

on the steam-bath, cooled and made alkaline with 40% sodium hydroxide and extracted with ether. The ether extract was washed successively with water and dilute potassium carbonate solution and then dried over anhydrous potassium carbonate. The dried extract was evaporated on the steam-bath and the residual oil distilled *in vacuo* yielding 7 g. of product.

7-Methoxy-5-(β -diethylaminoethyl)-aminoquinoxaline was a yellow oil, b. p. (1 mm.) 165–168°, after purification through the picrate.

Anal. Calcd. for $C_{15}H_{22}N_4O$: C, 65.60; H, 8.10; N, 20.40. Found: C, 65.47; H, 8.19; N, 20.32.

Di-picrate from alcohol, recrystallized from acetone-ether; purple-red needles, m. p. 184–185°.

Anal. Calcd. for $C_{27}H_{28}N_{10}O_{16}$: C, 44.3; H, 3.85; N, 19.1. Found: C, 44.79; H, 3.80; N, 18.94.

7-Methoxy-5-(γ -diethylaminopropyl)-aminoquinoxaline, yellow oil, b. p. (5 mm.) 185–186°.

Anal. Calcd. for $C_{14}H_{24}ON_4$: C, 66.60; H, 8.42; N, 19.50. Found: C, 66.25; H, 8.54; N, 19.41.

Di-picrate recrystallized from acetone-ether, deep brownish-red needles, m. p. 174°.

Anal. Calcd. for $C_{28}H_{30}O_{15}N_{10}$: C, 45.00; H, 4.05; N, 18.80. Found: C, 44.87; H, 4.00; N, 18.60.

Summary

1. *p*-Diacetylaminophenol was nitrated with a mixture of nitric acid and acetic anhydride to give 3,5-dinitro-*p*-diacetylaminophenol in good yield.

2. 7-Methoxy-5-aminoquinoxaline was synthesized by condensing 3,4,5-triaminoanisole (prepared from 3,5-dinitro-4-aminoanisole by catalytic reduction) with glyoxal bisulfite in aqueous solution.

3. 7-Methoxy-5-(β -diethylaminoethyl)-aminoquinoxaline and 7-methoxy-5-(γ -diethylaminopropyl)-aminoquinoxaline were synthesized from 7-methoxy-5-(*p*-toluenesulfonyl)-aminoquinoxaline by condensing the potassium salt with the appropriate diethylaminoalkyl chloride and subsequent hydrolysis.

BROOKLYN, N. Y.

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Syntheses with Styrene Oxide

BY WILLIAM S. EMERSON

In contrast to ethylene oxide, styrene oxide has had practically no use as a synthetic intermediate. Tiffeneau^{1,2,3,4} examined several of its reactions and recently its behavior with the Grignard reagent has received some attention.^{5,6}

The fact that styrene oxide reacts with dimethylamine to give a quantitative yield of β -dimethylamino- α -phenylethyl alcohol³ suggested that it would be a valuable source of β -amino- α -phenylethyl alcohol derivatives. We have treated styrene oxide with four secondary amines and obtained the expected tertiary amino alcohols in 80–92% yields. The alternative route from styrene chlorohydrin, which was also tested, gave yields of 63–66% in three cases. Each of these amino alcohols was esterified as a check on the presence of the hydroxyl group. When styrene oxide was slowly added to an excess of each of four primary amines, 56–70% yields of the corresponding β -alkylamino- α -phenylethyl alcohols resulted. In the case of *n*-butylamine, a by-product, whose analysis suggested it might be 4-*n*-butyl-2,6-diphenylmorpholine, was also isolated. With ammonia, side reactions predominated, so that only 18% of β -amino- α -phenylethyl alcohol was obtained. Some 2,6-diphenylmorpholine was also isolated in this reaction. After the completion of our experimental work, our results were borne out by the subsequent publication of the reaction of styrene

oxide with ethylenediamine to give 60% of β -(β -aminoethyl)-amino- α -phenylethyl alcohol.⁷

In the presence of sulfuric or phosphoric acid, styrene oxide reacted vigorously with ethyl and *n*-butyl alcohols to give 47–57% yields of the corresponding β -alkoxy- α -phenylethyl alcohols. The identity of these compounds was proved by synthesis from styrene chlorohydrin, potassium hydroxide and the alcohol in question, a method which Tiffeneau had previously used with styrene iodohydrin.⁸ In the preparation from styrene oxide, a high boiling by-product, probably 2,6-diphenyldioxane contaminated with some of the 2,5-isomer, was always produced. Seven esters of these two alcohols and of β -methoxy- α -phenylethyl alcohol were prepared by standard methods.

When refluxed with an excess of an organic acid in toluene solution in the presence of *p*-toluenesulfonic acid, styrene oxide yielded diesters of styrene glycol. Three of these compounds were prepared and characterized.

The author is grateful to Dr. C. A. Thomas and Dr. C. A. Hochwalt for suggesting the study of these reactions and to Dr. Josef Heyd for the preparation of large quantities of styrene oxide.

Experimental

Styrene oxide was prepared from styrene through styrene bromohydrin essentially by the method of Read and Reid.⁹

Styrene Chlorohydrin.—In a 5-liter three-necked flask equipped with a mercury-sealed stirrer, reflux condenser, gas inlet and dropping funnel was placed 218 g. (2.1 moles)

(1) Fournneau and Tiffeneau, *Compt. rend.*, **140**, 1595 (1905).

(2) Tiffeneau, *Ann. chim.*, [8] **10**, 345 (1907).

(3) Tiffeneau and Fournneau, *Compt. rend.*, **146**, 697 (1908).

(4) Tiffeneau and Tchoubar, *ibid.*, **207**, 918 (1938).

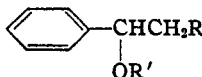
(5) Kharasch and Clapp, *J. Org. Chem.*, **3**, 355 (1938).

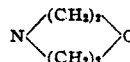
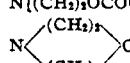
(6) Golumbic and Cottle, *THIS JOURNAL*, **61**, 996 (1939).

(7) Kitchen and Pollard, *J. Org. Chem.*, **8**, 342 (1943).

(8) Tiffeneau, *Compt. rend.*, **146**, 812 (1907).

(9) Read and Reid, *J. Chem. Soc.*, 1487 (1928).

TABLE I
COMPOUNDS PREPARED 

R	R'	Method of prepa. Yield, %	B. p., °C.	Mm.	n_D^{20}	d_{20}^{25}	Analyses, %				
							Calcd. C	H	Found C	H	
NH ₂	H	18	149-155	16 ^b				72.8	9.09	72.9	9.39
NHCH ₂ CH ₃	H	56	140-164	14 ^c							
NH(CH ₂) ₂ CH ₃	H	64	164-179	18 ^d							
NH(CH ₂) ₁₁ CH ₃	H	70	190-225	3 ^e				78.7	11.5	78.3	11.3
NH(CH ₂) ₂ OH	H	63	185-200	5 ^f				66.3	8.29	65.3	8.19
N(CH ₂ CH ₃) ₂	H	B 66	143-145	14	1.5101 ^g	0.984		74.6	9.85	74.8	9.89
N[(CH ₂) ₂ CH ₂] ₂	H	A 91	167-168	18	1.4970 (27°)	.948		76.0	10.4	76.6	10.7
N[(CH ₂) ₃ CH ₂] ₂	H	A 92	188-190	20	1.4961 (20°)	.938 (20°/25°)		77.1	10.84	78.0	10.87
N(C ₂ H ₅) ₂	H	B 63	192-195	14	1.4931	.935		78.0	11.2	77.7	10.8
N[(CH ₂) ₂ OH] ₂	H	{ B 63 A 89 }	218-222	3	1.5415	1.140		64.0	8.44	64.1	8.71
	H	A 80	183-198	18 ^h							
N(CH ₂ CH ₃) ₂	COCH(CH ₂ CH ₃)(CH ₂) ₂ CH ₃	D 53	193-195	14	1.4817	0.947		75.2	10.3	74.2	10.4
N[(CH ₂) ₂ CH ₂] ₂	CO(CH ₂) ₂ CH ₃	D 72	183-187	17	1.4829	.953		74.3	9.97	75.5	10.03
N[(CH ₂) ₃ CH ₂] ₂	COCH ₃	C 87	187-190	20	1.4821	.953		74.3	9.97	73.3	10.04
N(C ₂ H ₅) ₂	CO(CH ₂) ₂ CH ₃	D 54	177-180	2	1.4975	.952		76.5	10.8	76.8	10.5
N[(CH ₂) ₂ OCOCH ₃] ₂	COCH ₃	C 75	196-197	2	1.4925	1.129		61.5	7.12	60.7	7.12
	COCH ₂ CH ₃	D 77	188-192	14	1.5112	1.084		68.5	7.99	68.6	8.11
OCH ₃	H	E 61	128-131	18 ⁱ	1.5165 (26°)	1.070 ^j		71.1	7.90	70.7	7.85
OCH ₂ CH ₃	H	{ E 65 E ₁ 51 F 47 }	130.5-135.5	18	1.5109 ^k	1.037 ^k		72.3	8.58	72.3	8.79
O(CH ₂) ₂ CH ₃	H	{ E 52 F 57 }	155-158	18	1.5031	1.010		74.2	9.28	74.2	8.91
OCH ₃	COCH ₃	C 82	140-142	20	1.4985 (19°)	1.078 (19°/25°)	68.0	7.22	68.1	7.29	
OCH ₃	CO(CH ₂) ₂ CH ₃	D 55	175-177	18	1.4897 (24°)	1.010 (24°/25°)	72.0	8.80	72.8	8.60	
OCH ₂ CH ₃	COCH ₃	C 64	140-145	18	1.4900 (26°)	1.050		69.2	7.69	69.2	7.74
OCH ₂ CH ₃	CO(CH ₂) ₂ CH ₃	D 61	158-160	18	1.4828	1.020		71.2	8.48	70.5	8.29
OCH ₂ CH ₃	CO(CH ₂) ₁₀ CH ₃	D 32	205-213	4	1.4863	0.960		75.9	10.35	77.3	10.31
O(CH ₂) ₂ CH ₃	COCH ₃	C 79	158-160	18	1.4822	1.013		71.2	8.48	71.0	8.23
O(CH ₂) ₂ CH ₃	COCH ₃	D 51	175-177	2	1.5355 (23°)	1.071 (22°/25°)	76.5	7.39	75.9	7.30	
OCOCH ₂ CH ₃	COCH ₂ CH ₃	46	157-162	12	1.5013	1.110		67.2	7.20	67.0	7.01
OCO(CH ₂) ₂ CH ₃	CO(CH ₂) ₂ CH ₃		170-185	12	1.4917	1.062		69.1	7.92	69.4	7.77
OCO(CH ₂) ₁₀ CH ₃	CO(CH ₂) ₁₀ CH ₃		229-270	3 ^l				76.5	10.8	76.7	10.7
2,6-Diphenylmorpholine			170-185	3	1.5762 (26°)	1.097		80.4	7.12	80.1	7.19
4-n-Butyl-2,6-diphenylmorpholine			182-190	3	1.5532	1.040		81.4	8.49	80.2	8.44
Diphenyldioxane			207.5-210.5	18	1.5553 (24°)	1.100 (24°/25°)		80.0	6.67	79.7	7.06

^a All analyses are microanalyses performed by the Arlington Laboratories, Fairfax, Virginia. ^b Hess and Uibrig, *Ber.*, **48**, 1974 (1915), give b. p. 160° (17 mm.). ^c Crystallized twice from a benzene-hexane mixture, m. p. 76-78°. ^d Crystallized from hexane, m. p. 58-59°. Adams, Hyde and Browning, *THIS JOURNAL*, **50**, 2287 (1928), give the m. p. as 58-59°. ^e Crystallized twice from hexane, m. p. 74-75°. ^f Crystallized three times from benzene, m. p. 90-91°. ^g Marvel and du Vigneaud, *THIS JOURNAL*, **46**, 2093 (1924), give n_D^{20} 1.507. ^h Crystallized three times from a benzene-hexane mixture, m. p. 80-81°. Rubin and Day, *J. Org. Chem.*, **5**, 54 (1940), give m. p. 80.9-81.3°. ⁱ Tiffeneau, ref. 8, reported the b. p. as 132° (18 mm.) and d^0 as 1.080. ^k Tiffeneau, ref. 8, reported d^0 1.054. ^l Crystallized twice from alcohol, m. p. 33-34°.

of styrene, 1 g. of Santomerse No. 3 Paste (essentially an alkylbenzene sodium sulfonate) and 1.5 liters of water. While carbon dioxide was bubbled through the suspension with vigorous stirring at room temperature, a mixture of 260 g. (2.5 moles) of 70% HTH (calcium hypochlorite) and 1.5 liters of water was added over a seven-hour period. After seven and one-half hours, the mixture was filtered and the precipitate washed three times with benzene. These washings were combined with three benzene extracts of the filtrate and the entire solution distilled from a flask of at least 3-liters capacity. Because of severe foaming at the end of the distillation, an oversize flask is necessary to obtain a high yield. From four batches distilled together was obtained 953 g. (76%) of crude styrene chlorohydrin, b. p. 118-126° (14 mm.) (128° (17 mm.)),¹⁰ n_D^{20} 1.5520-1.5538.

(10) Deteouf, *Bull. soc. chim.*, [4] **31**, 169 (1922).

β -Amino- α -phenylethyl Alcohol.—A mixture of 48 g. (0.4 mole) of styrene oxide and 97 g. (1.6 moles) of ammonium hydroxide was heated in an autoclave at 90-125° for eight hours. After cooling, the mixture was removed from the bomb, the layers separated, and the aqueous portion twice extracted with benzene. The extracts were combined with the non-aqueous layer and distilled to give I, 17 g., b. p. 146-186° (12 mm.) and II, 16.5 g., b. p. 186° (12 mm.)-235° (4 mm.). Redistillation of fraction I yielded 10 g. of β -amino- α -phenylethyl alcohol, while a small quantity of 2,6-diphenylmorpholine was obtained from fraction II.

β -Alkylamino- α -phenylethyl Alcohols.—To 2 moles of the boiling primary amine (in the case of *n*-dodecylamine the temperature was 180°) 1.0 mole of styrene oxide was added over a two and one-half hour period. After boiling two hours longer, the mixture was distilled to isolate the

product. In the preparation of β -*n*-butylamino- α -phenylethyl alcohol further distillation yielded a small quantity of 4,*n*-butyl-2,6-diphenylmorpholine.

β -Dialkylamino- α -phenylethyl Alcohols.—Method A: A mixture of 0.2 mole of styrene oxide and 0.3 mole of the secondary amine was refluxed for four hours and then distilled to obtain the desired β -dialkylamino- α -phenylethyl alcohol.

Method B: An alternative procedure was to add 0.33 mole of styrene chlorohydrin over a one-half hour period to a boiling mixture of 0.33 mole of the secondary amine and 50 cc. of water containing 42 g. (0.5 mole) of sodium bicarbonate. After refluxing seven hours, the mixture was cooled and extracted with benzene. Distillation of the benzene extract yielded the desired β -dialkylamino- α -phenylethyl alcohol.

β -Dialkylamino- α -phenylethyl Esters.—Method C:¹¹ Acetates were prepared by refluxing the β -dialkylamino- α -phenylethyl alcohols with acetic anhydride containing sodium acetate.

Method D: Other esters were obtained by boiling a toluene solution of the amino alcohol and acid in question in the presence of *p*-toluenesulfonic acid, while the water was removed continuously by means of a Dean and Stark trap.

β -Alkoxy- α -phenylethyl Alcohols.—Method E: To a boiling solution of 20 g. (0.36 mole) of potassium hydroxide in 200 cc. of the corresponding alcohol was added 40 g. (0.26 mole) of styrene chlorohydrin over a five-minute period. After refluxing for one hour, the mixture was diluted with water, acidified with acetic acid and then extracted three times with benzene. Distillation of the combined benzene extracts yielded the desired β -alkoxy- α -phenylethyl alcohol.

Method E₁: β -Ethoxy- α -phenylethyl alcohol was also prepared in the same way from styrene bromohydrin.

Method F: An alternative procedure was to add 0.2

(11) Shriner and Fuson, "Identification of Organic Compounds," John Wiley and Sons, New York, N. Y., 1940, p. 137.

mole of styrene oxide over a fifteen minute period to 0.3 mole of the boiling alcohol containing 1 cc. of 85% phosphoric acid or two drops of concentrated sulfuric acid. After refluxing four more hours, the mixture was cooled, washed with enough aqueous sodium bicarbonate to neutralize the acid, and then distilled. In this case from 12 to 27% of diphenyldioxane was always isolated as a by-product.

β -Alkoxy- α -phenylethyl Esters.—These were prepared by the identical procedures (Methods C and D) used for the synthesis of the β -dialkylamino- α -phenylethyl esters.

Styrene Glycol Diesters.—A mixture of 0.2 mole of styrene oxide, 0.6 mole of the acid in question (0.4 mole in the case of lauric acid), 0.5 g. of *p*-toluenesulfonic acid and 100 cc. of toluene was refluxed eleven hours while the water was removed in a Dean and Stark trap. After cooling, it was washed with enough aqueous sodium bicarbonate to neutralize the sulfonic acid and then distilled to obtain the diester.

Compounds Prepared.—The methods of synthesis, physical properties and analyses of the compounds prepared are summarized in Table I.

Summary

Styrene oxide reacts with primary and secondary amines to give good yields of the corresponding β -alkylamino- or β -dialkylamino- α -phenylethyl alcohols.

In the presence of mineral acids it reacts with alcohols to give β -alkoxy- α -phenylethyl alcohols and with organic acids to give styrene glycol diesters.

Thirteen new esters of the β -dialkylamino- and β -alkoxy- α -phenylethyl alcohols have been prepared and characterized.

DAYTON, OHIO

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[CONTRIBUTION FROM THE CENTRAL RESEARCH DEPARTMENT, MONSANTO CHEMICAL COMPANY]

Vapor Phase Reactions of Styrene Chlorohydrin

BY WILLIAM S. EMERSON AND EDWARD P. AGNEW

When treated with steam in the presence of such widely different catalysts as alumina or calcium carbonate on silica, ethylene chlorohydrin has been reported to give acetaldehyde in good yield.¹ The same result has been effected with an aqueous suspension of magnesium oxide.² Similarly ethylene dichloride reacted with steam in the presence of a surface catalyst to give a mixture of acetaldehyde and vinyl chloride.³

Styrene chlorohydrin, $C_6H_5CHOHCH_2Cl$, was selected as a suitable unsymmetrical chlorohydrin for the detailed study of this type of reaction. In spite of the presence of steam the principal reaction of styrene chlorohydrin (I) over an acid catalyst, such as phosphoric acid on silica gel, was one of dehydration to yield β -chlorostyrene (II). This is in contrast to the reported reaction with acid in the liquid phase to give acetophenone,⁴

(1) Amos and Hooker, U. S. Patent 2,208,557; C. A., **35**, 135⁹ (1941).

(2) Ziese, U. S. Patent 2,245,377; C. A., **35**, 5907⁷ (1941).

(3) Amos, U. S. Patent 2,183,036; C. A., **34**, 1995³ (1940).

(4) Eberhardt and Stadler, U. S. Patent 2,246,299; C. A., **35**, 5914⁷ (1941).

and to the preparation of biacetyl by treating methyl vinyl ketone with hypochlorous acid and then mineral acid.⁴

In the presence of more neutral catalysts, such as silica skeleton, calcium carbonate on silica gel or sodium metaphosphate on silica gel, hydrolysis of styrene chlorohydrin predominated, although some dehydration still occurred, since the principal reaction product, phenylacetaldehyde (III), was always contaminated with some β -chlorostyrene (II). This reaction probably proceeds by much the same mechanism as the reaction of isobutylene with aqueous chlorine under pressure to produce isobutyraldehyde.⁵ The probable course of the styrene chlorohydrin reaction was hydrolysis to styrene glycol (V), followed by dehydration and rearrangement of this latter compound to phenylacetaldehyde. The postulated intermediate, styrene glycol, gave phenylacetaldehyde in good yield, under the nearly neutral conditions employed above, or, better, in the presence of an acid catalyst such as phosphoric acid on pumice.

(5) Kautter, U. S. Patent 2,060,086; C. A., **31**, 418⁴ (1937).