

melting point. In one run however a small amount of solid of m. p. 171–178° was obtained but was not studied.

Since the results of these reductions do not correspond with those reported by Campbell and Khanna,⁴ we repeated our experiments on dibenzoyl ethylene many times, and varied the concentration of the reagent, conditions and mode of hydrolysis. In several experiments freshly prepared unclarified aluminum isopropoxide solutions were used. The results were always approximately the same and in no case was dibenzoyl ethane isolated. The residual oils underwent resinification under attempts at distillation or evaporation under reduced pressure, and gave only oils when oxidized by chromic acid under conditions which converted the unsaturated glycols into the unsaturated diketones.

Reduction of IV in ethanol by platinum and hydrogen at room temperature and pressure on a small scale gave an 84% yield of VIa which upon crystallization from chloroform and petroleum ether melted at 113–114° and showed no mixture melting point depression with a sample prepared by a similar catalytic reduction of the acetylene glycol^{6b} of m. p. 142° (Va).

Oxidation of 1 g. of IV in 100 ml. of concd. acetic acid by 1 g. of chromic oxide in 20 ml. of 25% acetic acid, added dropwise over forty minutes at 20° and with continued stirring for a further thirty minutes, gave 0.7 g. of II of m. p. 111–112° (identified by mixture melting point). Oxidation similarly of III^{6b} gave a 50% yield of I of m. p. 134–135° (identified by mixture melting point).

Inversion of I to II on a small scale was accomplished by the action of 0.09 *N* aluminum isopropoxide in isopropyl alcohol under refluxing for 2.5 hours; only II was recovered (92%). Without the added aluminum isopropoxide the *cis* compound (I) could be largely recovered unchanged.

***trans*-1,2-Dimesitoylethylene** was recovered practically quantitatively unchanged after treatment under the usual conditions with aluminum isopropoxide (refluxing for

two and one-half hours). No acetone evolution was observed during the experiment.

Reduction of dibenzoyl ethane (VII) by aluminum isopropoxide as above but under reflux for four hours gave an oil which was fractionally crystallized from chloroform by additions of petroleum ether; the yield of VIb of m. p. 89–90° was 82% (identified by mixture melting point with an authentic sample^{6a} prepared by catalytic reduction of Vb).

Summary

Aluminum isopropoxide in low concentration caused *cis-trans* inversion of dibenzoyl ethylene, and in higher concentration caused reduction to the *trans*-unsaturated glycol which could be oxidized back to *trans*-dibenzoyl ethylene and catalytically hydrogenated to the higher-melting saturated glycol. The *cis*-unsaturated glycol of corresponding diastereo-configuration, made by partial hydrogenation of the acetylene glycol, was reducible to the higher-melting saturated glycol, and was oxidizable to *cis*-dibenzoyl ethylene. Dimesitoylethylene resisted reduction; and *trans*-dibenzoyldimethylethylene was reduced like dibenzoyl ethylene, but slowly, to the unsaturated glycol. Dibenzoyl ethane was reduced readily to the lower-melting saturated glycol.

A reduction mechanism involving a coordination complex with the reagent and a transitory quasi-ring phase facilitating transfer of hydrogen, is considered.

CHARLOTTESVILLE, VA.

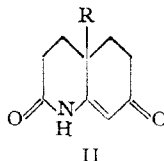
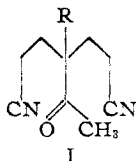
RECEIVED JULY 20, 1949

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

The Action of Sulfuric Acid on γ -Acetylpylimonitriles¹

BY C. F. KOELSCH* AND H. M. WALKER

γ -Acetyl- γ -phenylpimelonitrile (I, R = C₆H₅) has been converted to the corresponding acid with hot 10% sodium hydroxide, but the process is slow.² It was thought that a more rapid hydrolysis might be effected with sulfuric acid, but it has now been found that this reagent yields II, R = C₆H₅, rather than the expected acid. Such behavior appears to be characteristic of γ -substituted- γ -acetylpylimonitriles; the γ -methyl derivative gives II, R = CH₃, the γ -cyanoethyl derivative gives II, R = CH₂CH₂COOH, and the γ -carboxy derivative gives II, R = H.



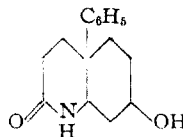
Structure II, R = C₆H₅, has been established

* Harvard University National Research Fellow 1931–1932.

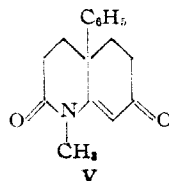
(1) From the Ph.D. Thesis of Harry M. Walker, May, 1949.

(2) Bruson and Riener, *THIS JOURNAL*, **64**, 2850 (1942).

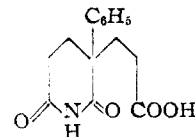
for the product from γ -acetyl- γ -phenylpimelonitrile by a study of the reactions of the substance. Drastic treatment with alkali converts the compound into γ -acetyl- γ -phenylpimelic acid, showing that sulfuric acid brought about no deep-seated change in the carbon skeleton. Formation of an oxime indicates a ketone group, as does catalytic reduction to an alcohol, III. Ozonolysis, with the formation of IV, indicates the presence and position of a double bond



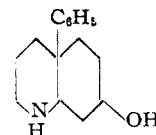
III



V



IV



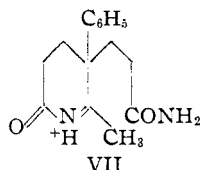
VI

Methylation, with the formation of V, which yields methylamine on hydrolysis, indicates an NH group. Finally, reduction with sodium and butyl alcohol, with the formation of an amino alcohol, VI, demonstrates a keto group and a lactam structure.

Proof of structure II, R = H, is furnished by dehydrogenation of the substance. This yields 2,7-dihydroxyquinoline, identical with the compound synthesized from known 7-amino-2-hydroxyquinoline.

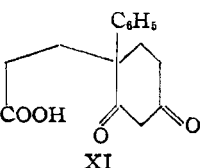
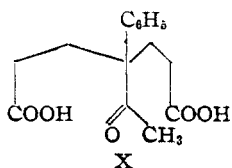
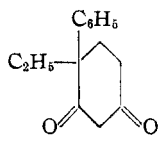
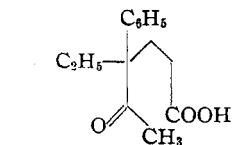
Structures II, R = CH₃, and R = CH₂CH₂-COOH, are based on analyses of the compounds and on analogy in properties and methods of preparation with the preceding substances.

The reactions whereby I is converted into II probably involve hydrolysis to a diamide, then cyclization to VII. Subsequent interaction of



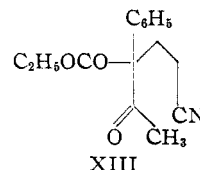
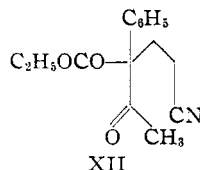
the methyl with the remaining amide group, dependent on electron attraction by $^+\text{NH}=\text{C}-$, is similar to acid-catalyzed aldol reactions in general, especially to those of α -picoline. Some support for these assumed intermediate stages is given by the observations that both the diamide and the ethyl ester-amide of γ -acetyl- γ -phenylpimelic acid yield II, R = C₆H₅, with sulfuric acid; and further, the bis-methylamide yields V.

A group $\text{HO}=\text{C}-$ apparently can activate an attached methyl in cyclizations analogous to the preceding ones. Thus it has been suggested that the product obtained by the action of hydroiodic acid and phosphorus on γ -acetyl- γ -phenylcaproic acid (VIII) is IX,³ and it has been found in the present work that sulfuric acid converts γ -acetyl- γ -phenylpimelic acid (X) into a dehydrocompound which probably is XI.



It has not been possible, however, to isolate cyclohexanediones from the products of the action of sulfuric acid on XII or XIII. Perhaps

this failure indicates that in acid-catalyzed cyclizations involving $\text{HO}=\text{C}-\text{CH}_3$, it is necessary that R be tertiary. When R is secondary, as it is in the products derived from XII and XIII by hydrolysis and decarboxylation, a nucleophilic center is formed in R rather than from the terminal carbon. Analogy supporting this suggestion is found in acid-catalyzed aldol reactions of ketones $\text{RCH}_2\text{COCH}_3$, where methylene and not methyl groups are involved.



Experimental

4a-Phenyl- Δ^8 -octahydro-2,7-quinolinedione, II, R = C₆H₅.—A mixture of 100 g. of γ -acetyl- γ -phenylpimelonitrile² with one liter of 1:1 (vol.) sulfuric acid was boiled (120–140°) and stirred for two and one-quarter hours, and then poured into three liters of water. The suspension was cooled, and the product was removed. It was freed of acidic material by warming it with 8% sodium bicarbonate, then washed and dried, giving 68.8 g. (68.5%), m. p. 232–234°. A colorless sample was obtained by solution in dilute sodium hydroxide, precipitation with acid and crystallization from alcohol; m. p. 237–239°.

Anal. Calcd. for C₁₅H₁₅NO₂: C, 74.6; H, 6.2; N, 5.8. Found: C, 74.1; H, 6.3; N, 5.9.

The oxime, prepared by heating the compound with hydroxylamine hydrochloride and sodium hydroxide in aqueous alcohol for ten minutes, formed colorless crystals from alcohol, m. p. 310–311° dec.

Anal. Calcd. for C₁₅H₁₆N₂O₂: C, 70.3; H, 6.3; N, 10.9. Found: C, 70.6; H, 6.6; N, 11.2.

Hydrolysis to γ -acetyl- γ -phenylpimelic acid, m. p. 163–165° alone or mixed with an authentic sample⁴ having the same m. p., was effected by boiling 2 g. of II, R = C₆H₅, with 15 ml. of 10% sodium hydroxide for eleven hours.

Ozonolysis of 5 g. of II, R = C₆H₅, in 200 ml. of methylene chloride was effected with 2% ozone. The ozonide was decomposed with boiling water, giving 4.5 g. of 3-phenyl-2,6-piperidinedione-3-propionic acid (IV), m. p. 160–165°; the anilide, prepared using thionyl chloride, had m. p. 198–200°; these two substances showed unchanged m. p.'s when they were mixed with authentic samples⁴ of the same compounds.

Methylation of 20 g. of II, R = C₆H₅, in 200 ml. of absolute alcohol was accomplished by adding 25 ml. of methyl sulfate and then a small excess of alcoholic potash. There was obtained 17.6 g. of 1-methyl-4a-phenyl- Δ^8 -octahydro-2,7-quinolinedione (V); colorless crystals from benzene, m. p. 169–170°.

Anal. Calcd. for C₁₆H₁₇NO₂: C, 75.3; H, 6.7. Found: C, 75.4; H, 6.9.

Catalytic reduction of 10 g. of II, R = C₆H₅, in 70 ml. of alcohol, was carried out with Raney nickel and hydrogen at 1000 p.s.i. and 165°. There was obtained a nearly quantitative yield of 7-hydroxy-4a-phenyldecahydro-2-quinolone, III; colorless crystals from benzene-ligroin, m. p. 117–119°.

Anal. Calcd. for C₁₅H₁₉NO₂: C, 73.5; H, 7.8. Found: C, 73.1; H, 7.5.

Reduction of 100 g. of II, R = C₆H₅, in two liters of absolute butyl alcohol by rapid addition of 165 g. of so-

(4) Reported m. p. 171–172°; ref. 2.

(5) Koelsch, to be published.

(3) Campbell, Carter and Slater, *J. Chem. Soc.*, 1741 (1948).

dium gave a sirupy mixture of bases. Crystallization of the mixed hydrochlorides from alcohol gave 4.5 g. of an easily soluble hydrochloride, which crystallized after it had stood for more than a year (Found: C, 67.3; H, 8.4), and 39.1 g. of **4a-phenyldecahydro-7-quinolinol hydrochloride**, which was difficultly soluble and crystallized readily; m. p. 300° dec.

Anal. Calcd. for $C_{15}H_{23}ClNO$: C, 67.3; H, 8.3. Found: C, 67.5; H, 8.3.

The **free base (VI)** corresponding to the latter salt was crystallized from dilute alcohol; m. p. 136–143°.

Anal. Calcd. for $C_{17}H_{21}NO$: C, 77.9; H, 9.2. Found: C, 78.0; H, 8.9.

With benzoyl chloride and aqueous alkali, VI gave the **N-benzoyl derivative**; crystals from benzene-ligroin, m. p. 166–167.5°.

Anal. Calcd. for $C_{22}H_{25}NO_2$: C, 78.8; H, 7.5. Found: C, 78.4; H, 7.5.

With excess hot acetic anhydride containing a trace of sulfuric acid, VI was converted nearly quantitatively into its **O,N-diacetyl derivative**; crystals from ether-ligroin, m. p. 165–166°.

Anal. Calcd. for $C_{19}H_{25}NO_3$: C, 72.4; H, 8.0; mol. wt., 315. Found: C, 72.6; H, 8.4; mol. wt., 312.

When the diacetyl derivative (6.2 g.) was boiled with 60 ml. of 8% alcoholic potash for five minutes, it gave 4.7 g. of the **N-acetyl derivative of VI**; crystals from alcohol, m. p. 239–240°.

Anal. Calcd. for $C_{17}H_{23}NO_2$: C, 74.7; H, 8.5. Found: C, 74.9; H, 8.6.

Nitration of 2.4 g. of II, $R = C_6H_5$, in 7 ml. of sulfuric acid with 1 g. of potassium nitrate gave 2.5 g. of crude product, from which there was obtained 1.3 g. of **4a-p(?) -nitrophenyl- Δ^8 -octahydro-2,7-quinolinedione**, colorless crystals from acetic acid, m. p. 320–324° dec.

Anal. Calcd. for $C_{15}H_{14}N_2O_4$: C, 62.9; H, 4.9. Found: C, 63.1; H, 5.0.

4a-Methyl- Δ^8 -octahydro-2,7-quinolinedione, II, $R = CH_3$.—Twenty-five grams of γ -acetyl- γ -methylpimelonitrile² was treated with a hot (130°) solution of 49 g. of sulfuric acid in 12 ml. of water. A vigorous reaction took place which subsided within five minutes. The mixture was boiled for five minutes more, and then poured into 300 ml. of water. The sulfuric acid was removed with calcium carbonate, and the solution was evaporated to a sirup and cooled. The product was recrystallized from water, giving 15.6 g. (62%) of colorless plates, m. p. 220–221°.

Anal. Calcd. for $C_{10}H_{18}NO_2$: C, 67.0; H, 7.3. Found: C, 67.0; H, 7.2.

The **oxime** had m. p. 248° dec.

Anal. Calcd. for $C_{10}H_{14}N_2O_2$: C, 61.8; H, 7.3. Found: C, 62.2; H, 7.6.

Δ^8 -Octahydro-2,7-quinolinedione-4a-propionic Acid, II, $R = CH_2CH_2COOH$.—Twenty-five grams of tri-(β -cyanoethyl)-acetone² was treated with 73.5 g. of sulfuric acid in 20 ml. of water, and the mixture was processed as in the preceding preparation. The residue from evaporation was gum, which was extracted with alcohol. Addition of ether to the concentrated extract gave 18.5 g. (67%) of product; colorless crystals from water, m. p. 243–245°.

Anal. Calcd. for $C_{12}H_{16}NO_4$: C, 60.7; H, 6.4; N, 5.9. Found: C, 60.6; H, 6.3; N, 5.9.

Δ^8 -Octahydro-2,7-quinolinedione, II, $R = H$.—One hundred and thirty-eight grams of γ -acetyl- γ -carboxypimelonitrile² was treated with a hot solution of 312 ml. of sulfuric acid in 138 ml. of water. After spontaneous reaction had ceased (ten minutes), the mixture was boiled for fifteen minutes, then poured into 1.5 liters of water and treated with calcium carbonate. Filtration and evaporation gave 42 g. (42.5%) of crystalline material. Recrystallization from water gave a colorless product, m. p. 225–233° dec.

Anal. Calcd. for $C_9H_{11}NO_2$: C, 65.4; H, 6.8. Found: C, 65.2; H, 6.9.

The **oxime** had m. p. 255° dec.

Anal. Calcd. for $C_9H_{12}N_2O_2$: C, 60.0; H, 6.7; N, 15.5. Found: C, 60.4; H, 6.8; N, 15.2.

Five grams of II, $R = H$, was heated at 240–260° for thirty minutes with 1.95 g. of sulfur. The melt was then extracted with six 30-ml. portions of water, and the crude product so removed (0.5 g.) was distilled under reduced pressure. It then melted at 310–315° dec., alone or mixed with 2,7-quinolinediol, and showed an ultraviolet absorption curve identical with this compound.

2,7-Quinolinediol.—A solution of 2.24 g. of 7-aminocarbostyryl³ in 80 ml. of 5% sulfuric acid was diazotized with 1 g. of sodium nitrite, then boiled, filtered and cooled. The product was dissolved in sodium hydroxide and treated with charcoal, and then recrystallized from water, giving 0.7 g. of fine needles, m. p. 308–315° dec. Absorption was measured in 95% alcohol; (λ_{max} , log ϵ): 230, 4.358; 250, 3.602; 260, 3.653; 285, 3.699; 325, 4.230; 340, 4.100.

Anal. Calcd. for $C_9H_7NO_2$: C, 67.1; H, 4.4. Found: C, 66.7; H, 4.5.

γ -Acetyl- γ -phenylpimelamide.—A mixture of 11 g. of γ -acetyl- γ -phenylpimelic acid and 25 ml. of thionyl chloride was boiled for thirty minutes and then distilled to a sirup under reduced pressure. The residue was dissolved in 90 ml. of benzene and added slowly to excess aqueous ammonia. The product separated from ethyl acetate-alcohol in the form of colorless plates (8.7 g.), m. p. 182°.

Anal. Calcd. for $C_{15}H_{20}N_2O_3$: C, 65.2; H, 7.3; N, 10.1. Found: C, 64.9; H, 7.6; N, 10.1.

Treatment of the amide with sulfuric acid in a procedure analogous to that used for the corresponding nitrile gave II, $R = C_6H_5$, in a yield of 86%.

γ -Acetyl- γ -phenylpimel-N,N'-dimethylamide.—From the crude chloride with 25% aqueous methylamine, there was obtained a product m. p. 179–180°.

Anal. Calcd. for $C_{17}H_{22}N_2O_3$: C, 67.1; H, 7.9. Found: C, 67.2; H, 8.1.

Treatment of the dimethylamide with sulfuric acid gave V in a yield of 57%.

Ethyl γ -Acetyl- γ -phenylpimelamate.—When an attempt was made to reduce ethyl γ -acetyl- γ -phenylpimelate by heating it in 95% alcohol with hydrogen and Raney nickel at 220°, the only reaction that took place was partial hydrolysis. **Ethyl acid γ -acetyl- γ -phenylpimelate** was separated with sodium carbonate in a yield of about 10%. It formed colorless crystals from ligroin, m. p. 107–108°.

Anal. Calcd. for $C_{17}H_{22}O_5$: C, 66.7; H, 7.2; neut. equiv., 306. Found: C, 66.9; H, 7.3; neut. equiv., 304.

The ester-acid (3 g.) was converted to the ester-chloride by heating it with excess thionyl chloride, and this was converted into the **ester-amide** by adding it to aqueous ammonia at 5–10°. The product was washed in ether and dried, but it formed an undistillable oil.

Anal. Calcd. for $C_{17}H_{23}NO_4$: N, 4.6. Found: N, 3.9.

Treatment of the ester-amide with hot 75% sulfuric acid gave II, $R = C_6H_5$, in good yield.

1-Phenyl-2,4-cyclohexanedione-1-propionic Acid, XI.—A mixture of 23 ml. of sulfuric acid, 10 ml. of water and 20 g. of γ -acetyl- γ -phenylpimelic acid was boiled for eight minutes and then poured into 300 ml. of water. The oily product was taken up in ether, washed with water and dried. Distillation of the ether left an oil that soon crystallized. Recrystallization from ethyl acetate-ligroin gave 11.8 g. of colorless crystals, m. p. 121–124° with gas evolution.

Anal. Calcd. for $C_{15}H_{16}O_4$: C, 69.2; H, 6.2. Found: C, 68.7; H, 6.6.

The material behaved as a dibasic acid; calcd. mol. wt., 260; found, neut. equiv., 139. Even when a glass electrode was used in an electrometric titration, only a single end-point was found.

When a solution of 1.5 g. of the compound and 2 g. of aniline in 15 ml. of alcohol was boiled for sixteen hours,

(6) Friedländer and Fritsch, *Monatsh.*, **23**, 534 (1902).

there was deposited 0.5 g. of an anil; colorless crystals from alcohol, m. p. 219–222°.

Anal. Calcd. for $C_{21}H_{21}NO_3$: C, 75.2; H, 6.3. Found: C, 74.9; H, 6.4.

Ethyl α -(β -Cyanoethyl)- α -phenylacetoacetate, XII.—Ethyl α -phenylacetoacetate (20.6 g.) was dissolved in 25 ml. of *t*-butyl alcohol which had been saturated with potassium hydroxide. Then 5.3 g. of acrylonitrile was added, and the mixture was stirred for one hour. Water and a little acetic acid were added; the product was removed with ether and fractionally distilled, giving 7 g., b. p. 180–220° at 0.003 mm.

Anal. Calcd. for $C_{18}H_{17}NO_3$: C, 69.5; H, 6.6. Found: C, 69.2; H, 6.5.

The material reacted with 75% sulfuric acid, and carbon dioxide was evolved, but careful search revealed no phenylcyclohexanedione in the products.

Ethyl α -(β -Cyanoethyl)- α -methylacetoacetate, XIII.—From 25 g. of ethyl α -methylacetoacetate and 9.2 g. of acrylonitrile with potassium hydroxide in *t*-butyl alcohol, there was obtained 20 g. of product, b. p. 118–118.5° at 4 mm., n_D^{25} 1.445.

Anal. Calcd. for $C_{16}H_{15}NO_3$: C, 60.9; H, 7.7. Found: C, 61.0; H, 7.7.

Carbon dioxide was evolved when the substance was treated with 75% sulfuric acid, but no methylenecyclohexanedione could be isolated.

Acknowledgment.—The authors thank the Monsanto Chemical Company for a Fellowship.

Summary

Treatment of γ -substituted- γ -acetylpimelonitriles with hot 40–80% sulfuric acid leads to the formation of 4a-substituted- Δ^8 -octahydro-2,7-quinolinediones. The structures of two such products have been established, and a mechanism for the reaction is suggested. An apparently similar reaction takes place when γ -acetyl- γ -phenylpimelic acid is treated with sulfuric acid.

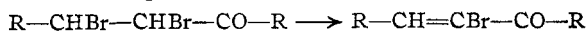
MINNEAPOLIS, MINNESOTA RECEIVED OCTOBER 15, 1949

[CONTRIBUTION FROM THE THOMPSON LABORATORY OF THE PHILLIPS EXETER ACADEMY]

The Debromination of α,β -Dibromo Ketones by Bases

BY CHARLES L. BICKEL*

The reaction of α,β -dibromo ketones with alcoholic solutions of bases has been carefully studied¹ and has been used extensively for the preparation of both β -diketones and α -diketones. The first step in the reaction is assumed to be the elimination of the beta bromine atom as hydrogen bromide, an unsaturated α -bromo ketone being formed.

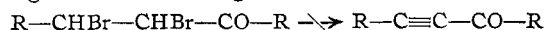


This assumption has been verified in many instances by the isolation of the monobromide. The subsequent action of bases on the monobromide leads to a variety of derivatives, the product or products in a particular case depending on the nature of the base, the solvent and the terminal groups.

Recent communications from this Laboratory² described the preparation of acetylenic ketones from unsaturated α -bromoketones, using acetone instead of an alcohol as the solvent.



In the light of the above, it seemed reasonable to predict that the intermediate preparation and isolation of the monobromides might be unnecessary and that the acetylenic ketones might therefore be prepared directly from the dibromides by the elimination of two molecules of hydrogen bromide, using acetone as the solvent.



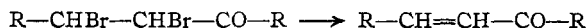
This is, however, not the case.

* Harvard University Ph.D. 1932.

(1) Kohler and Addinall, *THIS JOURNAL*, **52**, 3728 (1930). This paper summarizes the action of bases on α,β -dibromo ketones and cites the most important references.

(2) Bickel, *ibid.*, **69**, 73, 2134 (1947).

The action of potassium hydroxide on an acetone solution of the dibromides results in debromination and in the formation of the chalcones from which the dibromides were derived.



Six dibromides have been debrominated in this way, indicating that the reaction may be expected in the case of other dibromides not herein studied. The reaction appears to be clean-cut. The yields of the chalcones are high and there is no evidence of the formation of either the α -bromo ketones or the acetylenic ketones. The absence of acetylenic ketones among the reaction products necessarily means that the α -bromo ketones were not formed as intermediates.² Thus, in the absence of alcohols, the action of potassium hydroxide resembles that of zinc, iron and acetic acid, or potassium iodide, agents which convert chalcone dibromides into the parent chalcones.

Basic agents other than potassium hydroxide can be used for the debromination reaction but are not as effective. Sodium carbonate, potassium carbonate, sodium bicarbonate and potassium bicarbonate were so used and gave the corresponding chalcone as a product. On the other hand, the action of potassium acetate in acetone gave the α -bromo ketone, the same product that is obtained in alcohol solution.

Comparable experiments with 2-chlorochalcone dibromide and α -bromo-2-chlorochalcone indicate that the debromination of the dibromide is a faster process than is the elimination of hydrogen bromide from the α -bromo compound.