TABLE I

N-CARBALKOXY-α-AMINO ACIDS

Compound (Cbzo, carbobenzoxy; Cbetho, carbethoxy.)	Yield, %	M.p. (°C.) uncor.	Formula	Analyses, % Carbon Calcd.	Found	Hydrogen Calcd.	Found	Nitrogen Calcd.	Found
N-Cbetho-DL-phenylalanine	85	76	$C_{12}H_{15}NO_4$	60.8	60.6	6.3	6.4	5.9	6.2
N-Cbzo-DL-phenylalanine	80	102[a]	$C_{17}H_{17}NO_4$	68.2	68.5	5.7	5.8	4.7	4.8
N-Cbetho-DL-alanine	64	83[b]	$C_6H_{11}NO_4$	44.7	44.9	6.8	6.5	8.7	8.5
N-Cbzo-DL-alanine	76	114[c]	$C_{11}H_{13}NO_4$	59.2	59.0	5.8	5.9	6.3	6.5
N-Cbetho-DL-valine	86	56	$C_8H_{15}NO_4$	50.8	51.0	7.9	8.0	7.4	7.3
N-Cbzo-DL-valine	88	71	$C_{13}H_{17}NO_4$	62.2	62.4	6.8	6.6	5.6	5.8
N,N'-Dicbzo-L-lysine	82	150[d]	$C_{22}H_{26}N_2O_6$	63.8	63.6	6.3	6.6	6.8	7.1
N-Cbzo-sarcosine	87	53–54	$C_{11}H_{13}NO_4$	59.3	59.4	5.8	5.6	6.3	6.6
N-Cbetho-anthranilic acid	78	125 dec.	$C_{10}H_{11}NO_4$	57.4	57.4	5.3	5.4	6.7	6.8
N-Cbzo-anthranilic acid	55	141	$C_{15}H_{13}NO_4$	66.4	66.6	4.8	4.9	5.2	5.0

[a] M. Bergmann and L. Zervas, *Ber.*, **65**, 1192 (1932), give m.p. 103°. [b] E. Fischer and W. Axhausen, *Ann.*, **340**, 137 (1905), give m.p. 84° (cor.). [c] M. Bergmann and L. Zervas, ref. *a*, give m.p. 114–115° (cor.). [d] M. Bergmann, L. Zervas and W. F. Ross, *J. Biol. Chem.*, **111**, 245 (1935), give m.p. 150°. J. Bredt and H. Hof, *Ber.*, **33**, 26 (1900), give m.p. 126° (dec.).

TABLE II

N-CARBOXY-α-AMINO ACID ANHYDRIDES (OXAZOLIDINE-2,5-DIONES)

N-Carbalkoxy-α-amino acid	Oxazolidine-2,5-dione	Yield, %	M.p. (°C.) uncorrected	Formula	Analyses, % Carbon Calcd.	Found	Hydrogen Calcd.	Found	Nitrogen Calcd.	Found
N-Cbetho-DL-phenylalanine	4-Benzyl	82	125–126 (dec.)[a]	$C_{10}H_9NO_3$	62.8	62.7	4.7	4.9	7.3	7.4
N-Cbzo-DL-phenylalanine	4-Benzyl	84	125–126 (dec.)[a]	$C_{10}H_9NO_3$	62.8	62.6	4.7	4.7	7.3	7.4
N-Cbetho-DL-alanine	4-Methyl	60	44–45[b]	$C_4H_5NO_3$	41.7	41.9	4.4	4.6	12.2	12.4
N-Cbzo-DL-alanine	4-Methyl	68	44–45[b]	$C_4H_5NO_3$	41.7	41.7	4.4	4.6	12.2	12.3
N-Cbetho-DL-valine	4-Isopropyl	85	77–79[c]	$C_6H_9NO_3$	50.4	50.1	6.3	6.4	9.8	10.0
N-Cbzo-DL-valine	4-Isopropyl	88	77–79[c]	$C_6H_9NO_3$	50.4	50.3	6.3	6.4	9.8	10.1
N,N'-Dicbzo-L-lysine	4-(δ,N-Cbzo-aminobutyl)	85	99 (dec.)[d]	$C_{15}H_{18}N_2O_5$	58.8	58.7	5.9	5.9	9.2	9.0
N-Cbzo-sarcosine	3-Methyl	90	99 (dec.)[e]	$C_4H_5NO_3$	41.7	41.9	4.4	4.1	12.2	12.1

[a] H. Leuchs and W. Geiger, *Ber.*, **41**, 1721 (1908), give m.p. 127–128° (dec.). [b] J. L. Bailey, *J. Chem. Soc.*, 3461 (1950), gives m.p. 45–46°. [c] W. E. Hanby, S. G. Waley and J. Watson, *ibid.*, 3009 (1950), give m.p. 78–79°. [d] M. Bergmann, L. Zervas and W. F. Ross, *J. Biol. Chem.*, **111**, 245 (1935), give m.p. 100° (dec.). [e] F. Sigmund and F. Wessely, *Z. physiol. Chem.*, **157**, 91 (1926), give m.p. 99–100° (dec.).

by aqueous ammonia into anthranilamide; from chloroform, m.p. 108–109°.[6]

Anal. Calcd. for $C_7H_8ON_2$: N, 20.6. Found: N, 20.8.

(6) Kolbe, *J. prakt. Chem.*, [2] **30**, 487 (1884).

THE WEIZMANN INSTITUTE OF SCIENCE
REHOVOTH, ISRAEL

Substituted Benzimidazoles[1]

BY CARL TABB BAHNER, HENRY A. RUTTER, JR., AND LYDIA MOORE RIVES

RECEIVED MARCH 15, 1952

It has been reported[2] that benzimidazole is an antagonist of adenine and it seemed worthwhile to investigate whether substituted benzimidazoles would inhibit the growth of cancers. In addition to a number of previously described compounds the following have been prepared.

5,7(or 4,6)-Dinitrobenzimidazole.—A solution of 1.0 g. of 1,2-diamino-4,6-dinitrobenzene[3] (0.005 mole) and 0.37 g. of formic acid (0.008 mole) in 5 ml. of 4 *N* HCl was refluxed 40 minutes, cooled and neutralized with ammonia. The precipitate was recrystallized once from water and twice from ethanol (with activated charcoal) to yield 0.50 g. of yellow crystals, m.p. 239–240° (dec.).

Anal.[4] Calcd. for $C_7H_4N_4O_4$: C, 40.39; H, 1.94. Found: C, 40.55; H, 1.79.

4(or 7)-Amino-6(or 5)-nitrobenzimidazole.—A solution of 3.36 g. of 5-nitro-1,2,3-triaminobenzene (0.02 mole) and 1.38 g. of formic acid (0.03 mole) in 20 ml. of 4 *N* HCl was refluxed 40 minutes and cooled to room temperature. The black, needle-shaped crystals (probably a hydrochloride salt of the benzimidazole) were filtered off, dissolved in boiling concentrated HCl, diluted with water, and neutralized with ammonia to produce a red precipitate which, after one recrystallization from water and two recrystallizations from alcohol (with activated charcoal), yielded 0.8 g. of yellow crystals, m.p. 240–241° (dec.). An additional 0.2 g. of product was obtained by neutralizing the original reaction mixture with ammonia and recrystallizing the precipitate.

Anal. Calcd. for $C_7H_6N_4O_2$: C, 47.19; H, 3.37. Found: C, 47.37; H, 3.35.

5(or 6)-Chloro-2-hydroxymethylbenzimidazole.—Prepared from *p*-chloro-*o*-phenylenediamine and glycolic acid and recrystallized from ethyl acetate this product melted at 206–208° (dec.). (Water and ethyl alcohol were unsatisfactory solvents for recrystallization.)

Anal. Calcd. for $C_8H_7ClN_2O$: C, 52.71; H, 3.86. Found: C, 52.78; H, 3.60.

5(or 6)-Nitro-2-hydroxymethylbenzimidazole.—Prepared from *p*-nitro-*o*-phenylenediamine and glycolic acid and recrystallized from ethyl acetate the yellow crystals melted at 194–195° (dec.).

Anal. Calcd. for $C_8H_7N_3O_3$: C, 49.74; H, 3.63. Found: C, 49.56; H, 3.60.

5(or 6)-Chlorobenzimidazole Hydrochloride.—A solution of 5(or 6)-chlorobenzimidazole[5] in concentrated HCl was

(1) This research was supported, in part, by a grant from the National Cancer Institute of the National Institutes of Health, U. S. Public Health Service, and in part by a grant from the Damon Runyon Memorial Fund for Cancer Research.

(2) D. W. Wooley, *J. Biol. Chem.*, **152**, 225 (1944).

(3) *Cf.* R. Nietzke and H. Hagenbach, *Ber.*, **30**, 544 (1897).

(4) All carbon and hydrogen analyses by Galbraith Microanalytica Laboratories, Knoxville, Tennessee.

(5) O. Fischer, *Ber.*, **37**, 556 (1904).

evaporated to dryness. The residue was dissolved in warm isopropyl alcohol and thrown out by addition of acetone, m.p. 239–240° (dec.); solubility in water at 25° about 5%. *Anal.* Calcd. for $C_7H_6Cl_2N_2$: ionic Cl, 18.75. Found: Cl, 18.48, 18.71.

5(or 6)-Aminobenzimidazole Dihydrochloride.—Isopropyl alcohol was added to a saturated solution of 5(or 6)-aminobenzimidazole[6] in dilute HCl and the resulting light pink crystals were washed with isopropyl alcohol and with ether. A sample kept in a vacuum desiccator gave a low analysis, apparently because of gradual loss of HCl, but a sample dried at atmospheric pressure gave satisfactory analyses; m.p. 299° (dec.); water solubility at 25° > 20%. *Anal.* Calcd. for $C_7H_9Cl_2N_3$: Cl, 34.40. Found: Cl, 34.33, 34.63.

We wish to express our appreciation to Mr. Charles Chumley and Mr. Eddie Pace for the preparation of the 1,2-diamino-4,6-dinitrobenzene and 5-nitro-1,2,3-triaminobenzene used in these preparations and to Dr. Alfred Gellhorn of Columbia University College of Physicians and Surgeons for arranging to screen several of the products against tumors.

(6) G. M. van der Want, *Rec. trav. chim.*, **67**, 45 (1948).

CARSON-NEWMAN COLLEGE
JEFFERSON CITY, TENNESSEE

Bromomethylation; Preparation of 2,6-Bis-(bromomethyl)-4-alkyl Phenols

BY WILLARD M. BRIGHT[1] AND PETER CAMMARATA

RECEIVED JANUARY 22, 1952

This paper presents a direct method for the preparation of crystalline monomeric bromomethyl alkyl phenols. In it the phenol, dissolved in glacial acetic acid, is allowed to react with paraformaldehyde and anhydrous hydrogen bromide. The generality of the method is attested to by the simple preparations of 2,6-bis-(bromomethyl)-4-methylphenol,[2] 2,6-bis-(bromomethyl)-4-*t*-butylphenol, and 2,6-bis-(bromomethyl)-4-*t*-octylphenol.[3]

There seems to have been no direct bromomethylation procedure reported in the literature, although chloromethylation of non-phenolic materials is routine. In the latter connection, it has been noted that employing the usual procedures, phenols react so readily that the reaction goes too far, yielding polymeric material.[4] Buehler[5] has chloromethylated substituted phenols containing such strongly polar groups as $-NO_2$ and –COOH which have been found to retard the undesirable resinification reaction leading to polymeric materials. He treated the phenol in concentrated hydrochloric acid with formalin in the presence of a strong acid catalyst, such as H_2SO_4. A patent[6] exists in which it is claimed that monomeric, crystalline 2,6-bis-(chloromethyl)-4-methylphenol was obtained as a result of reaction of aqueous formaldehyde, cresol and concentrated hydrochloric acid. We were unable to confirm this claim, nor were we able to prepare the desired bromomethyl compound from aqueous systems.

The *t*-butyl and *t*-octyl compounds reported herein have not been described previously. They were characterized by direct comparison with samples prepared from 2,6-bis-(hydroxymethyl)-4-*t*-butylphenol[7] and 2,6-bis-(hydroxymethyl)-4-*t*-octylphenol,[8] by hydrogen bromide using the method of von Auwers.[2]

Experimental[9]

2,6-Bis-(bromomethyl)-4-methylphenol.—To 150 g. of glacial acetic acid was added 54 g. of *p*-cresol and 35 g. of paraformaldehyde. The flask containing the mixture was immersed in an ice-bath and anhydrous hydrogen bromide was passed into the reaction mixture. Heat was evolved and the admission of HBr was regulated in such a manner that the temperature of the mixture was never allowed to exceed 80°. Near the saturation point of HBr in acetic acid (evidenced by fuming at the mouth of the flask) the suspended paraformaldehyde disappeared and a clear solution was obtained. HBr addition was stopped when the solution was completely saturated and the *p*-cresol derivative precipitated immediately. After the solid product was filtered off, and recrystallized from heptane, approximately 60% yield was obtained; m.p. 115–117°.

Anal. Calcd. for $C_9H_{10}Br_2O$: C, 36.8; H, 3.4; Br, 54.4. Found: C, 36.7; H, 3.4; Br, 54.3.

Other Phenols.—2,6-Bis-(bromomethyl)-4-*t*-butylphenol was prepared in the same manner as the cresol derivative when 4-*t*-butylphenol was used; yield 50%, m.p. 92–93°.

Anal. Calcd. for $C_{12}H_{16}Br_2O$: C, 42.9; H, 4.8; Br, 47.6. Found: C, 42.6; H, 4.8; Br, 47.4.

2,6-Bis-(bromomethyl)-4-octylphenol was prepared similarly from the commercially available phenol, which was not further purified; yield 25%, m.p. 87–90°. Both the butyl and octyl derivatives required several hours of refrigeration to effect crystallization.

Anal. Calcd. for $C_{16}H_{24}Br_2O$: C, 49.0; H, 6.2; Br, 40.7. Found: C, 48.1; H, 6.3; Br, 40.0.

(1) Address communications to: Clark Laboratory, The Kendall Company, Cambridge 39, Massachusetts.

(2) This compound has been previously prepared by reaction of 2,6-bis-(hydroxymethyl)-phenol. See K. von Auwers, *Ber.*, **40**, 2532 (1907), and F. Uhlman and K. Brittner, *ibid.*, **42**, 2540 (1909).

(3) Nomenclature for parent methylol phenol given variously as: (a) 2,6-bis-(hydroxylmethyl)-4-*t*-octylphenol, (b) 2,6-bis-(hydroxymethyl)-4-diisobutylphenol, (c) α,α'-*m*-xylenediol-2-hydroxy-5-1,1,3,3-tetramethylbutyl.

(4) R. C. Fuson and C. H. McKeever, "Organic Reactions," Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1942, p. 65.

(5) (a) C. A. Buehler, *J. Tennessee Acad. Sci.*, **22**, 303 (1947); (b) C. A. Buehler, F. K. Kirchner and C. F. Deebel, *Org. Syntheses*, **20**, 59 (1940).

(6) I. G. Farbenind. A.-G., British Patent 347,887 (1931).

(7) F. Hanus, E. Fuchs and E. Ziegler, *J. prakt. Chem.*, **153**, 327 (1939).

(8) J. B. Niederl, *Ind. Eng. Chem.*, **30**, 1269 (1938).

(9) Analyses by Carol K. Fitz, 115 Lexington Ave., Needham Heights 94, Massachusetts.

RESEARCH LABORATORY
BAUER AND BLACK
CHICAGO 16, ILLINOIS

The Reaction between Niobium Pentachloride and Niobium Metal

BY C. H. BRUBAKER, JR., AND R. C. YOUNG

RECEIVED MARCH 18, 1952

Recently Schäfer, Göser and Bayer[1] have shown niobium tetrachloride is produced, when niobium pentachloride and niobium metal (in a molar ratio greater than 4/1) are caused to react at 350°. Their results were in agreement with those obtained in our own rather extensive study of the reaction between niobium pentachloride and niobium. Presented here, however, are certain of our results and conclusions which were not covered in their paper.

Large needles (*ca.* 1 cm. long) are obtained directly, after removal of excess pentachloride by vacuum sublimation at 120°, when the penta-

(1) H. Schäfer, C. Göser and L. Bayer, *Z. anorg. allgem. Chem.*, **265**, 258 (1951).