drolysis products, while phosphotungstic acid, as might be expected, leaves practically no peptides in solution. The large quantity of free amino nitrogen in the filtrate from the latter precipitation indicates the existence of amino acids in solution. This indication was verified by the isolation of glutamic acid. A more extended examination will doubtless show the presence of other amino acids in the free state.

Summary

In the fermentation of corn mash *B. granulobacter pectinovorum* brings about a rapid hydrolysis of the proteins. From 50 to 75% of the total protein is converted into soluble products during the fermentation which is approximately complete in from 3 to 4 days. One-half of the total soluble products may be formed in 24 hours.

The hydrolysis results chiefly in the formation of simple peptides and amino acids. Due to these buffers and to acids of low dissociation, a high titratable acidity may be produced without causing much change in the hydrogen-ion concentration.

MADISON, WISCONSIN.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY COLLEGE, NOTTINGHAM]

SOME NEW AROMATIC ORTHOFORMATES

BY JOHN EDMUND DRIVER

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Although numerous alkyl orthoformates have been described, the phenyl ester is the only simple aromatic compound of this type known.[1] It has been obtained by Tiemann[2] and by Auwers[3] as a by-product of the Reimer-Tiemann reaction. Tiemann stated that attempts were being made to prepare similar compounds from other phenols, but nothing else was published on the subject.

It has recently been shown[4] that phenyl orthoformate can be conveniently prepared by the action of chloroform on dry potassium phenolate at a fairly high temperature. This method has now been employed for the preparation of the *o*-, *m*- and *p*-tolyl esters from the corresponding cresols. The yields of these compounds are poor, and their purification is rendered difficult by the fact that they are accompanied by comparatively large quantities of dark, viscous, alkali-insoluble glues. The

[1] Since the completion of this work, the author finds that Keil [*Ann.*, **352**, 273 (1907)] records, in a footnote, the formation of the *p*-tolyl ester as a by-product of the action of chloroform on *p*-cresol in alkaline solution.

[2] Tiemann, *Ber.*, **15**, 2686 (1882).

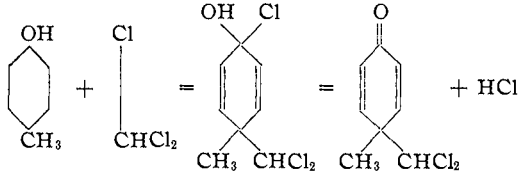
[3] Auwers, *Ber.*, **18**, 2657 (1885).

[4] Baines and Driver, *J. Chem. Soc.*, **125**, 907 (1924).

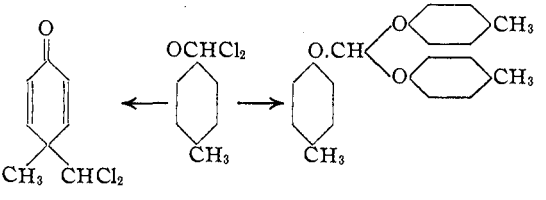
amounts of the pure esters finally obtained varied from about 3 to 7 g. per 100 g. of the cresolate employed. Dark colored, alkali-soluble substances are also formed, the alkaline solutions being deep red and reddish-brown, respectively, in the cases of the *o*- and *m*-cresolates and dark brown in the case of the *p*-cresolate. In the two former cases the alkali-soluble product doubtless contains the leuco compound of the corresponding trimethylaurine, the red color being due to partial atmospheric oxidation.[4] These products have not been further investigated, previous experience having shown that, in the case of phenol, the corresponding substance is difficult to purify and cannot be obtained crystalline.

The tolyl orthoformates are colorless, well-defined crystalline compounds. As in the case of the corresponding cresols, the *meta* compound melts at a much lower temperature than do the *ortho* and *para*. In chemical properties they behave like stable compounds of the ether type. Thus they are insoluble in dilute acids and in aqueous alkalies; they are not hydrolyzed by boiling alkalies, and are only very slowly oxidized by boiling neutral permanganate. Concd. nitric acid decomposes them in the cold or on gentle warming.

One of the main products of the action of chloroform on alkaline solutions of *p*-cresol is 1-methyl-1-dichloromethyl-Δ-2,5-cyclohexadiene-4-one.[5] Auwers explained the formation of this compound as being due to the production of an additive compound, from which hydrogen chloride is subsequently eliminated.



By the action of chloroform on dry potassium *p*-cresolate this cyclic ketone is formed in only small traces, the main product, even under widely differing conditions, being the orthoformic ester. This suggests that the first product is an unstable dichloromethoxytoluene, which can either react with potassium *p*-cresolate to form the orthoformic ester, or undergo intramolecular change to give the cyclic ketone.



[5] Auwers and Winternitz, *Ber.*, **35**, 465 (1902). Auwers and Keil, *Ber.*, **35**, 4207 (1902).

The molecular rearrangement evidently takes place most readily in aqueous solution. With other phenols, the reaction no doubt follows a similar course.

Experimental Part

Potassium cresolates were prepared from good commercial samples of the corresponding cresols by the method previously described.[6]

***p*-Tolyl Orthoformate,** $CH(O.C_6H_4.CH_3)_3$.—Chloroform vapor was passed over potassium *p*-cresolate, heated at 108°, for six to eight hours. The dark product was warmed with an excess of aqueous sodium hydroxide, the mixture cooled, and extracted with chloroform. After the chloroform extract was washed and dried, the solvent was distilled. There remained a black, viscous oil, which slowly solidified. The solid thus obtained was dissolved in benzene and, by slow evaporation of the solution in the cold, the ester was deposited in large crystals which were washed with a little acetone and purified by recrystallization, from alcohol.

The crystals were not suitable for goniometric measurement. They were colorless and transparent and of tabular habit, showing a tendency to hollow growth. Microscopic examination between crossed Nicols revealed symmetrical extinction when lying on the basal face. Irregular brushes indicating a biaxial figure were obtained. The crystals thus appear to belong to the orthorhombic system, and are tabular parallel to the basal plane (001). The mean values for the angles of the prism faces are 93° and 87°, respectively, as measured under the microscope.

The ester is easily soluble in chloroform, benzene, or ether, fairly easily in acetone or ligroin, and is somewhat less soluble in alcohol. It melts at 112°.

Anal. Calc. for $C_{22}H_{22}O_3$: C, 79.04; H, 6.59; mol. wt., 334. Found: C, 78.67; H, 6.64; mol. wt. in freezing benzene, 325.

Isolation of 1-Methyl-1-dichloromethyl-Δ-2,5-cyclohexadiene-4-one.—The alkali-insoluble glues and mother liquors from the preparation described above were mixed and distilled in a current of steam. 1-Methyl-1-dichloromethyl-Δ 2,5-cyclohexadiene-4-one was extracted from the distillate with benzene, and was obtained, after recrystallization from petroleum ether, in colorless needles; m. p., 53–55°. The yield from 30 g. of potassium *p*-cresolate was only about 0.02 g.

In other experiments, potassium *p*-cresolate (40 g.) was boiled with chloroform (100 cc.) for twelve hours. Potassium chloride separated and from the filtered solution 0.08 g. of the ketone and 3.5 g. of the crude orthoformic ester were isolated. Experiments in which the reaction was carried out in alcoholic solution in sealed tubes at 90–100° did not result in any appreciable increase in the yield of either compound.

***o*-Tolyl Orthoformate,** $CH(O.C_6H_4.CH_3)_3$, was most conveniently prepared at the boiling point of chloroform, the yield from 50 g. of potassium *o*-cresolate under these conditions being 3.5 g. The ester was purified by recrystallization three or four times from alcohol, the last trace of coloring matter being removed by extracting with petroleum ether and separating from the slight, insoluble brown residue.

The compound forms tufts of small, colorless needles (from petroleum ether). It is readily soluble in boiling alcohol, very readily in benzene, and melts at 96°.

Anal. Calc. for $C_{22}H_{22}O_3$: C, 79.04; H, 6.59; mol. wt., 334. Found: C, 78.86; H, 6.66; mol. wt. in freezing benzene, 316.

From the alkali-insoluble residues of this preparation there was isolated about 2 g. of an oil volatile with steam, which did not crystallize. It had a distinct odor

[6] Baines and Driver, *J. Chem. Soc.*, **123**, 1214 (1923).

resembling that of hexachloro-ethane, and boiled at about 210° with decomposition and evolution of hydrogen chloride.

m-**Tolyl Orthoformate,** $CH(O.C_6H_4.CH_3)_3$.—This compound was prepared from potassium *m*-cresolate at 110–120°, and was isolated as described above. It was purified by recrystallization first from pentane, and finally from alcohol containing a little water, being thus obtained as a silky mass of long, slender, colorless prisms. It is extremely soluble in all common organic solvents, but is comparatively sparingly soluble in 80% alcohol; m. p., 50°.

Anal. Calc. for $C_{22}H_{22}O_3$: C, 79.04; H, 6.59; mol. wt., 334. Found: C, 78.80; H, 6.56; mol. wt. in freezing benzene, 305.

The author wishes to express his thanks to Professor F. S. Kipping, F.R.S., for his encouragement and interest in this work, and to Dr. W. A. Richardson for examining microscopically the *p*-tolyl ester.

Summary

1. The action of chloroform on the potassium derivatives of the cresols has been investigated. The three isomeric tolyl orthoformates have been isolated and described.

2. A new mechanism is suggested for the formation of cyclic ketones by the action of chloroform on alkaline solutions of phenols.

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

PRESSOR ANESTHETICS. I

BY C. S. MARVEL AND V. DU VIGNEAUD

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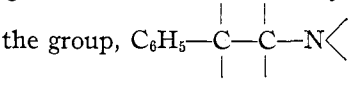
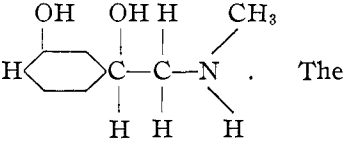
In medical practice, a pressor drug is always used with a local anesthetic in order to localize and prolong its action. The pressor substance also helps to reduce bleeding if an operation is performed. Since the chemical structures that produce pressor action and that produce local anesthesia are well known, an attempt was made to combine these two pharmacological properties in one molecule.

The work of Barger and Dale[1] has shown very clearly that pressor action is associated with the group,  and reaches a maximum in adrenaline,  . The pressor action is not strong in the compounds which do not contain a phenolic hydroxyl and the primary and secondary amines have been shown to have the greatest action.

[1] (a) *J. Physiol.*, **41**, 19 (1910). (b) See also Pyman, *J. Chem. Soc.*, **111**, 1121 (1917).