

experiment was any product found in this receiver). A slow flow of nitrogen (*ca.* 1-2 l. per hr.) was passed through the pyrolysis tube before and during the pyrolysis.

The temperature of the pyrolysis tube was controlled and measured as described previously.⁸ Control was accurate to within $\pm 5^\circ$.

The phosphoramidates were pyrolysed by dropping the melted compounds through the heated tube at the rates and temperatures listed in Table III. After pyrolysis was complete, the frozen solids in the receiver were quickly weighed and then warmed by the warmth of the hand to

melt the olefinic product, which was decanted from the still frozen phosphorus-containing by-products. The crude olefin was weighed and then analysed without purification by gas chromatography, essentially as described previously.⁷

The olefinic product from the pyrolysis at 350° of diphenyl *N*-(2-ethylhexyl)phosphoramidate was separated by simple distillation because the whole product melted at the same time, preventing mechanical separation of the olefin.

The amount of carbonization accompanying the pyrolyses varied considerably from very slight to fairly heavy; being the worst with diphenyl *N*-(2-ethylhexyl)-phosphoramidate.

Most of the pyrolysates had the faint odor of phenol and the infrared spectra of the phosphorus-containing residues contained, in addition to peaks to be expected of the organo phosphorus materials, the peaks characteristic of phenol.

LINCOLN 8, NEB.

[CONTRIBUTION FROM AVERY LABORATORY, UNIVERSITY OF NEBRASKA]

Cinnolines. IX. The Stollé-Becker Synthesis^{1,2}

HENRY E. BAUMGARTEN AND JAMES L. FURNAS

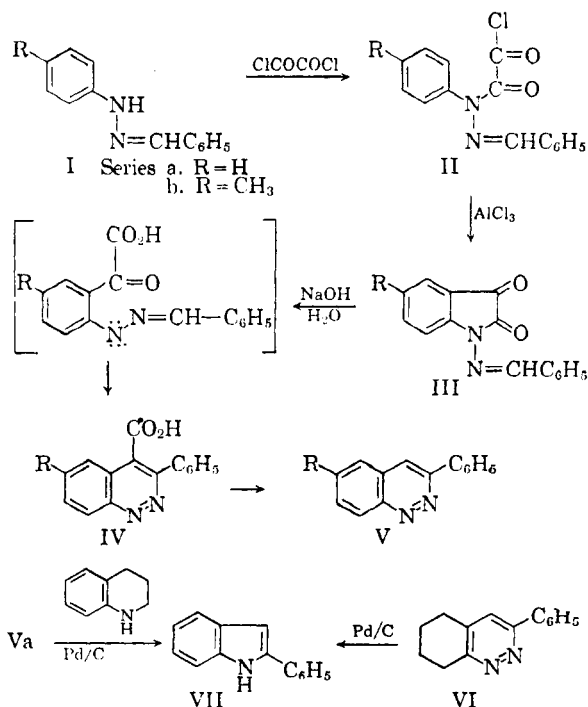
Treatment of *N*-benzylideneaminoisatin (IIIa) with aqueous base gave 3-phenyl-4-cinnolinecarboxylic acid (IVa) as suggested previously by Stollé and Becker. The structure of IVa was proved by conversion of IVa into 3-phenylcinnoline and into 2-phenylindole. By a similar sequence 6-methyl-3-phenyl-4-cinnolinecarboxylic acid (IVb) and 6-methyl-3-phenylcinnoline (Vb) were prepared.

In 1924 Stollé and Becker³ reported that the treatment of *N*-benzylideneaminoisatin (IIIa) with aqueous base yielded 3-phenyl-4-cinnolinecarboxylic acid (IVa). This transformation, which may be labelled the Stollé-Becker synthesis, has occupied a somewhat questionable position in cinnoline chemistry,⁴ for Stollé and Becker gave at best meager experimental details and offered no proof of structure other than an elementary analysis for nitrogen. The present communication offers experimental evidence supporting the validity of the Stollé-Becker synthesis.

The complete sequence used by Stollé and Becker is shown by the changes Ia \rightarrow IVa. Preliminary experiments based on such experimental detail as was given in their report quickly demonstrated the inadvisability of attempting to repeat their experiments exactly. Thus, although their sequence was followed, the experimental procedures were based on what appeared to be the best current practice.

The reaction of benzaldehyde phenylhydrazone (Ia) with a 100% excess of oxalyl chloride gave a 90-98% yield of crude *N*-benzylideneamino-*N*-phenyloxamyl chloride (IIa). Treatment of the latter with six moles of aluminum chloride in chloroform solution gave a 65-80% yield of IIIa, and the reaction of IIIa with hot 20% aqueous

sodium hydroxide gave a 75-85% (48-61% overall) yield of 3-phenyl-4-cinnolinecarboxylic acid (IVa).



(1) Paper VIII. *J. Org. Chem.*, **26**, 803 (1961).

(2) This work was supported in part by grant CY-3090 of the U. S. Public Health Service.

(3) R. Stollé and W. Becker, *Ber.*, **57**, 1123 (1924).

(4) Cf. T. L. Jacobs in R. C. Elderfield's *Heterocyclic Compounds*, Vol. 6, Wiley, New York, 1957, p. 152.

Although the unstable character of IIa prevented its complete characterization compounds IIIa and IVa gave analyses and infrared spectra (Table I) compatible with the structures assigned by Stollé and Becker. However, to establish the validity of

TABLE I
 INFRARED SPECTRA^a

Compound	Frequency, Cm. ⁻¹
IIIa ^b	3622w, 3460w, 2900bb w, 1825w, 1745s, 1619s, 1473s, 1391w, 1333m, 1310m, 1287m, 1097m, 1022w, 1002w, 968w, 921w, 875w.
IVa	3420bbw, 2800bbw, 2400bbm, 1716s, 1619w, 1587w, 1567m, 1542w, 1502m, 1577m, 1430m, 1478w, 1331m, 1322w, 1294m, 1246s, 1201m, 1187sh, 1152sh, 1137m, 1088w, 1072w, 1038m, 1026m, 987w, 970m, 862m, 856m, 808w, 783m, 766m, 728s, 707m, 691sh.
Va	3018w, 1624w, 1607w, 1591m, 1502m, 1450m, 1406w, 1367w, 1335m, 1216w, 1175w, 1141w, 1111msh, 1167m, 1104msh, 1027w, 969w, 939w, 916m, 878m, 806m, 786wsh, 776m, 754m, 708s.
Va ^b	3700w, 3400bbw, 3015msh, 2997s, 2475m, 1981w, 1891w, 1845w, 1820bbw, 1757w, 1657w, 1622m, 1592s, 1580s, 1563sh, 1500w, 1453m, 1443msh, 1398wsh, 1363w, 1328s, 1134m, 1095s, 1012w, 963m, 959m, 898s.
VII from Va	3418m, 3008w, 1608m, 1590sh, 1545w, 1470m, 1457m, 1411m, 1360m, 1346sh, 1305m, 1248w, 1238wsh, 1196w, 1153w, 1122w, 1108wsh, 1076w, 1057w, 1035w, 1016w, 939w, 911w, 805m, 768sh, 747s, 691m.
VII from VI	3418m, 3010w, 1602m, 1585sh, 1544w, 1489m, 1456m, 1410m, 1368m, 1345sh, 1305m, 1247sh, 1237w, 1192w, 1155w, 1120w, 1105sh, 1077w, 1056w, 1030w, 1015w, 936w, 910w, 804m, 768sh, 745s, 686m.
IIIb	3035w, 2335w, 1817w, 1725s, 1626s, 1573sh, 1497s, 1460w, 1399w, 1331sh, 1311s, 1284sh, 1237w, 1228w, 1293m, 1142m, 1041m, 1023sh, 1001w, 981w, 871w, 824m, 765m, 701m.
IVb	3400bbw, 3060w, 2910w, 2470bbm, 1710s, 1625m, 1492m, 1460m, 1370w, 1395m, 1240s, 1191m, 1174m, 1140w, 1101m, 1020w, 882m, 810w, 770m, 750s, 707m, 695m.
Vb	3019w, 1631m, 1587bbm, 1488m, 1463m, 1421m, 1363m, 1324m, 1221w, 1181w, 1167w, 1121m, 1106m, 1040w, 1029m, 976w, 921m, 831s, 776m, 704s, 686sh.

^a Determined using a Perkin-Elmer model 21 recording spectrophotometer and potassium bromide pellets. ^b Chloroform solution, 6 mg./ml.

these assignments more rigorously IVa was decarboxylated by heating in benzophenone solution, giving 51–74% of 3-phenylcinnoline (Va). At the time this work was done Va had not been reported. Therefore, attempts were made to prepare the 6-methyl (Vb) analog of Va by a sequence very similar to that used subsequently by Atkinson and Sharpe⁵ for the preparation of Va. However, as the results of these attempts were not particularly encouraging,⁶ a different approach to synthesis of Va was examined. It was hoped that the catalytic dehydrogenation of 3-phenyl-5,6,7,8-tetrahydrocin-

noline⁷ (VI) would give at least some of the desired Va.⁸ Unfortunately, the only product isolated from this dehydrogenation was 2-phenylindole (VII) (in 39% yield), which apparently resulted from the combined dehydrogenation of the benzo ring and hydrogenation of the pyridazine ring of VI.

Attempts were then made to reduce Va to VII using the various procedures reported in the literature for the reduction of cinnolines to indoles.⁹ From each of these attempts Va was recovered unchanged. However, when a mixture of Va and 1,2,3,4-tetrahydroquinoline was heated with palladium on charcoal, dehydrogenation of the latter combined with hydrogenation of the former occurred giving VII in 43% yield. The ease of separation of the basic 1,2,3,4-tetrahydroquinoline and its basic dehydrogenation product, quinoline, from the essentially neutral indole may recommend this procedure for the reduction of other cinnoline derivatives to indoles.

The conversion of Va into VII would appear to establish fairly definitely the structures of IVa and Va and to suggest strongly the validity of structure IIIa. This conclusion is further supported by the similarity of the properties of the compound prepared in this work and those of the 3-phenylcinnoline reported by Atkinson and Sharpe.⁵ Although their product was not fully characterized *per se*, it appears reasonable to conclude that both their product and ours were correctly identified.

Our attempts to establish the generality of the Stollé-Becker synthesis have been only partially successful. By using very similar experimental procedures 6-methyl-3-phenyl-4-cinnolinecarboxylic acid (IVb) was prepared in 53% over-all yield from benzaldehyde *p*-tolylhydrazone (Ib) and 6-methyl-3-phenylcinnoline (Vb) was obtained by the decarboxylation of IVb in 95% yield. However, these same procedures were not effective with benzaldehyde *p*-chlorophenyl-, *p*-anisyl-, or 1-naphthylhydrazones, none of which gave in our hands the entire Stollé-Becker sequence. Inasmuch as we cannot claim to have exhausted in these examples the possible experimental variations that might be employed with the Stollé-Becker sequence, we can conclude only that the experimental conditions reported here do not form the basis of a general cinnoline synthesis and that the question of the generality of the Stollé-Becker synthesis is still subject to further investigation.

(5) C. M. Atkinson and C. J. Sharpe, *J. Chem. Soc.*, 2858 (1959).

(6) Examination of ref. 5 will confirm that the procedure employed there is clearly inferior to the Stollé-Becker synthesis for the preparation of Va.

(7) H. E. Baumgarten, P. L. Creger, and C. E. Villars, *J. Am. Chem. Soc.* **80**, 6609 (1958).

(8) C. F. H. Allen and J. A. Van Allen, *J. Am. Chem. Soc.*, **73**, 5850 (1951).

(9) Ref. 4, p. 159–161.

EXPERIMENTAL¹⁰

N-Benzylideneamino-N-phenyloxamyl chloride (IIa). To a solution of 15 g. (0.077 mole) of benzaldehyde phenylhydrazone in 450 ml. of anhydrous ether was added dropwise with stirring 19.5 g. (0.154 mole) of oxalyl chloride. A bright yellow solution was obtained. The reaction mixture was heated under reflux in an oil bath for 3 hr., during which time no color change occurred and no precipitate formed. The ether was evaporated, leaving 10–12 g. (90–98% yield) of *N-benzylideneamino-N-phenyloxamyl chloride* as a bright yellow solid, m.p. 100–105° (lit.³ m.p. 110°), which had to be used immediately in the preparation of *N-benzylideneaminoisatin* because of rapid decomposition of the former on standing. In other experiments with quantities of benzaldehyde phenylhydrazone varying from 0.029–0.115 mole, the yields were 80–95%. In experiments using equimolar quantities of reactants, only intractable tars were obtained.

N-Benzylideneaminoisatin (IIIa). A suspension of 32.38 g. (0.2421 mole) of aluminum chloride in 200 ml. of chloroform¹¹ was cooled in an ice bath to 0–5° and a solution of the 10–12 g. (0.0349–0.0419 mole) *N-benzylideneamino-N-phenyloxamyl chloride* (obtained in the previous experiment) in 250 ml. of chloroform was added dropwise with stirring while the temperature was kept below 10°. After the addition was completed, the solution was stirred at room temperature for 15 min., then refluxed for 30 min. At the end of this heating period the reaction mixture was dark red in color. The mixture was allowed to stand overnight.

To the reaction mixture was added 200 g. of ice and water in such a fashion that the temperature of the mixture was kept below 10°. The solution was stirred at room temperature until all of the ice had melted. The gray solid which formed was separated by filtration. The aqueous and chloroform layers were separated, and the aqueous layer and the solid were extracted with chloroform. The combined chloroform solutions were evaporated, leaving a reddish-brown solid. The crude *N-benzylideneaminoisatin* was crystallized from absolute ethanol, giving 11–15 g. (65–80%) of brick red solid, m.p. 148–149° (lit.³ m.p. 147°). The *N-benzylideneaminoisatin* was soluble in hot benzene, hot ethanol; insoluble in Skellysolve B,¹² water, and cold ethanol; slightly soluble in ether, acetone, chloroform, and cold methanol. When the reaction was run in carbon disulfide, the yields were 16–21%.

Anal. Calcd. for $C_{15}H_{12}N_2O_2$: C, 71.99; H, 4.03; N, 11.20. Found: C, 71.72; H, 4.19; N, 11.20.

3-Phenylcinnoline-4-carboxylic acid (IVa). Five grams (0.0199 mole) of *N-benzylideneaminoisatin* was suspended in a solution of 20 g. of sodium hydroxide in 100 ml. of water. The color of the solution changed from red to yellow almost immediately. The mixture was heated on a water bath for 1 hr. at the end of which time all of the solid had dissolved. The solution was neutralized to pH 5 with 6*N* hydrochloric acid, cooled, and filtered. The yellow solid which was collected was recrystallized from 95% ethanol, giving 3.75–4.20 g. (75–85%) of 3-phenylcinnoline-4-carboxylic acid, m.p. 224–224.5° (lit.³ m.p. 244°). 3-Phenylcinnoline-4-carboxylic acid was soluble in hot ethanol; slightly soluble in chloroform, carbon tetrachloride, carbon disulfide, dioxane, and piperidine; insoluble in water and ether.

Anal. Calcd. for $C_{15}H_{10}N_2O_2$: C, 71.99; N, 11.20; H, 4.03. Found: C, 71.61; N, 11.18; H, 4.32.

(10) Melting points are corrected. Analyses were by Micro-Tech Laboratories, Skokie, Ill.

(11) The chloroform was freed from ethanol just prior to use by passage through a column of silicic acid and Celite (1:1) which had been heated at 80° for 6 hr.

(12) A hydrocarbon solvent, b.p. 60–69°.

(13) K. Schofield and J. C. E. Simpson, *J. Chem. Soc.*, 512 (1945)

3-Phenylcinnoline (Va). The procedure of Schofield¹³ and Simpson for the decarboxylation of 6-methoxycinnoline-3-carboxylic acid to 6-methoxycinnoline was used as a model.

A mixture of 4 g. (0.016 mole) of 3-phenylcinnoline-4-carboxylic acid and 20 g. (0.020 mole) of benzophenone was heated for 90 min. in the oil bath at 200° under an atmosphere of nitrogen. The gas which was evolved gave a turbidity when bubbled through barium hydroxide, indicating the gas to be carbon dioxide. After being cooled, the mixture was dissolved in 150 ml. of ether and the ethereal solution was extracted with 300 ml. of 6*N* hydrochloric acid. The yellow acidic solution was cooled in an ice bath, saturated with potassium carbonate, filtered, and extracted with ether. The ethereal solution was dried over anhydrous potassium carbonate, filtered, and saturated with hydrogen chloride. The yellow solid which precipitated was washed with 6*N* sodium hydroxide and recrystallized from Skellysolve B,¹² giving 2.14–3.20 g. (51–74%) of 3-phenylcinnoline, m.p. 118.5–119° (lit.⁶ m.p. 119–120°). The solid was soluble in ethanol and chloroform.

Anal. Calcd. for $C_{14}H_{10}N_2$: N, 13.59; C, 81.53; H, 4.88. Found: N, 13.66; C, 81.52; H, 5.04.

2-Phenylindole (VII) from 3-phenylcinnoline. A mixture of 5 g. (0.038 mole) of tetrahydroquinoline, 1 g. (0.048 mole) of 3-phenylcinnoline, and 0.5 g. of 10% palladium on charcoal was heated at 250° for 2 hr. The residue was extracted with 6*N* hydrochloric acid and then with chloroform, and the acidic aqueous solution was extracted with chloroform. The chloroform layer was dried over anhydrous magnesium sulfate, treated with charcoal, filtered, and evaporated in the rotating evaporator. The solid which remained was recrystallized from Skellysolve B¹² giving 0.36 g. (43%) of 2-phenylindole, m.p. 186.5–187° (lit.¹⁴ m.p. 188–189°), mixture m.p. with the 2-phenylindole prepared from 3-phenyl-5,6,7,8-tetrahydrocinnoline, 186–187°.

2-Phenylindole (VII) from 3-phenyl-5,6,7,8-tetrahydrocinnoline. A mixture of 1 g. (0.0048 mole) of 3-phenyl-5,6,7,8-tetrahydrocinnoline and of 0.5 g. of 10% palladium on charcoal was heated in an atmosphere of carbon dioxide in an apparatus such that the carbon dioxide swept out the hydrogen formed by the dehydrogenation of the sample, the hydrogen being collected over 50% aqueous potassium hydroxide. Most of the hydrogen came off at 270°, 200 ml. being collected at 25°. The crude solid product was dissolved in ether, and the solution was treated with hydrogen chloride. No solid precipitated. The ethereal solution was evaporated and the residue was suspended in 6*N* sodium hydroxide. The solid which resulted was recrystallized from Skellysolve B,¹² giving 0.37 g. (39%) of 2-phenylindole, m.p. 186–187°.

Anal. Calcd. for $C_{14}H_{11}N$: C, 87.01; H, 5.74; N, 7.25. Found: C, 86.67; H, 5.81; N, 7.38.

N-Benzylideneamino-N-(p-tolyl)oxamyl chloride (IIb). To a solution of 6.0 g. (0.029 mole) of benzaldehyde *p*-tolylhydrazone in 150 ml. of ether was added dropwise with stirring 9.5 g. (0.075 mole) of oxalyl chloride. The yellow solution was refluxed for 3 hr. Through evaporation of the solvent 6.3 g. (75%) of a yellow solid was isolated (m.p. not obtained). The product had to be used immediately in the preparation of *N-benzylideneamino-5-isatin*.

N-Benzylideneamino-5-methylisatin (IIIb). To a suspension of 10.8 g. (0.81 mole) of aluminum chloride in 70 ml. of chloroform a solution of the 6.3 g. (0.021 mole) of *N-benzylidene-N-(p-tolyl)oxamyl chloride* from the preceding preparation in 80 ml. of chloroform was added dropwise with stirring. The solution had to be kept cold during this addition. The reaction mixture was then refluxed for 1 hr. and allowed to stand overnight. After addition of 75 g. of crushed ice to the reaction mixture and removal by filtration of a gray solid, the water and chloroform layers were separated.

(14) R. L. Shriner, W. C. Ashley, and E. Welch, *Org. Syntheses*, Coll. Vol. III, 725 (1955).

rated. The chloroform layer was evaporated leaving a red solid, which was recrystallized from 95% ethanol. After several recrystallizations 4.45 g. (71%) of *N*-benzylidene-amino-5-methylisatin was obtained as a red solid, m.p. 145–145.5°.

Anal. Calcd. for $C_{16}H_{12}N_2O_2$: C, 72.71; H, 4.59; N, 10.60. Found: C, 72.53; H, 4.69; N, 10.53.

3-Phenyl-6-methylcinnoline-4-carboxylic acid (IVb). One gram (0.0038 mole) of *N*-benzylideneamino-5-methylisatin was suspended in a solution of 20 g. of sodium hydroxide dissolved in 100 ml. of water. The solution was refluxed for 5 hr. The reaction mixture was filtered and acidified with 6*N* hydrochloric acid. The yellow precipitate which formed was recrystallized from ethanol, giving 1 g. (100%) of 3-phenyl-6-methylcinnoline-4-carboxylic acid, m.p. 229–229.5°.

Anal. Calcd. for $C_{16}H_{12}N_2O_2$: C, 72.71; H, 4.59; N, 10.60. Found: C, 72.45; H, 4.69; N, 10.67.

6-Methyl-3-phenyl cinnoline (Vb). A mixture of 0.5 g. (0.0019 mole) of 3-phenyl-6-methylcinnoline-4-carboxylic acid and 2.5 g. (0.0025 mole) of benzophenone was heated for 60 min. at 260° under an atmosphere of nitrogen. The gas evolved gave a turbidity when bubbled through barium hydroxide, indicating the gas to be carbon dioxide. After being cooled, the mixture was dissolved in 250 ml. of ether and the ethereal solution was extracted with about 300 ml. of 6*N* hydrochloric acid. The yellow acidic solution was cooled in an ice bath, saturated with potassium carbonate, filtered, and extracted with ether. The ethereal solution was concentrated. The yellow solid which separated was recrystallized from Skellysolve B,¹² giving 0.40 g. (95%) of 3-phenyl-6-methylcinnoline, m.p. 138.5–139.5°.

Anal. Calcd. for $C_{15}H_{12}N_2$: C, 81.79; H, 5.49; N, 12.72. Found: C, 82.06; H, 5.48; N, 12.47.

LINCOLN 8, NEB.

[CONTRIBUTION FROM AVERY LABORATORY, UNIVERSITY OF NEBRASKA]

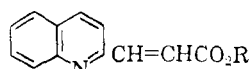
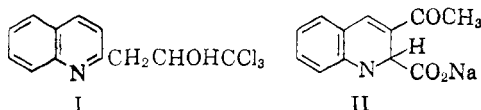
The Reaction of Chloralquinaldine with Pyridine and Alkali^{1,2}

HENRY E. BAUMGARTEN, RICHARD BECKERBAUER, AND MARJORIE R. DEBRUNNER

Received August 19, 1960

Chloralquinaldine reacts with pyridine and aqueous potassium hydroxide to yield a purple-black solid, $C_{17}H_{12}N_2O$, which is shown to be 2-(3-hydroxy-5,6-benzo)indolizyl pyridinium betaine (XI). Similar substances are obtained from chloral-2-picoline and chloral-2-methylbenzothiazole. Several reactions of these substances are described and the mechanism of their formation discussed.

Woodward and Kornfeld³ have shown that the reaction of chloralquinaldine (I) with aqueous alcoholic sodium hydroxide yields sodium 3-acetyl-1,2-dihydroquinaldate (II) in addition to the expected sodium β -(2-quinolyl)acrylate (IIIa).⁴ Mechanisms to explain the formation of II have been suggested by Woodward and Kornfeld,³



IIIa. R = Na

IIIb. R = H

by Brown, Hammick and Robinson,⁵ and by Dauben and Vaughan.⁶ Although the most recent of these, the mechanism of Dauben and Vaughan,⁶ appears to be for the most part quite reasonable,

(1) This work was supported in part by grant CY-3090 of the U. S. Public Health Service.

(2) Abstracted from the M. S. theses of R. B. (February 1960) and M. R. D. (July 1951).

(3) R. B. Woodward and E. C. Kornfeld, *J. Am. Chem. Soc.*, **70**, 2508 (1948).

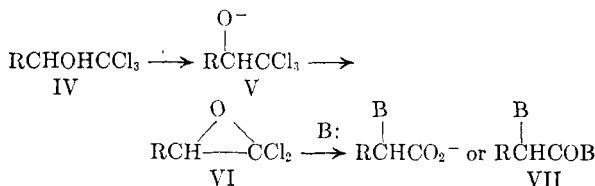
(4) Cf. A. Einhorn, *Ber.*, **19**, 904 (1886); A. Einhorn and P. Sherman, *Ann.*, **287**, 26 (1895).

(5) B. R. Brown, D. L. Hammick, and R. Robinson, *J. Chem. Soc.*, 780 (1950).

(6) W. G. Dauben and C. W. Vaughan, *J. Am. Chem. Soc.*, **75**, 4651 (1953).

the investigation described in this communication was undertaken to examine an alternative sequence for the *initial phases* of the reaction of I with alkali.

All of the previously reported mechanisms^{3,5,6} have been based on the premise that one of the hydrogens on the carbon atom *alpha* to the ring is removed by base in one of the early steps of the reaction. However, it would appear equally if not more likely that the initial proton exchange would involve removal by base of the hydrogen attached to the oxygen of the carbinol group. Thus, there have been a number of reports in the literature describing base-catalysed reactions of trichloromethylcarbinols which take place as shown in the following equation.⁷



(7)(a) K. Garzarolli-Thurnlackh, *Ann.*, **210**, 63 (1881). (b) J. Jocietz, *J. Russ. Phys. Chem. Soc.*, **29**, 97 (1897). (c) A. Wohl and H. Roth, *Ber.*, **40**, 212 (1907). (d) A. Kotz and K. Otto, *J. prakt. Chem.*, [2], **88**, 531 (1913). (e) A. Kotz and C. Diebel, *J. prakt. Chem.*, [2], **90**, 297 (1914). (f) P. Hebert, *Bull. soc. chim. France*, [4], **27**, 45 (1920). (g) G. Banti, *Gazz. chim. ital.*, **59**, I, 819 (1929). (h) C. Weizmann, M. Sulzbacher, and E. Bergmann, *J. Am. Chem. Soc.*, **70**, 1153 (1948). B = Cl: Ref. (a), (b). B = OH: Ref. (b), (d), (e), (f). B = OR: Ref. (a), (e), (f), (h). B = aniline: Ref. (g).