TABLE I

2-Oxomorpholinium Salts (II)

R_1, R_2	R_3	X	Yield, %	M.P., °C.	Analysis
C_2H_5,C_2H_5	H	Cl	95	204.5–205	Calcd. for $C_8H_{16}ClNO_2$: C, 49.74; H, 8.29; N, 7.25; Cl, 18.31. Found: C, 49.53; H, 8.37; N, 7.23; Cl, 18.70
C_2H_5, C_2H_5	H	Br	94	226–227 dec.	Calcd. for $C_8H_{16}BrNO_2$: Br, 33.60. Found: Br, 33.92
CH_3, CH_3	CH_3	Cl	80	242 dec.	Calcd. for $C_7H_{14}ClNO_2$: C, 46.92; H, 7.82; N, 7.82; Cl, 19.55. Found: C, 46.99; H, 7.85; N, 7.76; Cl, 19.93
CH_3, CH_3	CH_3	Br	95	240 dec.	Calcd. for $C_7H_{14}BrNO_2$: Br, 35.71. Found: Br, 35.92
CH_3, CH_2CH_2OH	H	Cl	89	185–186	Calcd. for $C_7H_{14}ClNO_3$: C, 43.07; H, 7.17; N, 7.17; Cl, 17.94. Found: C, 42.93; H, 6.93; N, 7.20; Cl, 18.13
$CH_2CH_2OCH_2CH_2$	H	Cl	85	260–262 dec.	Calcd. for $C_8H_{14}ClNO_3$: C, 46.30; H, 6.76; N, 6.76; Cl, 16.90. Found: C, 46.12; H, 6.74; N, 6.76; Cl, 16.87
$CH_2CH_2OCH_2CH_2$	H	Br	95	247–248	Calcd. for $C_8H_{14}BrNO_3$: Br, 31.74. Found: Br, 31.60
$(CH_2)_4$	H	Br	94	227	Calcd. for $C_8H_{14}BrNO_2$: Br, 33.89. Found: Br, 33.68
$(CH_2)_5$	H	Cl	86–87	256–258	Calcd. for $C_9H_{16}ClNO_2$: N, 6.85. Found: N, 6.55

salt (V) and the second is a ring closure in which alcohol is eliminated.

Spiro-2-oxomorpholinium salts are obtained in a similar manner when cyclic aminoalcohols such as β-(*N*-pyrrolidyl)ethanol and β-(*N*-piperidyl)-ethanol are used.

The reaction is performed by heating the dialkylaminoalcohol and the haloacetic ester in a solvent such as toluene, xylene, or benzene. Only small amounts of the quaternary salts can be prepared without using a solvent because of the strongly exothermic reaction. The alcohol formed is distilled off and the precipitated quaternary salt filtered and washed with acetone. The product is then recrystallized from absolute ethanol, methanol, or isopropyl alcohol.

The alcohols (ethanol, methanol) formed during the reaction have been characterized as their 3,5-dinitrobenzoyl derivatives.

The aqueous solutions of the quaternary 2-oxomorpholinium salts have a *p*H of 3 to 4. Some of them show biologic activity and influence phagocytosis.[3]

When β-(*N*-phenyl-*N*-ethylamino)ethanol and ethyl chloroacetate were allowed to react, only quaternization was observed and no ring closure occurred. Since this behavior might be attributed to a steric hindrance of the aromatic ring we plan to extend this preliminary experiment in order to study the influence of substituents on the ring closure.

The quaternary 2-oxomorpholinium salts prepared are listed in Table I.

EXPERIMENTAL

In order to obtain good yields the starting materials, particularly the aminoalcohols, have to be freshly distilled.

4,4-Diethyl-2-oxomorpholinium chloride. Methyl chloroacetate (108 g., 1 mole), 117 g. (1 mole) of β-(*N,N*-diethylamino)ethanol, and 300 ml. of dry xylene were heated and stirred for 3 hr. at 120 to 130°. The methanol which formed during the reaction was continuously removed and identified as the 3,5-dinitrobenzoyl derivative (m.p. 111–112°). The precipitated quaternary salt (184 g.) was filtered, washed with acetone, and recrystallized twice from absolute ethanol.

The salt is difficultly soluble in absolute ethanol but readily soluble in 95 to 98% ethanol.

About the same yield was obtained when ethyl chloroacetate was used instead of methyl chloroacetate.

2-Oxo-3-oxa-6-azoniaspiro[4.5]decane bromide. N-(β-Hydroxyethyl)pyrrolidine (11.5 g., 0.1 mole) and 15.3 g. (0.1 mole) of methyl bromoacetate were heated in 40 ml. of benzene for 1 hr. at 75 to 80°. The white precipitate, 22.2 g., was recrystallized from a mixture (1:1) of absolute ethanol and methanol.

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Melibiose Monohydrate[1]

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Melibiose was originally prepared from raffinose by controlled acid hydrolysis[2] and later by the action of baker's yeast,[3,4] and was isolated, not without difficulty,[3–5] as the dihydrate, m.p. 83°; this dihydrate was the β anomer since it showed in water $[\alpha]_D^{23}$ +111.7° changing to +129.5°.[3–7]

Whereas studies reported[5,7,8] in the literature appear to have been carried out with the β form of

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[1] Paper No. **3973** of the Scientific Journal Series, Minnesota Agricultural Experiment Station.

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melibiose dihydrate, chemical storehouses at the present time evidently supply what is sometimes referred to as a "monohydrate" or a "hydrate," but there is no evidence as to its anomeric form.

We have recently repeated the preparation of melibiose by the above method[9] using yeast, expecting to obtain the dihydrate, but instead we have obtained a monohydrate, m.p. 179–181°. This monohydrate of melibiose is evidently the α anomer since it shows $[\alpha]_D^{23}$ +157° changing to +137° in water (C, 1.0).

Anal. Calcd. for $C_{12}H_{22}O_{11}$. H_2O: C, 40.00; H, 6.71. Found: C, 39.95; H, 6.60.

When allowance was made for the change in molecular weight, the equilibrium rotation of +137° found for the new monohydrate agreed well with the value of +129.5° reported for the dihydrate.

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[9] "Polarimetry Saccharimetry and the Sugars," Circular C440 of the Natl. Bur. Standards, by Frederick J. Bates and Associates, 1942, p. 473.

Some Derivatives of *p*-Bis(β-hydroxyethyl)aminobenzaldehyde

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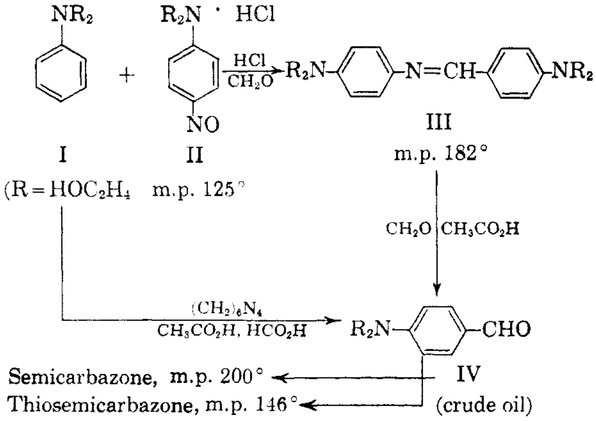
Although several *p*-dialkylaminobenzaldehyde derivatives are reported in the literature, including the butyl- and ethyl-β-hydroxyethyl- compounds,[2] the bis(β-hydroxyethyl) analog apparently has not been reported. Using a procedure similar to that for the preparation of *p*-dimethylaminobenzaldehyde,[3] it has not been possible to obtain a purified sample of the bis(β-hydroxyethyl) compound, although several derivatives of it have been isolated and identified.



EXPERIMENTAL[4]

p-Nitroso-bis(β-hydroxyethyl)aminobenzene hydrochloride (II). A stirred solution of 36.2 g. of bis(β-hydroxyethyl)-aniline in a mixture of 20 ml. of water and 40 ml. of concentrated hydrochloric acid was cooled in an ice-salt bath and a solution of 14.6 g. of sodium nitrite in 25 ml. of water was added, care being taken that the temperature did not rise above 5°. After stirring for a further period of 30 min., the orange crystalline nitroso compound was collected, washed with 40 ml. of cold 1:1 hydrochloric acid and dried first in air and then in a desiccator. On recrystallization from ethanol the compound melted with decomposition at 123–125°.

Anal. Calcd. for $C_{10}H_{15}N_2O_3Cl$: C, 48.68; H, 6.13; N, 11.36. Found: C, 48.33; H, 6.30; N, 11.16.

The nitroso compound seemed to be sensitive to light. The original color soon changed to greenish yellow and finally to black within a few days.

N-[p'-Bis(hydroxyethyl)aminobenzylidene]-p-[bis(hydroxyethyl)amino]-aniline (III). Wet nitroso hydrochloride, from a preparation using four times the quantities described above, was added all at once to a 5-liter beaker containing a solution made by warming for 10 min. on a steam bath a mixture of 173.6 g. of bis(β-hydroxyethyl)aniline, 192 ml. of concentrated hydrochloric acid and 100 ml. of 40% formaldehyde solution. The initial vigorous reaction soon subsided. After allowing the mixture to stand for an hour, about 1600 g. of crushed ice was added to the mixture and it was cautiously neutralized with a very slight excess of 40% sodium hydroxide solution. The aqueous portion was poured off from the plastic mass, which was washed by trituration and decantation with four 3.5-l. portions of cold water, care being taken to see that the wash liquor before decantation was neutral. The temperature throughout the latter operation was maintained below 15°. The plastic mass was warmed with 400 ml. of hot ethanol, seeded (a portion of the solution, diluted with 2–3 times its volume of ether, on cooling, scratching, and washing with cold ethanol gave the desired material for seeding) and cooled thoroughly, when yellow crystalline material separated. This was collected and washed with cold ethanol to yield 105 g., m.p. 176–178°. One recrystallization from ethanol raised the melting point to 181–182°.

Anal. Calcd. for $C_{21}H_{29}N_3O_4$: C, 65.09; H, 7.54; N, 10.86. Found: C, 64.77; H, 7.67; N, 10.83.

p-Bis(β-hydroxyethyl)aminobenzaldehyde semicarbazone. Compound III (27 g., 0.7 mole) was stirred at room temperature with a mixture of 42 ml. of glacial acetic acid and 40% formaldehyde for 4 hr. This mixture was then diluted with 70 ml. of water, cooled thoroughly, cautiously basified with a slight excess of ammonia, and extracted with chloroform in a liquid-liquid extractor for 16 hr. After drying and evaporation of solvent, the residual oil, containing some high-melting by-product, weighed 15.6 g. This oil, presumably the crude aldehyde (IV), could not be crystallized and did not distill at 285° (0.05 mm.). The *semicarbazone*, prepared in the usual way using sodium acetate, readily recrystallized from ethanol, m.p. 199–200°, dec.

Anal. Calcd. for $C_{12}H_{18}N_4O_3$: C, 54.12; H, 6.81; N, 21.04. Found: C, 54.08; H, 7.16; N, 21.32.

p-Bis(β-hydroxyethyl)aminobenzaldehyde thiosemicarbazone. (a) To a solution of 11 g. of the crude oil containing the aldehyde (IV) in 20 ml. of 95% ethanol and 60 ml. of water, 4.8 g. of thiosemicarbazide was added. After heating under reflux for 4 hr., the mixture was cooled and the supernatant liquor was decanted from the oily precipitate. After addition of 200 ml. of hot water, the mixture was heated to boil-

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[4] Analyses by Midwest Microanalytical Lab., Indianapolis.