Experimental(4)

2-Chloroethyl Benzohydryl Ether.—The crude, moist benzohydrol, obtained by following the procedure in "Organic Synthesis"(5) but using four times the amounts described therein, was dissolved in two liters of warm benzene. After separating the water layer, the solution was filtered, and dried by distillation until its volume was reduced to *ca.* one liter. Keeping the temperature of the solution at about 20°, it was saturated with dry hydrogen chloride. The aqueous layer was separated and the benzene removed by distillation from a steam-bath. To the residue, still containing a little benzene, was added 2116 g. (26.9 moles) of ethylene chlorohydrin. The solution was refluxed for six hours, using a reflux condenser with a take-off tube to remove the benzene which remained. A copious evolution of hydrogen chloride occurred during this period of reflux. About 800–900 ml. of ethylene chlorohydrin was then removed by distillation at atmospheric pressure. The remaining liquid was distilled *in vacuo*. The colorless product was collected at 184–189° (12 mm.) and weighed 941 g. This represents an over-all yield of 87%, based on the weight of benzophenone used in the initial reduction reaction.

Anal. Calcd. for $C_{15}H_{15}ClO$: Cl, 14.38. Found: Cl, 14.31.

2-Benzylaminoethyl Benzohydryl Ether.—A mixture of 50.7 g. (0.206 mole) of 2-chloroethyl benzohydryl ether and 220.4 g. (2.06 moles) of benzylamine was heated at a bath temperature of 160–165° for 117 hours. The cooled reaction mixture was suspended in a liter of ether and the benzylamine hydrochloride removed by filtration. After washing with ether and air-drying, the salt weighed 27.3 g., corresponding to a 92.5% conversion. The ether and excess benzylamine were removed from the filtrate by distillation and the residual liquid distilled *in vacuo*. The viscous yellow oil weighed 60.0 g. (92%), b.p. 169–172°.

Anal. Calcd. for $C_{22}H_{23}NO$: N, 4.41. Found: N, 4.33, 4.31.

The ratio of the reactants, the length of the heating period and the size of the run seem to be critical factors affecting the yield. Results of experiments where these were varied are summarized in Table I.

TABLE I

FACTORS AFFECTING THE YIELD OF 2-BENZYLAMINOETHYL BENZOHYDRYL ETHER

Benzylamine, moles	2-Chloroethyl ether, mole	Heating period, hours	Bath temp., °C.	Yield, %
0.2	0.1	25	105	48
0.800	.100	23	177–182	74
1.00	.100	68	160–165	87
2.06	.206	117	160–165	92
3.73	.3730	216	160–165	68
10.0	1.00	51	160–165	66

After this work had been completed, a publication appeared describing the preparation of this compound in 25% yield by the catalytic hydrogenation of a mixture of benzaldehyde and 2-aminoethyl benzohydryl ether.(6)

The hydrochloride was prepared by adding an ethereal hydrogen chloride solution to an ether solution of the base. On standing overnight at room temperature the oily base turned to a pink solid which melted at 146.5–147.5° (cor.) after recrystallization from acetone.

Anal. Calcd. for $C_{22}H_{23}NO \cdot HCl$: Cl, 10.02. Found: Cl, 9.87.

Reaction between 2-Bromopyridine and 2-Benzylaminoethyl Benzohydryl Ether.—A mixture of 15.8 g. (0.1 mole) of 2-bromopyridine and 63.5 g. (0.2 mole) of 2-benzylaminoethyl benzohydryl ether was heated at a bath temperature of 150–160° for 134 hours. The reaction mixture, while still warm, was dissolved in 100 ml. of chloroform. The solution was mixed well with 10 ml. of saturated aqueous potassium carbonate solution. Solid anhydrous potassium carbonate was added and, after standing overnight, the mixture was filtered. The filtrate was freed of chloroform and excess 2-benzylaminoethyl benzohydryl ether by distillation. Further distillation *in vacuo* yielded a small fraction distilling at 205–220° (1 mm.) which deposited a solid on standing. The mixture, after the addition of cold methanol, was filtered and the precipitate washed with the cold solvent. The product, melting at 196–202°, weighed 3.1 g. Recrystallized from ethanol, the white needles melted at 211–212°. Analysis revealed no nitrogen. Fox and Wenner[3] reported that their 1,1,2,2-tetraphenylethane melted at 211–212°. Mixed with an authentic sample,[2] the product showed no depression in melting point.

2-(2-Pyridyl)-aminoethyl Benzohydryl Ether.—A mixture of 14.1 g. (0.15 mole) of 2-aminopyridine, 3.5 g. of lithium amide and 100 ml. of dry toluene was refluxed for five hours. After adding a solution of 37 g. (0.15 mole) of 2-chloroethyl benzohydryl ether in 50 ml. of toluene, refluxing was continued 19 hours longer. The hot suspension was filtered and the insoluble material washed with ether. The solvents were removed from the filtrate *in vacuo* and the semisolid residue vacuum distilled. Five and one-half grams of 2-aminopyridine was recovered (39% of the starting compound). A dark brown viscous oil, weighing 8.8 g. (32%, corrected for the amount of 2-aminopyridine recovered), was collected at 167–188° (0.10–0.15 mm.). The large amount of tarry residue in the still-pot was not investigated. Redistillation yielded 5.8 g. (21% corrected) of a viscous yellow-orange oil, b.p. 152° (0.06 mm.).

Anal. Calcd. for $C_{20}H_{20}N_2O$: N, 9.20. Found: N, 9.07.

The picrate, prepared in ether and recrystallized from ethanol, melted at 141.5–142.5°.

Anal. Calcd. for $C_{20}H_{20}N_2O \cdot C_6H_3N_3O_7$: N, 16.53. Found: N, 16.42.

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DEPARTMENT OF CHEMISTRY
BROOKLYN COLLEGE
BROOKLYN 10, NEW YORK

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(4) All melting points are corrected; boiling points are not.

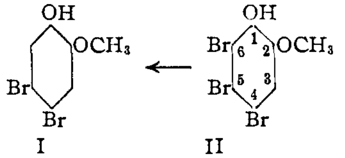
(5) H. Gilman and A. H. Blatt, "Organic Syntheses," Vol. 1, John Wiley and Sons, Inc., New York, N. Y., 1941, p. 90.

(6) L. H. Sutherland, S. L. Eberlin, J. D. Forsythe, I. F. Halverstadt, J. R. Vaughan, Jr., and R. C. Clapp, *J. Org. Chem.*, **14**, 235 (1949).

Bromination of Guaiacol and Debromination of Tribromoguaiacol

BY MORITZ KOHN AND SELMA KREISKY

It has been shown by Robinson and his coworkers[1] and by Raiford and Silker,[2] that Cousin's[3] dibromoguaiacol is the 4,5-dibromoisomer (I).



I II

This has now received further support by the reduction of 4,5,6-tribromoguaiacol[4] (II) with zinc dust and acetic acid. According to our earlier investigations on brominated phenols[5] it was to be expected that the bromine ortho to the hydroxyl group would be substituted by hydrogen. This reaction does take place and 4,5-dibromoguaiacol (I) results.

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(1) Hindmarsh, Knight and Robinson, *J. Chem. Soc.*, **111**, 942 (1917); Jones and Robinson, *ibid.*, **111**, 913 (1917).

(2) Raiford and Silker, *J. Org. Chem.*, **2**, 346 (1937–1938).

(3) Cousin, *Ann. chim. phys.*, [7] **29**, 63 (1903).

(4) The structure II has been established by Zangirolami, *Gazz. chim. ital.*, **62**, 570 (1932).

(5) M. Kohn and J. Sussmann, *Monatsh.*, **48**, 193 (1927); M. Kohn and J. Pfeifer, *ibid.*, **48**, 212 (1927); M. Kohn and L. Steiner, *ibid.*, **58**, 92 (1931).

Experimental

4,5-Dibromoguaiacol can be purified by boiling with 20% NaCl solution. The melting point of the substance prepared by this steam distillation is 94–95°. Methylation yields 4,5-dibromoveratrol, m.p. 92–93°. Dibromoguaiacol acetate melts at 101–102° in accordance with the value of Raiford and Silker[2]; m.p. of the benzoate 112–113° (Raiford and Silker[2] 110–111°).

Reduction of Tribromoguaiacol (II) with Zinc Dust and Acetic Acid.—Fourteen grams of tribromoguaiacol, 9 g. of zinc dust, 40 ml. of glacial acetic acid and 10 ml. of water were boiled under reflux for 4 minutes. The mixture was cooled, filtered and pieces of ice added. The oily precipitation solidified. The substance was filtered by suction, dried in vacuum (6 g.), triturated with petrol ether (b.p. 60–110°), filtered by suction and recrystallized from petrol ether; m.p. 94–95°.

Anal. Calcd. for $C_7H_6O_2Br_2$: Br, 56.73. Found: Br, 57.06, 56.87.

The melting points of its acetate, benzoate and methyl ether were in agreement with the values given above.

LABORATORY OF CHEMICAL TECHNOLOGY
UNIVERSITY OF VIENNA AND
LABORATORY OF THE AB PHARMACIA IN UPSALA

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Some 5-Alkyl-1-acetyl-2-thiohydantoins[1]

BY J. F. R. KUCK, J. J. HERDA, W. E. KOVAC AND J. V. KARABINOS

In the course of some work on the chromatography of amino acid derivatives in this Laboratory, we found it necessary to prepare 5-alkyl-1-acetyl-2-thiohydantoins from a number of α-amino acids.

TABLE I

5-ALKYL-1-ACETYL-2-THIOHYDANTOINS R—CH—CO—NH—CS—N—$COCH_3$

R-	Amino acid	M.p., °C.	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found
Isopropyl-	DL-Valine	115	47.98	47.92	6.04	6.27
n-Butyl-	DL-Norleucine	136	50.44	50.63	6.58	6.89
s-Butyl-	DL-Isoleucine	163	50.44	50.62	6.58	6.61
Methylthioethyl-	DL-Methionine	104	41.35	41.50	5.21	5.22
β-Amidoethyl-	L-Glutamine[a]	219	41.91	42.24	4.84	4.90
Indole-β-methyl-	DL-Tryptophan	170	58.52	58.50	4.56	4.27
p-Hydroxybenzyl-	L-Tyrosine[a]	248[b]	54.53	54.73	4.58	4.26
Hydrogen	Glycine	179[c]	37.96	38.21	3.82	3.63
Bis-thiomethyl-	L-Cystine[a]	208[d]				
s-Acetylthiomethyl-	L-Cysteine[a]	142[e]				
i-Butyl-	DL-Leucine[a]	129[f]				
Benzyl-	DL-Phenylalanine[a]	170[g]				
Amidomethyl-	DL-Asparagine[a]	224[g]				
Methyl-	DL-Alanine[a]	166[g]				

[a] Actually the optical identity of these acetylthiohydantoins is uncertain since acetic anhydride frequently acts as a racemizing agent. Furthermore the optical configuration of some of the amino acids was not given in the original reference and can only be surmised. [b] The oil which was precipitated by adding water was dissolved in 10 ml. of 5% sodium hydroxide and the yellow solution was filtered. The chilled filtrate was added slowly with stirring to a slight excess of 10% hydrochloric acid. The amorphous solid which separated was recrystallized from ethanol. The preparation reported was obtained only once; this procedure usually gave the unacetylated compound, 5-*p*-hydroxybenzyl-2-thiohydantoin of m.p. 211°. *Cf.* M. Jackman, *et al.*, THIS JOURNAL, **70**, 2884 (1948). [c] T. B. Johnson and B. H. Nicolet, *ibid.*, **33**, 1973 (1911). [d] B. H. Nicolet, *J. Biol. Chem.*, **88**, 395 (1930). [e] *Ibid.* [f] P. Schlack and W. Kumpf, *Z. physiol. Chem.*, **154**, 125 (1926). [g] Ref. 2.

Although several of these derivatives were known, we wish to report the preparation of additional ones and describe a method for obtaining crystalline derivatives of most of the naturally occurring monoamino-monocarboxylic acids, essentially according to the directions of Johnson and Nicolet.[2]

One-hundredth of a mole of amino acid was heated with 0.9 g. of ammonium thiocyanate in 10 ml. of acetic anhydride containing 1.3 ml. of acetic acid for 30 minutes at 100°. After the reaction mixture was poured into 50 ml. of water an oil separated from which the acetylthiohydantoin subsequently crystallized. Further purification was accomplished by recrystallization of the crude product from ethanol. For purposes of identification the melting points and analyses of the derivatives prepared in this study are listed in Table I along with the others previously reported. The amino acids which failed to give a precipitate upon addition to water included DL-serine, DL-threonine, L-tyrosine, L-proline and L-hydroxyproline as well as the monohydrochlorides of L-histidine, L-arginine, L-lysine and DL-ornithine. This may indicate the use of this reaction for the group separation of mixtures of the amino acids.

TOMECKO CHEMICAL LABORATORY
ST. PROCOPIUS COLLEGE
LISLE, ILLINOIS

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[1] Research supported by the Office of Naval Research under contract N7ONR-449.

[2] T. B. Johnson and B. H. Nicolet, *Am. Chem. J.*, **49**, 197 (1913).

The Action of Sodium on Di-*s*-butylmercury

BY JOHN F. LANE AND STEPHEN E. ULRICH

Previous studies in these laboratories[1,2] have shown that the major path of reaction in syntheses of the Wurtz type with *s*-alkyl halides proceeds through (ionic) interaction of an *s*-alkyl sodium with the halide. These studies have not, however, ruled out the possibility that a portion, at least, of the Wurtz product might have resulted from the dimerization of *s*-alkyl radicals formed by thermal dissociation of the *s*-alkyl sodium present, an energetically plausible process.[3] To throw further light upon this matter a study was undertaken on the interaction of sodium with di-*s*-butylmercury, in the hope of producing *s*-butylsodium through displacement of mercury. The interaction of sodium with mercury *n*-alkyls is

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[1] S. E. Ulrich, F. H. Gentes, J. F. Lane and E. S. Wallis, THIS JOURNAL, **72**, 5127 (1950).

[2] J. F. Lane and S. E. Ulrich, *ibid.*, **72**, 5132 (1950).

[3] *Cf.* N. G. Brink, J. F. Lane and E. S. Wallis, *ibid.*, **65**, 943 (1943).