to be able to determine the presence of unreacted positions ortho or para to the phenolic hydroxyl group. Thus, Niederl and McCoy[1] used the coupling reaction with a diazonium salt as a qualitative test for open end positions in a phenolic polymer. The general applicability of the coupling reaction to phenol–formaldehyde intermediates is, however, open to question because of the possible (or, indeed, probable) presence of hydroxymethyl groups. Thus, exploratory experiments carried out in 1944[2] showed that 2-hydroxy-α^1,α^3-mesitylenediol couples with benzenediazonium chloride even though this phenol contains no free ortho or para positions.

A more detailed study of this reaction was begun by the authors in 1949. Three alkylated phenols and three hydroxymethyl derivatives of these phenols were coupled with benzenediazonium chloride, and the reaction products were isolated, purified, and compared. After this work was completed there came to our attention a recent paper by Ziegler and Zigeuner[3] that contained essentially all of our results. It seems desirable, however, to record briefly our work, both for its confirmatory value and for the additional information that it provides.

We have found that 2-hydroxy-α^1-mesitylenol (I), 4-hydroxy-α^1-mesitylenol (II) and 2-hydroxy-α^1,α^3-mesitylenediol (III) couple with benzenediazonium chloride in alkaline solution with the liberation of formaldehyde, although these phenol alcohols contain no open positions ortho or para to the phenolic hydroxyl group. The purified azo dyes obtained from (I) and 2,4-dimethylphenol were found to be identical as were those obtained from (II) and 2,6-dimethylphenol. The product formed on coupling (III) differs from that obtained on coupling *p*-cresol in that the former still contains a single ortho hydroxymethyl group. The liberation of formaldehyde upon the coupling of phenol alcohols was confirmed by preparing methylene-di-β-naphthol, a derivative of formaldehyde, according to the procedure of Mulliken.[4]

Acknowledgment.—We wish to thank the U. S. Atomic Energy Commission whose support made this research possible.

(1) Niederl and McCoy, THIS JOURNAL, **65**, 629 (1943).

(2) I. W. Ruderman, M. S. Dissertation, New York University, 1944.

(3) Ziegler and Zigeuner, *Monatsh.*, **79**, 42 (1948); *C. A.*, **44**, 1929[g] (1950).

(4) S. P. Mulliken, "A Method for the Identification of Pure Organic Compounds," Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1904, p. 24.

DEPARTMENT OF PHYSICS
COLUMBIA UNIVERSITY
NEW YORK, N. Y.

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4-β-(β′-Hydroxy)-ethoxyethoxyphenylarsonic Acid and Some Acyl Derivatives[1,2]

BY ROBERT L. MCGEACHIN

In the search for an organic arsenical with a side chain to which a fat-solubilizing group might be added, we have studied the reaction of 4-hydroxyphenylarsonic acid with diglycolchlorohydrin (β-chloro-β′-hydroxy diethyl ether). This reaction gave 4-β-(β′-hydroxy)-ethoxyethoxyphenylarsonic acid,[3] a compound with an esterifiable hydroxyl group in the side chain.

Although the use of potassium iodide as a catalyst has been found to be essential in the reaction of some chloro compounds with 4-hydroxyphenylarsonic acid, in this case the reaction proceeded smoothly and in good yields without any catalyst.

In studying the esterification of the hydroxyl group of 4-β-(β′-hydroxy)-ethoxyethoxyphenylarsonic acid, we have found that the lower acyl chlorides will react but considerable decomposition accompanied the reactions. The same difficulty was encountered with acid anhydrides at elevated reaction temperatures so that the acylations were finally carried out at room temperature even though a prolonged reaction time was necessary at the lower temperature. Acetylation and butyrylation were accomplished by this method.

Attempts were made to prepare the stearyl derivative using stearyl chloride in pyridine but only the unreacted 4-β-(β′-hydroxy)-ethoxyethoxyphenylarsonic acid could be isolated from the reaction mixture. Attempts at benzoylation by the Schotten–Baumann method were likewise unsuccessful.

Experimental

Preparation of 4-β-(β′-Hydroxy)-ethoxyethoxyphenylarsonic Acid (I).—To a solution of 21.8 g. of 4-hydroxyphenylarsonic acid (prepared by decomposition of diazotized *p*-arsanilic acid) in 150 ml. of 2 *N* sodium hydroxide was added 24.9 g. of diglycolchlorohydrin and the mixture heated under reflux conditions for eight hours. The original insoluble layer of diglycolchlorohydrin gradually disappeared during the course of the reaction.

The hot reaction mixture was made just acid to congo red with concd. hydrochloric acid, filtered through a charcoal mat and placed in the ice-box overnight. On cooling the product, a white crystalline solid, separated from solution. This was filtered off, washed with ice-water and dried *in vacuo* over calcium chloride; yield 19.9 g. (65%); m.p. 127°.

Anal.[4] Calcd. for $C_{10}H_{15}O_6As$: As, 24.51. Found: As, 24.44, 24.48.

Preparation of 4-β-(β′-Acetoxy)-ethoxyethoxyphenylarsonic Acid.—Two grams of I was added to 10 ml. of acetic anhydride containing 4 drops of concd. sulfuric acid and the mixture shaken continuously for 20 hours, the arsonic acid gradually going into solution. Most of the acetic anhydride was then distilled off under reduced pressure and the product precipitated by addition of 15 ml. of ether. This white solid was filtered off, washed well with ether and finally a little water, then dried *in vacuo* at 80° for an hour and at room temperature for 24 hours; yield 1.0 g. (45%); m.p. 125°; mixed m.p. with I, 100–110°.

Anal. Calcd. for $C_{12}H_{17}O_7As$: As, 21.55. Found: As, 21.50, 21.35.

Preparation of 4-β-(β′-Butyroxy)-ethoxyethoxyphenylarsonic Acid.—Two grams of I was added to a mixture of 20 ml. of butyric anhydride and 5 ml. of dioxane containing 4 drops of pyridine. The arsonic acid went into solution slowly on shaking which was continued for 48 hours. Most of the dioxane and excess butyric anhydride were distilled off under reduced pressure, 10 ml. of ether added and the mixture placed in the ice-box overnight. A white solid crystallized out in the cold. This was filtered off, washed with cold ether and allowed to dry 24 hours in the air; yield 0.5 g. (20%); m.p. 69–70°.

(1) This work was begun in the Avery Laboratory of Chemistry of the University of Nebraska under the direction of Dr. C. S. Hamilton.

(2) The portion of the work done in this Laboratory was aided by a grant to the University of Louisville from the Kentucky State Medical Research Commission.

(3) First synthesized by J. Parker.

(4) A modification of the method of F. E. Cislak and C. S. Hamilton, THIS JOURNAL, **52**, 638 (1930), was used in the arsenic analyses.

Anal. Calcd. for $C_{14}H_{21}O_7As$: As, 19.92. Found: As, 19.90, 19.98.

DEPARTMENT OF BIOCHEMISTRY
UNIVERSITY OF LOUISVILLE
SCHOOL OF MEDICINE
LOUISVILLE, KY.

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Reaction of Polyethylenepolyamines with *p*-Dichloroarsinobenzoyl Chloride[1]

BY ROBERT L. MCGEACHIN AND OLIVER RAYMOND HUNT, JR.[2]

Doak, Eagle and Steinman[3] and Gough and King[4] have prepared many derivatives and homologs of *p*-arsenosobenzamide by the reaction of *p*-dichloroarsinobenzoyl chloride on various aliphatic amines. However, the reaction of *p*-dichloroarsinobenzoyl chloride with polythylenepolyamines has not previously been reported. We have studied the reaction with diethylenetriamine, aminoethylethanolamine, triethylenetetramine and tetraethylenepentamine. In a preliminary study of the reaction of *p*-dichloroarsinobenzoyl chloride with amino compounds we have also used several amines not previously tried, allylamine, monoisopropanolamine and morpholine.

In the preparation of *p*-benzarsonic acid (from which the *p*-dichlorarsinobenzoyl chloride is made) *via* the Bart reaction on *p*-aminobenzoic acid our yields were comparable with those reported by Lewis and Cheetham[5] and Lewis and Hamilton.[6] However, we have found that this procedure does not give a pure product directly. Only after four or five recrystallizations from alcohol, accompanied by a considerable loss in yield, does the analysis of the product agree with theoretical arsenic percentage. However, the impurities apparently are eliminated in the conversion of the *p*-benzarsonic acid to *p*-dichloroarsinobenzoyl chloride so that the initial crude *p*-benzarsonic acid may be used without further purification.

The reactions of diethylenetriamine and aminoethylethanolamine with *p*-dichloroarsinobenzyl chloride gave satisfactory products when a ten molar excess of the amines were used but triethylenetetramine and tetraethylenepentamine did not. Even when as high as a twenty molar excess of these amines were used, the products obtained contained from 4–7% excess arsenic indicating considerable formation of bis-compounds. Attempts to separate pure products from these mixtures were unsuccessful. Allylamine and monoisopropanolamine gave satisfactory products but with morpholine a pure product could not be isolated because of the extremely high water solubility.

Experimental

Reaction of *p*-Dichloroarsinobenzoyl Chloride with Amines.—These reactions were carried out following the method of Lewis and Hamilton[6] using a five molar excess of allylamine, monoisopropanolamine and morpholine, a ten molar excess with diethylenetriamine and aminoethylethanolamine and a 20 molar excess with tetraethylenepentamine and triethylenetetramine. All products were isolated as the arsenoso compounds by washing with bicarbonate, dissolving in sodium hydroxide solution, reprecipitating by addition of concd. hydrochloric acid and drying at 120°.

TABLE I

SUBSTITUTED *p*-ARSENOSOBENZAMIDES

Amine used	Formula	Analyses,[7] % Calcd.	Found
Allylamine	$C_{10}H_{10}O_2NAs$	29.8	29.3
Monoisopropanolamine	$C_{10}H_{12}O_3NAs$	27.7	27.1
Diethylenetriamine	$C_{11}H_{16}O_2N_3As$	25.3	25.8
Aminoethylethanolamine	$C_{11}H_{15}O_4N_2As$	25.1	25.0

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SCHOOL OF MEDICINE
UNIVERSITY OF LOUISVILLE
LOUISVILLE, KY.

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Wolff–Kishner Reduction of Pyruvic and 3-Formylpropionic Acids[1]

BY E. H. MOSBACH, E. F. PHARES AND S. F. CARSON

The Wolff–Kishner reduction has been applied to a large number of organic compounds,[2] but very few investigations have been reported concerning the reduction of low molecular weight aldehydo- and keto-acids. We have found that pyruvic-2-C^{14} acid and 3-(formyl-C^{14})-propionic acid could be reduced to propionic-2-C^{14} acid and butyric-4-C^{14} acid, respectively, in good yield. These and similar transformations have been used in this Laboratory for the synthesis and degradation of biochemically important compounds.

Table I summarizes specific radioactivity data determined in connection with the synthesis and stepwise degradation[3] of propionic-2-C^{14} acid. This compound was degraded in order to determine whether any rearrangement of the carbon skeleton had occurred during the reduction.

TABLE I

SYNTHESIS AND DEGRADATION OF PROPIONIC-2-C^{14} ACID

Compound or carbons	Specific radioactivity,[a] counts/min./mg. $BaCO_3$ Calcd.	Found
Pyruvic-2-C^{14} acid	..	126
Propionic-2-C^{14} acid	15.8[b]	16.2
Carbon 1	0.0	0.1
Carbon 2	47.4	46.1
Carbon 3	0.0	0.1

[a] $BaCO_3$ from wet combustion, G–M counting at infinite thickness, estimated over-all precision of radioassay ±5%. [b] Eight-fold dilution with non-radioactive carrier.

Table II shows similar data for the preparation of butyric-4-C^{14} acid from glutamic-1,2-C_2^{14} acid. This reaction was carried out by converting glutamic acid quantitatively to 3-formylpropionic acid with chloramine T, followed by a Wolff–Kishner reduction of the aldehydo-acid. As before, a step-

(1) This work was aided by a grant to the University of Louisville from the Kentucky State Medical Research Commission.

(2) Research Scholar 1949–1950. Present address: Edward W. Sparrow Hospital, Lansing, Michigan.

(3) G. O. Doak, H. Eagle and H. G. Steinman, THIS JOURNAL, **62**, 3012 (1940).

(4) G. A. C. Gough and H. King, *J. Chem. Soc.*, 669 (1930).

(5) W. L. Lewis and H. C. Cheetham, THIS JOURNAL, **43**, 2117 (1921).

(6) W. L. Lewis and C. S. Hamilton, *ibid.*, **45**, 757 (1923).

(7) A modification of the method of F. E. Cislak and C. S. Hamilton, *ibid.*, **52**, 638 (1930), was used in the arsenic analyses.

(1) Work performed at the Oak Ridge National Laboratory under Contract No. W-7405-Eng-26 for the Atomic Energy Commission.

(2) R. Adams, "Organic Reactions," Vol. IV, John Wiley and Sons, Inc., New York, N. Y., Chap. 8, 1946.

(3) E. F. Phares, *Arch. Biochem. Biophys.*, **32**, 173 (1951).