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-tetraphenyl-propanol-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.

(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
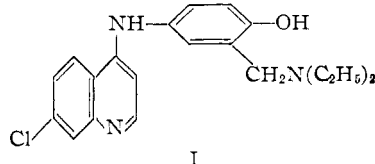

(1) Parke, Davis and Company trade name for SN 10,751 or 4-(7-chloro-4-quinolylamino)-α-diethylamino-*o*-cresol.

(2) Present address: Department of Pharmaceutical Chemistry, University of Kansas School of Pharmacy, Lawrence.

(3) Present address: Department of Chemistry, University of Illinois, Urbana.

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

II

III
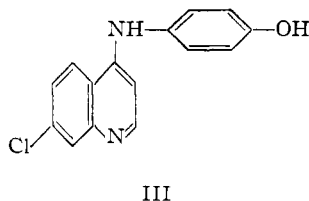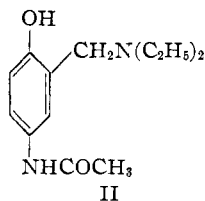
III and formaldehyde and a nine-fold excess of diethylamine, which may be recycled, over-all yields as high as 80% have been realized from 4,7-dichloroquinoline and *p*-aminophenol hydrochloride. It is of interest to note that this yield is much higher than that obtained when a primary amine—ethylamine—was used in the process.[5]

Experimental

7-Chloro-4-(4-hydroxyanilino)-quinoline (III).—Yields of the previously prepared hydrochloride[6] of III from 4,7-dichloroquinoline and *p*-aminophenol hydrochloride were virtually quantitative when the heated reaction mixture was stirred. To obtain the free base, the salt was suspended in an excess of ammonia and the mixture stirred vigorously. The free base (III) was collected and dried to constant weight; yield 128–135 g. (95–100%); m. p. 254–256°. Recrystallization from alcohol did not significantly affect the melting point.

Anal. Calcd. for $C_{15}H_{11}ClN_2O$: C, 66.54; H, 4.10. Found: C, 66.52; H, 4.18.

4-(7-Chloro-4-quinolylamino)-α-diethylamino-o-cresol (Camoquin, I).—A mixture of 27 g. (0.1 mole) of 7-chloro-4-(4-hydroxyanilino)-quinoline (III), 3.4 g. (0.11 mole) of 95% paraformaldehyde, 100 ml. (0.98 mole) of diethylamine and 100 ml. of isopropyl alcohol was stirred and heated under reflux for eight hours. Complete solution was effected within an hour. At the end of the reflux period, the mixture was well cooled and then filtered. The crystalline product, a light cream in color, was sucked dry; yield 29.8 g. (84% yield); m. p. 200–205° (dec.). Mixed m. p. determination with a sample prepared by the original process[7] showed no depression.

The filtrate was saved for subsequent runs. Before the second cycle, the diethylamine was replenished by washing the product prior to its removal from the funnel with 10 ml. (0.1 mole) of the amine. To the combined filtrates was added 0.1 mole of III, and the reaction was repeated. For six recycles the over-all yield was about 80%.

Camoquin Dihydrochloride.—A mixture of 25 g. (0.07 mole) of Camoquin base and 20 ml. of hot concentrated hydrochloric acid readily formed a solution. Upon cooling, the mass quickly began to crystallize. At this time 75 ml. of acetone was added and the mixture vigorously stirred and cooled. The product, a yellow crystalline monohydrate, was collected on a Buchner funnel and dried; yield 95–99%; m. p. 179–183°.[7]

(5) *Cf.* ref. 4, p. 1367.
(6) *Cf.* ref. 4, p. 1373.
(7) *Cf.* ref. 4, p. 1366.

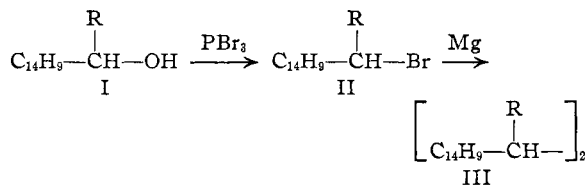RESEARCH LABORATORIES
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DETROIT 32, MICHIGAN   RECEIVED AUGUST 22, 1949

Some New Bis-9-phenanthryl Derivatives

BY CHARLES K. BRADSHER AND RICHARD S. KITTILA[1]
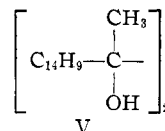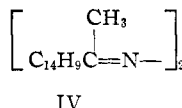
As a continuation of our study of phenanthrene derivatives having substituents at the 9 position, we have now prepared some new bis-9-phenan-

(1) U. S. Public Health Service Fellow (1948–1949).

thryl compounds. The two hydrocarbons prepared (III, R = CH_3 and R = C_2H_5) may be

$$C_{14}H_9\!-\!\overset{R}{\underset{|}{C}}H\!-\!OH \xrightarrow{PBr_3} C_{14}H_9\!-\!\overset{R}{\underset{|}{C}}H\!-\!Br \xrightarrow{Mg}$$
I   II

$$\left[C_{14}H_9\!-\!\overset{R}{\underset{|}{C}}H\!-\! \right]_2$$
III

considered as members of a series in which the 1,2-bis-(9-phenanthryl)-ethane (III, R = H) of Tarbell and Wystrach[2] is the simplest member.

The two new hydrocarbons were prepared by treatment of the appropriate halide (II) in ether with one-half gram atom of magnesium. Seeking alternate approaches to the synthesis of the bisphenanthrylbutane (III, R = CH_3), it was found that the phenanthrylbromoethane (II, R = CH_3) did not undergo the Wurtz reaction, and that the azine (IV) of 9-acetophenanthrene (IV) was not

$$\left[C_{14}H_9\overset{CH_3}{\underset{|}{C}}\!=\!N\!-\! \right]_2$$
IV

$$\left[C_{14}H_9\!-\!\overset{CH_3}{\underset{\underset{OH}{|}}{C}}\!-\! \right]_2$$
V

reduced to the tetrahydroazine under the conditions employed by Baker[3] in the synthesis of hexestrol derivatives.

It was found that 9-acetophenanthrene could be reduced to the corresponding pinacol (V) by the action of zinc and alkali or, less satisfactorily, by zinc and acetic acid.

Experimental

1-Bromo-1-(9-phenanthryl)-ethane (II, R = CH_3).—A solution of 4 g. of 1-(9-phenanthryl)-ethanol-1[4] in 30 ml. of dry ether was cooled and 1.2 ml. of phosphorus tribromide was added with shaking. After the solution had been allowed to stand for two hours in an ice-bath, the ether was removed under vacuum, and the residue triturated with 8 ml. of cold methanol. The resulting solid (5.1 g.) was collected, taken up in benzene and the benzene solution washed and dried. Upon concentration of the solution and addition of petroleum ether, the bromide was obtained as white crystals, m. p. 85.5–87.5°, yield 3.2 g. (62%). Recrystallization yielded a product, m. p. 86.5–89°, which was not improved by further recrystallization.

Anal.[5] Calcd. for $C_{16}H_{13}Br$: C, 67.38; H, 4.59. Found: C, 67.72; H, 4.60.

2,3-Bis-(9-phenanthryl)-butane (III, R = CH_3).—A solution containing 5.7 g. of the above bromide in 15 ml. of dry benzene was added slowly with mechanical stirring to 0.25 g. of magnesium and 15 ml. of dry ether. The mixture was refluxed on the steam-bath for six hours and the solid collected, m. p. 281.5–282.5°; yield 1.1 g. (27%). Recrystallization from benzene yielded a fine white powder, m. p. 283.5–284°.

Anal. Calcd. for $C_{32}H_{26}$: C, 93.61; H, 6.39; molecular weight, 411. Found[5]: C, 93.66; H, 6.13; molecular weight 388 (ebulliometric in chloroform).

(2) Tarbell and Wystrach, THIS JOURNAL, **65**, 2149 (1943).
(3) Baker, *ibid.*, **65**, 1572 (1943).
(4) Bachmann, *ibid.*, **56**, 1366 (1934).
(5) Analyses by Microanalytical Laboratory, University of Pittsburgh.