amine by shaking it with sodium carbonate solution, filtering, washing and recrystallizing the precipitate from ethanol.

Reduction of *cis*-Dibenzoyl-(morpholinomethyl)-ethylene (V), (a) Zinc-Acetic Acid Reduction.—One gram of the (morpholinomethyl)-ethylene (V) was dissolved in 20 ml. of acetic acid. To this solution was added a porcelain spatulaful of zinc dust. The resulting mixture was stirred for one minute (heat was generated), after which time it was filtered. The filtrate was diluted with water, made alkaline with sodium carbonate and extracted with ether. Evaporation of the ether extract, after it had been washed and dried, yielded 0.5 g. of material which melted at 79–80°. Several recrystallizations from ethanol changed the melting point to 85–86°. No depression occurred in a mixture melting point with known dibenzolyl-(morpholinomethyl)-ethane (IIa).

(b) Catalytic Reduction in Acetic Acid Solution.—Eight-tenths of a gram of the (morpholinomethyl)-ethylene (V) was reduced catalytically with the aid of 0.02 g. of platinum oxide in 35 ml. of glacial acetic acid. The rate of absorption began to decrease sharply after one equivalent of hydrogen had been absorbed and the reduction was stopped after about 1.5 equivalents had been absorbed. The mixture was filtered to remove the catalyst, diluted with water, neutralized with sodium carbonate and extracted with ether. The ether extract was dried over anhydrous sodium sulfate and evaporated under reduced pressure. Crystallization of the residue from ethanol yielded 0.3 g. of crystals which melted at 79–81° and was shown to be the (morpholinomethyl)-ethane (IIa) by a mixture melting point.

Treatment of *cis*- and *trans*-Dibenzoylmethylethylenes (I) with Triethylamine.—One gram of freshly prepared *trans*-dibenzoylmethylethylene was dissolved in a solution of 4 ml. of triethylamine and 10 ml. of ether, and the resulting solution was allowed to stand in the dark for twenty-four hours after which time it was evaporated under a stream of air. The crystalline residue upon recrystallization from ethanol weighed 0.5 g., melted at 62–64° and gave no mixture melting point depression with the *cis* isomer.

When the *cis* isomer was treated with triethylamine under the same conditions for three weeks, it was recovered unchanged.

The *cis* isomer does not react with ferric chloride solution or ethanolic bromine at room temperature and is not soluble in sodium hydroxide solution, showing that it exists in the keto form.

Treatment of *cis*- and *trans*-Dibenzoylethylenes with Triethylamine.—When 0.5 g. of *cis*-dibenzoylethylene was treated with triethylamine under the same conditions as were the dibenzoylmethylethylenes, 0.3 g. of the *trans* compound which melted at 108–110° was obtained as the product. It was identified by a mixture melting point with an authentic sample.

The *trans* compound when treated under these conditions was recovered unchanged.

Treatment of *cis*- and *trans*-dibenzoyldimethylethylenes with triethylamine and morpholine under the conditions which favored reaction with dibenzoylmethylethylene gave only unchanged material.

Treatment of *trans*-dibenzoylethylmethylene with the nitric–acetic acid reagent (1 g. in a solution of 1 ml. of nitric acid and 8 ml. of acetic acid) for five minutes at 10° followed by pouring into 25 ml. of cold water, gave 0.8 g. of nearly pure starting material.

This experiment shows that the *trans* compound is stable under conditions identical with those involved in the formation of the *cis* compound by the oxidation of 2,5-diphenyl-3-methylfuran.[7] Thus, there can be no doubt that the configurations assigned to the *cis* and *trans*-dibenzoylmethylethylenes on the basis of mode of synthesis, are correct.

Summary

Secondary amines react with dibenzoylmethylethylene to give (*t*-aminomethyl)-dibenzoylethanes. These are furanized to the 3-(*t*-aminomethyl)-2,5-diphenylfurans, the structures of which are proved by synthesis from known furans. Nitric acid oxidation of the (morpholinomethyl)-furan to *cis*-dibenzoyl-(morpholinomethyl)-ethylene and reduction of this to dibenzoyl-(morpholinomethyl)-ethane complete the cycle of reactions typical of this class of compounds.

trans-Dibenzoylmethylethylene is shown to be the *labile* isomer by conversion into the *cis* isomer by means of triethylamine. The bearing of this on the chelate ring structure proposed for the *cis* compound is discussed.

CHARLOTTESVILLE, VIRGINIA
RECEIVED SEPTEMBER 28, 1945

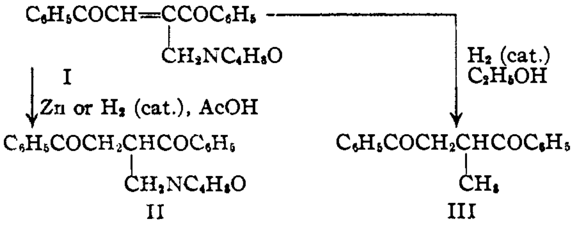
[CONTRIBUTION FROM THE COBB CHEMICAL LABORATORY OF THE UNIVERSITY OF VIRGINIA]

Some Reactions of *cis*-Dibenzoyl-(morpholinomethyl)-ethylene. Reduction and Cyclization

BY PHILIP S. BAILEY[1] AND ROBERT E. LUTZ

In the preceding paper[2] is discussed the conversion of 2,5-diphenyl-3-(morpholinomethyl)-furan by the characteristic nitric acid oxidation into *cis*-dibenzoyl-(morpholinomethyl)-ethylene (I). This compound has proved to be especially interesting in its reactions and is the subject of the present paper.

Reduction of the unsaturated diketone (I) in *acetic acid* solution, catalytically or with zinc dust, gave the corresponding saturated diketone (II).[3] In contrast with this straightforward result, catalytic hydrogenation *in ethanol* solution, of the free amine (I) or its hydrochloride, using either platinum or palladium–barium sulfate catalyst,



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[1] Holder of Philip Francis du Pont Fellowships 1942–1944.

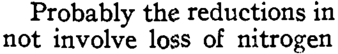
[2] Lutz and Bailey, THIS JOURNAL, 67, 2229 (1945).

[3] This reaction was carried out in the course of a structural proof (*cf.* ref. 2).

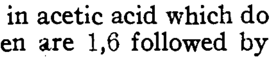
caused elimination of the nitrogen to give dibenzoylmethylethane (III).

In the reductive deamination nearly two equivalents of hydrogen was very rapidly absorbed before an appreciable decrease in the reaction rate occurred. In a separate experiment under the same conditions, dibenzoyl-(morpholinomethyl)-ethane (II) was found to undergo hydrogenation only very slowly, and consequently could not have been an intermediate. The two types of reductions, with and without deamination, therefore must involve different mechanisms and cannot represent merely two steps in reduction.

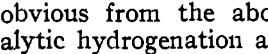
Probably the reductions in acetic acid which do not involve loss of nitrogen are 1,6 followed by ketonization[4] to the relatively stable morpholinomethyl saturated diketone (II). On the other hand, as is obvious from the above-described facts, the catalytic hydrogenation and deamination in ethanol solution must involve elimination of the morpholine *before* or simultaneously with, but not after, reduction of the double bond. Furthermore, the fact that both of the two equivalents of hydrogen are absorbed very rapidly, indicates that similar and easily reducible systems are involved in both stages of the reduction. We would be inclined, therefore, to assume that here the initial reduction step involves 1,6-hydrogenation of the system, O=C—C=C—C—N, of I, followed quickly by reduction of the resulting enol (IV) or its keto form (V or VI)[5]; however, of course, alternative mechanisms may involve 1,4-reduction of the allylamino system, C=C—C—N, of I, or direct 1,2-reductive deamination analogous to debenzylation, to give easily reducible intermediates such as V or VI.


$C_6H_5\underset{OH}{\underset{|}{C}}{=}CH-\underset{CH_2}{\underset{\parallel}{C}}-\underset{O}{\underset{\parallel}{C}}C_6H_5$

IV

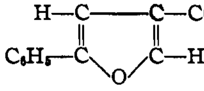

$C_6H_5COCH_2\underset{CH_2}{\underset{\parallel}{C}}-\underset{O}{\underset{\parallel}{C}}C_6H_5$

V


$C_6H_5COCH{=}\underset{CH_3}{\underset{|}{C}}COC_6H_5$

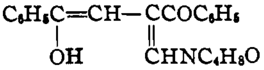
VI

The (morpholinomethyl)-ethylene (I) is stable in the form of the hydrochloride, but, surprisingly, as the free amine it spontaneously undergoes furanization over a period of time. The product was identified as the known 3-benzoyl-5-phenylfuran (VII) previously prepared by Fuson, Fleming and Johnson[6] by the selenium dioxide oxidation of *trans*-dibenzoylmethylethylene (VI).

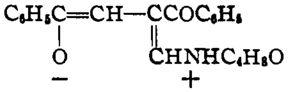


VII

A mechanism similar to the one proposed by the above authors for their reaction is applicable here, namely, 1,5-enolization of I to VIII from which morpholine is split out to give the benzoylfuran (VII). The loss of the amine from VIII may be direct, or perhaps an inner salt (IX) may


$C_6H_5\underset{OH}{\underset{|}{C}}{=}CH-\underset{CHNC_4H_8O}{\underset{\parallel}{C}}COC_6H_5$

VIII

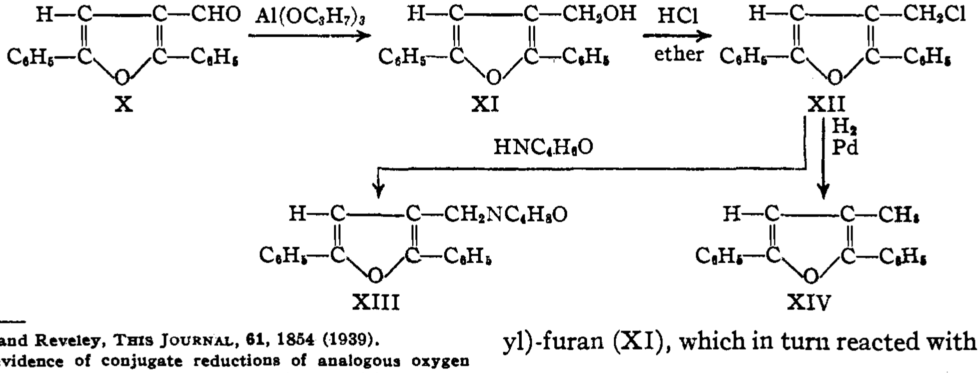

$C_6H_5\underset{\underset{-}{O}}{\underset{|}{C}}{=}CH-\underset{\underset{+}{CHNHC_4H_8O}}{\underset{\parallel}{C}}COC_6H_5$

IX

represent the point at which morpholine is eliminated. The possibility of this latter intermediate is related to the first step of the mechanism proposed for ordinary furanization in which the enolic hydroxyl reacts with a carbonyl group[4,7]; and it is also consistent with the fact that the hydrochloride of the (morpholinomethyl)-ethylene, unlike the free amine (I), is stable and does not spontaneously furanize, presumably because in that case an inner salt such as IX could not form.

When dibenzoyl-(morpholinomethyl)-ethylene (I) was dissolved in methanolic hydrogen chloride there was produced a new and interesting compound which contained neither nitrogen nor halogen. It had the same empirical formula as, but was different from, 3-benzoyl-5-phenylfuran (VII); it formed an oxime, and gave a positive silver mirror test for an aldehyde group. It was therefore believed to be 2,5-diphenyl-3-formylfuran (X), a conclusion which was subsequently demonstrated by the following series of reactions.

Upon reduction by means of aluminum isopropoxide the new compound (X) gave the corresponding alcohol, 2,5-diphenyl-3-(hydroxymethyl)-furan (XI), which in turn reacted with ethereal



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[4] Lutz and Reveley, THIS JOURNAL, 61, 1854 (1939).

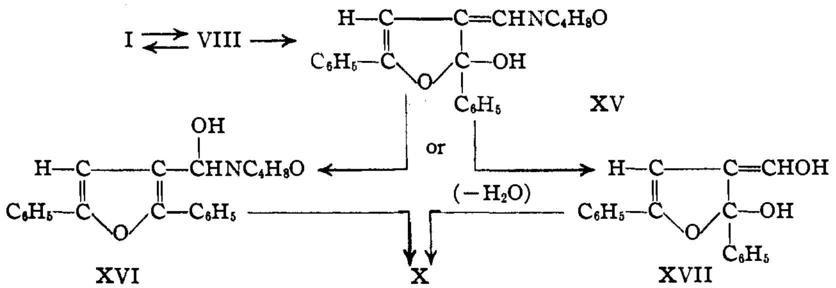
[5] For evidence of conjugate reductions of analogous oxygen allylic systems see (a) Lutz, *ibid.*, 56, 1378 (1934); (b) Lutz and Small, *ibid.*, 56, 1741 (1934).

[6] Fuson, Fleming and Johnson, *ibid.*, 60, 1994 (1938).

[7] Lutz and Wilder, *ibid.*, 56, 1193 (1934).

hydrogen chloride to form 3-(chloromethyl)-2,5-diphenylfuran (XII). From this compound was obtained two known compounds, 2,5-diphenyl-3-methylfuran (XIV) by reductive dehalogenation, and 2,5-diphenyl-3-(morpholinomethyl)-furan (XIII) by treatment with morpholine.

The striking feature in this cyclization reaction (I → X) is the fact that the furanization has proceeded in such a way as to produce an aldehyde group which, if it had been generated before or during ring closure, might have been expected to have taken part in the furanization because of its activity. With this point in mind, a mechanism is suggested for this reaction involving enolization to VIII or IX, cyclization to XV, and conversion thence by several possible paths into the furan (X), as is exemplified in the abbreviated diagram below.



Experimental[8]

Catalytic Reduction of *cis*-Dibenzoyl-(morpholinomethyl)-ethylene (I) in Ethanol Solution.—When a mixture of 0.3 g. of dibenzoyl-(morpholinomethyl)-ethylene (I),[2] 0.3 g. of palladium-barium sulfate catalyst and 75 ml. of ethanol was shaken with hydrogen, the rate of absorption did not decrease appreciably until 1.5 equivalents had been absorbed. The reduction was interrupted after the absorption of 2.5 equivalents. Filtration and evaporation yielded an oil which upon crystallization and recrystallization from ethanol gave 0.1 g. of material which melted at 100–104°. It was shown to be dibenzoylmethylethane (III) by a mixture melting point with an authentic sample.[9]

Reduction of the hydrochloride of I (one gram in 75 ml. of ethanol) using 0.02 g. of platinum oxide catalyst, proceeded at the same rate as did the above reduction of the free amine and did not decrease in rate appreciably until 1.5 equivalents had been absorbed. When the reaction mixture was worked up, 0.1 g. of dibenzoylmethylethane (III) was obtained.[10]

Catalytic reduction of the (morpholinomethyl)-ethane (II) using either palladium-barium sulfate or platinum oxide catalyst proceeded very slowly, beginning at a rate of about 0.75 ml. per minute and decreasing steadily almost to zero over forty-eight hours with absorption of three equivalents. The product was not isolated because the only information desired was the rate of reduction.

Spontaneous Furanization of *cis*-Dibenzoyl-(morpholinomethyl)-ethylene (I) to 3-Benzoyl-5-phenylfuran (VII).—The (morpholinomethyl)-ethylene (I), in contrast with its hydrochloride, is not stable. It spontaneously furanizes over a period of time. A sample of the ethylene which melted at 126–128° was set aside for three weeks. At the end of this time the material was recrystallized twice from ethanol and was found to melt at 114–115°. No depression occurred in a mixture melting point of this compound and a sample of 3-benzoyl-5-phenylfuran (VII), prepared in the manner described by Fuson, Fleming and Johnson.[6] Some samples required several months for the rearrangement to occur. The furanization is speeded up by an increase in temperature and takes place in two hours at 100°.

2,5-Diphenyl-3-formylfuran (X).—A solution of 12 g. of dibenzoyl-(morpholinomethyl)-ethylene (I) in 150 ml. of a 1.75 *N* methanolic hydrogen chloride solution was allowed to stand for eight hours after which time it was evaporated under reduced pressure. The residue was dissolved in ether and the resulting solution was washed first with water, then with sodium carbonate solution and finally again with water, after which it was dried over anhydrous sodium sulfate and evaporated under reduced pressure. Crystallization of the residue from isopropanol yielded 7 g. of material which melted at 86–88°. Several recrystallizations and a vacuum sublimation raised the melting point to 90–92°. The pure compound was white, gave no Beilstein test for halogen and was completely insoluble in hydrochloric acid. It gave a large mixture melting point depression with 3-benzoyl-5-phenylfuran (VII).[6] A positive test for an aldehyde group was obtained with Tollens reagent.

Anal. Calcd. for $C_{17}H_{12}O_2$: C, 82.24; H, 4.87. Found: 82.10; H, 5.00.

An **oxime** of the formylfuran (X) was formed by reaction with hydroxylamine hydrochloride in the usual way.[11] It melted at 171–173° after several recrystallizations from ethanol.

Anal. Calcd. for $C_{17}H_{13}NO_2$: N, 5.32. Found: N, 5.44.

2,5-Diphenyl-3-(hydroxymethyl)-furan (XI).—Five grams of 2,5-diphenyl-3-formylfuran (X) was dissolved in 125 ml. of a 1 *M* solution of aluminum isopropoxide in isopropanol and the resulting solution was refluxed for two hours in an apparatus similar to the one described in "Organic Reactions."[12] Positive acetone tests were obtained during the first ninety minutes of the refluxing period. In all, 50 ml. of the solvent was distilled over. The reaction mixture was then shaken with 100 ml. of 20% sodium hydroxide solution and the two layers were separated. The aqueous layer was extracted with ether and the ether extract was added to the isopropanol layer. The resulting solution was diluted with ether, washed several times with saturated salt solution, dried over anhydrous sodium sulfate and evaporated under reduced pressure. Recrystallization of the crude residue from 60% ethanol yielded 4.5 g. of material which melted at 121–123°. Further recrystallization raised the melting point to 123–124°.

Anal. Calcd. for $C_{17}H_{14}O_2$: C, 81.58; H, 5.60. Found: C, 81.30; H, 5.45.

3-(Chloromethyl)-2,5-diphenylfuran (XII) was prepared by dissolving 4 g. of 2,5-diphenyl-3-(hydroxymethyl)-furan (XI) in 100 ml. of 3 *N* ethereal hydrogen chloride solution. After standing for three days the solution was evaporated under reduced pressure. The residue weighed 4 g. and melted at 56–59°. Several recrystallizations from ethanol raised the melting point to 62–63°. The compound gave a positive Beilstein test for halogen.

Anal. Calcd. for $C_{17}H_{13}ClO$: C, 75.98; H, 4.88. Found: C, 75.79; H, 4.95.

Treatment of 3-(Chloromethyl)-2,5-diphenylfuran (XII) with Morpholine.—To a solution of 0.2 g. of the chloromethyl compound in 10 ml. of dry ether was added 5 ml. of morpholine. After three days the mixture was filtered

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[8] All melting points reported in this paper are corrected.

[9] Lutz and Taylor, THIS JOURNAL, 55, 1177 (1933).

[10] For the reduction in acetic acid solution which yielded dibenzoyl-(morpholinomethyl)-ethane (II) see ref. 2.

[11] Shriner and Fuson, "Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., p. 145.

[12] Wilds, in "Organic Reactions," Vol. 2, John Wiley and Sons, New York, N. Y., 1944, p. 178.

and the filtrate was diluted with ether and extracted with 10% hydrochloric acid. The acid extract was diluted with water and neutralized with sodium carbonate, after which the resulting mixture was extracted with ether. The ether extract was washed, dried, and evaporated under reduced pressure. Acidification of an acetone solution of the residue with ethereal hydrogen chloride yielded 0.3 g. of a hydrochloride which melted at 217–221° and was shown by a mixture melting point to be 2,5-diphenyl-3-(morpholinomethyl)-furan (XIII) hydrochloride.[2]

Catalytic dehalogenation of 3-(chloromethyl)-2,5-diphenylfuran (XII) (1 g. in 50 ml. of ethanol) using 1 g. of palladium–barium sulfate proceeded at a steady rate until one equivalent of hydrogen had been absorbed. At this point the rate of absorption decreased greatly and for this reason the reaction was stopped. The reaction mixture was filtered and evaporated to a low volume under an air blast, after which the resulting mixture was cooled and filtered. Thus was obtained 0.4 g. of material which melted at 54–57° and gave a large mixture melting point depression with starting material. It was shown to be 2,5-diphenyl-3-methylfuran (XIV) by a mixture melting point with an authentic sample.[13]

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[13] Lutz and McGinn, THIS JOURNAL, **64**, 2585 (1942).

Summary

Catalytic reduction of *cis*-dibenzoyl-(morpholinomethyl)-ethylene in ethanol solution is found to involve saturation of the double bond and deamination, yielding dibenzoylmethylethane; in contrast reductions in acetic acid solution involve retention of the morpholino group and yield dibenzoyl-(morpholinomethyl)-ethane.

cis - Dibenzoyl - (morpholinomethyl) - ethylene furanizes in two different ways, one spontaneously to the known 3-benzoyl-5-phenylfuran, and the other under the influence of methanolic hydrogen chloride to 2,5-diphenyl-3-formylfuran. The structure of the latter compound is demonstrated. Possible mechanisms for these reactions are suggested.

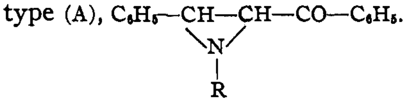
CHARLOTTESVILLE, VIRGINIA

RECEIVED SEPTEMBER 28, 1945

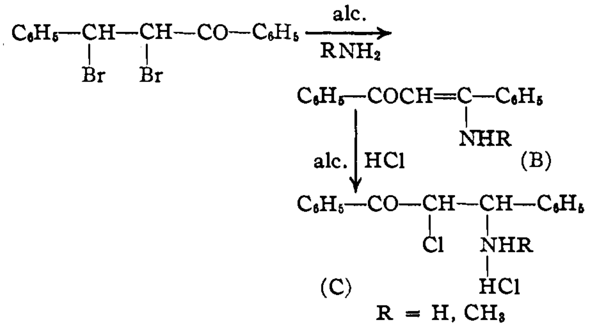
[CONTRIBUTION FROM THE AVERY LABORATORY OF CHEMISTRY OF THE UNIVERSITY OF NEBRASKA]

Ethylene Imine Ketones

BY NORMAN H. CROMWELL AND JOHN A. CAUGHLAN

In a previous communication[1] the reactions of primary amines with α-bromobenzalacetophenone and with α,β-dibromobenzylacetophenone were shown to produce ethylene imine ketones of the type (A),  $C_6H_5\text{—}\underbrace{CH\text{—}CH}_{\underset{R}{N}}\text{—}CO\text{—}C_6H_5$.

Algar, Hickey and Sherry[2] have published an article in which they describe some interesting experiments involving the reactions of ammonia and methylamine with α,β-dibromobenzylacetophenone. These investigators did not attempt to isolate the immediate products from these reactions, but treated the resulting crude products with alcoholic hydrogen chloride to obtain, as isolable products, dichlorides for which they wrote the structure (C). The mechanisms of the reactions were described as indicated.



The Irish workers refer to the early work of Ruhemann and Watson[3] in assigning the structures for their intermediate products (B). The structure of the intermediate bromobenzalacetophenone has long been known to be α-bromobenzalacetophenone[4] and not β-bromobenzalacetophenone as Ruhemann and Watson wrote it. Moreover, the work of Dufraisse and Moureu[5] has since shown that the product from the reaction of ammonia with α,β-dibromobenzylacetophenone cannot have the β-aminobenzalacetophenone structure (B). By analogy with the behavior of secondary amines in such reactions the French investigators wrote the structure for this product as α-aminobenzalacetophenone. Our recent investigations[1,6] indicate the true structures for the products of the reactions of ammonia and primary amines with these dibromo ketones to be ethylene imine ketones of type (A).

It seemed important to reinvestigate some of the reactions described by the Irish workers and attempt to isolate the intermediate ethylene imine ketone which we expected resulted from the reaction of methylamine with α,β-dibromobenzylacetophenone. Also, a more careful study of the structures of the dihalides of type (C), which we also had reported as resulting from the

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[1] Cromwell, Babson and Harris, THIS JOURNAL, **65**, 312 (1943).

[2] Algar, Hickey and Sherry, *Proc. Roy. Irish Acad.*, **49B**, 109–119 (1943). A communication to the Editor from Professor Algar points out that their paper was read before the Royal Irish Academy on Feb. 22, 1943, and published on June 11, 1943, and that the paper by us (ref. 1), published in March, 1943, was not available to them until sometime later because of difficult overseas communication.

[3] Ruhemann and Watson, *J. Chem. Soc.*, **85**, 1181 (1904).

[4] Kohler, *Am. Chem. J.*, **33**, 36 (1905); Dufraisse, *Compt. rend.*, **171**, 1062 (1920).

[5] Dufraisse and Moureu, *Bull. soc. chim.*, (4) **41**, 861 (1927).

[6] Cromwell and Johnson, THIS JOURNAL, **65**, 316 (1943).