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THE ALKALI PHOSPHATE-CATALYZED EPOXIDATION AND OXIDATION BY A MIXTURE OF NITRILE AND HYDROGEN PEROXIDE

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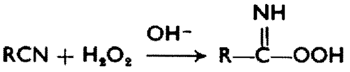
Abstract—The reaction of nitrile with alkaline hydrogen peroxide is inhibited almost completely by the presence of phosphate; therefore, the epoxidation of styrene in this mixture gives nearly a quantitative yield of epoxide on the basis of consumed peroxide. This oxidizing agent was used to epoxidize styrene and cyclohexene in the yield of 74–95% and to oxidize dimethylaniline to its N-oxide (73–78%) and aniline to azoxybenzene (71%).

It has been reported that nitrile and alkaline hydrogen peroxide form a peroxycarboimidic acid (I), which can be used as a strong oxidizing agent; e.g., olefins are converted to epoxides and even hydrogen peroxide itself to oxygen.[1,2] Although this method has the advantage of being effective under weakly alkaline conditions without the Baeyer–Villiger reaction,[2] the basicity of the reaction media must be controlled to ca. pH 8 with aqueous alkali[1] or potassium bicarbonate for the duration of the reaction time.[2] These difficulties may, however, be overcome by the addition of alkali phosphate to the mixture of nitrile and hydrogen peroxide.



$$RCN + H_2O_2 \xrightarrow{OH^-} R{-}\overset{\overset{\displaystyle NH}{\|}}{C}{-}OOH \qquad (1)$$

I

The epoxidation of styrene with a mixture of nitrile and hydrogen peroxide was examined in a 75% methanolic solution with various buffers and is summarized in Table 1. The reaction of nitrile with alkaline hydrogen peroxide alone[3,4] is retarded almost completely by the addition of phosphate (runs 3 and 14) and the yield of styrene oxide is almost quantitative on the basis of consumed peroxide (runs 1, 2 and 13), according to the stoichiometric equation:

$$RCN - H_2O_2 + C_6H_5CH{=}CH_2 \longrightarrow RCONH_2 + C_6H_6\underbrace{CH{-}CH_2}_{O} \qquad (2)$$

Acetonitrile is less reactive than benzonitrile (run 13).

On the other hand, the Radziszewski's reaction[4] ($RCN + 2H_2O_2 \rightarrow RCONH_2 + O_2 + H_2O$), with a borate buffer, results in a low yield of styrene oxide (runs 15 and 16) and similarly when ammonia–ammonium chloride is used as buffer except that the consumption of peroxide was ca. 1/5 (runs 19 and 20).

The addition of sodium phosphate suppresses the Radziszewski's reaction in an

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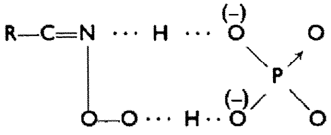
[1] G. B. Payne, P. H. Deming and P. H. Williams, *J. Org. Chem.* **26**, 659 (1961).

[2] G. B. Payne, *Tetrahedron* **18**, 763 (1962).

[3] K. B. Wiberg, *J. Amer. Chem. Soc.* **75**, 3961 (1953)

[4] B. Radziszewski, *Ber. Dtsch. Chem. Ges.* **17**, 1389 (1884).

ammonia–ammonium chloride buffer (run 21), but not in run 18 (borate buffer). The addition of sodium borate or boric acid to the phosphate buffer also reduces the effect of the phosphate (runs 10, 11 and 12), while sodium carbonate, sulfate and silicate have no effect (runs 7, 8 and 9). The action of phosphate may be explained by assuming the formation of a stable complex (II) between HPO_4^{2-} and I, but an unstable complex between I and H_3BO_3.[5]



II

However, when the water content in methanol is increased, the Radziszewski's reaction becomes apparent (runs 4, 5 and 6), suggesting a diminution in the interaction between phosphate and I. Therefore, methanol containing more than 35% water is not suitable for the epoxidation.

TABLE 1. THE REACTION OF BENZONITRILE WITH HYDROGEN PEROXIDE WITH OR WITHOUT STYRENE IN 75% METHANOL AT 40° FOR 5 HR; INITIAL CONC. $[C_6H_5CN] = [H_2O_2] = 0{\cdot}1M$

Run no.	Buffer composition	Added compd 0·0025M	$[C_6H_5CH{=}CH_2]$, M × 10^3	Consumed $[H_2O_2]$, M × 10^3	$\left[\underset{\diagdown O \diagup}{C_6H_5CH\text{—}CH_2}\right]$ / $[H_2O_2]$ %
1	KH_2PO_4—NaOH[a]	—	100	36·2	96·8
2		—	300	60·6	96·7
3		—	—	0·4	—
4		H_2O[d]	—	3·4	—
5		H_2O[e]	—	10·3	—
6		H_2O[f]	—	16·3	—
7		Na_2CO_3	—	1·9	—
8		Na_2SO_4	—	1·9	—
9		Na_2SiO_4	—	1·1	—
10		$Na_2B_4O_7$	—	45·3	—
11		$Na_2B_4O_7$	100	44·2	51·0
12		H_3BO_3	—	7·3	—
13		CH_3CN[g]	100	16·8	96·0
14		CH_3CN[g]	—	1·8	—
15	H_3BO_3—NaOH[b]	—	200	44·7	33·0
16		—	100	46·2	21·2
17		—	—	48·0	—
18		Na_2HPO_4	—	47·9	—
19	NH_4Cl—NH_4OH[c]	—	100	8·5	38·0
20		—	—	8·2	—
21		Na_2HPO_4	—	1·6	—
22		H_3BO_3	—	24·7	—

[a] A mixture of 0·2M KH_2PO_4–0·2N NaOH (4:5) (15 ml) was added to the reaction mixture (200 ml). The pH value observed in the absence of reactants was 11·35 and the addition of reactants decreased the value by ca. 0·5 pH unit, where the pH held constant during the reaction.

[b] 0·41M H_3BO_3–0·1N NaOH (1:1) (15 ml) was added to the reaction mixture (200 ml). Observed pH value was 9·02.

[c] 0·1M NH_4Cl–0·1N NH_4OH (1:2) (15 ml) was used, pH being 9·00.

[d,e,f] Reaction in 65%, 50% and 40% methanol, respectively.

[g] Acetonitrile was used in place of benzonitrile.

The results of the epoxidation of styrene and cyclohexane and the oxidation of aniline and dimethylaniline in the presence of alkali phosphate are summarized in Table 2.

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[5] Y. Ogata and Y. Sawaki, *Bull. Chem. Soc. Japan* **37**, in press (1964).

TABLE 2. PHOSPHATE CATALYZED EPOXIDATION AND OXIDATION WITH NITRILE AND HYDROGEN PEROXIDE

Oxidant	Substrate	Reaction		Yield (%)[a]	
		Temp (°C)	Time (hr)	Titrated[b]	Isolated
C_6H_5CN—H_2O_2	Cyclohexene	40	2	91	65
C_6H_5CN—H_2O_2	Styrene	50	2	95	—[c]
C_6H_5CN—H_2O_2	N,N-Dimethylaniline	30	1	—	73[d]
CH_3CN—H_2O_2	Cyclohexene	50	3	74	60
CH_3CN—H_2O_2	Styrene	50	3	82	76
CH_3CN—H_2O_2	N,N-Dimethylaniline	60	1	—	78[d]
CH_3CN—H_2O_2	Aniline	50	4	—	71[e]

[a] Yield based on the used substrate.

[b] Yield calculated from oxirane content by titrimetry.[6]

[c] No attempt was made to isolate styrene oxide, but benzamide (92%) was isolated.

[d] Dimethylaniline oxide picrate.

[e] Azoxybenzene.

The consumption of peroxide is over 90% and the epoxidation of styrene and cyclohexane using benzonitrile and hydrogen peroxide is complete in 2 hr. The titration for oxirane oxygen[6] also confirms a 90% yield of epoxide. In the case of acetonitrile, a longer reaction time is necessary and the yield of epoxide is lower.

The oxidation of dimethylaniline to its N-oxide is complete within 1 hr, the yield of picrate being 73–78%. Aniline may be oxidized to azoxybenzene in 71% yield.

EXPERIMENTAL

Materials. Commercial benzonitrile (b.p. 190–191°), acetonitrile (b.p. 83–84°), aniline (b.p. 185–186°), dimethylaniline (b.p. 192–193°) and styrene (b.p. 58° const. (35 mm)) were purified by fractional distillation. Cyclohexene was obtained from cyclohexanol,[7] b.p. 82·5–83·5. Hydrogen peroxide (30%), phosphate and other inorganic reagents were all of guaranteed grade.

Examination of the effect of phosphate catalyst. An aqueous buffer solution (15 ml; Table 1) was added to a 75 vol% methanolic solution (200 ml) containing 0·1M nitrile and 0·1M H_2O_2 and if necessary, styrene or other compounds were also added. The mixture was kept at 40° for 5 hr, then the concentration of peroxide determined iodometrically, and the content of epoxide estimated by the pyridinium chloride-chloroform method.[6]

Epoxidation of cyclohexene with benzonitrile–hydrogen peroxide. In a 300 ml 3-necked, round-bottom flask equipped with a mechanical stirrer, a reflux condenser and a thermometer, methanol (150 ml), cyclohexene (16·4 g, 0·20 mole), benzonitrile (25·8 g, 0·25 mole), 30% H_2O_2 (28·5 g, 0·25 mole), 0·1M Na_2HPO_4 aq (5 ml) and finally 0·5N NaOH aq (5 ml) were added. The mixture was stirred at 40° for 2 hr while 0·5N NaOH aq (4 × 5 ml) was added gradually. Titration indicated the consumption of 0·191 mole of peroxide and the presence of 0·182 mole of epoxide (91% based on olefin). The mixture was diluted with water (50 ml) and extracted with 3 × 50 ml portions of $CHCl_3$. The combined extract, after washing and drying, was distilled to give 13·0 g (65%) cyclohexene oxide, b.p. 57–58° (55 mm); n_D^{25} 1·4526 (lit.[1] b.p. 54–55° (50 mm); n_D^{20} 1·4525).

Epoxidation of styrene by benzonitrile–hydrogen peroxide. Styrene (20·8 g, 0·20 mole) was added in place of cyclohexene, and the reaction temp (50°), was raised up to 64° for the first 20 min. After working up, the titration indicated the conversion of 0·193 mole (97%) peroxide and the presence of 0·190 mole (95%) epoxide. No attempt was made to isolate the epoxy compound. Instead, the remaining H_2O_2 (0·057 mole) was decomposed with $Na_2S_2O_3$ and the mixture was concentrated

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[6] After extraction with $CHCl_3$, epoxide was determined by the pyridinium chloride–$CHCl_3$ method. See J. L. Jungnickel, E. D. Peters, A. Polgár and F. T. Weiss, *Organic Analysis* Vol. I, p. 136. Interscience, New York (1953).

[7] G. H. Coleman and H. F. Johnstone, *Organic Synthesis* Coll. Vol. I, p. 183. J. Wiley, New York (1948).

in vacuo, extracted with hot $CHCl_3$, filtered and condensed by evaporation. Dilution of the condensed filtrate with excess pet. ether caused benzamide (m.p. 126–127°, 22·4 g, 0·184 mole, 92%) to precipitate.

Epoxidation of cyclohexene by acetonitrile–hydrogen peroxide. Acetonitrile (10·3 g, 0·25 mole) was used at 50° and after 3 hr, titration indicated the conversion of 0·177 mole (89%) peroxide and the presence of 0·148 mole (74%) epoxide. Extraction and distillation gave 11·7 g (60%) cyclohexene oxide, b.p. 58–59° (58 mm); n_D^{25} 1·4522.

Epoxidation of styrene by acetonitrile–hydrogen peroxide. Epoxidation was started by the addition of 0·5N NaOH aq (5 ml) to a mixture of methanol (200 ml), styrene (41·6 g, 0·40 mole), acetonitrile (20·6 g, 0·50 mole), 30% H_2O_2 (57 g, 0·50 mole) and 0·1M Na_2HPO_4 aq (5 ml). The mixture was stirred at 50° for 3 hr during the gradual addition of 0·5N NaOH aq (6 × 5 ml). After the reaction, the consumed peroxide was estimated as 0·388 mole (97%) and the yield of epoxide 0·326 mole (82%). Extraction and distillation gave styrene oxide, 36·2 g (85% on the basis of consumed styrene), b.p. 86–87° (27 mm); n_D^{20} 1·5335 (lit.[1] b.p. 98–99° (35 mm); n_D^{20} 1·5348), styrene (5 g), b.p. 55–56° (27 mm), being recovered.

Oxidation of dimethylaniline with benzonitrile–hydrogen peroxide. A mixture of methanol (150 ml), dimethylaniline (12·1 g, 0·10 mole), benzonitrile (11·4 g, 0·11 mole), 30% H_2O_2 (12·5 g, 0·11 mole), 0·1M Na_2HPO_4 (5 ml) and 1N NaOH (5 ml) was stirred at 30° for 1 hr with an addition of 1N NaOH (5 ml) in 30 min. Iodometry indicated 90% conversion of peroxide. The mixture was condensed *in vacuo*; water (50 ml) was added and dimethylaniline extracted with ether. The aqueous layer was poured into a boiling aqueous solution of picric acid (23 g in 450 ml water) to precipitate 26·6 g (73%) dimethylaniline oxide picrate, m.p. 138–139° (lit.[8] m.p. 137–138°).

Oxidation of dimethylaniline by acetonitrile–hydrogen peroxide. Acetonitrile was used in place of benzonitrile at 60° according to the above procedure. The yield of N-oxide picrate was 28·5 g (78%), m.p. and mixture m.p. 137–138°.

Oxidation of aniline by acetonitrile–hydrogen peroxide. A mixture of methanol (150 ml), aniline (9·3 g, 0·10 mole), acetonitrile (20·5 g, 0·40 mole), 30% H_2O_2 (46·5 g, 0·46 mole) and 0·1M Na_2HPO_4 (5 ml) was stirred at 50° for 4 hr with the gradual addition of 1N NaOH (6 × 5 ml). After 4 hr, 0·45 mole of peroxide was consumed; the mixture diluted with water and extracted with benzene. The extract, after washing with dil. HCl and then water, dried and evaporated to dryness (8·6 g). Recrystallization from a small amount of pet. ether gave 7·0 g (71%) azoxybenzene, m.p. and mixture m.p. 35·3–35·5°.

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[8] E. Bamberger and F. Tschirner, *Ber. Dtsch. Chem. Ges.* **32**, 342 (1899).