The spectrum of choline is closely similar to that of betaine, as would be expected from their similarity of structure. However, there are some very striking differences. Both compounds show lines in the regions 700–715 and 770–785 cm.$^{-1}$. In betaine the higher of these frequencies is by far the more intense; in choline, the lower. In choline, no lines at 1400 or near 1740 are found; whereas they are strongly present in betaine and its hydrochloride, owing to the presence of the carboxyl group.

Summary

1. Raman spectra are reported for choline chloride, ethanolamine hydrochloride, sarcosine, betaine and certain betaine derivatives and their hydrochlorides; also for the hydrochloride of ethylene diamine.

2. Certain correlations between Raman spectrum and structure, previously found in certain simpler compounds, are shown also to be present in the substances studied here.

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[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF THE STATE UNIVERSITY OF IOWA]

Hexahydroxybenzene and Some of its Derivatives[1]

BY IRA E. NEIFERT AND EDWARD BARTOW

Hexahydroxybenzene, $C_6H_6O_6$, was first prepared by Lerch[2] from potassium carbonyl, $K_6C_6O_6$. Nietzki and Benckiser[3] obtained hexahydroxybenzene by the action of a zinc chloride–hydrochloric acid solution on triquinoyl. They found it difficult to separate hexahydroxybenzene, prepared from potassium carbonyl and hydrochloric acid, from its first oxidation product, tetrahydroxyquinone.

Gelormini and Artz[4] stated that some hexahydroxybenzene may have been produced in the oxidation of *i*-inositol, cyclohexanehexol, $C_6H_6(OH)_6$, with nitric acid. They obtained several compounds related to tetrahydroxyquinone, one of which was hexahydroxybenzene acetate. No free hexahydroxybenzene was reported.

It was our thought that the separation would be unnecessary, if the tetrahydroxyquinone formed could be reduced completely to hexahydroxybenzene, the hexahydroxybenzene might be prepared by reduction of tetrahydroxyquinone made from *i*-inositol, which, because of its composition and cyclic structure, and absence of a metal, is an ideal material for the preparation of tetrahydroxyquinone and hexahydroxybenzene.

The purpose of this research was to prepare hexahydroxybenzene from *i*-inositol, to prepare derivatives and study their properties. *i*-Inositol was prepared in sufficient quantity from starch factory steep water by the method of Bartow and Walker[5a,b] modified by Hoglan and Bartow.[6] Tetrahydroxyquinone was prepared by oxidizing *i*-inositol with concentrated nitric acid, neutralizing with sodium bicarbonate, and then adding the crystals to one part of 45% hydriodic acid (sp. gr. 1.50) and ten parts of hydrochloric acid (sp. gr. 1.19), heating the mixture and stirring for half an hour. Crystals of tetrahydroxyquinone are obtained on cooling.

Sometimes these crystals are brown, but if an equal volume of water is added and the mixture warmed and stirred for about fifteen minutes, coal-black crystals are obtained. These crystals should be filtered out on a Büchner funnel, washed with a little water to dissolve any crystals of sodium chloride and sodium iodide, then with cold alcohol and finally with ether. Since tetrahydroxyquinone is somewhat more soluble in alcohol and ether than in water, excessive amounts should not be used. The combined filtrate and wash liquids may be evaporated on a steam-bath and more of the tetrahydroxyquinone will crystallize out. The yield is approximately 80% of the theoretical. The apparent catalytic effect of the hydriodic acid is the important part of the above method. Fair yields have been obtained when dilute hydrochloric acid (6 *N*) has been substituted for the concentrated hydrochloric acid, provided hydriodic acid is used in conjunction with it. Diluted acid is not recommended.

(1) Original manuscript received August 10, 1939.

(2) J. U. Lerch, *Ann.*, **124**, 20–42 (1862).

(3) R. Nietzki and Th. Benckiser, *Ber.*, **18**, 499–515 (1885).

(4) O. Gelormini and N. E. Artz, THIS JOURNAL, **52**, 2483–2494 (1930).

(5) (a) E. Bartow and W. W. Walker, *Ind. Eng. Chem.*, **30**, 300–303 (1938); (b) U. S. Patent 2,112,553, March 29, 1938.

(6) F. A. Hoglan and E. Bartow, *Ind. Eng. Chem.*, **33**, 2397 (1939).

TABLE I

ESTERS OF HEXAHYDROXYBENZENE

Ester	Formula	Melting point, °C.	Molecular weight—Theoretical	Molecular weight—Found
Hexaacetate[a]	$C_6(CH_3CO_2)_6$	203	427.9	dec.
Hexapropionate	$C_6(CH_3CH_2CO_2)_6$	133	512.6	494
Hexa-*n*-butyrate	$C_6(CH_3CH_2CH_2CO_2)_6$	135	597.3	595
Hexa-isobutyrate	$C_6[(CH_3)_2CHCO_2]_6$	164.5	597.3	583
Hexa-*n*-valerate	$C_6[CH_3(CH_2)_3CO_2]_6$	103	682	679
Hexa-isovalerate	$C_6[(CH_3)_2CHCH_2CO_2]_6$	155	682	640
Hexa-*n*-caproate	$C_6(C_5H_{11}CO_2)_6$	97	767	765
Hexa-*n*-caprylate	$C_6(C_7H_{15}CO_2)_6$	86	936	dec.
Hexa-*n*-caprate	$C_6(C_9H_{19}CO_2)_6$	85	1105	dec.
Hexamonochloroacetate	$C_6(CH_2ClCO_2)_6$	212	635	...
Hexadichloroacetate	$C_6(CHCl_2CO_2)_6$	Not formed	841	...
Hexatrichloroacetate	$C_6(CCl_3CO_2)_6$	245d.	1048	...
Hexabenzoate[a]	$C_6(C_6H_5CO_2)_6$	254	803	675–812

[a] Hexaacetate and hexabenzoate have been reported previously.

The following method has been developed: Dissolve one part by weight of tetrahydroxyquinone in 10 parts of hot 95% alcohol (denatured alcohol, 10% methyl and 90% ethyl alcohol may be used). Add at least 3 parts of 45% hydriodic acid (sp. gr. 1.5), and boil gently for about an hour. On cooling, the hexahydroxybenzene crystallizes out. Wash the crystals on a filter, first with a minimum amount of water, then with alcohol and finally with ether. The yield is about 70%. If acetone is substituted for alcohol, crystallization is considerably slower, but the crystals are unusually well formed and are almost colorless. Hexahydroxybenzene is considerably more soluble in acetone than in alcohol. By slow evaporation of acetone, crystals usually will appear in two or three days.

Zinc and acid was not satisfactory as a reducing agent, for the zinc forms a salt that is decidedly troublesome in the separation of the crystals from the mother liquor. Hydrogen sulfide was not tried.

Derivatives of Hexahydroxybenzene

Esters.—Mix hexahydroxybenzene with approximately twice as much of an acid chloride as would be required to react with 6 hydroxyl groups, reflux for six hours on an oil-bath at a sufficiently high temperature to maintain gentle boiling, evaporate the excess liquid, dissolve the remaining solid in the least amount of hot alcohol, filter and allow to cool to crystallize. The compounds were purified by recrystallizing from alcohol, washing with a small amount of alcohol and drying in a desiccator charged with solid potassium hydroxide and solid calcium chloride.

Esters were prepared using acetyl, propionyl, *n*-butyryl, isobutyryl, *n*-valeryl, isovaleryl, *n*-caproyl, *n*-caprylyl, *n*-capryl, monochloroacetyl, dichloroacetyl, trichloroacetyl and benzoyl chlorides. Only the acetyl and benzoyl esters have been reported previously. The melting points of the series of esters from the acetate through the normal caprate, in general, decrease with increase in molecular weights, determined by the method of Rast[7] (Table I). The solubility in alcohol was noted to increase, in general, as the molecular weight increases. The melting points of the isobutyrate and the isovalerate are considerably higher than those of the corresponding normal esters.

All of the hydroxyl groups acted alike, forming esters containing six acid radicals.

Amino Derivatives.—Nietzki and Schmidt[8] in 1888 reported that hexahydroxybenzene and aniline in dilute alcohol, if stirred in air, formed glistening gold-colored plates which appeared carmine-red by transmitted light. We confirmed this observation. However, when the glistening gold-colored plates were washed thoroughly with alcohol, they became green and glistening by reflected light, and red by transmitted light.

Determination of nitrogen by the Kjeldahl-Gunning method gave the following results

	I	II	Calcd. for $C_6(OH)_6 \cdot 2NH_2C_6H_5$	Calcd. for $C_6(OH)_6 \cdot NH_2C_6H_5$
Nitrogen	7.04	7.20	7.77	5.24

The compound produced probably has the formula $C_6(OH)_6 \cdot 2NH_2C_6H_5$, the addition of two molecules of aniline instead of a condensation with one, which is at variance with the claim of Nietzki and Schmidt that the monoanilide of tetrahydroxyquinone is produced.

Hexahydroxybenzene and the Chloroanilines.—When the chloroanilines were added to 50% alcohol in which hexahydroxybenzene was suspended, *o*-chloroaniline did not form a compound, *m*-chloroaniline yielded a small amount of product, and the *p*-chloroaniline easily formed a derivative. Nitrogen and chlorine determinations of the para derivative lead to the conclusion that its formula is $C_6(OH)_6 \cdot 2NH_2C_6H_4Cl$, and that two molecules of *p*-chloroaniline have been added to one molecule of hexahydroxybenzene.

		Found	Calcd. for $C_6(OH)_6 \cdot 2NH_2C_6H_4Cl$
Nitrogen	I	7.6	6.32
	II	7.68	
Chlorine	I	17.6	16.5
	II	17.1	

(7) K. Rast, *Ber.*, **55**, 1051–1054, 3727–3728 (1922).

(8) R. Nietzki and A. W. Schmidt, *ibid.*, **21**, 1850–1856 (1888).

Compounds of Hexahydroxybenzene and the Toluidines.—When *o*-toluidine, *m*-toluidine and *p*-toluidine were added to hexahydroxybenzene in the same manner that aniline was added, solid products were formed. When these were washed, dried and the nitrogen determined, it was found that two molecules of the toluidines had added to one molecule of hexahydroxybenzene, giving the formula $C_6(OH)_6 \cdot 2NH_2C_6H_4CH_3$ (Table II).

A second compound of *o*-toluidine was formed when the reaction was carried out with exclusion of air. The derivative was buff-colored in the mass, and decidedly crystalline and almost colorless under the microscope, instead of the strikingly colored compound usually obtained. Nitrogen determination showed that the formula of this compound was probably $C_6(OH)_6 \cdot NH_2C_6H_4CH_3$ (Table II).

TABLE II

AROMATIC AMINO COMPOUNDS OF HEXAHYDROXYBENZENE

Reagent	Formula of compound	Color	Form
Aniline	$C_6(OH)_6 \cdot 2NH_2C_6H_5$	Green-red	Plates
o-Toluidine	$C_6(OH)_6 \cdot NH_2C_6H_4CH_3$	Buff	Plates
o-Toluidine	$C_6(OH)_6 \cdot 2NH_2C_6H_4CH_3$	Red	Needles
m-Toluidine	$C_6(OH)_6 \cdot 2NH_2C_6H_4CH_3$	Orange-red	Plates
p-Toluidine	$C_6(OH)_6 \cdot 2NH_2C_6H_4CH_3$	Red	Plates
o-Chloroaniline	Not formed		
m-Chloroaniline	$C_6(OH)_6 \cdot 2NH_2C_6H_4Cl$	Orange-red	Plates
p-Chloroaniline	$C_6(OH)_6 \cdot 2NH_2C_6H_4Cl$	Red	Plates

Summary

1. Tetrahydroxyquinone has been prepared by the action of a mixture of hydriodic acid and hydrochloric acid on disodium tetrahydroxyquinone prepared from oxidized *i*-inositol; yield, 80%.

2. Hexahydroxybenzene has been prepared by the action of hydriodic acid on an alcoholic solution of tetrahydroxyquinone; yield, 70%.

3. Fatty acid esters of hexahydroxybenzene, from the acetate to the normal caprate have been prepared. Hexamonochloroacetate, hexatrichloroacetate and hexabenzoate of hexahydroxybenzene also have been prepared.

4. Aniline, *m*-chloroaniline, *p*-chloroaniline, *o*-toluidine, *m*-toluidine and *p*-toluidine addition compounds with hexahydroxybenzene have been prepared. Two molecules of the amino compound combine with one of the hexahydroxybenzene.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

The Synthesis of 3′-Alkyl-1,2-cyclopentenophenanthrenes

BY BYRON RIEGEL, MARVIN H. GOLD[1] AND MICHAEL A. KUBICO

The importance of thoroughly testing the tumor producing activity of hydrocarbons having the tetracyclic steroid ring structure was pointed out to us by Dr. M. J. Shear of the National Cancer Institute. Since the side chains of the various steroids are attached to the 17-position, the corresponding 3′-position of 1,2-cyclopentenophenanthrene is of particular interest. A few derivatives of 1,2-cyclopentenophenanthrene have been reported, but the methods of preparation are so laborious that sufficient quantities for biological testing have not been prepared.

The most obvious approach to the 3′-alkyl-1,2-cyclopentenophenanthrenes would be through 3′-keto-1,2-cyclopentenophenanthrene which has been prepared by Bachmann and Kloetzel.[2] Low yields, however, prohibited the adaptation of their method, and other attempts at its preparation in this Laboratory involving the cyclization of 2-[β-halopropionyl]-phenanthrenes were unsuccessful.

The series of reactions outlined below proved to be the most successful means of synthesizing the desired compounds. The readily available 2-acylphenanthrenes[3] (I) were reduced by means of aluminum isopropoxide to the corresponding carbinols which were in turn converted to bromides. Condensation of the bromides with sodiomalonic ester followed by saponification and decarboxylation gave the β-[2-phenanthryl]-substituted acids (II). This is an adaptation of the method used by Bachmann and Struve[4] in their synthesis of chrysene derivatives. Ring closure of the corresponding acid chlorides was best effected by means of aluminum chloride in nitrobenzene. Clemmensen reduction of the resulting ketones (III) gave the desired homologs (IV) of Diels' hydrocarbon. The latter part of this synthesis is an adaptation of the method employed for the preparation of 3′-methyl-1,2-cyclopentenophenanthrene by Bergmann and Hillemann[5] who made the acid II

(1) Anna Fuller Fund Research Associate, 1940-1942.

(2) W. E. Bachmann and M. C. Kloetzel, THIS JOURNAL, **59**, 2207 (1937).

(3) B. Riegel, M. H. Gold and M. A. Kubico, *ibid.*, **64**, 2221 (1942).

(4) W. E. Bachmann and W. S. Struve, *J. Org. Chem.*, **5**, 426 (1940).

(5) E. Bergmann and H. Hillemann, *Ber.*, **66**, 1302 (1933).