dissolved in water, made alkaline with aqueous ammonia, evaporated to dryness, and the residue extracted again. Only a little sirup that did not crystallize was obtained.

Summary

1. The causes for the varying stability of substituted uric acids toward alkali are discussed.
2. The action of alkali on tetramethyl-uric acid and on 1,3,9-trimethyl-uric acid has been studied. Tetramethyl-uric acid gives 1,3-dimethyl-hydantoyl-methylamide, and trimethyl-uric acid gives 3-methylhydantoyl-methylamide.
3. Tetra-substituted uric acids give hydantoins as final decomposition products; 1,3,9-tri-substituted uric acids give ureas.
4. An intermediate compound that would show where the first break in the uric acid ring occurs could not be isolated.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF KENTUCKY]

SOME NEW SUBSTITUTED BENZYL ESTERS[1]

BY CHARLES BARKENBUS AND JOHN B. HOLTZCLAW

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The anti-spasmodic action of opium alkaloids has been shown by Macht[2] to be due to the presence of the benzyl group in the alkaloids. Benzyl benzoate and many other benzyl esters have been shown to possess this physiological property.[3] In the last few years many benzyl esters have been made, chiefly with the desire of finding some new ester that would have the physiological properties of benzyl benzoate but have physical properties that would allow it to be more readily dispensed.

The object of this work was to prepare a substituted benzyl benzoate, namely *p*-carboxybenzyl benzoate, that would have a carboxyl group in the *para* position of the benzyl nucleus. It was hoped that this ester might form a soluble salt which would be superior to benzyl benzoate for dispensing purposes, since the latter is a water-insoluble oil. So far we have been unable to obtain this ester in a pure state but have thought it expedient to publish the results obtained, since other workers[4] are preparing esters of this kind and we do not expect to continue this work.

p-Carboxybenzyl alcohol can be esterified to give three types of esters.

$$HOOCC_6H_4CH_2OH \longrightarrow HOOCC_6H_4CH_2OOC{-}R \qquad (1)$$
$$HOOCC_6H_4CH_2OH \longrightarrow HOCH_2C_6H_4COOC{-}R_3 \qquad (2)$$
$$HOOCC_6H_4CH_2OH \longrightarrow R{-}COOCH_2C_6H_4COOC{-}R_3 \qquad (3)$$

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[1] This paper is based upon the thesis presented by John B. Holtzclaw to the Faculty of the Graduate School of the University of Kentucky in partial fulfilment of the requirements for the degree of Master of Science, June, 1924.

[2] Macht, *J. Pharmacol.*, **9,** 287 (1917); **11,** 263 (1918).

[3] Macht, *ibid.*, **13,** 509 (1919). Shonle and Row, THIS JOURNAL, **43,** 361 (1921).

[4] Case, THIS JOURNAL, **47,** 1143 (1925).

Case[4] has recently prepared some esters of Type 2 and Type 3. We were primarily interested in the esters of Type 1.

The method first used in preparing esters of Type 1 was that of Gomberg and Buchler[5] in making benzyl esters. When the sodium salt of *p*-carboxybenzyl chloride was used in place of benzyl chloride a complex mixture was always obtained. It was found that when a neutral water solution of the sodium salt of *p*-carboxybenzyl chloride was heated an ester, *p*-carboxybenzyl-*p*-chloromethyl benzoate, was precipitated as indicated by the reaction, $3\ NaOOCC_6H_4CH_2Cl + H_2O \longrightarrow 2\ NaCl + NaOOCC_6H_4CH_2OH + HOOCC_6H_4CH_2OOCC_6H_4CH_2Cl$. This ester hydrolyzes quantitatively when heated in a slightly alkaline solution to form the sodium salt of *p*-carboxybenzyl alcohol: $NaOOCC_6H_4CH_2OOCC_6H_4CH_2Cl + 2\ NaOH \longrightarrow 2\ NaOOCC_6H_4CH_2OH + NaCl$. The fact that we have a benzyl chloride nucleus and a sodium salt in the same molecule accounts for this reaction and makes the preparation of esters by this method impossible. The esterification of *p*-carboxybenzyl alcohol was tried next. This acid was first made by Kekulé and Dittmar[6] by heating *p*-carboxybenzyl bromide with barium hydroxide. Case[4] prepared it by heating *p*-cyanobenzyl bromide with concd. hydrochloric acid. The corresponding chloride under similar conditions gives only the *p*-carboxybenzyl chloride. We made the acid by hydrolyzing *p*-carboxybenzyl chloride with *dil.* sodium hydroxide solution. By avoiding an excess of sodium hydroxide, ether formation, first pointed out by Günther,[7] was minimized.

The *p*-carboxybenzyl alcohol was heated with acetyl chloride, and *p*-carboxybenzyl acetate was obtained as a white crystalline solid. All attempts to prepare the corresponding benzoate gave us a mixture from which the ester has not been obtained in a pure state.

Some work was done on the *ortho*-substituted esters. *o*-Carboxybenzyl alcohol readily forms phthalide, and no esters of it have ever been made.[8] By heating *o*-cyanobenzyl chloride with sodium acetate or with sodium benzoate the corresponding new esters, *o*-cyanobenzyl acetate and *o*-cyanobenzyl benzoate were obtained. We attempted to hydrolyze the nitrile group in *o*-cyanobenzyl acetate in the presence of absolute alcohol, hoping to esterify the carboxyl group as fast as it was formed and thus obtain the double ester of the unstable acid. In all cases, however, phthalide and ethyl acetate were the only products formed.

Experimental Part

_p_-Cyanobenzyl Chloride.—Chlorine gas was passed into 100 g. of *p*-tolyl nitrile at a temperature of 120–130° until it had gained 30 g. About two hours was sufficient for

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[5] Gomberg and Buchler, THIS JOURNAL, **42**, 2059 (1920).

[6] Kekulé and Dittmar, *Ann.*, **162**, 342 (1872).

[7] Günther, *Ber.*, **23**, 1061 (1890).

[8] Hessert, *Ber.*, **10**, 1446 (1877). Gabriel, *Ber.*, **20**, 2234 (1887). Hjelt, *Ber.*, **25**, 525 (1892).

the chlorination when a tungsten lamp was placed beside the reaction flask. A higher temperature, the boiling point of *p*-tolyl nitrile, is given in the literature[9] but at this temperature more of the *p*-cyanobenzal chloride is formed. The chlorinated product was poured into an evaporating dish and allowed to cool. The crystalline mass was triturated with ice-cold alcohol and filtered with suction. One more trituration gives a product melting at 77–78°. This is pure enough for most purposes. It can be crystallized from alcohol; yield, 76 g., or 58.7%. The wash-alcohol filtrates from several runs were combined, evaporated and fractionally distilled. Some more of the product was obtained as well as some unchanged *p*-tolyl nitrile and some *p*-cyanobenzal chloride. This recovery brings the yield to about 70%.

o-**Cyanobenzyl Chloride.**—The procedure is the same as for the *para* compound except that the chlorination temperature was 140–150°. Seventy five g. of *o*-tolyl nitrile gave 60 g. of *o*-cyanobenzyl chloride; yield, 61.7%; m. p., 60–61°.

p-**Carboxybenzyl Chloride.**—Fifty g. of *p*-cyanobenzyl chloride was heated for six hours with 500 cc. of 50% sulfuric acid at a temperature of 110–120° (temperature of oil-bath). The mixture was vigorously stirred, 100 cc. of water was added and the mixture cooled with ice and filtered. The crude acid was suspended in 300 cc. of water and neutralized with sodium hydroxide solution. The resulting solution was filtered from a small amount of slimy material and the acid precipitated with concd. hydrochloric acid. The precipitate was filtered off and recrystallized from alcohol; yield, 43 g., or 76.5%; m. p., 199–200°.

p-**Carboxybenzyl Alcohol.**—Forty g. of *p*-carboxybenzyl chloride was suspended in 300 cc. of water and exactly neutralized with sodium hydroxide solution, using phenolphthalein as an indicator. The solution was heated to boiling during stirring, and 10% sodium hydroxide solution added as fast as used up. When the color no longer disappeared, the solution was treated with animal charcoal, filtered and the acid precipitated with concd. hydrochloric acid. The crude acid was crystallized from water; yield, 26 g., or 72.9%; m. p., 178–179°.

Action of the Sodium Salt of *p*-**Carboxybenzyl Chloride when Heated in Water Solution.** *Preparation of p-Carboxybenzyl-p-chloromethyl Benzoate.*—Twenty g. of *p*-carboxybenzyl chloride was neutralized in the cold with 10% sodium hydroxide solution and the mixture filtered. When this solution was heated a precipitate commenced to form at 60°. The solution was boiled for ten minutes and then filtered hot. Thirteen g. of crude, amorphous material was obtained. This was crystallized from alcohol and after several crystallizations obtained as a white, crystalline solid; yield, 6 g., or 52.1%. This new ester forms white microscopic needles; m. p., 221°. It is insoluble in water and soluble in alkali and alcohol. It is difficult to obtain in a crystalline form. By acidifying the filtrate from the original crude product, 3 g. of *p*-carboxybenzyl alcohol was obtained.

Anal. Calcd. for $C_{16}H_{13}O_4Cl$: Cl, 11.64. Found: 11.23, 11.37.

This ester is hydrolyzed quantitatively to *p*-carboxybenzyl alcohol: *p*-$HOOC-C_6H_4CH_2OOCC_6H_4CH_2Cl + 3\ NaOH \longrightarrow 2\ p\text{-}HOCH_2C_6H_4COONa + NaCl + H_2O$.

Hydrolysis. 0.1004 g. requires 9.9 cc. of 0.1 *N* sodium hydroxide solution. Found: 9.8 cc.

o-**Cyanobenzyl Esters.** (a) *o*-**Cyanobenzyl Acetate.**—Fifty g. of *o*-cyanobenzyl chloride was heated at 100–110° for five hours with 75 g. of sodium acetate dissolved in 300 cc. of water, the mixture being well stirred. The reddish-brown oil that separated was extracted with ether. The ether extract was washed with water, dried and distilled. The resulting oil was fractionally distilled under diminished pressure. From the low-boiling fractions, 9.8 g. of unchanged *o*-cyanobenzyl chloride was recovered. The fraction boiling at 180–190° (20 mm.) was redistilled and 26 g. of an oil distilling at

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[9] Mellinghoff, *Ber.*, **22**, 3207 (1889).

180–182° (24 mm.) was obtained. Analysis showed this oil to be the ester; yield, 55.9%, after deducting the unchanged chloride recovered. This ester is a heavy, colorless oil with slight aromatic odor. It is insoluble in water but soluble in the common solvents.

Anal. Calcd. for $C_{10}H_9O_2N$: N, 8.0. Found: (Kjeldahl) 7.8.

(b) **o-Cyanobenzyl Benzoate.**—Sixty g. of benzoic acid was dissolved in the calculated amount of 10% sodium hydroxide solution and the whole made up to 300 cc. Fifty g. of o-cyanobenzyl chloride was added and the mixture stirred for seven hours at 100–110°. A reddish-brown, crystalline mass settled as the liquid cooled; this was extracted with ether. The ether extract was washed with water, dried and the ether distilled. The unchanged o-cyanobenzyl chloride was distilled under diminished pressure and 17 g. was recovered. The residue in the flask was fractionally crystallized from alcohol. This ester is a white, odorless, crystalline solid. It is insoluble in water but soluble in the common solvents; m. p., 54–55°; yield, 18 g., or 34.8%, calculated on the amount of unchanged chloride recovered.

Anal. Calcd. for $C_{15}H_{11}O_2N$: N, 5.9. Found: (Kjeldahl) 5.8.

p-Carboxybenzyl Acetate.—Ten g. of p-carboxybenzyl alcohol and 15 g. of acetyl chloride were heated together for five hours on a boiling water-bath. The resulting clear oil was poured into 200 cc. of water, and 12 g. of a crude, white solid was obtained. This was crystallized from a mixture of ether and petroleum ether; yield, 7.5 g., or 58.6%; m. p., 123–124°. This ester is soluble in the common solvents and in alkaline solutions but insoluble in water.

Anal. Calcd. for $C_{10}H_{10}O_4$: C, 61.83; H, 5.19. Found: C, 61.59; H, 5.12.

Summary

An improvement in the preparation of o- and p-cyanobenzyl chloride has been described and some new esters of o-cyanobenzyl alcohol and p-carboxybenzyl alcohol have been made. The reaction that the sodium salt of p-carboxybenzyl chloride undergoes in a neutral water solution has been investigated and the new ester, p-carboxybenzyl-p-chloromethyl benzoate has been isolated.

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[CONTRIBUTION FROM THE DEPARTMENT OF PHARMACOLOGY OF JOHNS HOPKINS UNIVERSITY]

THE INFRA-RED ABSORPTION SPECTRA OF ORGANIC DERIVATIVES OF AMMONIA. I. ANILINE AND SOME MONO- AND DIALKYL ANILINES

BY FREDERICK K. BELL

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Introduction

The relation between light absorption and chemical constitution is a subject that has received considerable attention. Aside from the theoretical significance of such a relation, its practical aspect which presents the possibility of both qualitative and quantitative analysis of unknown substances is of especial interest to the chemist.

A survey of the literature reveals clearly that, in the case of organic com-