TABLE II

ANALYSIS OF BIS-(TRIMETHYLENEDIAMINO)-CUPRIC SULFATE HYDRATE[6]

	% C	% H	% Cu	% N	% S
Calcd. for $C_6H_{20}CuN_4SO_4 \cdot H_2O$	22.11	6.81	19.51	17.19	9.84
Determined	21.88	6.40	19.51	16.80	9.66
Determined	21.98	6.44	19.69	16.54	9.99

When heated it changes to the blue anhydrous form and finally decomposes at 276–277° cor. with evolution of gas, leaving a brown residue. Samples of the hydrate were heated to 35, 57, 78 and 100° and kept at these temperatures, all samples being reweighed after 1, 3, 8, 10, and 14 days. At 35° there was no dehydration. At 57° dehydration progressed so slowly that it was not quite complete even after fourteen days. At both 78 and 100° the dehydration was complete after one day. At 100° the change appeared to take place instantly, but at 78° even the visible color change required about an hour. The anhydrous compound apparently is stable at 100° for no additional change in weight occurred during the fourteen-day period of heating. The product does not contain unreacted cupric sulfate because when a sample of it was treated with additional trimethylenediamine and water and dried, it went back to its original weight.

(6) All determinations were made by the Laboratory of Michrochemistry, 366 Fifth Avenue, New York, N. Y.

VENEREAL DISEASE RESEARCH LABORATORY
U. S. MARINE HOSPITAL
STATEN ISLAND, NEW YORK

RECEIVED SEPTEMBER 8, 1944

Configuration of Acetylmethylcarbinol

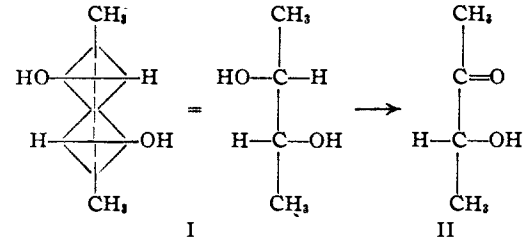
BY R. H. BLOM

The configurations of the optically active 2,3-butylene glycols have recently been correlated with the configurational system which Emil Fischer established for glucose, as D-(−) and L-(+)- for the levo- and dextro-rotatory forms, respectively.[1] The proof depends upon the established relationship of configuration between the methylethylcarbinols and the lactic acids.[2] In turn, the place of the lactic acids in the Fischer sugar system follows, for example, from the oxidation of the methyl 6-desoxy-hexopyranosides to the corresponding lactic acids.[3] In studying the vapor-phase oxidation of D-(−)-2,3-butylene glycol (I), it has been found that the acetylmethylcarbinol so formed (II) is levorotatory. Although extensive racemization occurred during the reaction, the rotation of the product was sufficient to establish the configurational relationship. Since the glycol and the carbinol can exist in only two active forms, D- or L-, racemization would form only the racemic structures in both cases. The acetylmethylcarbinols and the 2,3-butylene glycols which exhibit the same sign of rotation therefore possess the same configuration:

(1) S. A. Morell and A. H. Auernheimer, THIS JOURNAL, **66**, 792 (1944).

(2) P. A. Levene, A. Walti and H. L. Haller, *J. Biol. Chem.*, **71**, 465 (1927).

(3) W. D. Maclay, R. M. Hann and C. S. Hudson, THIS JOURNAL, **61**, 1660 (1939).



I II

D-(−)-2,3-Butylene glycol[4] D-(−)-Acetylmethylcarbinol

A sample of D-(−)-2,3-butylene glycol,[5] $[\alpha]^{21}D$ −12.20° (C = 100%, 1-dcm. tube) was heated to 140° and vaporized by means of a stream of air. The vapors were passed through a Pyrex tube packed with copper turnings and maintained at 315°. On condensation and fractional distillation, the main products obtained were diacetyl (33% yield), b. r. 88–88.5° (uncor.) and acetylmethylcarbinol (25% yield), b. r. 142–144° (uncor.), $n^{21}D$ 1.4186, which values are in good agreement with the literature.[6] The latter was levorotatory, $[\alpha]^{21}D$ −1.39° (C = 100%, 1-dcm. tube). On standing for twenty-four hours at 4° crystals of the optically inactive dimer of acetylmethylcarbinol were deposited.[7] Since an optically pure isomer of acetylmethylcarbinol has not yet been conclusively obtained,[8] it is not possible to calculate the concentration of the active form present in the product. The acetylmethylcarbinol was identified by acetylation with acetic anhydride, acetoin acetate, b. r. 167–168°[9] being obtained.

The assistance of Dr. S. A. Morell in the preparation of this paper is gratefully acknowledged.

(4) The structural formulas used conform with the fundamental convention of Emil Fischer in that the lower edges of the tetrahedra lie in a straight line in the plane of the paper, the corners which carry (H) and (OH) groups thus being above the paper.

(5) G. E. Ward, O. G. Pettijohn, L. B. Lockwood and R. D. Coghill, THIS JOURNAL, **66**, 541 (1944).

(6) J. R. Pound and A. M. Wilson, *J. Phys. Chem.*, **39**, 1135 (1935).

(7) T. M. Lowry and W. C. G. Baldwin, *J. Chem. Soc.*, 704 (1935).

(8) W. Dirscherl and A. Schollig, *Ber.*, **71**, 418 (1938).

(9) M. Bergmann and S. Ludewig, *Ann.*, **438**, 173 (1924).

NORTHERN REGIONAL RESEARCH LABORATORY
BUREAU OF AGRICULTURAL AND INDUSTRIAL CHEMISTRY
AGRICULTURAL RESEARCH ADMINISTRATION
U. S. DEPARTMENT OF AGRICULTURE
PEORIA, ILLINOIS

RECEIVED DECEMBER 14, 1944

Carbobenzoxy Derivatives of Aromatic Amines

BY NORMAN C. BERGSTROM AND A. E. MARTELL[1]

A number of aromatic amines were treated with benzyl chlorocarbonate in order to determine the ease of acylation and the possible use of the reagent for obtaining crystalline derivatives of amines. The acylation of amines and amino acids with benzyl chlorocarbonate has been thoroughly described by Bergmann[2] and his method is essentially the one used here.

(1) Now at Clark University, Worcester, Mass.

(2) Bergmann and Zervas, *Ber.*, **65**, 1192 (1932).

The derivatives tabulated below were obtained merely by shaking the corresponding amine with slightly more than a molar equivalent of benzyl-chlorocarbonate in the presence of excess 10% sodium hydroxide solution. The product solidified in a few minutes, was filtered and then recrystallized from ethyl alcohol. The yields of recrystallized material were between 60 and 90% of the theoretical amount.

Product, carbonate	M. p., °C.	Nitrogen, % Calculated	Found
N-Phenyl-benzyl	77	6.16	6.11
N-*p*-Tolyl-benzyl	83	5.81	5.64
N-*o*-Tolyl-benzyl	83.5	5.81	5.62
N-*p*-Methoxy-phenyl-benzyl	98.0	5.83	5.65
N-*m*-Bromophenyl-benzyl	58.0	4.58	4.45

Orthoanisidine produced a liquid derivative which was not further investigated. Three of the above compounds have been prepared previously by the isocyanate method: N-phenyl-benzyl carbamate,[3] N-*o*-tolyl-benzyl carbamate,[4] and N-*p*-methoxyphenyl-benzyl carbamate.[5] The remaining two benzyl carbamates have not previously been reported. Nitrogen analyses were made by the Dumas method. Carbobenzoxy chloride was prepared by the method of Bergmann and Zervas.[2]

The low melting points and low melting point spread of these derivatives indicate that they would be of little value in the identification of the amines investigated. On the other hand they are prepared in excellent yield and seem to offer a convenient method for "masking" amino groups.

(3) Soden and Rojahn, *Ber.*, **34**, 2809 (1901).
(4) Gattermann and Cantzler, *ibid.*, **25**, 1807 (1892).
(5) Brunner and Wohol, *Monatsh.*, **63**, 374 (1930).

DEPARTMENT OF CHEMISTRY
WORCESTER POLYTECHNIC INSTITUTE
WORCESTER, MASS. RECEIVED NOVEMBER 22, 1944

Percain Analogs. The Preparation of β-Diethylaminoethoxyethyl 2-Alkoxy-cinchonates

BY CHI-CHIEK CHANG AND NENG-YÜAN WOO

Most 2-alkoxy-cinchonic acid derivatives exhibit a local anesthetic effect. In a series of β-diethylaminoethylamides of this acid prepared by Aeschlimann,[1] percain, the butoxy derivative, is the strongest, being ten times as active as cocaine, and is used in medicine.

Luré[2] showed that in a series of amino esters of these acids the anesthetic effect was to some extent dependent on the nature of the alkoxy group in the 2-position, but more on the side chain in the 4-position, the effect increasing with the increase of the number of the carbon atoms.

In a series of a different type of amides of these acids Magidson[3] proved that an increase in the number of the hydroxyl groups in the side chain in the 4-position decreases the anesthetic effect.

With these views in mind, we prepared a series of β-diethylaminoethoxyethanol esters of 2-alkoxy-cinchonic acids containing an O-atom in the side chain in the 4-position, and studied the change in the local anesthetic effect when the alkoxy group in the 2-position was varied.

β-Diethylaminoethoxyethanol was prepared by the method of Horne and Shriner.[4] 2-Chlorocinchonic acid was prepared by the method of Aeschlimann[1] or Thielepape,[5] and it was converted into a series of 2-alkoxycinchonic acids by the action of sodium alcoholate in the corresponding alcohols. From these, the acid chlorides, the esters, and finally the ester hydrochlorides were prepared.

2-Alkoxy-cinchonic Acid Chloride.—This was prepared by the action of thionyl chloride on a solution of the corresponding alkoxy-cinchonic acid[1,5] in benzene following the procedure of Gardner and Hammel.[6] In several repetitions of this procedure we found the yield to be dependent on the time of heating, as follows

Time of heating, min.	Amount of 2-alkoxy-cinchonic acid used, g.	Amount of acid recovered, g.
10	0.38	0.30
35	1.20	.25
60	1.40	.19

β-Diethylaminoethoxyethyl 2-Alkoxy-cinchonate Hydrochloride.—To a solution of the alkoxy-cinchonate chloride in about ten times its weight of benzene was added a slight excess of β-diethylaminoethoxyethanol. The mixture was heated at 60° for fifteen minutes. After cooling, the benzene solution was extracted with dilute hydrochloric acid. The ester was precipitated by neutralizing the acid solution with sodium carbonate, and was extracted with benzene. The benzene solution was dried with anhydrous sodium sulfate and treated with the calculated amount of hydrogen chloride gas. The mixture was allowed to stand for several hours and the precipitate was filtered off, washed with benzene, and dried in a desiccator. Yields and melting points are given in the table.

β-DIETHYLAMINOETHOXYETHYL 2-ALKOXY-CINCHONATE HYDROCHLORIDES

Alkoxy	Yield, %	M. p., °C.	Formula	Percentage composition Nitrogen Calcd.	Nitrogen Found	Chlorine Calcd.	Chlorine Found
-ethoxy-	64	80	$C_{20}H_{33}O_4N_2Cl$	7.02	7.10	8.94	9.03
-isopropoxy-	68	75	$C_{21}H_{35}O_4N_2Cl$	6.95	6.94	8.64	8.72
-butoxy-	66	108	$C_{22}H_{37}O_4N_2Cl$	6.72	6.77	8.35	8.50
-pentoxy-	66	78	$C_{23}H_{39}O_4N_2Cl$	6.50	6.53	8.08	8.12

These compounds, in 1% aqueous solution, produce a local anesthetic effect when tested by the tongue, but the pharmacological properties will be further investigated.

(4) Horne and Shriner, THIS JOURNAL, **54**, 2925–2930 (1932).
(5) Thielepape, *Ber.*, **55**, 133–134 (1922).
(6) Gardner and Hammel, THIS JOURNAL, **58**, 1360–1361 (1936).

DEPARTMENT OF CHEMISTRY
NATIONAL CHEKIANG UNIVERSITY
MAITAN, KWEICHOW, CHINA
RECEIVED NOVEMBER 22, 1944

Derivatives of Phenothiazine

BY STEWART E. HAZLET AND CHARLOTTE E. RODERUCK

In connection with other investigations[1] at this institution, several new derivatives of pheno-

(1) Aeschlimann, *J. Chem. Soc.*, 2906 (1926).
(2) Luré, *J. Gen. Chem.* (U. S. S. R.), **9**, 287 (1938).
(3) Magidson, *ibid.*, **9**, 2097–2103 (1939).

(1) Nicholson and McCulloch, *J. Am. Vet. Med. Assoc.*, **101** (No. 786), 205 (1942).