[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE UNIVERSITY OF TEXAS]

Preparations and Reactions with Amines of Some 1,2-Dibenzoylalkenes[1]

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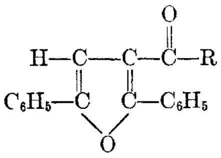
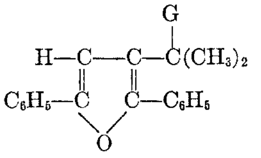
The reactions of several dibenzoylalkenes with amines are compared with the reaction of 1,2-dibenzoylpropene with amines to give 1-amino-2,3-dibenzoylpropanes. The Wolff-Kishner reduction of 3-benzoyl-2,5-diphenylfuran gave 3,5-diphenyl-4-(β-phenylethyl)pyrazole as a by-product.

In earlier papers the reactions of 1,2-dibenzoylpropene,[2] 1,2-dibenzoyl-1-butene,[3] and 2,3-dibenzoyl-1-(4-morpholinyl)-2-butene[4] with morpholine to give 1,2-dibenzoyl-3-(4-morpholinyl)propane and butane and 2,3-dibenzoyl-1,4-di(4-morpholinyl)-butane, respectively, and of 1,2-dibenzoylpropene with hydrogen halides to give 1,2-dibenzoyl-3-halopropanes or 3-halomethyl-2,5-diphenylfurans[5,6] have been reported. In the present paper the syntheses and reactions with amines of three similar compounds, *cis*-1,2-dibenzoyl-3-methyl-1-butene (VIa), *cis*-2,3-dibenzoyl-2-butene (VIc), and *cis*-1,2-dibenzoyl-3-phenylpropene (VIb) are described.

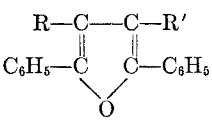
The synthesis of *cis*-1,2-dibenzoyl-3-methyl-1-butene (VIa) started with 3-acetyl-2,5-diphenylfuran (Ia) and involved as the first step reaction with methylmagnesium iodide to give 3-(2-hydroxy-2-propyl)-2,5-diphenylfuran (IIa), which spontaneously dehydrated to 3-isopropenyl-2,5-diphenylfuran (IV). Catalytic reduction of IV gave 3-isopropyl-2,5-diphenylfuran (IIIa) which underwent the characteristic nitric acid oxidative cleavage[7] to the desired dibenzoylisopropylethylene (VIa). Attempts to produce IIIa by a direct Friedel-Crafts reaction between 2,5-diphenylfuran (IIId) and isopropyl chloride failed.



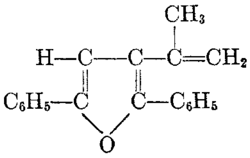
I (a) R = CH_3
(b) R = phenyl



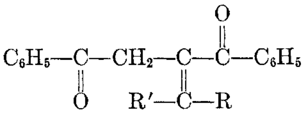
II (a) G = OH
(b) G = Cl



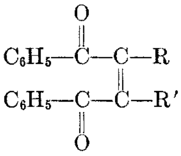
III (a) R = H; R′ = isopropyl
(b) R = H; R′ = benzyl
(c) R = R′ = CH_3
(d) R = R′ = H
(e) R = R′ = CH_2Br



IV



V (a) R = R′ = CH_3
(b) R = H; R′ = phenyl



VI (a) R = H, R′ = isopropyl
(b) R = H, R′ = benzyl
(c) R = R′ = CH_3
(d) R = CH_3, R′ = $CH_2NC_4H_8O$

The synthesis of *cis*-1,2-dibenzoyl-3-phenylpropene (VIb) involved the Wolff-Kishner reduction of 3-benzoyl-2,5-diphenylfuran (Ib) to 3-benzyl-2,5-diphenylfuran (IIIb) followed by nitric acid oxidation of IIIb to VIb. The *cis* configuration is assigned to both VIa and VIb by analogy to the nitric acid oxidations of similar furans.[7] The reductive cyclization of each back to the corresponding furans (IIIa and b) is evidence that no unexpected structural changes occurred during the oxidations.

cis-2,3-Dibenzoyl-2-butene (VIc) was obtained as shown previously,[8] by the nitric acid oxidation of 3,4-dimethyl-2,5-diphenylfuran (IIIc). The latter was synthesized by a new method, however, which involved the dibromomethylation of 2,5-diphenylfuran (IIId to IIIe) followed by reductive dehalogenation.

The dibenzoylisopropylethylene (VIa) failed to undergo addition with dimethylamine, morpholine, or piperidine. Instead, whether in ether solution at room temperature or with the amine direct, even at 90°, it isomerized to 1,2-dibenzoyl-3-methyl-2-

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(1) Taken in part from the M.A. Thesis of W. F. T. (January 1950) and H. H. N. (January 1951) and from a portion of the Ph.D. dissertation of S. S. B. (soon to be presented). This work was supported in part by grants-in-aid from the Research Corporation, New York, N. Y., and The University of Texas Research Institute.

(2) Lutz and Bailey, *J. Am. Chem. Soc.*, **67**, 2229 (1945).

(3) Bailey and Hakki, *J. Am. Chem. Soc.*, **71**, 2886 (1949).

(4) Bailey and Nowlin, *J. Am. Chem. Soc.*, **71**, 732 (1949).

(5) Bailey, Nowlin, Pomerantz, Waggoner, and Kawas, *J. Am. Chem. Soc.*, **73**, 5560 (1951).

(6) Bailey and Pomerantz, *J. Am. Chem. Soc.*, **75**, 281 (1953).

(7) Lutz and Wilder, *J. Am. Chem. Soc.*, **56**, 978 (1934).

(8) Lutz and Kibler, *J. Am. Chem. Soc.*, **62**, 1520 (1940).

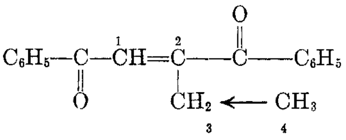
butene (Va). Under more drastic conditions it gave a tar. The structure of Va was proven by reductive cyclization to IIIa and by ozonolysis, whereby acetone was produced. In contrast, VIa gave no acetone upon ozonolysis.

In an earlier paper[3] it was suggested that the cause for the difficulty with which 1,2-dibenzoyl-1-butene underwent the amine addition in comparison to 1,2-dibenzoylpropene might be the inductive effect of the additional methyl group (carbon 4 in structure VII) which could conceivably decrease the ease with which the hydrogens on carbon 3 (of VII) could undergo the 1,3-shift necessary to bring about the reaction.[2,5] However the results with the isopropyl compound (VIa) show that this is not so, since the 1,3-hydrogen shift occurs readily but addition to the product (Va) does not occur. Instead, it appears much more likely that steric hindrance in the product of the 1,3 hydrogen shift is the reason why homologs and structurally similar derivatives of 1,2-dibenzoylpropene undergo the novel amine addition less readily than does 1,2-dibenzoylpropene. Indeed, a Fisher-Hirschfelder model of Va shows that it would be extremely difficult for addition with an amine as large as morpholine or piperidine to occur.

The benzyldibenzoylethylene (VIb) also reacted in accordance with this picture. In a dilute solution of morpholine in ether, VIb simply isomerized to 2,3-dibenzoyl-1-phenylpropene (Vb). When treated with a concentrated morpholine-ether solution or with morpholine alone, however, addition occurred to give 1,2-dibenzoyl-3-(4-morpholinyl)-3-phenylpropane (VIIIa). It was under the same conditions that 1,2-dibenzoyl-1-butene reacted with morpholine to give 1,2-dibenzoyl-3-(4-morpholinyl)-butane.[3] Fischer-Hirschfelder models of 2,3-dibenzoyl-1-phenylpropene (Vb) and of 1,2-dibenzoyl-2-butene (the product of the 1,3-hydrogen shift with 1,2-dibenzoyl-1-butene) show that whereas these molecules are sterically hindered, they are not as sterically hindered as Va and morpholine addition should occur.

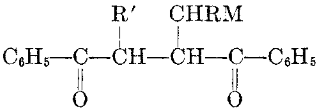
The structural proof of Vb consisted of its ozonolysis to the enol of 1,4-diphenyl-1,2,4-butanetrione (X)[9] which is a known compound. The odor of benzaldehyde was also apparent, but no attempt was made to isolate the material.

The structure of VIIIa was proven by cyclization to XIb which in turn was synthesized from 3-benzyl-2,5-diphenylfuran (IIIb) by bromination with N-bromosuccinimide to XIa followed by aminolysis of XIa to XIb. The bromo compound (XIa) had previously been made another way by Kohler and Jones.[10]



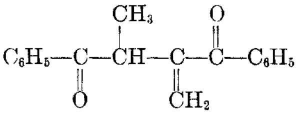
$$C_6H_5-\underset{\underset{O}{\|}}{C}-\overset{1}{C}H=\overset{2}{\underset{\underset{\underset{3}{CH_2}\ \longleftarrow\ \underset{4}{CH_3}}{|}}{C}}-\overset{\overset{O}{\|}}{C}-C_6H_5$$

VII



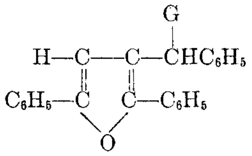
$$C_6H_5-\underset{\underset{O}{\|}}{C}-\overset{\overset{R'}{|}}{C}H-\overset{\overset{CHRM}{|}}{C}H-\underset{\underset{O}{\|}}{C}-C_6H_5$$

VIII M = morpholinyl
(a) R′ = H; R = phenyl
(b) R = H, R′ = CH₃

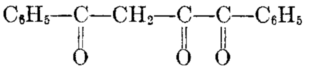


$$C_6H_5-\underset{\underset{O}{\|}}{C}-\overset{\overset{CH_3}{|}}{C}H-\underset{\underset{CH_2}{\|}}{C}-\overset{\overset{O}{\|}}{C}-C_6H_5$$

IX



XI (a) G = Br
(b) G = morpholinyl
(c) G = OH



$$C_6H_5-\underset{\underset{O}{\|}}{C}-CH_2-\underset{\underset{O}{\|}}{C}-\underset{\underset{O}{\|}}{C}-C_6H_5$$

X

As with 2,3-dibenzoyl-1-(4-morpholinyl)-2-butene (VId),[4] it was necessary to heat a morpholine solution of 2,3-dibenzoyl-2-butene (VIc) for 24 hours in order to bring about reaction. The product was the known 2,3-dibenzoyl-1-(4-morpholinyl)-butane (VIIIb).[4] Since not even isomerization occurred with VIc under milder conditions it is reasonable to suppose that in the case of VIc and VId not only is steric hindrance a factor, but also the extent to which the product of the 1,3-shift of hydrogen occurs in the equilibrium mixture produced by treating the original olefin with morpholine. For example, IX (the product of the 1,3-shift of hydrogen with VIc) should be much less stable than VIc, and therefore present to a much lesser extent in the equilibrium mixture, because it not only possesses a shorter conjugated system than VIc, but also is stabilized through the hyperconjugation of only one hydrogen atom whereas VIc is stabilized through the hyperconjugation of six hydrogen atoms. With the other systems discussed, hyperconjugation either makes no difference, or else stabilizes the product of the 1,3-shift to a greater extent than the original olefin, thus making the equilibrium more favorable for the product of the 1,3-shift than in the case of VIc.

During the work leading to the preparation of IIIa and IIIb the corresponding bis-furans (XIIa and b) were obtained. The bis-isopropylfuran (XIIa) was obtained, instead of IIIa, by reduction of IV with hydriodic acid or stannous chloride and hydrochloric acid. Stannous chloride-hydrochloric acid reductions of VIa and Va likewise gave XIIa. It was also produced by treatment of IV, Va or VIa with a hydrochloric acid-acetic acid mixture followed by coupling with copper bronze. Evi-

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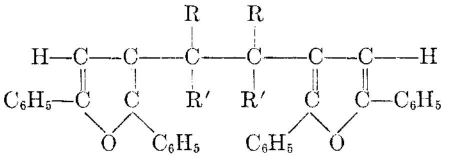
[9] Lutz, Wilder, and Parrish, *J. Am. Chem. Soc.*, **56**, 1980 (1934); Lutz and Stuart, *J. Am. Chem. Soc.*, **58**, 1885 (1936); Lutz and King, *J. Org. Chem.*, **17**, 1519 (1952).

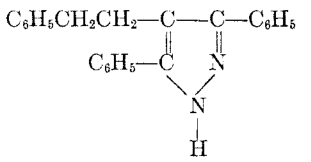
[10] Kohler and Jones, *J. Am. Chem. Soc.*, **41**, 1249 (1919).

dently in these last reactions, at least, halogen derivatives are intermediates, IIb from IV, and either or both IIb and the product of a conjugate addition of hydrogen chloride to Va in the cases of Va and VIa.[11] A Fisher-Hirschfelder model of Va shows that hydrogen chloride addition could much more easily occur than the morpholine addition discussed earlier.

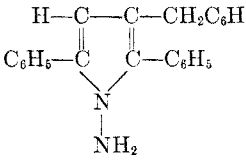
Similarly, XIIb was produced by Ponndorf reduction[12] of the benzoylfuran (Ib) to the corresponding alcohol (XIc) followed by stannous chloride–hydrochloric acid reduction of XIc. It was also obtained from the coupling of the bromobenzylfuran (XIa) by means of copper bronze.



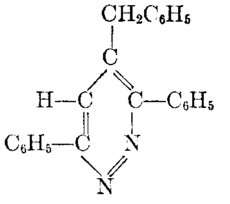
XII (a) R = R′ = CH_3
(b) R′ = H; R = phenyl



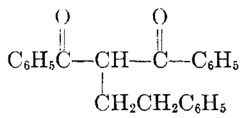
XIII



XIV



XV

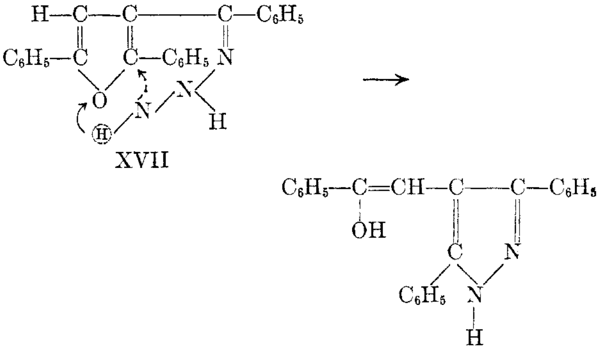


$C_6H_5C(=O)-CH(CH_2CH_2C_6H_5)-C(=O)-C_6H_5$

XVI

The Wolff-Kishner reduction of 3-benzoyl-2,5-diphenylfuran (Ib) produced not only the corresponding benzylfuran (IIIb), but also a nitrogen-containing compound which, judging from its percentage composition and origin, would have to be 3,5-diphenyl-4-phenylethylpyrazole (XIII), 1-amino-3-benzyl-2,5-diphenylpyrrole (XIV), or the 1,2-dihydro derivative of 4-benzyl-3,6-diphenylpyridazine (XV). Since dihydropyridazines are known to be oxidized to the corresponding pyridazines, XV itself was also considered a possibility. Synthesis of XV by a general method, however, proved it to be different. The unknown substance was resistant to mild permanganate oxidation, and yielded a mono hydrochloride and a mono sulfonamide which was insoluble in sodium hydroxide solution. These reactions are entirely typical only of the pyrazole (XIII). The material was shown to be the pyrazole by an unambiguous synthesis, the principal step of which was the conversion of the corresponding 1,3-diketone (XVI) to the pyrazole by the general method of treating with hydrazine.

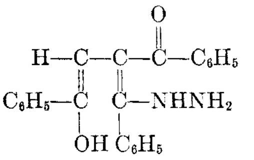
A possible course by which the benzoylfuran (Ib) was converted to the pyrazole (XIII) involves first the formation of the hydrazone (XVII). The hydrazone could then be converted to the benzylfuran (IIIb) on the one hand and on the other undergo an internal simultaneous aminolytic cleavage of the furan ring and formation of the pyrazole ring to form XVIII which would ketonize and undergo Wolff-Kishner reduction to XIII.



XVII

XVIII

An alternative route to XVIII (or its keto form) involves first the aminolytic cleavage of the furan ring of Ib by hydrazine to give XIX, followed by the intramolecular interaction of the substituted hydrazine group and the carbonyl group of XIX.



XIX

EXPERIMENTAL[13]

3-Isopropenyl-2,5-diphenylfuran (IV). To 66 ml. of a 1 *M* methylmagnesium iodide solution (0.066 mole) was added dropwise with stirring, over a period of one hour, a solution of 15 g. (0.057 mole) of 3-acetyl-2,5-diphenylfuran[14] in 300 ml. of dry ether. After the reaction had subsided, the mixture was refluxed for 30 minutes and then was poured into a mixture of ice and 30 ml. of 10% hydrochloric acid. The ether layer was separated, washed, and evaporated leaving 15 g. of a viscous yellow oil which resisted crystallization. An accumulation of 80 g. of the oil was distilled; yield, 51 g., b.p. 188–190°/2 mm.; redistilled for analytical sample at 157°/0.2 mm.

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[11] See footnotes 5 and 6 for references to analogous additions with 1,2- and 2,3-dibenzoylpropenes.

[12] Wilds in Adams, *Org. Reactions*, **2**, 178 (1944).

[13] The melting points reported here are corrected. Some of the microanalyses were done by the Clark Microanalytical Laboratory of Urbana, Illinois, and the G. Weiler and F. B. Strauss Microanalytical Laboratory of Oxford, England.

[14] Lutz and Rowlett, *J. Am. Chem. Soc.*, **70**, 1359 (1948).

Anal. Calc'd for $C_{19}H_{16}O$: C, 87.66; H, 6.20; M.W. 260. Found: C, 87.70, 87.56; H, 6.07, 6.19; M.W. (Rast), 259, 259.

After standing for several months the oil crystallized; after recrystallization from ethyl alcohol, it had m.p. 37–38°.

Anal. Calc'd for $C_{19}H_{16}O$: C, 87.66; H, 6.20. Found: C, 87.58; H, 6.27.

3-Isopropyl-2,5-diphenylfuran (IIIa). A solution of 2.5 g. (0.01 mole) of 3-isopropenyl-2,5-diphenylfuran (IV) in 50 ml. of ethyl alcohol was allowed to absorb hydrogen in the presence of 0.1 g. of Adam's catalyst[15] at atmospheric pressure; 0.009 mole was absorbed. The catalyst was removed by filtration and the filtrate was cooled; the product formed colorless crystals, recrystallized from ethyl alcohol, 2.2 g. (88%), m.p. 48–49°.

Anal. Calc'd for $C_{19}H_{18}O$: C, 86.98; H, 6.92. Found: C, 86.85, 86.78; H, 7.11, 7.07.

Attempts to prepare the isopropylfuran (IIIa) from 2,5-diphenylfuran by the Friedel-Crafts reaction using isopropyl chloride in benzene and in carbon disulfide solutions at room temperature, −10°, or 0° failed. Only viscous tars were obtained with an aluminum chloride catalyst and no reaction occurred using a stannic chloride catalyst.

cis-1,2-Dibenzoyl-3-methyl-1-butene (VIa). To a solution of 7.5 g. of 3-isopropyl-2,5-diphenylfuran (IIIa) and 40 ml. of propionic acid cooled to 0° was added a solution of 13.5 ml. of nitric acid and 40 ml. of propionic acid also cooled to 0°. After 5 minutes standing without further cooling the solution was poured onto cracked ice, whereupon a yellow solid precipitated; 6.5 g. (81%), m.p. 64–65° after several recrystallizations from petroleum ether (b.p. 60–68°).

Anal. Calc'd for $C_{19}H_{18}O_2$: C, 81.98; H, 6.52. Found: C, 81.85, 82.03; H, 6.57, 6.49.

Reductive cyclization of cis-1,2-dibenzoyl-3-methyl-1-butene (VIa). To a solution of 1 g. of VIa in 20 ml. of glacial acetic acid was added a porcelain spatulaful of zinc dust. The mixture was heated over a steam-bath for 20 minutes, after which it was filtered. The filtrate was poured into water, and the resulting mixture was extracted with ether and the ether extract was evaporated. The residue failed to crystallize. Therefore it was dissolved in 10 ml. of acetic anhydride and the resulting solution was treated with 10 drops of sulfuric acid in order to convert to the furan (IIIa). After 15 minutes, the mixture was poured into ice-water, neutralized with sodium carbonate, and extracted with ether. The ether extract was evaporated. The residue crystallized from ethyl alcohol after standing in the refrigerator; 0.4 g. (43%), m.p. 47–48°, no depression in melting point with a known sample of 3-isopropyl-2,5-diphenylfuran (IIIa).

1,1,2-Tribenzoylethane. To a vigorously stirred solution of 4.6 g. (0.2 mole) of sodium in 75 ml. of absolute ethanol was added a solution of 44.8 g. (0.2 mole) of dibenzoylmethane[16] and 40 g. (0.2 mole) of phenacyl bromide[17] in 120 ml. of ethanol. Stirring was continued for 45 minutes, after which time the mixture was cooled and filtered; 48 g. (70%), m.p. 150–155°. Additional recrystallization from methanol raised the melting point to 158–159°. Kleinfeller and Trommsdorff[18] report a melting point of 155°.

3-Benzoyl-2,5-diphenylfuran (Ib). (*a*) *From 1,1,2-tribenzoylethane.* To a cold solution of 20 g. of 1,1,2-tribenzoylethane in 200 ml. of acetic anhydride was added, with stirring, 15 drops of conc'd sulfuric acid. The mixture was poured into ice-water, and the aqueous layer was decanted from the oily layer. The oily layer was dissolved in ether, the ether solution was washed and evaporated, and the residue was crystallized from ethyl alcohol; yield, 15.7 g. (83%), m.p. 76–78°. Kohler and Jones[10] report a melting point of 77°.

(*b*) *From 2,5-diphenylfuran* (IIId). To a solution of 5 g. of 2,5-diphenylfuran (IIId) in 40 ml. of dry benzene was slowly added, with stirring, at a temperature of 10° a solution of 3.5 g. of benzoic anhydride in 20 ml. of dry benzene followed by a solution of 6 g. of stannic chloride in 20 ml. of dry benzene. Stirring was continued for 4 hours at a temperature of 18–25° and 1 hour at 30°. The dark mixture then was poured onto crushed ice mixed with 10 ml. of conc'd hydrochloric acid. The resulting mixture was extracted with ether and the ether extract was washed with sodium carbonate solution and with water, dried over sodium sulfate, and evaporated under an air jet. The residue was crystallized and recrystallized from ethyl alcohol yielding 3 g. (41% yield) of material melting at 79–81°; it showed no depression in a mixture melting point with the material obtained in the preceding experiment.

Bis-(3-benzoyl-2,5-diphenylfuran) hydrazone. This material was obtained in a preliminary effort to carry out the Wolff-Kishner reduction of 3-benzoyl-2,5-diphenylfuran (Ib). A solution of 5 g. of Ib and 10 ml. of 85% hydrazine hydrate in 100 ml. of 0.7 *molar* sodium isoamyl alkoxide solution was refluxed 5 hours after which 5 ml. of hydrazine hydrate was added and refluxing was continued for 11 hours. The mixture was shaken with 400 ml. of 5% hydrochloric acid, after which the isoamyl alcohol layer was separated, washed, and evaporated. Crystallization of the residue from ethyl alcohol gave yellow crystals melting at 195–209°; recrystallized from an acetone-ethyl alcohol mixture, m.p. 220–221°.

Anal. Calc'd for $C_{46}H_{32}N_2O_2$: C, 85.69; H, 5.00; N, 4.35. Found: C, 85.40, 85.16; H, 5.38, 5.22; N, 4.56, 4.46.

3-Benzyl-2,5-diphenylfuran (IIIb). To 40 ml. of ethylene glycol was added 1.4 g. of sodium and then 5 g. of the semicarbazone (m.p. 222–225°)[19] of 3-benzoyl-2,5-diphenylfuran (Ib). The mixture was refluxed for 70 hours, after which time it was poured into cold water and acidified with dilute hydrochloric acid. Extraction with ether and evaporation of the ether layer gave a residue which was crystallized from ethyl alcohol (Norit) yielding 2.6 g. (64%) of material melting at 79–81°; recrystallized from ethyl alcohol, m.p. 83–84°.

Anal. Calc'd for $C_{23}H_{18}O$: C, 89.00; H, 5.85. Found: C, 89.34; H, 5.85.

In later experiments using one-gram quantities of Ib, either sodium or sodium methoxide and ethylene glycol, and refluxing for 10 to 20 hours, yields of 75–85% of IIIb were obtained.

cis-1,2-Dibenzoyl-3-phenylpropene (VIb). A cold solution (−15°) of 20 ml. of conc'd nitric acid and 50 ml. of propionic acid was added slowly to a cold solution (−15°) of 4.8 g. of 3-benzyl-2,5-diphenylfuran (IIIb) and 50 ml. of propionic acid. After 10 minutes at −15° the mixture was poured onto crushed ice. Crystallization occurred after a few hours and the material was filtered, washed, dried, and recrystallized from petroleum ether (b.p. 60–68°) which contained a small amount of ethanol; yield, 3.3 g. (65%), m.p. 78–79°.

Anal. Calc'd for $C_{23}H_{18}O_2$: C, 84.64; H, 5.58. Found: C, 84.85; H, 5.59.

Reductive cyclization of cis-1,2-dibenzoyl-3-phenylpropene (VIb). To a solution of 3 g. of stannous chloride, 6 ml. of glacial acetic acid, and 6 ml. of conc'd hydrochloric acid was added a solution of 0.4 g. of VIb in 6 ml. of glacial acetic acid. The mixture was refluxed for 8 minutes and then was allowed to cool, whereupon a semicrystalline material precipitated. Filtration and crystallization from ethyl alcohol yielded 0.05 g. of material melting at 78–81°; no depression in mixture melting point with 3-benzyl-2,5-diphenylfuran (IIIb).

1,2-Dibenzoyl-3-phenylpropane. To a solution of 1.5 g. of

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(15) Adams, Voorhees, and Shriner in Gilman and Blatt, *Org. Syntheses*, Coll. Vol. I, 2nd Ed., 463 (1941).

(16) Allen, Abell, and Normington in Gilman and Blatt, *Org. Syntheses*, Coll. Vol. I, 2nd Ed., 205 (1941); Dreiding and Hartman, *J. Am. Chem. Soc.*, **75**, 3725 (1953).

(17) Cowper and Davidson in Blatt, *Org. Syntheses*, Coll. Vol. II, 480 (1943).

(18) Kleinfeller and Trommsdorf, *Ber.*, **71**, 2448 (1938).

(19) Lutz and Smith, *J. Am. Chem. Soc.*, **63**, 1148 (1941).

1,2-dibenzoyl-3-phenylpropene (VIb) in 35 ml. of glacial acetic acid was added a spatulaful of zinc dust. After 15 minutes the excess zinc was filtered off, water was added, and the resulting mixture was neutralized with sodium carbonate and extracted with ether. The ether extract was washed and evaporated and the residue was crystallized from isopropyl alcohol, yielding 1 g. of material melting at 95–98°; recrystallized from isopropyl alcohol, m.p. 97–98°.

Anal. Calc'd for $C_{23}H_{20}O_2$: C, 84.12; H, 6.14. Found: C, 84.18; H, 6.15.

3,4-Dibromomethyl-2,5-diphenylfuran (IIIe). To a solution of 12.6 g. of paraformaldehyde in 120 g. of 30% hydrogen bromide-acetic acid reagent was added a solution of 31 g. of 2,5-diphenylfuran (IIId)[14] in 210 ml. of glacial acetic acid. The mixture was stirred for 2 hours after which time the crystals which formed were filtered off; 54 g. (90%), m.p. 155–160°; recrystallized from acetone, m.p. 164–165°.

Anal. Calc'd for $C_{18}H_{14}Br_2O$: C, 53.23; H, 3.47. Found: C, 53.38; H, 3.57.

Treatment of IIIe with morpholine gave the known 3,4-di-4-morpholinylmethyl-2,5-diphenylfuran;[20] m.p. 137–139°, identification by the mixture melting point method.

3,4-Dimethyl-2,5-diphenylfuran (IIIc). 3,4-Di-(bromomethyl)-2,5-diphenylfuran (IIIe) (8 g.) and a porcelain spatulaful of Raney nickel catalyst was added to a solution of 1.6 g. of sodium hydroxide in 500 ml. of ethyl alcohol. The mixture was allowed to absorb hydrogen at atmospheric pressure (872 ml. absorbed). Removal of the catalyst by filtration, evaporation of the filtrate by a stream of air, and crystallization of the residue from acetone gave 4.4 g. (90% yield) of 3,4-dimethyl-2,5-diphenylfuran (IIIc), m.p. 113–116°. Lutz and Taylor[21] reported 116°.

cis-2,3-Dibenzoyl-2-butene (VIc) was made from 3,4-dimethyl-2,5-diphenylfuran (IIIc) by the same method that VIa was made from IIIa except that the temperature was −10° and the reaction mixture was slowly diluted with ice-water until precipitation of VIc was complete; yield 94%, m.p. 75–85°. Recrystallization from isopropyl alcohol raised the melting point to 82–84°; Lutz and Kibler[8] reported a melting point of 86–87°.

1,2-Dibenzoyl-3-methyl-2-butene (Va). A solution of 0.5 g. of *cis*-1,2-dibenzoyl-3-methyl-1-butene (VIa), 8 ml. of dry ether, and 2 ml. of morpholine was allowed to stand at room temperature for 24 hours, after which time it was diluted with additional ether, washed thoroughly with water and evaporated, leaving 0.3 g. (60% yield) of material melting at 64–67°. The material gave a large depression in a mixture melting point with VIa. Similar results were obtained with morpholine alone at room temperature, with piperidine alone at room temperature and at 90° for 2 hours (10 hours at 90° gave a resin, but no sign of an addition product) and with dimethylamine in ether solution at room temperature or in a sealed tube at 83° for 18 hours. Recrystallization from ethyl alcohol raised the melting point to 69–70°.

Anal. Calc'd for $C_{19}H_{18}O_2$: C, 81.98; H, 6.52. Found: C, 82.16, 81.92; H, 6.53, 6.58.

Ozonolysis of 1,2-dibenzoyl-3-methyl-2-butene (Va).[22] Into a solution of 2 g. of Va in 35 ml. of absolute methanol was passed a stream of oxygen containing 3% ozone at −50° until the solution became blue in color. After the solution had come to room temperature, 4.5 g. of sodium iodide was added (iodine precipitated) followed first by a solution of 3 g. of sodium hydroxide in 50 ml. of water (iodoform precipitated) and then by a solution of 4 g. of iodine and 8 g. of sodium iodide in 50 ml. of water. The total yield of iodoform produced was 2 g. (showing a 70% yield of acetone); m.p. 120–122°, no depression in a mixture melting point with a known sample.

In a similar experiment, 1,2-dibenzoyl-3-methyl-1-butene (VIa) gave no iodoform.

Reduction of 1,2-dibenzoyl-3-methyl-2-butene (Va) *to 3-isopropyl-2,5-diphenylfuran* (IIIa). (*a*) *1,2-Dibenzoyl-3-methylbutane.* The reductive cyclization method used to convert VIa to IIIa failed with Va. Therefore, Va (1.7 g.) was catalytically hydrogenated [Adams' catalyst[15] in ethyl alcohol] at atmospheric pressure. The catalyst was filtered off and the filtrate was cooled, producing 1.2 g. (70% yield) of material melting at 61–63°; recrystallized from ethyl alcohol, m.p. 63–64°.

Anal. Calc'd for $C_{19}H_{20}O_2$: C, 81.39; H, 7.19. Found: C, 81.14; H, 7.03.

(*b*). *3-Isopropyl-2,5-diphenylfuran* (IIIa). Conc'd sulfuric acid (10 drops) was added to a solution of 1 g. of 1,2-dibenzoyl-3-methylbutane in 10 ml. of acetic anhydride. After 10 minutes the resulting mixture was poured into ice-water and neutralized with sodium carbonate. Extraction with ether, evaporation of the ether extract, and crystallization of the residue from ethyl alcohol gave 0.6 g. (64%) of IIIa; m.p. 48–49°, identification by the mixture melting point method.

2,3-Dibenzoyl-1-phenylpropene (Vb). A solution of 0.3 g. of *cis*-1,2-dibenzoyl-3-phenylpropene (VIb), 3 ml. of morpholine, and 10 ml. of dry ether was allowed to stand for 23 hours, after which time it was poured into cold water. The resulting mixture was extracted with ether and the ether layer was extracted with dilute hydrochloric acid. A slight precipitate formed and was filtered off and discarded. The ether layer was washed, dried, and evaporated leaving a residue which crystallized from ethyl alcohol after standing in the refrigerator for 24 hours; 0.17 g. (57% yield), m.p. 87–90°; recrystallized from ethyl alcohol, m.p. 89–90°.

Anal. Calc'd for $C_{23}H_{18}O_2$: C, 84.64; H, 5.58. Found: C, 84.60; H, 5.53.

Ozonolysis of 2,3-dibenzoyl-1-phenylpropene (Vb). A solution of 0.3 g. of Vb in 17 ml. of dry methanol was ozonized with 4% ozone at −80° until the solution became pale blue. The solution then was decomposed with potassium iodide, the released iodine was reduced with sodium thiosulfate solution, and the resulting mixture was extracted with ether. Evaporation of the ether extract and recrystallization of the residue from 80% ethyl alcohol solution gave 0.05 g. of colorless crystals melting at 79–81° which showed no depression in a mixture melting point with the colorless isomer (m.p. 81–84°) of 1,4-diphenyl-1,2,4-butanetrione enol (X).[9] The material was converted to the yellow isomer of X by melting and resolidifying; m.p. 66–67°, no depression in a mixture melting point with a known sample (m.p. 65–68°).[9] The quinoxaline derivative (m.p. 166–168°) likewise showed no depression in a mixture melting point with a known sample (m.p. 165–168°).[9]

2,3-Dibenzoyl-1-(4-morpholinyl)-1-phenylpropane (VIIIa). A solution of 3 g. of 1,2-dibenzoyl-3-phenylpropane (VIb) in 35 ml. of morpholine was allowed to stand for 24 hours, after which time it was poured into ice-water. The resulting mixture was extracted with ether, the ether extract was washed and evaporated, and the residue was crystallized from ethyl alcohol; 2.7 g. (72%), m.p. 152–155°, recrystallized (ethyl alcohol) m.p. 153–154°.

Anal. Calc'd for $C_{27}H_{27}NO_3$: C, 78.42; H, 6.58. Found: C, 78.70; H, 6.60.

The addition compound was recovered unchanged after heating with glacial acetic acid for 5 minutes.

3-(α-4-Morpholinylbenzyl)-2,5-diphenylfuran (XIb). (*a*). *From 2,3-Dibenzoyl-1-(4-morpholinyl)-1-phenylpropane* (VIIIa). To a solution of 1.4 g. of VIIIa in 25 ml. of acetic anhydride was added dropwise 0.6 g. of conc'd sulfuric acid

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(20) Lutz and Bailey, *J. Am. Chem. Soc.*, **68**, 2002 (1946).

(21) Lutz and Taylor, *J. Am. Chem. Soc.*, **55**, 1593 (1933).

(22) The senior author wishes to thank Professor R. Criegee for allowing him to carry out this extracurricular experiment during his stay as a Fulbright grantee at the Institut für Organische Chemie der Technischen Hochschule, Karlsruhe, Germany, 1953–1954. This method appears to be a useful one for determining acetone from ozonolysis.

over a period of 15 minutes. The resulting light green solution was allowed to stand for 30 minutes after which time it was poured into ice-water. Neutralization with solid sodium carbonate produced an oil which crystallized upon agitation. Filtration and recrystallization from ethyl alcohol gave 1.1 g. (83% yield) of material melting at 138–140°. Further recrystallizations (ethyl alcohol) raised the melting point to 139–140°.

Anal. Calc'd for $C_{27}H_{25}NO_2$: C, 82.04; H, 6.38. Found: C, 82.20; H, 6.53.

(*b*). *From 3-benzyl-2,5-diphenylfuran* (IIIb). A mixture of 1 g. of IIIb, 0.6 g. of N-bromosuccinimide, and 50 ml. of reagent grade carbon tetrachloride was refluxed for 20 minutes. The resulting succinimide was filtered off and the filtrate was evaporated under a vacuum. The residue (see next experiment for characterization) was dissolved in 40 ml. of dry ether where it was treated with 8 ml. of morpholine. After 10 minutes the resulting morpholine hydrobromide was filtered off. The filtrate was washed first with water and then with dilute hydrochloric acid, whereupon the amine hydrochloride precipitated. This was filtered off and decomposed by treatment with sodium carbonate solution. The resulting mixture was extracted with ether. Evaporation of the ether extract and recrystallization of the residual crystals from ethyl alcohol gave 0.2 g. of XIb melting at 139–140°; the substance showed no depression in a mixture melting point with XIb produced by cyclization of VIIIa.

3-(α-Bromobenzyl)-2,5-diphenylfuran (XIa). The product of the N-bromosuccinimide reaction with 3-benzyl-2,5-diphenylfuran (IIIb) (preceding experiment) was crystallized (after evaporation of the carbon tetrachloride solvent) from acetic acid giving a 75% yield of material melting at 92–94°. Recrystallization from ligroin did not change the melting point. The material resisted further purification attempts.[23]

Anal. Calc'd for $C_{23}H_{17}BrO$: C, 70.96; H, 4.40. Found: C, 71.43; H, 4.48.

3-(α-Hydroxybenzyl)-2,5-diphenylfuran (XIc). (*a*). *From 3-benzoyl-2,5-diphenylfuran* (Ib). A solution of 40 g. of Ib and 300 ml. of 0.33 *M* aluminum isopropoxide solution was slowly distilled until tests for acetone were negative. The reaction mixture was poured onto ice and excess 6*N* hydrochloric acid and the resulting mixture was extracted with ether. The ether extract was dried and evaporated and the residue was crystallized from methanol, yielding 39 g. (97%) of material melting at 104–106°.

(*b*). *From 3-(α-bromobenzyl)-2,5-diphenylfuran* (XIa). The hydroxy compound (XIc) prepared by the method of Kohler and Jones[10] melted at 103–105° and showed no depression in a mixture melting point with the material obtained by reduction of 3-benzoyl-2,5-diphenylfuran (Ib).

Addition of morpholine to 2,3-dibenzoyl-2-butene (VIc). A solution of 1 g. of 2,3-dibenzoyl-2-butene (VIc) and 25 ml. of morpholine was refluxed for 24 hours. The morpholine was evaporated by a stream of air, the residue was extracted with dilute hydrochloric acid, and the hydrochloric acid extract was neutralized with ammonium hydroxide. The resulting mixture was extracted with ether and the ether extract was washed and evaporated. Crystallization of the residue from dilute methanol gave 0.5 g. (38% yield) of material melting at 108–112° which showed no depression in a mixture melting point with known 2,3-dibenzoyl-1-(4-morpholinyl)butane (VIIIb) (m.p. 112–113°).[4]

When 1.1 g. of VIc was treated with a solution of 10 ml. of morpholine in 70 ml. of ether for 42 hours, it was recovered unchanged in 80% yield; m.p. 79–83°.

2,3-Dimethyl-2,3-di-(2,5-diphenyl-3-furyl)butane (XIIa). (*a*). *By stannous chloride reduction of* IV, Va, or VIa. To a solution of 2 g. of 3-isopropenyl-2,5-diphenylfuran (IV) in 10 ml. of glacial acetic acid was added a warm mixture of 10 g. of stannous chloride in 14 ml. of acetic acid and 10 ml. of hydrochloric acid. The resulting mixture was heated over a steam-bath for 10 minutes during which time a gummy material precipitated. Decantation of the mother liquor and trituration of the precipitate with hot ethyl alcohol gave 0.5 g. (25% yield) of crystals melting at 168–172°. Several recrystallizations from an ethyl alcohol-acetone solution raised the melting point to 172–173°.

Anal. Calc'd for $C_{38}H_{34}O_2$: C, 87.32; H, 6.56; M.W. 523. Found: C, 87.62, 87.17; H, 6.31, 6.19; M.W. (Rast) 483, 497.

By an identical procedure both *cis*-1,2-dibenzoyl-3-methyl-1-butene (VIa) and 1,2-dibenzoyl-3-methyl-2-butene (Va) were converted to XIIa in 50% yields; m.p. 172–173°, identifications by the mixture melting point method.

(*b*). *By hydriodic acid reduction of* IV. A mixture of 2 g. of IV and 40 ml. of hydriodic acid (*sp. gr.* 1.7) was refluxed for 10 minutes. Cooling produced 1 g. (50% yield) of crystals which melted at 172–173° after recrystallization from an ethyl alcohol-acetone mixture. The material was identified as XIIa by the mixture melting point method.

(*c*). *By treatment of* IV, VIa or Va *with acetic acid, hydrochloric acid, and copper.* A mixture of 2 g. of IV, 30 ml. of glacial acetic acid, and 10 ml. of hydrochloric acid was allowed to stand at room temperature for an hour after which it was extracted with benzene. The benzene extract was evaporated under reduced pressure leaving a viscous oil which resisted crystallization. The crude oil was dissolved in 30 ml. of benzene, a small spatulaful of copper bronze was added, and the resulting mixture was refluxed for 2 hours. The mixture was filtered, the filtrate was evaporated, and the residue was crystallized by trituration with hot ethyl alcohol. A 50% yield of XIIa was obtained, m.p. 172–173° after recrystallization from an ethyl alcohol-acetone solution. Similarly Va and VIa were converted to XIIa in 21% and 43% yields respectively; m.p. 172–173°. Identifications were by the mixture melting point method.

1,2-Diphenyl-1,2-di-(2,5-diphenyl-3-furyl)ethane (XIIb). (*a*). *From 3-(α-hydroxybenzyl)-2,5-diphenylfuran* (XIc). A hot solution of 10 g. of XIc and 20 ml. of glacial acetic acid was added to a refluxing solution of 50 g. of stannous chloride, 100 ml. of glacial acetic acid, and 50 ml. of conc'd hydrochloric acid. After 10 minutes of reflux the mixture was poured into cold water where an oily precipitate separated. Treatment of the oily precipitate with hot ligroin dissolved part of it and converted the remainder to colorless crystals (4.2 g., 44% yield) melting at 185–189°. Several recrystallizations from an isopropyl alcohol-acetone mixture raised the melting point to 203–204°.

Anal. Calc'd for $C_{46}H_{34}O_2$: C, 89.29; H, 5.54; M.W. 618. Found: C, 89.27; H, 5.54; M.W., 588, 603.

Evaporation of the ligroin filtrate gave an intractable yellow oil.

(*b*). *From 3-(α-bromobenzyl)-2,5-diphenylfuran* (XIa). A mixture of 1.8 g. of XIa, 5 g. of copper bronze, and 80 ml. of dry benzene was refluxed for 2 hours, after which time the unreacted copper bronze was filtered off. The filtrate was evaporated by an air jet and the residue was crystallized and several times fractionally recrystallized from an acetone-isopropyl alcohol (50–50) mixture. Two products were obtained. The first weighed 0.25 g., melted at 201–203° and showed no depression in a mixture melting point with XIIb prepared in the first experiment. The second weighed 0.15 g. and melted at 228–229°. Judging from its analysis and preparative method it is probably stereoisomeric with XIIb.

Anal. Calc'd for $C_{46}H_{34}O_2$: C, 89.29; H, 5.54. Found: C, 89.05; H, 5.57.

3,5-Diphenyl-4-(β-phenylethyl)pyrazole (XIII) *from 3-benzoyl-2,5-diphenylfuran* (Ib). In a typical experiment 1.5 g. of sodium was allowed to react with 50 ml. of ethylene glycol, after which time 3 g. of 3-benzoyl-2,5-diphenylfuran (Ib) and 10 ml. of 95% hydrazine hydrate was added. The

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[23] Kohler and Jones[10] report a melting point of 110°. The acetoxy derivative, prepared by the method of K. and J., melted at 80–82° (K. and J. report 84°) and the hydroxy derivative (see next experiment) melted at 103–105° (K. and J. report 105°).

mixture was allowed to reflux for 5 hours, after which time the condenser was removed and the water was allowed to boil out. When the boiling temperature had reached 200° the condenser was replaced and refluxing was continued for about 45 hours. The reaction mixture then was poured in about 150 ml. of 5% hydrochloric acid where a precipitate formed. The precipitate was dissolved in ether and the ether extract was washed, dried, and evaporated. The residue was dissolved in ethyl alcohol and cooled, yielding 1.4 g. of material melting at 77–110°; further recrystallizations showed this material to consist largely of the benzylfuran (IIIb), m.p. 78–80°, no depression in a mixture melting point with an authentic sample. The filtrate from IIIb was evaporated and the residue was recrystallized; yield, 0.8 g. of m.p. 140–168°. Further recrystallizations from ethyl alcohol gave 0.4 g. of material melting at 177–178°.

Anal. Calc'd for $C_{23}H_{20}N_2$: C, 85.15; H, 6.21; N, 8.64. Found: C, 84.90, 84.97; H, 6.32, 6.10; N, 8.72, 8.75.

The material was recovered unchanged after treatment with excess potassium permanganate in acetone solution.

Treatment of XIII with ethereal hydrogen chloride solution gave a *hydrochloride* melting at 205–210°. Attempts to purify the material by recrystallization led to its decomposition.

Anal. Calc'd for $C_{23}H_{21}ClN_2$: Cl, 9.83. Found: Cl, 9.86, 9.89.

The *sulfonamide* was made by adding 0.1 g. of XIII to a mixture of 2.5 ml. of pyridine and 0.6 ml. of benzenesulfonyl chloride, refluxing the resulting mixture for 15 minutes, and then pouring it into water. Crystallization was produced by means of cooling and scratching on the sides of the vessel; yield, 0.13 g. (91%), m.p. 140–145°. Several recrystallizations from ethyl alcohol gave material melting at 145–146°. The material was not soluble in dilute sodium hydroxide.

Anal. Calc'd for $C_{29}H_{24}N_2O_2S$: C, 74.97; H, 5.21. Found: C, 75.19; H, 4.87.

1,4-Diphenyl-2-benzoyl-1-butanone (XVI). The general alkylation procedure of Adkins[24] was applied to this preparation. A mixture of 0.5 g. of granulated sodium,[25] 125 ml. of absolute ether, and 5.3 g. of dibenzoylmethane[16] was refluxed for 36 hours. The ether then was removed by distillation and to the residual sodium enolate was added 100 ml. of dry acetone[26] followed by a solution of 5.4 g. of β-phenylethyl iodide[27] in 25 ml. of dry acetone. The mixture was stirred and gently refluxed for 5 days, during which time an additional 2 g. of β-phenylethyl iodide was added. The material was poured into water and the resulting mixture was extracted with ether. Some unreacted sodium enolate remained insoluble; more was produced when the ether extract was washed with water. The ether layer was finally washed with dilute hydrochloric acid and with water, dried, and evaporated. Several recrystallizations of the residue from methanol gave 0.9 g. of material melting at 91–92°.

Anal. Calc'd for $C_{23}H_{20}O_2$: C, 84.12; H, 6.14. Found: C, 84.07; H, 5.92.

The filtrates from the purification of XVI plus the sodium enolate filtered off during the working-up process yielded 1.5 g. of unreacted dibenzoylmethane, purified through the chelate formed with copper acetate[16]; m.p. 76–78°.

3,5-Diphenyl-4-(β-phenylethyl)pyrazole (XIII) *from 1,4-diphenyl-2-benzoyl-1-butanone* (XVI). The general procedure of Wislicenus[28] was followed. To a solution of about 0.2 g. of XVI in 10 ml. of absolute ethanol was added 1.2 ml. of 50% hydrazine hydrate. The mixture was allowed to stand at room temperature for 20 hours during which time it changed in color from yellow to colorless and a colorless precipitate formed. The material upon recrystallization from ethyl alcohol weighed 0.1 g. and melted at 177–178°. It showed no depression in a mixture melting point with XIII produced by reaction of Ib with hydrazine hydrate.

4-Benzyl-3,6-diphenylpyridazine (XV). The general method of Campbell and Khanna[29] was employed. To a solution of 0.1 g. of *cis*-1,2-dibenzoyl-3-phenylpropene (VIb) in 10 ml. of ethyl alcohol was added a solution of 4 ml. of 85% hydrazine hydrate and 4 ml. of ethyl alcohol. The resulting solution was allowed to stand for 48 hours after which it was cooled in the refrigerator. Crystallization occurred; 0.06 g. (52% yield), m.p. 112–115°. Several recrystallizations from 90% ethyl alcohol raised the melting point to 115–116°.

Anal. Calc'd for $C_{23}H_{18}N_2$: C, 85.68; H, 5.63; N, 8.69. Found: C, 85.49; H, 5.51; N, 8.73.

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[24] Sprague and Adkins, *J. Am. Chem. Soc.*, **56**, 2668 (1934).

[25] Vogel, "*Textbook of Practical Organic Chemistry,*" Longmans, Green and Co., London, 1951, p. 189.

[26] Vogel, *ibid.*, p. 170.

[27] Prepared by treating an acetone solution of Eastman's phenylethyl bromide with sodium iodide. The material distilled at 110–111°/10 mm.

[28] Wislicenus, *Ann.*, **308**, 254 (1899).

[29] Campbell and Khanna, *J. Chem. Soc.*, S33 (1949).