

There are other indications in the literature that *o*-carboxyl and related substituents have a highly specific influence on reactions at aromatic side chains. For example in chloroform, bis-(*o*-iodobenzoyl) peroxide rearranges to a cyclic substance resembling compound A at a rate several thousand times as large as the dissociation rates of other *o*-substituted benzoyl peroxides.⁹ Also α -bromo-*o*-toluic acid and related compounds can be converted to phthalide with great ease.¹⁰ Furthermore it has been demonstrated neatly that *o*-carboxyl, or its anine, functions as an "internal" nucleophilic catalyst in the hydrolysis of phthamic acid, methyl hydrogen phthalate and related compounds.¹¹ This terminology might well be applied in the interpretation of the results of the present investigation.

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(11) (a) M. L. Bender, Y. Chow and F. Chloupek, *THIS JOURNAL*, **80**, 5380 (1958); (b) M. L. Bender, F. Chloupek and M. C. Neveu, *ibid.*, **80**, 5384 (1958); (c) M. L. Bender and M. C. Neveu, *ibid.*, **80**, 5388 (1958).

Electronically the activation process for solvolytic displacement reactions of benzyl halides and related compounds, which are presumed to react *via* benzylcarbonium ion intermediates,¹² is similar to that for dissociation of iodobenzene dichloride. One may anticipate, therefore, that an *o*-carboxyl substituent would greatly enhance the rates of solvolysis of α -substituted toluenes. There seems to be no quantitative kinetic evidence, pro or con, of such enhancement. (It is noteworthy that certain appropriate model compounds decompose rather readily to form phthalide.¹³) Accordingly, plans are now being made to investigate the kinetics of acetolysis of appropriately substituted benzyl tosylates.

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DAVIS, CALIF.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF PURDUE UNIVERSITY]

Alkylation of Nitroparaffins and Oximes with Epoxides¹

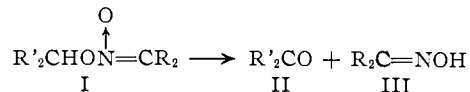
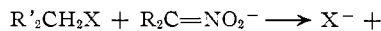
BY G. BRYANT BACHMAN AND TAKEO HOKAMA²

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The reactions of epoxides with nitroparaffin salts have been found to lead through O-alkylation to oximes and their β -hydroxyalkyl ethers. A number of these oxime ethers have been prepared and characterized.

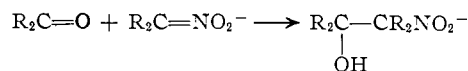
The nitronate ion is an "ambident anion"³ and may react with reagents such as alkyl halides at one of the oxygens of the nitro group (O-alkylation) or at the carbon attached to the nitro group (C-alkylation). Numerous workers have investigated the reactions of nitroparaffin salts with such alkylating agents as alkyl halides,⁴ alkyl sulfates,^{5,6} diazomethane,^{5,6} benzyltrimethylammonium iodides⁷ and various other onium salts.³

Except for a few special cases^{4a,4b,7} these reactions have generally resulted in O-alkylation. The nitronate esters (I) have been isolated in several cases^{4b,5,9} but usually they decompose during the reaction to form a carbonyl compound (II) and an oxime (III). The process has been used as a



method of oxidizing alkyl halides to aldehydes and ketones.¹⁰

In striking contrast to these results aldehydes and ketones give C-alkylation with nitronate anions.^{4c}



Since olefin oxides resemble aldehydes and ketones in many of their reactions it seemed reasonable to study the reaction of some typical olefin oxides with nitroparaffins in alkaline solution in the hope of achieving C-alkylations. However, instead of the hoped for γ -nitroalcohols which would result from C-alkylation, we obtained instead, oximes and oxime ethers, whose formation can be explained as resulting from the preliminary O-alkylation of the nitronate ion and the decomposition of this to a carbonyl compound and an oxime.

Since β -hydroxyalkyl ethers of oximes seem not to have been prepared previously, we synthesized a number of them for purposes of comparison by treating oximes with olefin oxides under basic conditions. The products so obtained corresponded

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(1) Abstracted from a thesis submitted by T. Hokama to the Faculty of the Graduate School of Purdue University in partial fulfillment of the requirements for the Ph.D. degree, August, 1958.

(2) American Cyanamid Fellow, 1957-1958.

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(4) (a) L. Weisler and R. W. Helmkamp, *ibid.*, **67**, 1167 (1945); (b) M. L. Bender and H. B. Hass, *ibid.*, **71**, 3842 (1949); prior literature on the alkylation of nitroparaffins may be found in the Ph.D. theses of L. Weisler, University of Illinois, and M. L. Bender, Purdue University; (c) H. B. Hass and E. F. Riley, *Chem. Revs.*, **32**, 406 (1943).

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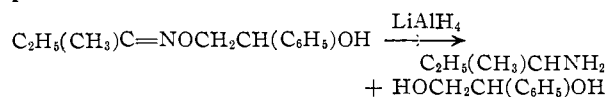
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TABLE II
 PROPERTIES AND ANALYSES OF OXIME ETHERS

Compound	B.p., (°C.) (mm.)	<i>d</i> ²⁰ ₄	<i>n</i> ²⁰ _D	3,5-Dinitrobenzoate, m.p., °C.	Formula	Carbon, %		Hydrogen, %		Nitrogen, %	
						Calcd.	Found	Calcd.	Found	Calcd.	Found
1 HOCH ₂ CH ₂ ON=C(CH ₃) ₂	38 (2)	1.019	1.4416	82	C ₁₁ H ₁₁ N ₃ O ₇	44.45	44.15	3.73	3.92	14.14	14.33
2 HOCH ₂ CH ₂ ON=C(CH ₃) ₂	54 (4)	0.9981	1.4488	102	C ₁₂ H ₁₃ N ₃ O ₇	46.30	46.39	4.21	4.35	13.50	13.67
3 HOCH ₂ CH ₂ ON=C(CH ₃)C ₂ H ₅	61 (4)	0.9754	1.4498	93	C ₁₃ H ₁₅ N ₃ O ₇	48.00	47.75	4.65	4.52	12.92	13.12
4 HOCH ₂ CH ₂ ON=C(CH ₃)C ₆ H ₅	114 (1)	1.0931	1.5545	93	C ₁₇ H ₁₅ N ₃ O ₇	54.92	54.69	4.05	4.16	11.26	11.48
5 HOCH ₂ CH ₂ ON=C(C ₆ H ₅) ₂	160 (1)	1.134	1.6036	94	C ₂₂ H ₁₇ N ₃ O ₇	60.69	60.37	3.94	3.83	9.65	9.75
6 CH ₃ CH(OH)CH ₂ ON=C(CH ₃) ₂	54 (2)	0.9633	1.4424	57 ^a	C ₁₂ H ₁₃ N ₃ O ₇	55.71	55.81	5.75	5.29	10.00	9.60
7 CH ₃ CH(OH)CH ₂ ON=C(CH ₃)C ₂ H ₅	62 (2)	.9449	1.4446	Oil	C ₇ H ₁₃ NO ₂	57.90	57.83	10.41	10.60	9.65	9.95
8 CH ₃ CH(OH)CH ₂ ON=CHC ₂ H ₅	53 (1)	.932	1.4426	Oil	C ₇ H ₁₃ NO ₂	57.90	57.63	10.41	10.41	9.65	9.69
9 CH ₃ CH(OH)CH ₂ ON=C(CH ₃)C ₆ H ₅	112 (1)	1.055	1.5412	104	C ₁₈ H ₁₇ N ₃ O ₇	55.81	56.04	4.42	4.70	10.83	11.00
10 CH ₃ CH(OH)CH ₂ ON=C(C ₆ H ₅) ₂	154 (1)	1.108	1.5866	114	C ₂₃ H ₁₉ N ₃ O ₇	61.47	61.78	4.26	4.50	9.35	9.53
11 C ₆ H ₅ CH(OH)CH ₂ ON=C(CH ₃) ₂	123 (1)	1.064	1.5262	^b	C ₁₁ H ₁₃ NO ₂	68.37	68.07	7.82	7.93	7.25	7.53
12 C ₆ H ₅ CH(OH)CH ₂ ON=C(CH ₃)C ₂ H ₅	132 (1)	1.041	1.5206	^b	C ₁₂ H ₁₇ NO ₂	69.54	69.78	8.27	8.46	6.76	7.24
13 C ₆ H ₅ CH(OH)CH ₂ ON=C(CH ₃)C ₆ H ₅	175 (1)	1.113	1.5873	^b	C ₁₈ H ₁₇ NO ₂	75.27	75.01	6.71	6.81	6.47	5.45
14 C ₆ H ₅ CH(OH)CH ₂ ON=C(C ₆ H ₅) ₂	213 (1)	^c	^c	^b	C ₂₁ H ₁₉ NO ₂	79.47	79.24	6.03	6.07	4.41	4.30

^a *p*-Nitrobenzoate derivative. ^b Did not form. ^c Exceedingly viscous.

reduction by lithium aluminum hydride to primary amines. Thus the 2-hydroxy-2-phenylethyl ether of butanone oxime gave styrene glycol and 2-butylamine (isolated as the benzoyl and benzenesulfonyl derivatives in 72% yield) as the only isolatable products. Moreover, salt formation was not ob-



served to occur upon treatment of the oxime ethers with gaseous hydrochloric acid in ether or with picric acid in benzene, reactions which are usually observed to take place readily with N-alkylated oximes¹³ (nitrones).

Experimental

These experiments illustrate the procedure employed.

2-Hydroxyethyl Ether of Acetone Oxime. Reaction of Ethylene Oxide with Lithium 2-Propanenitronate.—2-Nitropropane (45 g., 0.5 mole) was added in 0.5 hr. to a cooled solution of lithium ethoxide formed by treating lithium metal (3.45 g., 0.5 mole) with absolute ethanol, 300 ml., in a 500 ml., 3-necked flask equipped with stirrer, dropping funnel and reflux condenser protected with a sodium hydroxide tube. The dropping funnel then was replaced with a gas inlet tube extending to the bottom of the flask, and ethylene oxide (50 g., 1.1 moles) was introduced in 3 hr. at 50–60°. The mixture was stirred for an additional hour, cooled, and neutralized with acetic acid. The major portion of the solvent was removed by distillation at reduced pressure. The residue was taken up in a mixture of ether, 200 ml., and water, 100 ml., and the aqueous solution was extracted five times with ether (25-ml. portions). The ether solutions were combined, dried, and distilled. The 2-hydroxyethyl ether of acetone oxime, b.p. 54° (2–4 mm.), *n*²⁰_D 1.4488, 20 g. (27% of theoretical), was obtained.

The 3,5-dinitrobenzoate derivative, m.p. 102°, from petroleum ether, b.p. 65–67°, was prepared by the procedure of Brewster and Ciotti.¹⁴

2-Hydroxyethyl Ether of Acetophenone Oxime. Reaction of Ethylene Oxide with Acetophenone Oxime.—Acetophenone oxime (41 g., 0.3 mole) was added to a solution of lithium ethoxide formed by treating lithium metal (0.69 g., 0.1 mole) with ethanol, 200 ml., in a 500-ml., 3-necked flask equipped with a stirrer, condenser and a gas inlet tube extending to the bottom of the flask. Ethylene oxide (22 g., 0.5 mole) was introduced through the gas inlet tube in 1.25 hr. at 50–60°, and the reaction mixture was stirred for an additional 0.75 hr. The cooled solution was acidified with acetic acid (6 g., 0.1 mole) and worked up as above. The

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2-hydroxyethyl ether of acetophenone oxime, b.p. 114° (1 mm.), *n*²⁰_D 1.5545, 30.5 g. (57%), was isolated by fractional distillation.

2-Hydroxy-1-propyl Ether of Butanone Oxime. Reaction of Propylene Oxide with Sodium 2-Butanenitronate.—2-Nitrobutane (50 g., 0.5 mole) was added to a cooled solution of sodium ethoxide (0.4 mole) in ethanol, 300 ml. Propylene oxide (56 g., 1.0 mole) was added in 3 hr. to the solution at 50°, and the mixture was stirred for an additional 3 hr. The reaction mixture yielded the 2-hydroxy-1-propyl ether of butanone oxime, b.p. 62° (1–2 mm.), *n*²⁰_D 1.4446, 21 g. (29%).

2-Hydroxy-1-propyl Ether of Butyraldehyde Oxime. Reaction of Propylene Oxide with Butyraldehyde Oxime.—Propylene oxide (28 g., 0.5 mole) was added in 0.75 hr. to a solution of butyraldehyde oxime (43 g., 0.5 mole) and lithium ethoxide (0.1 mole) in ethanol, 200 ml., at 50°, and the reaction mixture was stirred for an additional 3.25 hr. 2-Hydroxy-1-propyl ether of butyraldehyde oxime, b.p. 53° (1 mm.), *n*²⁰_D 1.4426, 20 g. (28%), was isolated as before.

2-Hydroxy-2-phenylethyl Ether of Acetone Oxime. Reaction of Styrene Oxide with Acetone Oxime.—Styrene oxide (57 g., 0.48 mole) was added in 3 hr. to a refluxing solution of acetone oxime (36 g., 0.49 mole) and sodium ethoxide (0.2 mole) in ethanol, 200 ml., and the mixture was stirred for an additional 3 hr. The mixture yielded the 2-hydroxy-2-phenylethyl ether of acetone oxime, b.p. 121–125° (1 mm.), *n*²⁰_D 1.5262, 55 g. (60%).

Reduction of 2-Hydroxy-2-phenylethyl Ether of Butanone Oxime.—2-Hydroxy-2-phenylethyl ether of butanone oxime (4 g., 0.02 mole), diluted with ether, 10 ml., was added in 10 minutes to a suspension of lithium aluminum hydride, 3 g., in ether, 100 ml., in a 300-ml., 3-necked flask equipped with a stirrer, dropping funnel and reflux condenser protected with a drying tube. The mixture was refluxed for 3 hr., and the cooled mixture was treated successively with moist ether, 20 ml., 10% hydrochloric acid, 50 ml., and concentrated hydrochloric acid, 30 ml., and stirred for 2 hr. The ether layer was separated and the aqueous layer was extracted twice with ether (20-ml. portions). One-half of the aqueous solution was treated with benzoyl chloride, 2 g., and basified. N-(2-Butyl)-benzamide, m.p. 69–70°, 1.5 g. (70% yield), was isolated; lit.¹⁵ m.p. 70°. The other portion upon treatment with benzenesulfonyl chloride in alkaline medium gave N-(2-butyl)-benzenesulfonamide, m.p. 75–76°, 1.8 g. (72%); lit.¹⁶ m.p. 76–77°. Authentic samples of these derivatives were prepared for mixture melting point determinations. These showed no depression. The ether solution upon distillation gave styrene glycol, m.p. 67°, 1.4 g. (51%); lit.¹⁶ m.p. 65–66°.

LAFAYETTE, IND.

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