[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

A Synthesis of 3-Benzoyl-2-phenylcyclopentanone

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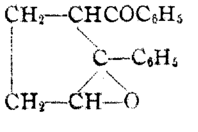
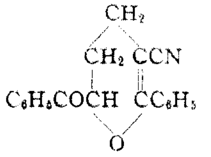
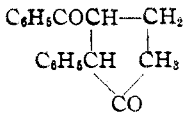
3-Benzoyl-2-phenylcyclopentanone (III) has been obtained by rearrangement of 1-phenyl-5-benzoylcyclopentene oxide (I),[1] and by the action of hot phosphoric acid on 2-phenyl-3-cyano-6-benzoyl-5,6-dihydro-1,4-pyran (II).[2]



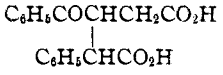
I



II



III



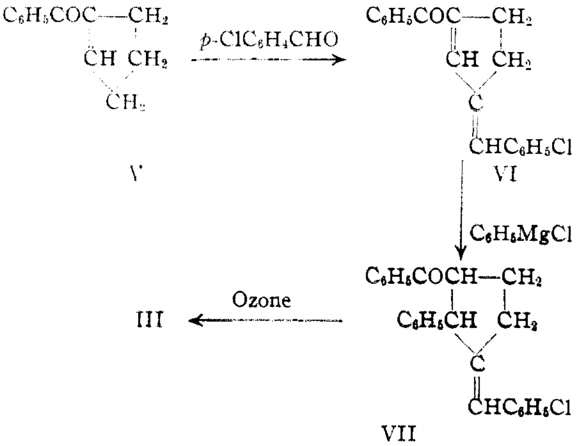
$$\begin{array}{l} C_6H_5COCHCH_2CO_2H \\ \qquad | \\ C_6H_5CHCO_2H \end{array}$$

IV

The structure of the cyclopentanone (III) could hardly be deduced from the manner in which it originates, for the transformations which lead to its formation might be expected to yield a variety of products. It was necessary, therefore, to establish the structure of III in some other way. The first attempt consisted in oxidizing the cyclopentanone to the open-chain dibasic acid, β-benzoyl-α-phenylglutaric acid (IV). This compound was isolated in the two forms required by theory,[3] but since these had not been synthesized hitherto the proof of structure was inconclusive.

We have now established the structure of the cyclopentanone (III) by a synthesis based on the principle of vinylogy.[4] From this principle it was to be expected that 1-benzoylcyclopentene (V) like 1-benzoylcyclohexene and similar α,β-unsaturated ketones would have active hydrogen atoms in the γ-position,[5] and may condense with aldehydes.

This expectation was realized. 1-Benzoylcyclopentene reacted with *p*-chlorobenzaldehyde to give the normal *p*-chlorobenzal derivative (VI). The next step in the synthesis was the addition of phenylmagnesium bromide to the benzal derivative. It was foreseen that 1,2-, 1,4- and 1,6-addition are possible, but because of the phenyl groups in positions 1 and 6 the addition was expected to be primarily of the 1,4-type. This proved to be the case. 1-Benzoyl-2-phenyl-3-(*p*-chlorobenzal)-cyclopentane (VII) was obtained in two forms which were evidently stereoisomers since they yielded the same ozonization products. These were *p*-chlorobenzaldehyde and the desired cyclopentanone (III). The latter proved to be identical with the compound derived from the oxide (I) and the cyanopyran (II).



Experimental

1-Benzoylcyclopentene (V).—This material was prepared by the Friedel–Crafts reaction. Forty-four grams of aluminum chloride was added slowly to a mixture of 20 g. of cyclopentene, 43 g. of benzoyl chloride and 180 g. of carbon disulfide, which was kept at −5° during the addition. Decomposition with ice gave a crude addition product which, after three hours of heating with 28 g. of diethylaniline at 180°, yielded 16 g. (32% of the theoretical) of 1-benzoylcyclopentene, boiling at 119–122° (3 mm.); $n^{20}\text{D}$ 1.5668.

Anal. Calcd. for $C_{12}H_{12}O$: C, 83.72; H, 7.00. Found: C, 83.41; H, 7.15.

1-Benzoyl-3-(*p*-chlorobenzal)-cyclopentene (VI).—A sodium methylate solution prepared from 2.5 g. of sodium and 25 cc. of methanol was added to a methanol solution of 10 g. of benzoylcyclopentene and 14 g. of *p*-chlorobenzaldehyde. After standing at room temperature for twelve hours, the solution was acidified with glacial acetic acid and cooled; the product separated as crystals. These were recrystallized from methanol; the yield of the condensation product, melting at 118°, was 8.2 g. (48% of the theoretical).

Anal. Calcd. for $C_{19}H_{15}OCl$: C, 77.43; H, 5.09; Cl, 12.05. Found: C, 77.26; H, 4.92; Cl, 12.30.

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(1) Fuson and Farlow, THIS JOURNAL, **56**, 1593 (1934).

(2) Fuson, Kuykendall and Wilhelm, *ibid.*, **53**, 4187 (1931).

(3) Babcock and Fuson, *ibid.*, **58**, 2325 (1936).

(4) Fuson, *Chem. Rev.*, **16**, 1 (1935).

(5) Christ and Fuson, THIS JOURNAL, **59**, 893 (1937).

1-Benzoyl-2-phenyl-3-(*p*-chlorobenzal)-cyclopentane (VII).—A Grignard reagent containing 0.0046 mole of phenylmagnesium bromide was added to a solution of 1 g. of 1-benzoyl-3-(*p*-chlorobenzal)-cyclopentene in anhydrous ether. The mixture was refluxed for one hour, then hydrolyzed by shaking with 5% hydrochloric acid. The product was recrystallized from ethanol, yielding 1 g. (79% of the theoretical) of the addition compound, melting at 171° (corr.). Larger runs were made with equivalent yields.

Anal. Calcd. for $C_{25}H_{21}OCl$: C, 80.56; H, 5.64; Cl, 9.52. Found: C, 80.76; H, 5.74; Cl, 9.53.

A solution of 0.7 g. of the addition product in 400 cc. of ethanol was refluxed with excess hydroxylamine. Concentration of the solution gave a small quantity of an oxime, melting at 115–120°.

Anal. Calcd. for $C_{25}H_{22}ONCl$: N, 3.62. Found: N, 3.69.

A solution of 1 g. of the addition compound (m. p. 171°) in 20 cc. of methanol was refluxed with 0.25 cc. of 10% sodium hydroxide solution for twenty minutes. An isomer melting at 178° (corr.) crystallized when the solution was cooled.

Anal. Calcd. for $C_{25}H_{21}OCl$: C, 80.56, H, 5.64. Found: C, 80.55; H, 5.91.

This isomerization seemed to be hastened by the presence of a small quantity of *p*-chlorobenzaldehyde, for in the presence of this aldehyde the compound underwent rearrangement in ten minutes. A mixture of these two isomers melted at 158–161°.

Ozonization of 1-Benzoyl-2-phenyl-3-(*p*-chlorobenzal)-cyclopentane.—One-half gram of the addition product (either form) was suspended and partly dissolved in 200 cc. of glacial acetic acid. This suspension was treated with ozone for four hours at 10°; during this time the material dissolved completely. The ozonide was decomposed with a mixture of 100 cc. of water, 3 g. of zinc dust and 1 cc. of 5% silver nitrate solution. This mixture was then filtered to remove zinc, steam distilled to remove the aldehyde and most of the acetic acid, and neutralized with sodium bicarbonate. Concentration of the ether extract of neutral material yielded crystals of 3-benzoyl-2-phenylcyclopentanone (III) which, after recrystallization from methanol and from ethyl acetate–petroleum ether, melted at 158°. A mixture of this material with a sample (m. p. 159°) prepared by Babcock and Fuson[3] also melted at 158°.

When the lower-melting isomer of 1-benzoyl-2-phenyl-3-(*p*-chlorobenzal)-cyclopentane was used in the ozonization, the yield of 3-benzoyl-2-phenylcyclopentanone was 0.08 g. (22% of the theoretical amount); when the higher-melting isomer was used, the yield was 0.2 g. (56% of the theoretical amount).

Oxidation of the crude aldehyde with hydrogen peroxide gave 0.1 g. of *p*-chlorobenzoic acid, melting at 239–240°. This acid was also precipitated by acidification of the sodium bicarbonate washings.

3-Benzoyl-2-phenylcyclopentanone formed an *oxime* which after recrystallization from ethyl alcohol melted at 222–224°.

Anal. Calcd. for $C_{18}H_{17}O_2N$: C, 77.4; H, 6.1; N, 5.02. Found: C, 77.1; H, 6.2; N, 5.08.

3-Benzoyl-2-phenyl-5-(*p*-chlorobenzal)-cyclopentanone.—A solution of 0.2 g. of 3-benzoyl-2-phenylcyclopentanone and 0.2 g. of *p*-chlorobenzaldehyde in 7 cc. of methanol containing one drop of 10% sodium hydroxide solution was refluxed for eight minutes. When the solution was cooled, crystals of 3-benzoyl-2-phenyl-5-(*p*-chlorobenzal)-cyclopentanone separated. These melted at 207° and gave no depression in melting point when mixed with the compound prepared by the method of Babcock and Fuson.[3]

Summary

1-Benzoylcyclopentene has an active methylene group, in accordance with the prediction based on the principle of vinylogy, and condenses with *p*-chlorobenzaldehyde.

This condensation product gives 1,4-addition of phenylmagnesium bromide as shown by ozonization of the addition compound to give *p*-chlorobenzaldehyde and 3-benzoyl-2-phenylcyclopentanone.

This synthesis of the cyclopentanone constitutes a proof of structure.

URBANA, ILLINOIS RECEIVED MAY 2, 1938