs. sigma* is a straight line,[2] with the exception of the point representing *p*-nitrostyrene oxide.

All of the oxides are believed to react by S_N2 mechanisms, but a somewhat different transition state is probably involved in the reaction of *p*-nitrostyrene oxide. The negative *rho* value for the reaction suggests that the electron density at the benzyl carbon atom is lower in the transition state than in the initial molecule, a condition which is stabilized by electron-donating substituents. On the other hand, the *p*-nitrostyrene oxide molecule is somewhat electron-deficient at the benzyl carbon atom, facilitating C–H bond formation and inhibiting C–O bond rupture. In attaining the transition state there is an increase in electron density at the benzyl carbon atom. The extreme examples of such a mechanism involve preliminary addition of the nucleophile, and may occur with silicon halides, aryl halides, and, in some cases, acyl halides. The coordination number of the central atom is increased before halide ion departs.

From this transition state—substituent effect relationship one would predict that any factor further decreasing the electron density in the transition state should increase the reactivity of the benzyl carbon atom of *p*-methylstyrene oxide and decrease the reactivity of the benzyl carbon atom of *p*-nitrostyrene oxide. Experimentally, this has been realized by adding magnesium bromide as an electrophile. The opposite effect should be observed by increasing the nucleophilicity (or, pos-

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[1] Fuchs and VanderWerf, *J. Am. Chem. Soc.*, **76**, 1631 (1954).

[2] Fuchs, *J. Am. Chem. Soc.*, **78**, 5612 (1956).

sibly, the base strength) of the borohydride ion by the addition of triethylamine.[3]

Unfortunately, the latter premise could not be verified, because the produce of reduction of *p*-nitrostyrene oxide with lithium borohydride and triethylamine detonated during distillation.

Reduction of *p*-nitrostyrene oxide at room temperature in the presence of magnesium bromide afforded mixtures of the isomeric *p*-nitrophenylethanols which contained 16 and 7% 2-(*p*-nitrophenyl)ethanol. The product contained 62% of this component[1] in the absence of magnesium bromide. Reductions of *p*-methylstyrene oxide yield mixtures of the isomeric *p*-tolylethanols, which were 84 and 93% 2-(*p*-tolyl)ethanol in the presence of, and 67%[2] in the absence of magnesium bromide.

Other possible explanations of the change in product ratios will be considered. If magnesium borohydride were the reducing agent the steric requirement might be greater. This would lead to a smaller amount of attack at the benzyl atom of both oxides, which is not observed. A more serious consideration is the possible magnesium bromide-catalyzed isomerization[4] of *p*-methylstyrene oxide to *p*-tolylacetaldehyde, and of *p*-nitrostyrene oxide to *p*-nitroacetophenone, followed by borohydride reduction of the carbonyl compounds. Isomerization experiments with *p*-nitrostyrene oxide at room temperature in the absence of lithium borohydride yielded mainly non-distillable materials. At 0° the products were unchanged oxide and *p*-nitrostyrene bromohydrin. The latter compound was unaffected by treatment with lithium borohydride and magnesium bromide under the conditions used for the oxide. In the lithium borohydride–magnesium bromide reduction of the oxide little bromohydrin was formed, so the rates of the several possible reactions of *p*-nitrostyrene oxide are: reduction > bromide attack > isomerization. Isomerization cannot be an important influence on the product composition.

Treatment of *p*-methylstyrene oxide at 0° with magnesium bromide yielded an oil which polymerized when distillation was attempted at a bath temperature of 40° Partial isomerization to *p*-tolylacetaldehyde cannot be ruled out in the reduction with lithium borohydride and magnesium bromide, particularly in the light of the observation[5] that the reduction of styrene oxide with lithium aluminum deuteride and aluminum chloride gives 2-phenylethanol-1-*d*, presumably through phenylacetaldehyde as an intermediate.[6] The magnesium bromide used in the present study would be expected to be a less effective isomerization catalyst than aluminum chloride, but lithium borohydride is also a weaker reducing agent than lithium aluminum hydride. It is therefore, difficult to predict how the ratios of $k_{isomerization}/k_{reduction}$ should compare for the two reducing mixtures. It is probable that the ratio is larger for *p*-methylstyrene oxide than for *p*-nitrostyrene oxide.

Electrophilic catalysis probably causes the increased reactivity of sodium borohydride in the presence of aluminum chloride,[7] lithium halides,[3,8] and magnesium halides.[3] In all cases borohydride ion could be the reducing agent, which is, however, insufficiently nucleophilic to react with any but highly polarized carbonyl bonds, or bonds which are polarized by coordination of a metal cation or metal halide at the oxygen atom.

EXPERIMENTAL

Reduction of oxides. *p*-Nitrostyrene oxide[1] or *p*-methylstyrene oxide[2] (0.10 mole) was added to a solution of magnesium bromide[9] (0.05 mole) and lithium borohydride (0.20–0.25 mole) in ether at room temperature. The products were isolated and analyzed by the methods previously reported.[1,2] The yields were 75–80%, which included 17–20% of unchanged oxide in the experiments with *p*-nitrostyrene oxide.

Isomerization of p-nitrostyrene oxide. A mixture of 0.075 mole of oxide and 0.05 mole of magnesium bromide stood in ether solution for 2 hours at 0°. After hydrolysis with dilute acid, 8.8 g. of the oily product was distilled, giving 2.7 g. of oxide, m.p. 78–82°, 5.7 g. of *p*-nitrostyrene bromohydrin, and 0.4 g. of residue. Similar treatment of *p*-methylstyrene oxide yielded an oil which polymerized when low temperature distillation was attempted.

p-Nitrostyrene bromohydrin (214 mg.) was treated with lithium borohydride and magnesium bromide under the conditions used for the reduction of the oxides. The product (115 mg., 54%) had the same melting point as the original bromohydrin (80–84°) as had a mixture of the two.

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(3) Brown, Mead, and Subba Rao, *J. Am. Chem. Soc.*, **77**, 6209 (1955).

(4) The isomerization of styrene oxide to phenylacetaldehyde has been reported by Tiffeneau and Tchoubar, *Compt. rend.*, **207**, 918 (1938).

(5) Ernest L. Eliel, private communication.

(6) The reduction of a number of oxides with lithium aluminum hydride and aluminum chloride has been reported by Eliel and Delmonte, *J. Am. Chem. Soc.*, **78**, 3226 (1956).

(7) Brown and Subba Rao, *J. Am. Chem. Soc.*, **78**, 2582 (1956).

(8) Kollenitsch, Fuchs, and Gabor, *Nature*, **173**, 125 (1954).

(9) Prepared in ether solution from bromine and magnesium.

The Aconite Alkaloids. XXXIII. The Identity of γ-Oxodelphinine

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Early in the study of delphinine,[1] the action of hot, dilute nitrous acid upon this alkaloid was in-

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* Dr. Rathgeb's participation occurred in 1950–1951.

(1) W. A. Jacobs and S. W. Pelletier, *J. Am. Chem. Soc.*, **78**, 3542 (1956).