dry ether was added to the reaction mixture and the addition was continued to the end. The mixture resolidified and was allowed to stand overnight under nitrogen, refluxed for 1 hour, cooled, decomposed cautiously with ice-water, and worked up. After removal of solvent (bath, 28°, pressure 25 mm.), the residue was distilled through a helix packed column. After a forerun of 0.9 g., 2.7 g. (10.4% based on pyrazine) of 2-butylpyrazine, b.p. 84° (19 mm.), $n^{26}D$ 1.4963 was obtained.

Anal. Calcd. for $C_8H_{12}N_2$: N, 20.57. Found: N, 19.07.

The **picrate** crystallized with extreme difficulty on long standing in the cold, m.p. 39–42°. Attempted recrystallization from ethanol produced great loss.

The **chloroplatinate** was a pale yellow microcrystalline powder.

Anal. Calcd. for $C_{16}H_{22}N_4PtCl_6$: Pt, 28.65. Found: Pt, 29.00.

2-Chloropyrazine.—An improved preparation of this compound from 2-hydroxypyrazine[10] was mentioned by Hort and Spoerri.[11] Details of this method are now given:

To 9.6 g. (0.1 mole) of 2-hydroxypyrazine in a 250-ml. 3-necked flask fitted with a stirrer and a reflux condenser bearing a drying tube, 30 ml. (0.3 mole) of freshly distilled $POCl_3$ was added. The mixture was warmed for a few minutes, refluxed for 40 minutes and cooled in an ice-water-bath. The cooled mixture was poured onto 300 g. chopped ice and stirred until all the excess $POCl_3$ was decomposed. The black solution was extracted with ether, the combined extracts dried over calcium chloride and the solvent evaporated. The residue was distilled through a jacketed modified Widmer column, collecting 8.1 g. (71%) of product, b.p. 62.5° (29 mm.), $n^{28}D$ 1.5340.

2,5-Dimethyl-6-chloropyrazine.—Prepared from 2,5-dimethylpyrazine-1-oxide[12] as described above in 92% yield, b.p. 66–69° (8.6 mm.), $n^{25}D$ 1.5250. The *picrate* melted at 100–101°.

Acknowledgment.—We are indebted to Dr. B. S. Gordon, Chief, Laboratory Service, Veterans Administration Hospital, Bronx 63, New York, for his sustained interest and assistance during the course of this investigation.

(10) J. Weijlard, M. Tishler and A. E. Erickson, THIS JOURNAL, **67**, 805 (1945).

(11) E. Hort and P. E. Spoerri, *ibid.*, **70**, 1657 (1948).

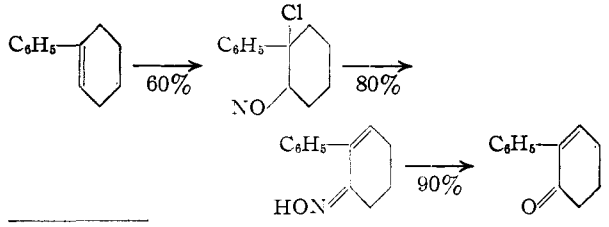
(12) G. T. Newbold and F. S. Spring, *J. Chem. Soc.*, 1183 (1947).

POLYTECHNIC INSTITUTE OF BROOKLYN
BROOKLYN, 2, N. Y. RECEIVED DECEMBER 26, 1950

Use of 2-Phenylcyclohexenone in Experiments on the Synthesis of Morphine

BY C. F. KOELSCH

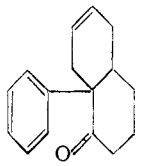
2-Phenyl-Δ^2-cyclohexenone and its reaction with ethyl malonate have been described recently, and it has been indicated that a promising route for synthesis of the morphine structure is thereby opened.[1,2] Certain aspects of that route were investigated in this Laboratory in 1944 with disappointing results, and it appears desirable to record these negative results now to prevent further duplication.



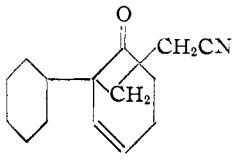
(1) W. E. Bachmann and L. B. Wick, THIS JOURNAL, **72**, 3388 (1950).

(2) W. E. Bachmann and E. J. Fornefeld, *ibid.*, **72**, 5529 (1950).

2-Phenylcyclohexenone was prepared by the reactions diagrammed, different from those used by Bachmann and Wick. The ketone could not be induced to react with butadiene, and a pure product was not obtained with acrylonitrile. Oxidation of the product expected from butadiene (I) to a diacetic acid, or Reformatzky reaction with the product expected from acrylonitrile (II)[3] would have given substances of considerable interest in syntheses of the morphine skeleton

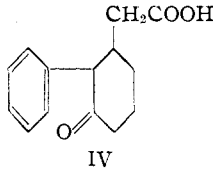


I

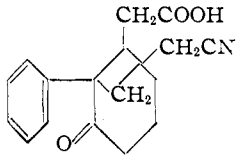


II

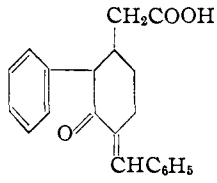
3-Oxo-2-phenylcyclohexaneacetic acid (IV) was obtained using the Michael reaction, a preparation differing only in detail from that used by Bachmann and Fornefeld. A pure product could not be obtained from the keto acid or its ester when reactions with acrylonitrile were attempted (expected formation of V), although a fair yield of benzal derivative (VI) was obtained from the keto acid and benzaldehyde in alkaline medium. This benzal derivative and its ester gave only resinous products when condensations with acrylonitrile were attempted.



IV

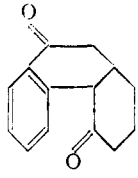


V



VI

The keto acid (IV) reacted with sulfuric acid to form 1,2,11,12-tetrahydrophenanthrene-4(3),9(10)-dione (VII). Possible uses of this substance were not investigated.



VII

Experimental

2-Phenyl-2-cyclohexenone.—A mixture of 48 g. of phenylcyclohexene, 100 ml. of acetic acid and 35 ml. of concentrated hydrochloric acid was cooled to 7° and treated dropwise with 35 g. of butyl nitrite in 30 ml. of acetic acid. The mixture was then stirred for 15 minutes while it was kept in a freezing mixture, and finally it was treated with 100 ml. of methanol. The precipitated product was removed, washed with two 25-ml. portions of methanol, then with water, and dried, giving 39 g. (57%) of nearly pure **phenylcyclohexene**

(3) H. A. Bruson and T. W. Riener, *ibid.*, **65**, 18 (1943).

nitrosochloride, colorless prisms from chloroform–methanol, m.p. 133–134° dec.

Anal. Calcd. for $C_{12}H_{14}ClNO$: Cl, 15.9. Found: Cl, 15.9.

When the acetic acid–methanol mother liquor from the above preparation was poured into one liter of water, there was deposited an oil which soon solidified. This material was ground up with ligroin and then with dilute sodium carbonate and crystallized from alcohol, giving 9 g. (16%) of phenylcyclohexenone oxime. Larger scale (2–3×) preparations gave less nitrosochloride (45–40%) and more oxime (28–35%).

To a stirred boiling suspension of 175 g. of the nitrosochloride in 600 ml. of 95% ethanol was added 125 g. of 85% potassium hydroxide in 150 ml. of water. A clear solution resulted, except for precipitated potassium chloride, after 2.25 hours, but boiling was continued for three hours. The mixture was then neutralized with acetic acid, cooled, and filtered. The precipitate was washed with water, giving 113 g. (77%) of nearly pure **2-phenyl-2-cyclohexenone oxime**, and 4.6 g. more was obtained from the filtrates. Crystallization from alcohol gave coarse colorless needles, m.p. 157–158°.

Anal. Calcd. for $C_{12}H_{13}NO$: C, 77.0; H, 6.9. Found: C, 77.0; H, 7.1.

Reduction of 1 g. of the oxime with 2 g. of sodium and 25 ml. of butyl alcohol gave 0.9 g. of **2-phenylcyclohexylamine** a colorless oil, b.p. 137–139° at 14 mm. **The hydrochloride** had m.p. 250–254° (Found: C, 67.8; H, 8.6; N, 6.9, $C_{12}H_{18}ClN$ requires C, 68.2; H, 8.5; N, 6.6). The **benzoyl derivative** formed fine needles from alcohol, m.p. 183–184° (Found: C, 82.5; H, 8.0. $C_{19}H_{21}NO$ requires C, 82.1; H, 7.6).

A solution of 180 g. of phenylcyclohexenone oxime in 360 ml. of concentrated hydrochloric acid and 180 ml. of water was warmed on a water-bath for 30 minutes. The mixture was then cooled and filtered, and the solid was washed with water and dried. The filtrate was diluted with 3 l. of water, which caused 22 g. of unchanged oxime to precipitate. There was obtained 140 g. of crude phenylcyclohexenone, a yield of 84%, or 96% on the basis of oxime actually consumed. Distillation gave 127 g., b.p. 169–171° at 14 mm., of pure product, colorless needles from alcohol, m.p. 94–95° (reported[1] 95–95.5°).

Anal. Calcd. for $C_{12}H_{12}O$: C, 83.7; H, 7.0. Found: C, 83.3; H, 7.2.

As a derivative characteristic of an α,β-unsaturated ketone,[4] **2-phenyl-3-*p*-toluenesulfonylcyclohexanone** was prepared by boiling 0.7 g. of phenylcyclohexenone with 0.7 g. of *p*-toluenesulfinic acid in 5 ml. of alcohol for two hours; it formed long white needles from alcohol, m.p. 158–159° with slow gas evolution.

Anal. Calcd. for $C_{19}H_{20}O_3S$: C, 69.5; H, 6.2. Found: C, 69.5; H, 6.5.

3-Oxo-2-phenylcyclohexaneacetic Acid (IV).—A mixture of 126 g. of phenylcyclohexenone, 100 g. of methyl malonate (ethyl malonate did not react under similar conditions), and 100 ml. of methanol was boiled, then cooled to 40° and treated with a solution of 1 g. of sodium in 15 ml. of methanol. The mixture became homogeneous after nine minutes, and its temperature rose (39 to 47.7°) during 13 minutes, then began to fall slowly. After ten hours, 700 ml. of water containing 70 g. of sodium hydroxide was added, and the mixture was boiled under reflux for 30 minutes. It was then cooled, and unchanged phenylcyclohexenone (60–65 g.) was removed by filtration. The filtrate was concentrated somewhat, 400 ml. of dilute methanol being distilled, and then acidified with dilute sulfuric acid. The sirupy dibasic acid (102 g.) was separated using 150-, 100- and 50-ml. portions of ether, and heated at 220° for a few minutes. The residue (80 g., 96%) was crystallized from benzene and dried for six hours in air. There was obtained 82 g. of white needles that sintered at 95° and melted at 104–105° with effervescence; this was a complex of the acid with benzene (Found: C_6H_6, 24.4. $C_{14}H_{16}O_3 + C_6H_6$ requires C_6H_6, 25.1). From dilute acetic acid, solvent-free needles were obtained, m.p. 124–125° (reported[3] 124–125°).

Anal. Calcd. for $C_{14}H_{16}O_3$: C, 72.4; H, 6.9; neut. equiv., 232. Found: C, 72.0; H, 6.9; neut. equiv., 232.

(4) E. P. Kohler and M. Reimer, *Am. Chem. J.*, **31**, 163 (1904).

A mixture of 10 g. of the keto-acid IV, 25 ml. of ethanol and 5 ml. of sulfuric acid was boiled for one hour, then poured into dilute soda solution. There was obtained 2.5 g. of unchanged acid, and 8.1 g. of **ethyl 3-oxo-2-phenylcyclohexaneacetate**, plates from alcohol, m.p. 73–75°; b.p. 205–210° at 13 mm.

Anal. Calcd. for $C_{16}H_{20}O_3$: C, 73.9; H, 7.7. Found: C, 74.3; H, 7.8.

4-Benzal-3-oxo-2-phenylcyclohexaneacetic Acid (VI).—A solution of 15.5 g. of solvated oxophenylcyclohexaneacetic acid and 2.5 g. of sodium hydroxide in 50 ml. of water was boiled to remove benzene, then cooled to 45°, treated with 5.5 g. of benzaldehyde, and shaken for 30 minutes. The mixture was then boiled for 15 minutes and finally acidified, yielding an oil that became solid when it was rubbed with ether. Crystallization from 75% acetic acid gave 9.5 g. of small pale yellow prisms, m.p. 151–153°.

Anal. Calcd. for $C_{21}H_{20}O_3$: C, 78.8; H, 6.3. Found: C, 79.0; H, 6.3.

When 8.5 g. of VI was boiled for three hours with 40 ml. of ethanol containing 2 ml. of sulfuric acid, there was obtained 8.9 g. of the ethyl ester of VI, pale yellow prisms from alcohol and then from benzene–ligroin, m.p. 92–94°.

Anal. Calcd. for $C_{23}H_{24}O_3$: C, 79.3; H, 6.9. Found: C, 79.3; H, 6.9.

1,2,11,12-Tetrahydrophenanthrene-4(3),9(10)-dione (VII).—A solution of 1 g. of solvated IV in 3 ml. of 96% sulfuric acid was heated in a boiling water-bath for 30 minutes, then poured onto ice and ether. The product was washed with dilute soda solution and distilled, giving 0.35–0.43 g. of pale yellow oil, b.p. 215–220° at 14 mm., that crystallized when it was rubbed with ether. Recrystallization of 0.6 g. from benzene–ligroin and then from dilute acetic acid gave 0.25 g. of faintly colored prisms, m.p. 94–95°.

Anal. Calcd. for $C_{14}H_{14}O_2$: C, 78.5; H, 6.6. Found: C, 78.5; H, 6.6.

The author thanks Mr. L. A. Errede for most of the analyses reported in this note.

SCHOOL OF CHEMISTRY
UNIVERSITY OF MINNESOTA
MINNEAPOLIS 14, MINN. RECEIVED FEBRUARY 5, 1951

The Use of C^{14}-Labeled Formaldehyde in the Mannich Reaction[1,2,3]

BY ALBERT V. LOGAN, JOHN L. HUSTON AND DONALD L. DORWARD

In the course of a study of the mechanism of the Mannich reaction C^{14} labeled paraformaldehyde was incorporated in a Mannich base to determine the possibility of the transposition of the carbon atoms. The reaction investigated involved the condensation of acetophenone, radioactive paraformaldehyde[4] and dimethylamine hydrochloride. The Mannich base, βC^{14}-β-dimethylaminopropiophenone, was pyrolyzed by steam and the resulting vinyl phenyl ketone subjected to ozonolysis. The ozonide was hydrolyzed and the products, phenyl glyoxal and formaldehyde, were separated. The radioactivity of each product was determined.

If no transposition of carbon atoms occurs the formaldehyde should contain all of the C^{14}. We found that the phenyl glyoxal monohydrate counted as the pure compound showed an initial activity

(1) Published with the approval of the Monograph Publications Committee, Oregon State College, as Research Paper No. 174, School of Science, Department of Chemistry.

(2) The work reported here was done with the aid of a grant from the Research Corporation, New York, N. Y.

(3) This note is based upon a thesis submitted by Donald L. Dorward in partial fulfillment of the requirements for the degree of Master of Science at Oregon State College, June, 1949.

(4) C. E. Spencer, thesis submitted to Oregon State College, 1949.