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 osubstituted benzoyl peroxides.⁹ Also α -bromo-otoluic 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 phthalamic 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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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.

Acknowledgment.—The authors are indebted to the National Science Foundation for a grant in support of this research.

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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

Received December 27, 1958

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.⁸

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

(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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method of oxidizing alkyl halides to ald ehydes and ketones. $^{\rm 10}$

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

$$R_2C = 0 + R_2C = NO_2^- \longrightarrow R_2C - CR_2NO_2^-$$

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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TABLE I

REACTIONS OF EPOXIDES WITH NITROPARAFFINS AND OXIMES											
	Epoxide ^a	Nitroparaffin or oxime	Baseb	Time, hr.	Тетр., °С.	Products	Vi el d, %				
1	Ethylene oxide	$CH_{3}CH(NO_{2})CH_{3}$	LiOC₂H₅	4	50 - 60	$HOCH_2CH_2ON = C(CH_3)_2$	27				
2	Ethylene oxide	$(CH_3)_2C = NOH$	NaOH	3	50	$HOCH_2CH_2ON = C(CH_3)_2$	31				
3	Ethylene oxide	$CH_3CH_2NO_2$	$LiOC_2H_5$	4	50 - 60	HOCH ₂ CH ₂ ON=CHCH ₃	7				
4	Ethylene oxide	$CH_3CH_2(CH_3)C = NOH$	NaOC₂H₅	3	50	$HOCH_2CH_2ON = C(CH_3)CH_2CH_3$	40				
5	Ethylene oxide	C ₆ H ₅ (CH ₃)C=NOH	LiOC ₂ H ₅	2	50 - 60	$HOCH_2CH_2ON = C(CH_3)C_6H_5$	57				
6	Ethylene oxide	(C ₆ H ₅)C=NOH	LiOC ₂ H ₅	2	50 - 60	$HOCH_2CH_2ON = C(C_6H_5)_2$	82				
$\overline{7}$	Propylene oxide	$CH_3CH(NO_2)CH_3$	LiOC₂H₅	6	50 - 60	$CH_3CH(OH)CH_2ON = C(CH_3)_2$	37				
8	Propylene oxide	$(CH_3)_2C = NOH$	$LiOC_2H_5$	6	50-60	$CH_2CH(OH)CH_2ON = C(CH_3)_2$	51				
9	Propylene oxide	$CH_3CH(NO_2)CH_2CH_3$	LiOC₂H₅	6	50 - 60	CH ₃ CH(OH)CH ₂ ON=C(CH ₃)CH ₂ CH ₃	39				
10	Propylene oxide	$CH_{3}CH_{2}(CH_{3})C = NOH$	$NaOC_2H_5$	5	50 - 60	$CH_3CH(OH)CH_2ON = C(CH_3)CH_2CH_3$	48				
11	Propylene oxide	CH ₃ CH ₂ CH ₂ CH=NOH	LiOC₂H₅	4	50–6 0	CH ₃ CH(OH)CH ₂ ON=CHCH ₂ CH ₂ CH ₃	28				
12	Styrene oxide	$(CH_3)_2C = NOH$	LiOC₂H₅	6	80	$C_6H_5CH(OH)CH_2ON=C(CH_3)_2$	60				
13	Styrene oxide	$C_2H_5(CH_3)C$ =NOH	LiOC₂H₅	6	80	$C_6H_5CH(OH)CH_2ON = C(CH_3)C_2H_5$	63				
	Styrene oxide	$C_2H_5(CH_3)C$ =NOH	NaOC₂H₅	6	80	$C_6H_5CH(OH)CH_2ON = C(CH_3)C_2H_5$	47				
14	Styrene oxide	C ₆ H ₅ CH=NOH	$NaOC_2H_5$	4	80	C ₆ H ₆ CH(OH)CH ₂ OH	82				
						C ₆ H ₅ CN	65				
15	Styrene oxide	$C_6H_5(CH_3)C$ mon	LiOC₂H₅	8	80	$C_6H_5CH(OH)CH_2ON=C(CH_3)C_6H_5$	63				
16	Styrene oxide	$(C_6H_5)_2C = NOH$	LiOC₂H₅	8	80	$C_6H_5CH(OH)CH_2ON=C(C_6H_5)_2$	72				
17	Styrene oxide	$CH_3CH_2CHNO_2CH_3$	LiOC₂H₅	3	60	$CH_3CH_2C(CH_3) = NOH$	57				
						C4H5COCH2OH	8				

^a A 2:1:1 mole ratio of epoxide, nitroparaffin and base was used except in reaction 14 where the mole ratio was 1:2:1 and in reaction 17 where the mole ratio was 2:2:1. A 1:1:0.1 mole ratio of epoxide, oxime and base was used. ^b The solvent used was ethanol except in reaction 2. ^c The solvent was water.

in all respects with those obtained from the nitroparaffin reactions. The by-products of these reactions, α -hydroxyaldehydes, were not usually isolated, but probably polymerized to form some of

$$\begin{array}{c} \mathbf{R'CH-CH_2 + R_2C=NO_2^- \longrightarrow} \\ \mathbf{O} \\ \begin{bmatrix} \mathbf{O} \\ \uparrow \\ \mathbf{O}^- \end{bmatrix} \xrightarrow{\mathbf{R}_2C=NO^-} \mathbf{R}_2C=NO^- \\ \mathbf{R'CH(CH_2ON=CR_2} \\ \uparrow \\ \mathbf{R'CH(OH)CH=O} \\ \mathbf{R}_2C=NO^- + C_2H_5OH \xrightarrow{\mathbf{C}} C_2H_5O^- + R_2C=NOH \\ \mathbf{R'CH-CH_2 + R_2C=NO^- \longrightarrow R_2C=NOCH_2CHR'O^-} \end{array}$$

 $\begin{array}{r} R_2C = \text{NOCH}_2\text{CHR'O}^- + C_2H_5\text{OH} \longrightarrow \\ R_2C = \text{NOCH}_2\text{CHR'OH} + C_2H_5\text{O}^- \end{array}$

the high boiling by-products noted in all cases. However, in the reaction of styrene oxide with 2nitrobutane, a small amount of α -hydroxyacetophenone (a rearrangement product of α -hydroxyphenylacetaldehyde) was isolated. The results of this investigation are summarized in Tables I and II.

Discussion of Results

The reactions of nitroparaffin salts with epoxides were first run in an aqueous medium using a 1:1 mole ratio of reactants, and oxime ethers were isolated as products in low yields (8-12%). No oxime ethers were isolated under similar conditions when the reactions were run in methanol. However, increased yields of oxime ethers (28-39%) were obtained by using an excess of the epoxide either in aqueous or alcoholic solution. Better yields of oxime ethers were obtained from lithium alkanenitronates than from sodium alkanenitronates under similar conditions. The ketoxime ethers were found to be reasonably stable compounds preparable in fair yields. The aldoxime ethers were less stable. Only a 28% yield of oxime ether was obtained from butyraldehyde oxime and propylene oxide while a 48% yield of ether was obtained from butanone oxime and the same epoxide. The product from styrene oxide and benzaldoxime decomposed during the reaction to styrene glycol and benzonitrile.

$$C_{\$}H_{5}CH = NOCH_{2}CHOHC_{6}H_{5} \longrightarrow$$

 $C_{6}H_{5}CN + HOCH_{2}CHOHC_{6}H_{5}$

This instability of the aldehyde oxime ethers doubtless explains why primary nitroparaffins react more poorly than secondary nitroparaffins with 1,2epoxides to give oxime ethers. The instability of aldehyde oxime ethers in alkaline media has been noted before. Thus Hauser and Vermillion¹¹ found that the methyl ethers of p-methoxybenzaldehyde oxime decomposed to give p-methoxybenzonitrile, p-methoxybenzamidine and methanol in the presence of potassium amide.

The oxime ethers from propylene and styrene oxides are assigned secondary alcohol structures because of the recognized tendency of such oxides to react at the primary carbon under alkaline conditions with nucleophilic agents of relatively weak acidity and large steric requirements.¹² The difficulty encountered in attempting to prepare 3,5dinitrobenzoates of the products from styrene oxide also suggests that the alcohol groups are secondary rather than primary.

The oxime derivatives were assigned the O- rather than the N-alkylated structure on the basis of their

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TABLE II

PROPERTIES AND ANALYSES OF OXIME ETHERS

2 5

		B.p., (°C.)		Dinitro- benzoate			Carbon. %		Hydrogen, %		Nitrogen %	
	Compound	(mm.)	d^{26} 4	$n^{20}D$	m.p., °C.	Formula	Calcd.	Found	Calcd.	Found	Calcd.	Found
1	HOCH_CH_ON=CHCH;	38 (2)	1.019	1.4416	82	C11H11N8O7	44.45	44.15	3.73	3.92	14.14	14.33
2	HOCH2CH2ON=C(CH3)2	54 (4)	0.9981	1.4488	102	C12H18N8O7	46.30	46.39	4.21	4.35	13.50	13.67
3	HOCH2CH3ON=C(CH3)C2H5	61 (4)	0.9754	1.4498	93	C13H15N3O7	48.00	47.75	4,65	4.52	12.92	13,12
4	HOCH2CH2ON=C(CH3)C6H5	114 (1)	1.0931	1.5545	93	C17H15N8O7	54.92	54.69	4.05	4.16	11.26	11.48
5	HOCH2CH2ON=C(C6H6);	160 (1)	1.134	1.6036	94	C22H17N3O7	60.69	60.37	3.94	3.83	9.65	9.75
6	CH3CH(OH)CH2ON=C(CH3)2	54 (2)	0.9633	1.4424	57^a	$C_{12}H_{16}N_2O_7$	55.71	55. 8 1	5.75	5.29	10.00	9.60
7	CH3CH(OH)CH2ON=C(CH3)C2H5	62 (2)	.9449	1.4446	Oil	$C_7H_{15}NO_2$	57.90	57.83	10.41	10.60	9.65	9.95
8	CH2CH(OH)CH2ON=CHC2H7	53 (1)	.932	1.4426	Oil	C7H16NO2	57.90	57,63	10.41	10.41	9.65	9.69
9	CH ₂ CH(OH)CH ₂ ON=C(CH ₃)C ₃ H ₄	112 (1)	1.055	1.5412	104	C18H17N3O7	55.81	56.04	4.42	4.70	10.83	11.00
10	$CH_{3}CH(OH)CH_{2}ON = C(C_{3}H_{4})_{3}$	154 (1)	1.108	1.5866	114	C22H19N2O7	61.47	61.78	4.26	4.50	9.35	9,53
11	CeH5CH(OH)CH2ON=C(CH2)2	123 (1)	1.064	1.5262	ь	C11H15NO2	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	ь	C12H17NO2	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	ь	C16H17NO2	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	Ъ	$C_{21}H_{19}NO_{2}$	79.47	79.24	6.03	6.07	4.41	4.30

• 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-

$$C_{2}H_{5}(CH_{3})C = NOCH_{2}CH(C_{6}H_{5})OH \xrightarrow{L1AIH_{4}} C_{2}H_{5}(CH_{3})CHN$$

H, + HOCH₂CH(C₆H₅)OH

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 hy-droxide 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^{29} 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} p 1.5545, 30.5 g. (57%), was isolated by fractional distillation.

2-Hydroxy-1-propyl Ether of Butanone Oxime. Reac-tion of Propylene Oxide with Sodium 2-Butanenitronate. tion of Propylene Oxide with Sodium 2-Butanenitronate.— 2-Nitrobutane (50 g., 0.5 mole) was added to a cooled solu-tion 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 addi-tional 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.), n²⁰D 1.4426, 20 g. (28%), was isolated as before.
2-Hydroxy-2-phenylethyl Ether of Acetone Oxime. Re-

action 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.), n²⁰D 1.5262, 55 g. (60%). **Reduction of 2-Hydroxy-2-phenylethyl Ether of Butanone** Oxime.—2-Hydroxy-2-phenylethyl ether of butanone ox-ime (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 pro-tected 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 con-centrated 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 1.5 g. (70%) yield), was isolated; ht.³⁰ m.p. 70°. The other portion upon treatment with benzenesulfonly 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°.

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