butyl ester by using butanol-1 and *either* malonic ester. In the case of the reactions using butanol, the solution was concentrated by a current of air after acidification, the butyl ester then being taken up in ether and handled in the usual way. The yields of esters ranged from 70 to 85%.

A warm alcohol solution of one of the pyrone esters was treated with a trace of sodium alcoholate, allowed to cool to room temperature, acidified with glacial acetic acid and then worked up as in the preceding paragraph. Each of the pyrone esters was converted into each of the other esters by this method. No other products were detected.

The pyrone acid IV was esterified either by refluxing an anhydrous ether solution with an excess of silver oxide and an excess of alkyl iodide or by refluxing an alcoholic solution with concentrated sulfuric acid, the ester products being isolated in the usual way. Each of the four esters was obtained as the sole product, except for traces of recovered pyrone acid when the Fischer method was used.

Methyl 4-(*o*-chlorophenyl)-6-phenyl-2-pyrone-3-carboxylate is fairly soluble in acetone, sparingly soluble in methanol and ether, and insoluble in petroleum ether. It crystallizes as pale yellow stout plates and melts at 121–122°.

Anal. Calcd. for $C_{19}H_{13}O_4Cl$: C, 67.0; H, 3.85. Found: C, 66.9; H, 3.88.

Ethyl 4-(*o*-chlorophenyl)-6-phenyl-2-pyrone-3-carboxylate is very soluble in acetone, soluble in ethanol, sparingly soluble in ether and insoluble in petroleum ether. It crystallizes as very pale yellow thin plates and melts at 133–134°.

Anal. Calcd. for $C_{20}H_{15}O_4Cl$: C, 67.6; H, 4.26. Found: C, 67.9; H, 4.35.

Propyl 4-(*o*-chlorophenyl)-6-phenyl-2-pyrone-3-carboxylate is very soluble in acetone, soluble in propanol and ether, and sparingly soluble in petroleum ether. It crystallizes as very pale yellow long thin plates and melts at 101°.

Anal. Calcd. for $C_{21}H_{17}O_4Cl$: C, 68.4; H, 4.65. Found: C, 68.4; H, 4.90.

Butyl 4-(*o*-chlorophenyl)-6-phenyl-2-pyrone-3-carboxylate is very soluble in acetone, butanol and ether, and sparingly soluble in petroleum ether. It crystallizes as very pale yellow long thin plates and melts at 62°.

Anal. Calcd. for $C_{22}H_{19}O_4Cl$: C, 68.9; H, 5.01. Found: C, 69.0; H, 5.13.

The Pyrone Acid, IV.—The next two paragraphs indicate the formation of the pyrone acid by basic hydrolysis and by acidic hydrolysis of the pyrone esters.

One equivalent of 0.2 normal aqueous sodium hydroxide (73.5 ml.) was added over a period of thirty minutes to a warm solution of 5.00 g. of the methyl pyrone ester in 100 ml. of alcohol-free acetone. After standing for one hour, the yellow solution was diluted with about 200 ml. of water and extracted with ether. The ether solution, twice extracted with sodium bicarbonate solution, gave 0.46 g. of unchanged methylpyrone ester. The combined aqueous solution, acidified with hydrochloric acid, gave a precipitate of the pyrone acid which was filtered, washed with water, allowed to dry and finally crystallized from ether. The weight of pyrone acid was 4.25 g., a 98% yield based on the ester consumed. In another run, one normal sodium hydroxide was used and the time of standing before extraction was increased to five hours. The amount of recovered ester was 0.75 g. and the weight of pyrone acid was 3.91 g., indicating that the more dilute base gives the better result.

A mixture of 4.95 g. of the methylpyrone ester, 50 ml. of glacial acetic acid and 50 ml.of six normal sulfuric acid was refluxed for one and one-half hours, cooled, diluted with water and extracted with ether. The ether solution was washed with water and then extracted with sodium bicarbonate solution. The extracted ether solution gave 1.20 g. of the pyrone V; the sodium bicarbonate extract gave 3.30 g. of the pyrone acid IV, a 70% yield of acid based on the methyl ester used. In another run, an increase of the refluxing period to four hours gave more of the pyrone, 2.70 g., at the expense of the acid produced, 1.50 g.

Hydrolysis of the pyrone esters by an excess of base resulted in a much lower yield of the pyrone acid and of the pyrone. The bulk of the material was converted into an oily mixture which has resisted identification.

4-(*o*-Chlorophenyl)-6-phenyl-2-pyrone-3-carboxylic acid is soluble in acetone, insoluble in petroleum ether and moderately soluble in ether. It dissolves with difficulty in ether but forms supersaturated solutions from which it precipitates when seeded or scratched. The acid crystallizes from ether as clusters of small stout sulfur-yellow plates and melts at about 178–180° with decomposition.

Anal. Calcd. for $C_{18}H_{11}O_4Cl$: C, 66.1; H, 3.40. Found: C, 66.0; H, 3.28.

The Pyrone, V.—The best method of preparing the pyrone appears to be the one described in the preceding section, namely, the acidic hydrolysis of the pyrone esters and the subsequent decarboxylation of the acid formed. One may start either with the pyrone ester or the pyrone acid. For example, 5.0 g. of the recrystallized pyrone was obtained when 6.0 g. of the pyrone acid was refluxed for eleven hours with 60 ml. of glacial acetic acid and 60 ml. of six normal sulfuric acid, a 95% conversion into the pyrone.

The action of an excess of alcoholic sodium hydroxide or alcoholic sodium alcoholate on the pyrone esters or the pyrone acid gave a mixture of products, the best yield of the pyrone obtained in this way being about 50%.

4-(*o*-Chlorophenyl)-6-phenyl-2-pyrone is soluble in glacial acetic acid, moderately soluble in acetone and methanol, sparingly soluble in ether and insoluble in petroleum ether. It crystallizes as long colorless needles, resembling fine glass wool, and melts at 141°.

Anal. Calcd. for $C_{17}H_{11}O_2Cl$: C, 72.2; H, 3.93. Found: C, 72.1; H, 4.04.

The Hydroxy Pyridine, VI.—Five grams of the methylpyrone ester was added to 30 ml. of methanol saturated with ammonia gas. The ester dissolved completely in one and one-half hours, giving a yellow solution from which colorless crystals began to separate in another hour. After standing overnight, the solid was filtered and washed with methanol, the yield of product being 2.5 g.

2-Hydroxy-4-(*o*-chlorophenyl)-6-phenylpyridine is very sparingly soluble in the common solvents, crystallizes as long thin colorless plates and melts at 232°.

Anal. Calcd. for $C_{17}H_{12}ONCl$: C, 72.6; H, 4.30. Found: C, 72.6; H, 4.50.

The filtrate from the above hydroxypyridine was evaporated in a current of air, giving an oily mixture from which only one pure substance could be obtained. This substance was β-methoxy-2-chlorochalcone,[1,3,7] identified by a mixed melting point with a known sample. The formation of this compound can be logically explained only by assuming that *o*-chlorophenylbenzoylacetylene was formed by a cleavage of the pyrone ring and that methanol then added to the acetylene.

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[7] Bickel, THIS JOURNAL, **68**, 865 (1946).

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Action of Organometallic Compounds on Geoisomeric Styrenes

BY J. C. BOND AND GEORGE F WRIGHT

The reaction of an excess of phenyllithium or phenylmagnesium bromide with either *cis-* or *trans*-styryl cyanide[1] gives β,β-diphenylpropiophenone and the known isomer of benzalacetophenone. A mixture of the geoisomers of styryl

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[1] Ghosez, *Bull. soc. chim. Belg.*, **41**, 477 (1932).

cyanide is recovered when either the *cis*- or *trans*-isomer is used initially.

The *cis*-isomer of cinnamic acid reacts with phenyllithium more rapidly than the *trans*-modification, but unchanged acid was recovered, in each case, geometrically identical with that introduced into the reaction. The hydrolyzed reaction mixtures also yield the known isomer of benzalacetophenone (1,2-addition) as well as β,β-diphenylpropionic acid (1,4-addition) and β,β-diphenylpropiophenone (1,4- and 1,2-addition). When a large excess of phenyllithium is used with *trans*-cinnamic acid the latter two products are not found, but 1,1,3,3-tetraphenylpropanol-1 is obtained instead. It is obvious that the lithium alkoxide from which this compound is derived could not have formed from an immediate pregenitor containing a carbonyl group. In consequence an ionic mechanism of organometallic addition must be operative. In this circumstance it is not surprising that specific geoisomeric configuration is lost in the formation of benzalacetophenone.

In the experiments described above, the reaction media were hydrolyzed by cold aqueous acid, but this does not seem to account for the appearance of but one of the two possible isomers of benzalacetophenone. This isomer alone is also obtained when the reaction mixture from either *cis*- or *trans*-styryl cyanide is hydrolyzed with aqueous ammonium chloride. The yield is low, however, since the principal product is a new compound of empirical formula $C_{15}H_{13}N$. This formula corresponds to that of styryl phenyl ketimine, but the compound cannot be converted to benzalacetophenone. Its structure will be discussed in a subsequent paper.

Experimental

Styryl Cyanides with Phenyllithium.—A solution of 0.35 mole of phenyllithium (from bromobenzene in 95% yield) in 300 cc. of ether under nitrogen was evaporated to 125 cc. volume and 200 cc. of dry benzene was added. To this stirred solution at 0° was added 5.1 g. (0.04 mole) of either *cis*- or *trans*-styryl cyanide in 50 cc. of dry benzene over fifteen minutes. After ninety minutes the homogeneous solution was poured into ice to which 15.5 cc. of *concd.* sulfuric acid had been added. The gum was dissolved in dioxane to which solution was added a chloroform extract of the aqueous layer. Distillation at about 0.001 mm. yielded first biphenyl, then an equilibrium mixture of styryl cyanides, and finally 4.5 g. boiling at 125–175°. After this fraction had partially crystallized it was washed with methanol at 0° to leave 0.85 g. of β,β-diphenylpropiophenone, m. p. 94–95° (about 7% of theoretical). The methanol solution yielded 3.4 g. of impure benzalacetophenone. Only the single pure isomer (m. p. 57°) could be isolated from this material by crystallization. The yield, estimated on the amount of benzalacetophenone dibromide which could be formed, varied between 20 and 30%.

In addition to these two products small amounts were obtained of a white crystalline substance which melted at 183° after crystallization from ethanol. This was the principal product which could be isolated (in 30–40 weight % yield) when a comparable reaction mixture of styryl cyanide and phenylmagnesium bromide was hydrolyzed with an excess of cold ammonium chloride, and the resulting gummy precipitate was extracted with ethanol.

***trans*-Cinnamic Acid with Phenyllithium.**—To 0.4 mole of phenyllithium in ether was added 5.92 g. (0.04 mole) of *trans*-cinnamic acid in 150 cc. of dry benzene over two hours at 25°. The clear red solution was then poured into ice plus 10.6 cc. of *concd.* sulfuric acid. The yellow non-aqueous layer was washed with alkali and distilled, finally under 0.001 mm. to yield first biphenyl, then 0.8 g. (10% yield) of benzalacetophenone, m. p. 52–53°, and finally (125–150°) 4.1 g. of 1,1,3,3-tetraphenylpropanol-1, m. p. 85–96° (30% yield). The propanol was identified by conversion to 1,1,3,3-tetraphenylpropene (m. p. 126–127° and mixed melting point not lowered) by boiling with 22% hydrochloric acid for eight hours.[2]

An otherwise identical experiment was carried out with a 1.5 instead of a fivefold excess of phenyllithium. Acidification of the alkaline wash liquors yielded an acid mixture from which 2.7 g. (45% recovery) of *trans*-cinnamic acid and 0.63 g. (7% yield) of β,β-diphenylpropionic acid (m. p. 150–150.5°) were separated. The non-aqueous portion was distilled at 0.001 mm. to yield first biphenyl, then 2.8 g. (33%) of benzalacetophenone, m. p. 50–53°, and finally (b. p. 170°) 0.05 g. of β,β-diphenylpropiophenone.

***cis*-Cinnamic Acid with Phenyllithium.**—To 0.06 mole of phenyllithium in 2:5 ether–benzene solution at 0° was added 2.96 g. (0.02 mole) of *cis*-cinnamic acid in 25 cc. of dry benzene over fifteen minutes. After one hundred minutes at 0° and sixty minutes at 30° the clear red solution was poured into 200 g. of ice containing 10 cc. of concd. sulfuric acid. The non-aqueous layer was extracted with alkali to remove an acid mixture which was separated, after acidification, into 0.059 g. (2% recovery) of *cis*-cinnamic acid and 1.35 g. (30% yield) of β,β-diphenylpropionic acid by means of extraction with petroleum ether (b. p. 60–70°). The alkali-washed ether-benzene solution was distilled, finally at 0.0001 mm., to yield biphenyl, and a 2.4-g. fraction (57% yield) of benzalacetophenone, m. p. 50–53°, identified by mixed melting point.

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[2] D. Vorlander and C. Siebert, *Ber.*, **39**, 1032 (1906).

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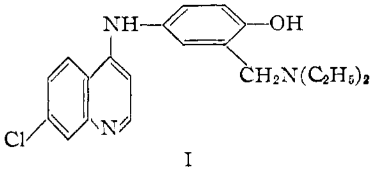
An Alternate Synthesis of Camoquin[1]

BY J. H. BURCKHALTER,[2] H. A. DEWALD[3] AND F. H. TENDICK

Camoquin (I) dihydrochloride may be obtained from 4-acetamido-α-diethylamino-*o*-cresol (II) and 4,7-dichloroquinoline in 90% yield.[4] We wish to report an alternate method for preparing this economically important antimalarial which involves the treatment of 7-chloro-4-(4-hydroxyanilino)-quinoline (III) with formaldehyde and diethylamine. By using equivalent amounts of



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[1] Parke, Davis and Company trade name for SN 10,751 or 4-(7-chloro-4-quinolylamino)-α-diethylamino-*o*-cresol.

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[4] Burckhalter, Tendick, Jones, Jones, Holcomb and Rawlins, THIS JOURNAL, **70**, 1363 (1948).