desiccator over sulfuric acid. The material was triturated with acetone, filtered, and placed in a vacuum desiccator over potassium hydroxide pellets. There was obtained 1.0 g. of a colorless solid, m.p. 105° dec.

Anal. Calcd. for $C_7H_{13}NO_4 \cdot HCl$: C, 39.72; H, 6.67; N, 6.62. Found: C, 39.81; H, 6.96; N, 6.82.

KALAMAZOO, MICHIGAN

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF THE UPJOHN CO.]

Some Reactions of Glycidaldehyde Diethylacetal

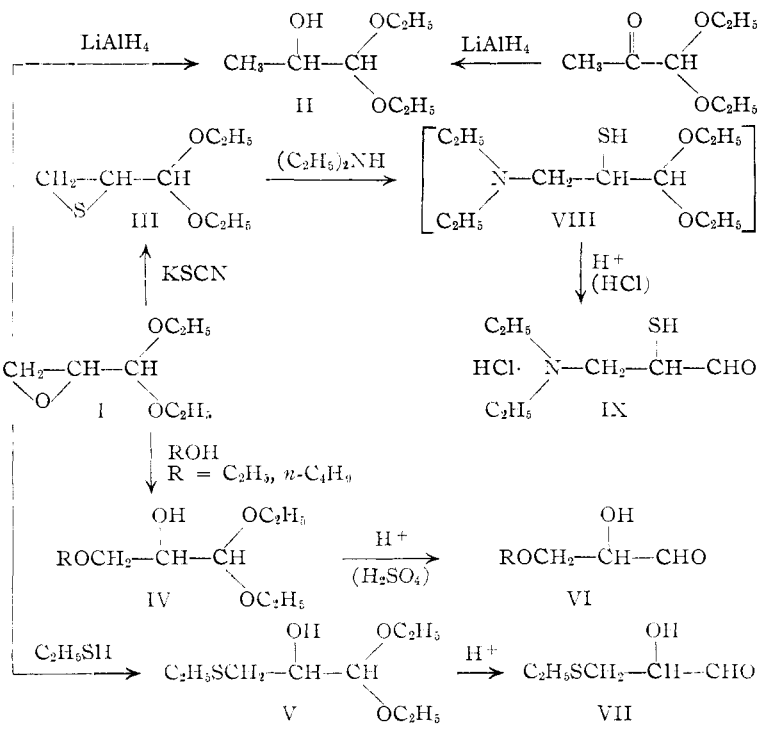
BY JOHN B. WRIGHT

RECEIVED JUNE 12, 1956

Glycidaldehyde diethylacetal (I) was found to react readily with lithium aluminum hydride, alcohols and mercaptans (ethyl mercaptan) with opening of the oxirane ring. Treatment with potassium thiocyanate gave thioglycidaldehyde diethyl acetal (III). The latter substance with diethylamine gave β-diethylamino-α-mercaptopropionaldehyde diethylacetal. The acetals obtained in this reaction were cleaved with acid to the corresponding aldehydes.

Glycidaldehyde diethylacetal (I) is a highly versatile intermediate that may be prepared readily in good yield from acrolein diethylacetal.[1] In the previous paper[2] are reported the reactions of various amines with this compound. In this paper we wish to report some additional studies on the chemistry of this substance.

Reduction of glycidaldehyde diethylacetal with lithium aluminum hydride gave lactaldehyde diethylacetal (II) in excellent yield.



The infrared spectrum of this substance was identical with that of the product from the reduction of pyruvaldehyde diethylacetal, indicating that the opening of the oxirane ring with lithium aluminum hydride proceeded in a manner to give a secondary hydroxyl group.

Treatment of glycidaldehyde diethylacetal with potassium thiocyanate[3] gave thioglycidaldehyde diethyl acetal (III) in good yield. Reaction with alcohols and with mercaptans (ethyl mercaptan) gave the corresponding β-alkoxylactaldehyde diethylacetals (IV) and β-ethylmercaptolactaldehyde diethylacetal (V), respectively. The latter reactions were carried out using methods identical to those that have been used with propylene oxide and in which the oxirane ring is known to open in such a manner as to give a secondary hydroxyl group. The structure of these compounds is assigned on the basis of this analogy with propylene oxide. The acetals IV and V were cleaved with acid to give the corresponding β-alkoxylacetaldehydes VI and β-ethylmercaptolactaldehyde (VII), respectively.

Thioglycidaldehyde diethyl acetal (III) reacted with diethylamine to give a compound thought to be the aminomercaptan VIII. However, when this compound was subjected to distillation under reduced pressure only thioglycidaldehyde diethyl acetal was isolated, indicating that diethylamine is probably split out readily from this compound. Treatment of crude undistilled VIII with dilute hydrochloric acid gave β-diethylamino-α-mercaptopropionaldehyde hydrochloride (IX).

Infrared spectra of the aldehydes VI, VII and IX indicated that these compounds contain no carbonyl group and hence probably exist in a dimeric (or polymeric) form. Lactaldehyde is reported[4] to exist in a similar dimeric form.

The aldehydes VI, VII and IX were tested for their antiviral activity. The results[5] of these tests are indicated in Table I.

Acknowledgments.—We wish to thank Dr. James L. Johnson and his associates for the infra-

(1) D. I. Weisblat, *et al.*, THIS JOURNAL, **75**, 5895 (1953).

(2) J. B. Wright, E. H. Lincoln and R. V. Heinzelman, *ibid.*, **79**, 1690 (1957).

(3) (a) J. M. Stewart and H. P. Cordts, *ibid.*, **74**, 5880 (1952); (b) H. R. Snyder, J. M. Stewart and J. B. Ziegler, *ibid.*, **69**, 2672 (1947).

(4) A. Wohl, *Ber.*, **41**, 3599 (1908).

(5) For these results we are indebted to the Staff of our Department of Infectious Diseases.

TABLE I

ANTIVIRAL ACTIVITY

	Compound	Virus: Newcastle (N.J.K.D.)	Virus: Influenza (PR-8)
1	$C_2H_5OCH_2CHOHCHO$ (VI)	+[a]	+[a]
2	$C_4H_9OCH_2CHOHCHO$ (VI)	−[b]	[c]
3	$C_2H_5SCH_2CHOHCHO$ (VII)	−[b]	[c]
4	$HCl\cdot(C_2H_5)_2NCH_2\underset{\displaystyle SH}{\underset{\vert}{C}}HCHO$ (IX)	++	+

[a] ++ = >50% survivors, + = 10–50% survivors, − = <10% survivors when tested in 11-day embryonated eggs. [b] The low activity of this compound possibly is due to its low solubility in water. [c] Not tested as yet.

red data reported, Mr. William A. Struck and his associates for the microanalyical data, and Mr. Arthur Barton for technical assistance. We wish to thank Dr. McLimans[6] and his associates for the antiviral data reported.

Experimental

Lactaldehyde Diethylacetal (from Glycidaldehyde Diethylacetal).—A mixture of 9.5 g. (0.287 mole) of lithium aluminum hydride in 200 ml. of anhydrous ether was heated under reflux for 1 hour. To the stirred mixture was then added very slowly 51.0 g. (0.35 mole) of glycidaldehyde diethylacetal. A vigorous reaction took place immediately. When addition of the acetal was completed the mixture was heated under reflux for 1 hour and then hydrolyzed by adding 10 ml. of water, 7.5 ml. of 20% sodium hydroxide solution and 35 ml. of water in succession. The mixture was diluted with an additional 300 ml. of ether, filtered, and the white solid washed well with ether. The ethereal filtrate was dried over anhydrous magnesium sulfate, the ether removed and the residue distilled under reduced pressure through a short column. There was obtained 43.5 g. (84%) of a colorless liquid boiling at 63° (13 mm.), $n^{20}D$ 1.4132. Infrared spectral analysis indicated strong hydroxyl absorption.

Lactaldehyde Diethylacetal (from Pyruvaldehyde Diethylacetal).—To a stirred suspension of 17.9 g. (0.471 mole) of lithium aluminum hydride in 300 ml. of anhydrous ether was added dropwise a solution of 68.9 g. (0.472 mole) of pyruvaldehyde diethylacetal in 50 ml. of anhydrous ether.

After standing overnight the mixture was cautiously decomposed by successive addition of 19 ml. of water, 14.1 ml. of a 20% sodium hydroxide solution and 61 ml. of water. The mixture was stirred thoroughly, the ether was decanted from the inorganic residue and the residue washed with ether. The ethereal extracts were dried and worked up as described above. The infrared spectrum of the product was identical to that obtained above (from glycidaldehyde diethylacetal).

Thioglycidaldehyde Diethylacetal.—To a solution of 97.0 g. (1.0 mole) of potassium thiocyanate in 100 ml. of water was added 146 g. (1.0 mole) of glycidaldehyde diethylacetal and 20 ml. of ethanol with vigorous stirring. Upon continued stirring the solution soon became turbid with the separation of two layers and the temperature rose to 32°. Stirring was continued for 18 hours.

The liquid material was decanted from the small amount of solid present, saturated with salt and extracted[7] with 400 ml. of ether. The ether was removed through a short column. An additional 50 g. of potassium thiocyanate dissolved in 100 ml. of water was added to the residue, and the resulting mixture was stirred vigorously for 18 hours. The mixture was worked up as described above, the ether extracts were dried over anhydrous sodium sulfate, the ether removed, and the residue distilled under reduced pressure giving 92.1 g. (57%) of a colorless liquid boiling at 84° (14 mm.), $n^{20}D$ 1.4613.

Anal. Calcd. for $C_7H_{14}O_2S$: S, 19.73. Found: S, 19.80.

β-Diethylamino-α-mercaptopropionaldehyde Hydrochloride.—A solution of 8.1 g. (0.05 mole) of thioglycidaldehyde diethylacetal and 3.66 g. (0.05 mole) of diethylamine was heated for 45 min. under reflux and then the excess diethylamine was allowed to distil away. The light yellow solution[8] was cooled to room temperature and dissolved in 33 ml. of 4 *N* hydrochloric acid whereupon the temperature rose spontaneously to 51°. After standing overnight under nitrogen the solution was concentrated under reduced pressure from a water-bath at 60°. The yellow viscous residue was triturated with acetone, then with ether, and finally the ether was replaced with anhydrous ethanol and the mixture brought to the boiling point. A fine white solid separated. This was filtered and washed with anhydrous ether, wt., 1.1 g., m.p. 148–150° dec. Infrared analysis indicated that the substance exists in the dimeric or polymeric modification.

Anal. Calcd. for $C_7H_{15}NOS\cdot HCl$: C, 42.52; H, 8.16; Cl, 17.93; N, 7.09. Found: C, 42.15; H, 7.96; Cl, 17.80; N, 7.26.

β-Ethoxylactaldehyde Diethylacetal.—The procedure used was essentially that of Chitwood and Freure[9] for the preparation of β-ethoxy-2-propanol from ethanol and propylene oxide.

To a stirred and refluxing solution of 1.0 g. of sodium hydroxide in 230 g. (291 ml., 5 moles) of commercial anhydrous ethanol was added dropwise during 1 hour 146 g. (1 mole) of glycidaldehyde diethylacetal. The solution was heated under reflux for 4 hours, the excess ethanol was removed under reduced pressure, and the residue distilled. There was obtained 134.6 g. (70%) of a colorless liquid boiling at 106° (14 mm.), together with an appreciable amount of higher boiling material, $n^{20}D$ 1.4230.

Anal. Calcd. for $C_9H_{20}O_4$: C, 56.22; H, 10.49. Found: C, 56.38; H, 10.25.

β-Ethoxylactaldehyde.—A solution of 40.32 g. (0.21 mole) of β-ethoxylactaldehyde diethylacetal in 300 ml. of 0.1 *N* sulfuric acid was kept at room temperature for 8 days. The acid was neutralized with 0.35 *N* barium hydroxide solution. Super-Cel was added and the precipitated barium sulfate removed by filtration. The colorless filtrate was concentrated under reduced pressure (15 mm.) from a water-bath at 35–40°. The colorless viscous residue was stored in a vacuum desiccator over concentrated sulfuric acid; however, the material did not crystallize on long standing. Infrared analysis indicated that the material exists in the dimeric or polymeric form.

Anal. Calcd. for $C_5H_{10}O_3$: C, 50.83; H, 8.53. Found: C, 50.84; H, 8.50.

β-*n*-Butoxylactaldehyde Diethylacetal.—The procedure for the β-ethoxylactaldehyde diethylacetal was modified in that the temperature was 100° (water-bath) and 1-butanol was used. There was obtained 101.2 g. (46%) of a colorless liquid boiling at 92–96° (1.2 mm.), $n^{20}D$ 1.4281.

Anal. Calcd. for $C_{11}H_{24}O_4$: C, 59.97; H, 10.98. Found: C, 60.00; H, 10.65.

β-*n*-Butoxylactaldehyde.—The procedure for β-ethoxylactaldehyde was used. Sufficient dioxane (188 ml.) was added to obtain a homogeneous solution and the solution was allowed to stand for 12 days. The product, after 2 weeks in a vacuum desiccator over sulfuric acid, partially solidified and upon trituration with acetone gave 11 g. (34%) of a white solid, m.p. 70–71°.

Anal. Calcd. for $C_7H_{14}O_3$: C, 57.51; H, 9.65. Found: C, 57.27; H, 9.57.

β-Ethylmercaptolacetaldehyde Diethylacetal.—To a stirred ice-cold solution of a small excess of ethyl mercaptan in a solution of 28 g. (0.05 mole) of potassium hydroxide in 300 ml. of 80% ethanol was added dropwise during about 0.5 hour, 73 g. (0.5 mole) of glycidaldehyde diethyl acetal. After standing overnight without cooling, the solution was concentrated under reduced pressure at about room temperature. To the residue was added 250 ml. of water and the resulting mixture was extracted three times with 300-ml. portions of ether. The ethereal extracts were dried over anhydrous magnesium sulfate, the ether removed and the residue distilled under reduced pressure giving 91.1 g.

(6) Wistar Institute, Philadelphia, Penna.

(7) Very troublesome emulsions formed.

(8) When this solution was subjected to fractional distillation *in vacuo* the only product isolated was thioglycidaldehyde diethyl acetal, evidently formed by the splitting out of diethylamine from the molecule.

(9) H. C. Chitwood and B. T. Freure, THIS JOURNAL, **68**, 680 (1946).

(88%) of a colorless liquid boiling at 132.5–133° (13 mm.), $n^{20}D$ 1.4623.

Anal. Calcd. for $C_9H_{20}O_3S$: S, 15.37. Found: S, 15.45.

β-Ethylmercaptolactaldehyde.—To 21.8 g. (0.105 mole) of β-ethylmercaptolactaldehyde diethylacetal was added 150 ml. of 0.1 *N* sulfuric acid and enough dioxane (100 ml.) to form a homogeneous solution which was allowed to stand for 10 days. The solution was exactly neutralized with 0.35 *N* barium hydroxide solution and the filtrate was concentrated under reduced pressure from a water-bath at about 40°. The residue was diluted with 300 ml. of water and extracted with ether. The ethereal extracts were dried over anhydrous magnesium sulfate and the ether removed, the last traces under reduced pressure. The semi-solid residue was triturated with *n*-hexane, filtered and recrystallized from methyl ethyl ketone. Additional material was obtained from the mother liquors by concentration and dilution with *n*-hexane for a total of about 1.0 g. of a colorless solid, m.p. 114.5° (cor.). Infrared analysis indicated that the material exists in the dimeric or polymeric form.

Anal. Calcd. for $C_6H_{10}O_2S$: C, 44.77; H, 7.52; S, 23.86. Found: C, 44.97; H, 7.55; S, 23.96.

KALAMAZOO, MICHIGAN

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING, STANFORD UNIVERSITY]

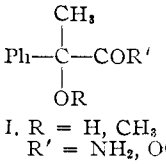
The Stereochemistry of Raney Nickel Action. VIII. Carbon–Carbon Bond Hydrogenolyses Catalyzed by Raney Nickel[1]

BY JOHN A. ZDERIC, WILLIAM A. BONNER AND THOMAS W. GREENLEE[2]

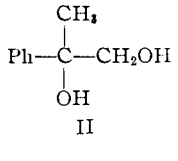
RECEIVED AUGUST 13, 1956

On treatment with Raney nickel in refluxing ethanol (reductive desulfuration conditions) 2-phenyl-1,2-propanediol (II) yields primarily ethylbenzene instead of the anticipated 2-phenyl-1-propanol. The main reaction thus involves carbon–carbon hydrogenolysis between C_1–C_2 of the aliphatic chain. Since reductive desulfuration is an important tool in degradative structure determination, we have investigated the carbon cleavage potentialities of 19 compounds related to II, characterizing the reaction products with the aid of vapor–liquid partition chromatography and infrared spectrophotometry. Our results permit us to conclude that the principal structural requirement for carbon–carbon hydrogenolysis is a hydroxyl or aldehyde function on a primary carbon adjacent to a carbon bearing an aromatic nucleus. In molecules where these structural features were absent, carbon–carbon hydrogenolysis failed to occur, or did so only insignificantly.

Catalytic hydrogenolyses resulting in dehydroxylation[3,4] and demethoxylation[4] have been studied recently from a stereochemical viewpoint in the 2-phenyl-2-hydroxypropionic acid series, I. Such



I. R = H, CH_3
R′ = NH_2, OCH_3



II

hydrogenolyses occurred with predominant retention of stereochemical configuration, an observation which was rationalized[4] by the postulation of a stereospecifically adsorbed carbonium ion intermediate. In order to assess what effect the unsaturation electrons of the carboxamide or carbalkoxyl functions in I had on determining the observed stereochemical consequences of such dehydroxylations and dealkoxylations, we recently undertook a similar study of the optically active reduced analog of I, 2-phenyl-1,2-propanediol (II), and related compounds.

When II was heated in refluxing ethanol with an excess of Raney nickel the anticipated dehydroxylation product, 2-phenyl-1-propanol, was not obtained. Instead, a hydroxyl-free oil resulted. Rectification of this oil followed by formation of a solid derivative proved the main product to be ethylbenzene. Subsequent examination of the crude hydrocarbon product with the aid of vapor–liquid partition chromatography indicated that the product was a mixture of ethylbenzene containing smaller amounts of isopropylbenzene. Traces of the anticipated 2-phenyl-1-propanol were only occasionally noted in the residues from the hydrocarbon isolation.

The main reaction thus occurring during Raney nickel treatment of II was thus one of carbon–carbon bond cleavage, presumably between carbon-1 and carbon-2 of the diol II, and probably involving the intermediate formation of 2-phenyl-1-propanol (*cf.* Table I). While such catalytic

TABLE I

PRODUCTS OBTAINED BY ACTION OF RANEY NICKEL ON VARIOUS ALCOHOLS AND RELATED COMPOUNDS UNDER REDUCTIVE DESULFURATION CONDITIONS

No.	Reactant	Products[a,b]
1	$PhC(CH_3)(OH)CH_2OH$	$PhCH(CH_3)CH_2OH$, *$PhCH_2CH_3$*(2), $PhCH(CH_3)_2$(1)
2	$PhCH(CH_3)CH_2OH$	*$PhCH_2CH_3$*(10), $PhCH(CH_3)_2$(1)
3	$PhCH(CH_3)CH{=}O$	*$PhCH_2CH_3$*(10), $PhCH(CH_3)_2$(1)
4	$PhCH(CH_3)CH_2OCH_3$	Starting material
5	$PhCH_2CH_2OH$	*$PhCH_3$* (1), $PhCH_2CH_3$(2)
6	$Ph_2CH{-}CH_2OH$	*$C_6H_{11}{-}CH_2{-}Ph$*, Ph_2CHCH_3
7	$PhC(OH)(CH_3)_2$	$PhCH(CH_3)_2$
8	$PhCH(CH_3)_2$	Starting material
9	$Ph_2C(OH)CH_3$	Ph_2CHCH_3
10	$Ph_2CHCH(OH)Ph$	Ph_2CHCH_2Ph
11	$PhCH_2CH(OH)CH_3$	$PhCH_2CH_2CH_3$
12	$PhCH(CH_3)CH(OH)CH_3$	$PhCH(CH_3)CH_2CH_3$[c,d]
13	$PhCH_2C(OH)(CH_3)_2$	$PhCH_2CH(CH_3)_2$[c,d]
14	$PhCH_2CH_2CH_2OH$	$C_6H_{11}{-}CH_2CH_2CH_2OH$[c]
15	$C_6H_{11}CH_2CH_2OH$	Starting material[c]
16	$CH_3(CH_2)_6CH_2OH$	Starting material
17	2-(1-Pyridyl)-ethanol	*1-Picoline* (2,5), by-product(1)[e]
18	$PhCH_2CH_2NH_2$	*$PhCH_3$*(1), $PhCH_2CH_3$(23)
19	$PhCH_2CH_2Cl$	$PhCH_2CH_3$
20	$PhCH_2CH_2Br$	$PhCH_2CH_3$

[a] Cleavage products are italicized. [b] Numbers in parentheses give approximate product ratios. [c] Plus traces of cleavage products; *cf.* Experimental. [d] Plus small amounts of unreacted starting material. [e] Unidentified.

(1) We gratefully acknowledge support of a portion of this research by the Petroleum Research Fund Advisory Board.

(2) Graduate Fellow Under the American Chemical Society Petroleum Research Fund.

(3) W. A. Bonner, J. A. Zderic and G. Casaletto, THIS JOURNAL, **74**, 5086 (1952).

(4) W. A. Bonner and J. A. Zderic, *ibid.*, **78**, 3218 (1956).