chloroform); ultraviolet; $\lambda_{max}^{MeOH}$ 230 m$\mu$; $\epsilon$, 17,820; log $\epsilon$ 4.25: $\lambda_{max}^{MeOH}$ 237 m$\mu$; $\epsilon$, 19,290; log $\epsilon$, 4.29: $\lambda_{max}^{MeOH}$ 245.5 m$\mu$; $\epsilon$, 12,250; log $\epsilon$, 4.09.

*Anal.* Calcd. for $C_{27}H_{44}$: C, 87.98; H, 12.02. Found: C, 87.74; H, 12.14.

Elution with benzene-ether (4:1) (Fractions 20–23) gave a small amount of a compound which had all the properties of cholesteryl acetate indicating that the double bond in the 4–5 position is playing a role in the solvolysis.

*Hydrolysis of epi-ψ-cholesteryl tosylate.* To a solution of 500 mg. of epi-ψ-cholesteryl tosylate (XII) in 35 ml. of purified acetone and 9 ml. of water was added 1.4 g. of anhydrous potassium acetate. This mixture was held at the reflux temperature for 9 hr., cooled, and poured into water. This aqueous solution was extracted 3 times with ether and the combined ethereal extracts were washed 3 times with water and dried over magnesium sulfate. Concentration *in vacuo* gave a clear oil, (340 mg.) which was chromatographed on 12 g. of neutral alumina. Elution with pentane (Fractions 3–13) gave 248 mg. (61.5%) of crystalline product which was recrystallized from acetone, m.p. 87.5–90.2. Examination of the infrared and ultraviolet spectra showed that this product was identical to cholesta-4,6-diene (IV). Elution with benzene-ether (4:1) (Fractions 25–27) gave a white crystalline product, 23 mg. (5.4%), m.p. 85.2–87.1° $[\alpha]_D^{23}$ +58° (c, 0.981 in chloroform).

*Anal.* Calcd. for $C_{27}H_{46}O$: C, 83.87; H, 11.99. Found: C, 83.96; H, 11.94. From an examination of the physical data and the infrared spectrum, this compound was assigned the structure of cholest-4-en-6$\beta$-ol (XIII). Further elution with benzene-ether (4:1) (Fractions 28–32) gave 40 mg. (9.5%) of a white crystalline product, m.p. 129.5–132°; $[\alpha]_D^{23}$ −55.2° (c, 1.19 in chloroform).

*Anal.* Calcd. for $C_{27}H_{46}O$: C, 83.87; H, 11.99. Found: C 83.59; H, 11.72. The physical data and the infrared spectrum of this compound suggest that it is cholest-5-en-4$\beta$-ol (XIV).

*Acetolysis of epi-ψ-cholesteryl tosylate with potassium acetate–acetic anhydride mixture.* To a solution of 1.43 g. of anhydrous potassium acetate and 24 ml. of acetic anhydride at 50° was added 500 mg. of epi-ψ-cholesteryl tosylate (XII) in several portions. This mixture was stirred at 75° for 38 hr. (yellow coloration). After concentration to dryness the residue was taken up in ether-water mixture and the layers separated. The aqueous phase was washed 3 times with ether and the combined ethereal extract was washed once with a 10% sodium bicarbonate solution and twice with water. The ethereal solution was dried over anhydrous magnesium sulfate and taken to dryness *in vacuo* to give 283 mg. (70.2%) of a dark yellow solid which was chromatographed on 14 g. of neutral alumina. Elution with pentane (Fractions 2–11) gave 250 mg. (62%) of a white crystalline solid which was recrystallized from acetone, m.p. 85.5–91.0°. Examination of the infrared and ultraviolet spectra showed that this material was identical to cholesta-4,6-diene(IV).

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PRINCETON, N. J.

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

# Reaction of the Enol Form of 1,2-Cyclohexanedione with the Phenyl Grignard Reagent[1]

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*Received March 2, 1959*

Spectroscopic evidence indicates that 4-, 5-, and 6-membered 1,2-cycloalkanediones exist exclusively in the enol form. 2-Hydroxy-2-cyclohexen-1-one reacts with the phenyl Grignard reagent to form the conjugate addition product, 2-hydroxy-3-phenylcyclohexanone. Treatment of this compound with the phenyl Grignard reagent results in the formation of 1,3-diphenyl-1,2-cyclohexanediol. The structures of these adducts are established by oxidative degradation.

The nature of the keto-enol equilibrium in 1,2-diketones has been the subject of considerable discussion, but with the advent of spectroscopic methods, investigations have established with certainty which of the tautomers predominates. Selected absorption maxima for various ketones are presented in Table I. The conjugated ketone chromophore (as exemplified by isophorone) absorbs near 235 m$\mu$ with a relatively high intensity. This same feature is found (with a bathochromic shift) in the ultraviolet spectra of all enolic 1,2-diketones. Characteristic infrared absorptions also identify these conjugated systems; the C=C stretching vibration occurs near 1640 cm.$^{-1}$ and the conjugated C=O absorption near 1670 cm.$^{-1}$

On the other hand, the 1,2-diketones which cannot enolize, such as camphorquinone[17] and 3,3,6,6-tetramethyl-1,2-cyclohexanedione, exhibit completely different spectra. The ultraviolet and visible absorption of the diketone chromophore is characterized by a relatively weak, broad band in the 380–450 m$\mu$ region. The infrared carbonyl absorption frequency is near the normal position. In a series of substituted 1,2-cycloalkanediones in which the ring contained from nine to fourteen carbon atoms,[18] the carbonyl absorptions were in the range 1704–1708 cm.$^{-1}$. Thus, from an examination of the

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[1] Presented in part at the 134th Meeting of the American Chemical Society, Chicago, Ill., September 1958; Abstracts, p. 56-P. This work was supported by a research grant from the University of Minnesota.

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[3] R. S. Rasmussen, D. D. Tunnicliff, and R. R. Brattain, *J. Am. Chem. Soc.*, **71**, 1068 (1949).

TABLE I

SPECTRAL PROPERTIES OF VARIOUS KETONES

| | Ultraviolet Absorption | | Infrared Absorption | | | |
|---|---|---|---|---|---|---|
| Compound[a] | $\lambda_{max}$, m$\mu$ | Log $\epsilon$ | Cm.$^{-1}$ | Solvent | % Enol | Refs. |
| Isophorone (3,5,5-trimethyl-2-cyclohexen-1-one | 235<br>310 | 4.2<br>1.7 | 1672 (C=O)<br>1639 (C=C) | none | . . . | 3 |
| Dimedone (5,5-dimethyl-1,3-cyclohexanedione) | 258 | 4.08 | 1702<br>1605<br>2640 | $CHCl_3$ | 95[b]<br>(di-enol) | 3, 4<br>5 |
| Diisophenol (3-methyl-6-isopropyl-1,2-cyclohexanedione) | 275 | 3.95 | 1675 (C=O)<br>1646 (C=C)<br>3460 (O—H) | $C_6H_6$ | 100 | 6, 7 |
| 3-Phenyl-1,2-cyclobutanedione | . . . | . . . | 1653 (C=C)<br>3480 (O—H) | ? | 100 | 8 |
| 1,2-Cyclopentanedione | 246 | 4.003 | . . . | | 100[b] | 9, 10 |
| 1,2-Cyclohexanedione | 263 | 3.919[c] | 1676[d] (C=O)<br>1661 (C=C)<br>3440 (O—H) | $CS_2$ | 100[b] | 9, 10<br>11 |
| 3-Phenyl-1,2-cyclohexanedione | 309 | 4.273 | 1668 (C=O)<br>1631 (C=C)<br>3380 (O—H) | $CS_2$ | 100 | 11 |
| 1,2-Cycloheptanedione | 215<br>280[e] | 1.948<br>1.3 | . . . | | 3[b] | 9 |
| Camphorquinone | 457<br>466 | 1.45<br>1.48 | 1775<br>1759 | $CS_2$ | 0 | 11, 12<br>13 |
| 3,3-6,6-Tetramethyl-1,2-cyclohexanedione | 297.5<br>380 | 1.46<br>1.04 | 1709 | none | 0 | 12, 13 |
| Biacetyl | 272<br>432 | 1.25<br>1.41 | 1721 | $CCl_4$ | 0.0056[b] | 13, 14 |

[a] Name refers to diketone form. [b] Determined by a modified bromine titration method, refs. 5, 9, 10, 14. [c] Wilson and Read[15] reported a value of 3.43 which is apparently in error. [d] An absorption at 1721 cm.$^{-1}$ ($CHCl_3$) attributed to the diketone form has been observed by Lavie and Willner.[16] This band does not appear in the spectrum of freshly prepared material.[11] [e] Several longer wave-length bands also are present in the published spectrum, but their position and intensity are not clearly indicated.

infrared absorption spectra alone, the enolic content of 1,2-diketones can be estimated: the four-, five-, and six-membered cyclic diketones are completely enolized, whereas those in larger rings are ketonic. Hammond[19] has suggested that the electrostatic repulsion between the coplanar carbonyl dipoles in certain 1,2-diketones results in destabilization of the diketone form with respect to the enolized form; stabilization of the enol form by hydrogen bonding does not seem to be an important consideration. In the larger rings (seven members and above), the flexibility of the ring permits rotation of the carbonyl groups away from the coplanar configuration toward the more stable *trans* arrangement.

Conjugate addition of organometallic reagents to $\alpha,\beta$-unsaturated cyclic ketones has been well established. Perhaps the recent investigations of the structures of Grignard reagents[20] combined with suitable modifications[21] of the quasi-six-membered transition state theory[22,23] may form the bases for more accurate explanations of conjugate addition.

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(4) R. B. Woodward and E. R. Blout, *J. Am. Chem. Soc.*, **65**, 562 (1943).

(5) G. Schwarzenbach and E. Felder, *Helv. Chim. Acta*, **27**, 1044 (1944).

(6) A. E. Gillam, J. I. Lynas-Gray, A. R. Penfold, and J. L. Simonsen, *J. Chem. Soc.*, **60** (1941).

(7) R. J. W. LeFèvre, F. Maramba, and R. L. Werner, *J. Am. Chem. Soc.*, 2496 (1953).

(8) E. F. Silversmith and J. D. Roberts, *J. Am. Chem. Soc.*, **80**, 4083 (1958).

(9) G. Hesse and G. Krehbiel, *Ann.*, **593**, 35 (1955).

(10) G. Schwarzenbach and C. Wittwer, *Helv. Chim. Acta*, **30**, 663 (1947).

(11) See Experimental Section.

(12) N. J. Leonard and P. M. Mader, *J. Am. Chem. Soc.*, **72**, 5388 (1950).

(13) K. Alder, H. K. Schäfer, H. Esser, H. Kreiger, and R. Reubke, *Ann.*, **593**, 23 (1955).

(14) G. Schwarzenbach and C. Wittwer, *Helv. Chim. Acta*, **30**, 669 (1947).

(15) N. A. B. Wilson and J. Read, *J. Chem. Soc.*, 1269 (1935).

(16) D. Lavie and D. Willner, *J. Am. Chem. Soc.*, **80**, 711 (1958).

(17) V. J. Shiner, Jr., and C. R. Wasmuth, *J. Am. Chem. Soc.*, **81**, 37 (1959).

(18) N. J. Leonard, J. C. Little, and A. J. Kresge, *J. Am. Chem. Soc.*, **79**, 6436 (1957).

(19) G. S. Hammond, *Steric Effects in Organic Chemistry*, M. S. Newman, ed., John Wiley and Sons, Inc., New York, 1956, p. 450.

(20) R. E. Dessy and G. S. Handler, *J. Am. Chem. Soc.*, **80**, 5824 (1958).

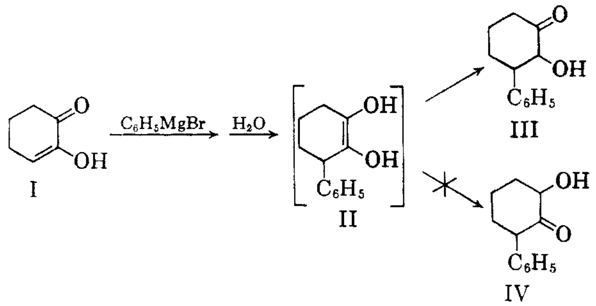
(21) M. S. Kharasch and O. Reinmuth, *Grignard Reactions of Nonmetallic Substances*, Prentice-Hall, Inc., New York, N. Y., 1954, p. 223.

(22) R. E. Lutz and W. G. Reveley, *J. Am. Chem. Soc.*, **63**, 3180 (1941).

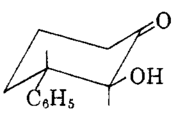
(23) For a recent discussion, see G. F. Wright, *Steric Effects in Organic Chemistry*, M. S. Newman, ed., John Wiley and Sons, Inc., New York, 1956, pp. 406–423.

Because the enol form of 1,2-cyclohexanedione (2-hydroxy-2-cyclohexen-1-one, I) contains such an $\alpha,\beta$-unsaturated system, conjugate addition might be expected. Treatment of enol I with an excess of the phenyl Grignard reagent furnished 2-hydroxy-3-phenylcyclohexanone (III) in 29% yield. The ketol was isolated from the crude reaction mixture by chromatography. Yields of this order are not uncommon in conjugate addition reactions, especially those involving the phenyl reagent. A considerable amount of extremely polar material also was formed; these products presumably resulted from condensation reactions of enol I in basic solution. This mixture could not be purified by crystallization and could not be eluted when adsorbed on an alumina column. No evidence for any discrete adduct other than ketol III was found. This appears to be the first example of conjugate addition to an enolic 1,2-diketone. Normal addition to enol I has been observed with the methyl[15,24] and ethyl[25] Grignard reagents, to form, respectively, 2-hydroxy-2-methylcyclohexanone and 2-hydroxy-2-ethylcyclohexanone.[26] The tendency for 1,2-addition with aliphatic reagents and 1,4-addition with aromatic reagents has many analogies in more complex systems.[29] This difference in reaction is usually attributed to the smaller size of the aliphatic reagent.

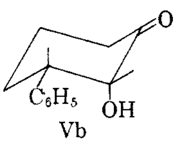
After hydrolysis of the Grignard complex, the intermediate enediol II underwent transformation to 2-hydroxy-3-phenylcyclohexanone (III) rather than 2-hydroxy-6-phenylcyclohexanone (IV). Because no isomerization was noted after treatment of ketol III with either acid or base, this product is assumed to be the more stable.



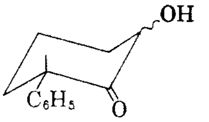
If the phenyl group occupies an equatorial position,[30] then the following additional stereochemical features would contribute to the stability of the ketol product: (a) a minimum of interaction between the equatorial benzene ring and the other substituents on the cyclohexane ring, (b) equatorial location of the hydroxyl group, and (c) hydrogen bonding between the ketone oxygen and the hydrogen of the hydroxyl group. Factor (a) is the most important energetically, and must determine whether ketol III or IV is formed. Since the product is III, then there must be less steric interaction between the benzene ring and the hydroxyl group (Va or Vb) than between the benzene ring and the carbonyl system (Vc). An examination of molecular models supports this theory.



Va



Vb



Vc

If condition (a) exists (as in Va), then condition (b) will follow, although some hydrogen bonding may occur if the hydroxyl group is axial (Vb). The infrared spectrum of ketol exhibits intramolecular hydrogen bonded O—H absorption[33] at 3460 cm.$^{-1}$ Structure Va should also be more stable since the phenyl and hydroxyl groups are both *trans* to each other and equatorial.[34] Additional data that indicate that Va represents the stereochemical configuration of the ketol was obtained from infrared analysis of diol VIII (*vide infra*).

Chemical evidence for the structure of ketol III was obtained from oxidation studies. Mild oxidation with cupric acetate or bismuth oxide in acetic acid furnished 2-hydroxy-3-phenyl-2-cyclohexen-1-one (VI), the enolic form of 3-phenyl-1,2-cyclohexanedione. This enol exhibits infrared absorption similar to that of 2-hydroxy-2-cyclohexen-

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(24) L. W. Butz, B. L. Davis, and A. M. Gaddis, *J. Org. Chem.*, **12**, 122 (1947).

(25) P. R. Jefferies and B. Milligan, *J. Chem. Soc.*, 4384 (1956).

(26) If enol I existed in the diketo form, addition to both carbonyl groups might be expected; although camphorquinone gives only mono adducts (ref. 27), benzil undergoes reaction at one or both carbonyl sites (ref. 28).

(27) J. Gripenberg, *Suomen Kemistilehti*, **18B**, 53 (1945); **19B**, 46 (1946).

(28) S. F. Acree, *Am. Chem. J.*, **33**, 180 (1905); M. A. Mihailescu and J. P. Caragea, *Bull sect. sci. acad. roumaine*, [12], **4/5**, 7 (1929), [*Chem. Abstr.*, **24**, 2116 (1930)]; E. Bergmann and W. Schreiber, *Ann.*, **500**, 122 (1933); O. Neunhoeffer and F. Nerdel, *Ann.*, **526**, 47 (1936); H. M. Crawford, M. E. Saeger, and F. E. Warneke, *J. Am. Chem. Soc.*, **64**, 2862 (1942).

(29) For a recent example, see R. C. Fuson and G. W. Griffin, *J. Am. Chem. Soc.*, **79**, 1941 (1957).

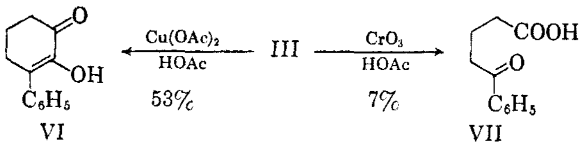
(30) This assumption is justified if the phenyl and isopropyl (or *t*-butyl) groups are considered to be of similar size in relation to their interactions with ring substituents. This similarity is supported by kinetic data on the acetylation of *cis*- and *trans*-4-*t*-butyl- and 4-phenylcyclohexanol (ref. 31). Spectral data on *trans*-1-isopropyl-1,2-cyclohexanediol confirm the equatorial assignment of the isopropyl group (ref. 32).

(31) E. L. Eliel and C. A. Lukach, *J. Am. Chem. Soc.*, **79**, 5986 (1957).

(32) A. R. H. Cole and P. R. Jefferies, *J. Chem. Soc.*, 4391 (1956).

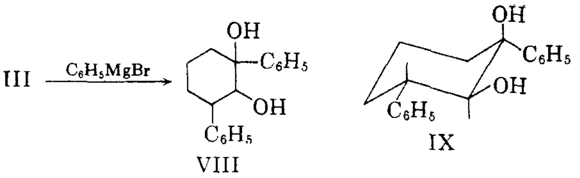
(33) L. J. Bellamy, *The Infra-red Spectra of Complex Molecules*, 2nd. ed., John Wiley and Sons, Inc., New York, 1958, pp. 96–99, 102–103.

(34) The predicted kinetically controlled product of ketonization [H. E. Zimmerman, *J. Am. Chem. Soc.*, **79**, 6554 (1957)] would be Vb or Vc (axial OH), but under the isomerizing conditions of the work-up, only Va is isolated.



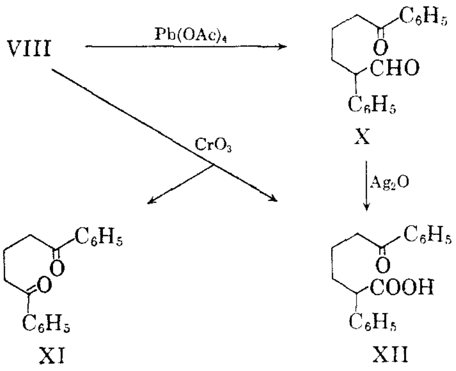
1-one (I). The position of the double bond in compound VI is indicated by the ultraviolet absorption spectrum (Table I) ,which resembles that of 3-phenyl-2-cyclohexen-1-one[35]: $\lambda_{max}$ 221 m$\mu$ (log $\epsilon$ 4.00) and 283 m$\mu$ (log $\epsilon$ 4.29). The bathochromic shift of the longer wave-length absorption band is a characteristic of $\alpha$-hydroxy-$\alpha,\beta$-unsaturated ketones.[36] Further evidence for the enolic 1,2-diketone system was the formation of 1-phenyl-1,2,-3,4-tetrahydrophenazine by treatment of compound VI with *o*-phenylenediamine.

Chromic acid oxidation of ketol III furnished 4-benzoylbutanoic acid (VII). This acid was also isolated after air oxidation of the product obtained from the action of periodic acid on ketol III. In this case or with lead tetraacetate oxidation, no discrete aldehyde was isolated, although there was spectral evidence for an aldehyde intermediate.[37] Finally, the structure for III was confirmed by reaction with phenylmagnesium bromide to form 1,3-diphenyl-1,2-cyclohexanediol (VIII) in 53% yield.



The suggested stereochemistry of this diol is illustrated by structure IX. Assuming the equatorial assignments of the phenyl and hydroxyl groups for ketol III (structure Va), then only two choices for diol VIII are possible—compound IX or its C$_1$ epimer. Diol IX would be favored energetically since the C$_1$ phenyl group is equatorial. The infrared spectrum of the diol measured by the technique of Kuhn[38] indicates that intramolecular hydrogen bonding does occur; the $\Delta\nu$ value is 28 cm.$^{-1}$ This establishes the relationship of the two hydroxyl groups—either both are equatorial or one is equatorial and one axial.[32,38,39] Thus IX is the only structure that can be written which both satisfies the infrared data and places the bulky aromatic groups in the equatorial position.

Oxidation of 1,3-diphenyl-1,2-cyclohexanediol (VIII) with chromic acid yielded a mixture of 1,3-dibenzoylpropane (XI) and a keto acid which is proposed to be 5-benzoyl-2-phenylpentanoic acid (XII). The structure assigned to this acid is based on the mode of formation, the neutralization equivalent, the infrared spectrum, and the isolation of this acid from an alternate degradation of diol VIII. By means of lead tetraacetate, the diol was converted in 81% yield to a keto aldehyde, assigned the structure 5-benzoyl-2-phenylpentanal (X). Treatment of compound X with silver oxide furnished a keto acid (22% yield), identical to that formed by chromic acid oxidation of diol VIII.



## EXPERIMENTAL[40]

*2-Hydroxy-2-cyclohexen-1-one* (I). This compound was prepared by the conventional selenium dioxide oxidation of cyclohexanone. In agreement with the published description,[41] the yields were in the 60% range and the colorless crystalline product turned yellow upon exposure to air. It was noted, however, that this color indicated decomposition of the ketone, since a liquid phase appeared and infrared spectrum changed. The spectrum of a freshly prepared sample contained bands at 3440 (hydrogen bonded alcohol group), 3020 (vinyl hydrogen), 1676 (conjugated ketone), and 1661 cm.$^{-1}$ (double bond). The spectra of yellow or semisolid samples exhibited an additional band at 1720 cm.$^{-1}$ which may be due to the diketo form. Only the colorless crystalline ketone was used in the experiments described below.

*2-Hydroxy-3-phenylcyclohexanone* (III). To the phenyl Grignard reagent prepared from 19.5 g. (0.124 mole) of bromobenzene and 2.60 g. (0.108 g. atom) of magnesium in 30 ml. of ether was added slowly a solution of 2.85 g. (0.0254 mole) of 2-hydroxy-2-cyclohexen-1-one in 6 ml. of ether. The resulting homogeneous red-brown solution was stirred under reflux (internal temperature 40°) for 15 hr. before hydrolysis with ice and dilute hydrochloric acid. The organic layer was removed and the solvent was distilled. The crude semisolid reaction product (5.41 g.) was subjected to chroma-

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(35) G. N. Walker, *J. Am. Chem. Soc.*, **77,** 3664 (1955).

(36) A. E. Gillam and E. S. Stern, *Electronic Absorption Spectroscopy*, 2nd. Ed., Edward Arnold, London, 1957, pp. 111–113

(37) The instability of a substituted phenylacetaldehyde intermediate is not surprising, especially in basic solution. Triebs and Krumbholz, *Chem. Ber.*, **85,** 1116 (1952), observed that only oils and resins were formed when phenylacetaldehyde was treated with base.

(38) L. P. Kuhn, *J. Am. Chem. Soc.*, **74,** 2492 (1952); **76,** 4323 (1954).

(39) J. S. Brimacombe, A. B. Foster, M. Stacey, and D. H. Whiffen, *Tetrahedron*, **4,** 351 (1958).

(40) All melting points are corrected. The microanalyses were performed by Mrs. Olga Hamerston and Mr. William Kuryla. Infrared spectra of 2–5% carbon disulfide solutions were measured on a calibrated Perkin-Elmer Model 21 spectrophotometer. The ultraviolet spectra were obtained from a Cary Model 11 spectrophotometer.

(41) C. C. Hach, C. V. Banks, and H. Diehl, *Org. Syntheses*, **32,** 35 (1952).

tography on an activated alumina column. Elution with hexane, methylene chloride, ethyl acetate, and finally methanol gave a total of 3.15 g. of material in addition to a large nonelutable yellow fraction. Combination and crystallization of fractions from this and two succeeding chromatographic separations yielded 0.66 g. of biphenyl, 1.40 g. (29%) of 2-hydroxy-3-phenylcyclohexanone (m.p. 119–120°), and 0.19 g. of yellow semisolid residue from the crystallizations. No evidence for heterogeneity of the ketol was found, either in the infrared spectra of various samples or in the melting points of samples obtained by crystallization from different solvents. The analytical specimen of the ketol crystallized from hexane-benzene in the form of fine needles, m.p. 120–121°.

*Anal.* Calcd. for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.46; H, 7.67.

The infrared spectrum exhibits hydrogen bonded OH absorption at 3460 cm.$^{-1}$ (sharp) and carbonyl absorption at 1719 cm.$^{-1}$. Other characteristic bonds occur at 1250, 1100, 1025, and 890 cm.$^{-1}$

The *2,4-dinitrophenylhydrazone* of 2-hydroxy-3-phenylcyclohexanone melted at 184–185° (dec.), after three crystallizations from ethanol.

*Anal.* Calcd. for $C_{18}H_{18}O_5N_4$: C, 58.37; H, 4.90; N, 15.13. Found: C, 58.15; H, 5.20; N, 15.70.

After three crystallizations from aqueous ethanol, the *semicarbazone* melted at 199–201°, with decomposition.

*Anal.* Calcd. for $C_{13}H_{17}O_2N_3$: C, 63.14; H, 6.93; N, 16.99. Found: C, 63.21; H, 6.98; N, 16.61, 16.50.

The spectrum of the crude reaction product contained (in addition to bands assigned to the ketol and biphenyl) three other carbonyl bands (1710, 1687, and 1662 cm.$^{-1}$), hydrogen bonded OH absorption (3390 cm.$^{-1}$), and unassigned absorption at 1650, 1627, 1377, and 1043 cm.$^{-1}$. These bands apparently were associated with the extremely polar components which could not be eluted from the column.

The yellow semisolid crystallization residue (0.19 g.) showed ketone and alcohol absorption similar to that of the ketol, but attempted further purification was not successful.

In other similar experiments, some employing chromatographic analysis, no discrete compounds other than ketol III and biphenyl were obtained. Sublimation, distillation, and crystallization were not effective in separating the mixture of products.

The ketol was recovered essentially unchanged after a 30-min. treatment on a steam bath with either 5% methanolic potassium hydroxide solution or acetic acid containing 10% hydrochloric acid, provided that an inert atmosphere was maintained in the reaction flask. Exposure of solutions of the ketol to oxygen at steam bath temperatures resulted in the formation of considerable amounts of 2-hydroxy-3-phenyl-2-cyclohexen-1-one.

*2-Hydroxy-3-phenyl-2-cyclohexen-1-one* (VI). Oxidation of 2-hydroxy-3-phenylcyclohexanone was effected by a modification of the usual method.[42] A mixture of 305 mg. of ketol, 550 mg. of cupric acetate, and 5 ml. of acetic acid was heated under reflux in an inert atmosphere for 20 min. The solution became light green and a copper salt precipitated. The mixture was filtered and the solution was concentrated. The residue was taken up in methylene chloride and washed with 5% potassium hydroxide solution to remove an acidic impurity. Removal of the solvent left 160 mg. (53%) of light tan crystals, m.p. 86–88°. Several crystallizations furnished the analytical sample in the form of colorless platelets, m.p. 89–90°.

*Anal.* Calcd. for $C_{12}H_{12}O_2$: C, 76.57; H, 6.43. Found: C, 76.90; H, 6.35.

The infrared spectrum contains the following assignable bands: 3380 cm.$^{-1}$ (sharp), hydrogen bonded OH absorption; 1668 cm.$^{-1}$, conjugated carbonyl; and 1631 cm.$^{-1}$, double bond. Other strong bands occur at 1377, 1327, 1295, and 1160 cm.$^{-1}$ The ultraviolet spectrum (isooctane) exhibited maxima at 226 mμ (log ε 3.828), 233 mμ (log ε 3.700), and 309 mμ (log ε 4.273).

Oxidation of the ketol with bismuth oxide in acetic acid[43] or cupric sulfate in pyridine[44] furnished the same product, but the yields were lower.

*1-Phenyl-1,2,3,4-tetrahydrophenazine.* A mixture of 2-hydroxy-3-phenyl-2-cyclohexen-1-one and *o*-phenylenediamine in acetic acid was heated under reflux for 5 hr. in an argon atmosphere. The acetic acid was removed and the mixture was basified. Following benzene extraction, chromatography on alumina, and two crystallizations from hexane, the phenazine was obtained as yellow clusters of crystals; m.p. 106–108°.

*Anal.* Calcd. for $C_{12}H_{16}N_2$: C, 83.04; H, 6.20, N, 10.76. Found: C, 83.20; H, 6.03, N, 10.77.

*Chromic acid oxidation of 2-hydroxy-3-phenylcyclohexanone.* To 5 ml. of ice-cold 50% acetic acid containing 350 mg. (1.84 mmoles) of the ketol was added 380 mg. (3.80 mmoles) of chromic anhydride. The mixture was then allowed to stand at room temperature for 20 hr. before water and methylene chloride were added. The organic layer yielded 60 mg. of crystalline material; this was dissolved in benzene and extracted with potassium carbonate solution. By infrared analysis, the neutral layer was found to contain mostly starting material. Acidification of the basic extract precipitated 25 mg. (7% yield) of 4-benzoylbutanoic acid, m.p. 125.5–126°. The identity of this compound was established by comparison of infrared spectra and by a mixture melting point determination with an authentic sample.[45] Changes in the conditions or amounts of reactants did not improve the yield of the keto acid.

*Periodic acid oxidation of 2-hydroxy-3-phenylcyclohexanone.* A mixture of 0.80 g. (3.5 mmoles) of periodic acid dihydrate, 0.60 g. (3.2 mmoles) of the ketol, 2 ml. of water, and 10 ml. of purified dioxane was stirred for 24 hr. at room temperature. Benzene extraction furnished 0.58 g. of yellow semisolid. The infrared spectrum of the crude product contained aldehyde and acid bands. Crystallization of this substance from benzene and from water eventually produced 0.055 g. (9%) of 4-benzoylbutanoic acid, m.p. 125–126°. Presumably the acid was a result of air oxidation of the aldehyde.

Attempted oxidations of the intermediate aldehyde acid by means of silver oxide and potassium hydroxide, or sodium permanganate and magnesium sulfate, did not produce any discrete acid, but did form base insoluble yellow oils.

*Attempted lead tetraacetate oxidation of 2-hydroxy-3-phenylcyclohexanone.* A mixture of 0.30 g. (1.58 mmoles) of ketol and 0.80 g. (1.80 mmoles) of lead tetraacetate was stirred for 3 hr. at room temperature in 6 ml. of benzene. The mixture was filtered and the solvent was removed under an argon stream. The product was an acidic pale yellow oil which exhibited two carbonyl bands (1752, 1736 cm.$^{-1}$) as well as an aldehyde C—H stretching vibration (2720 cm.$^{-1}$).

*Anal.* Calcd. for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84. Found: C, 69.75; H, 6.61.

No satisfactory derivatives of this material could be obtained; decomposition seemed to occur upon treatment with acid or base, or upon exposure to air. Both an oxime and a 2,4-dinitrophenylhydrazone were prepared but neither could be purified. The oil gave a positive Tollens' test. Attempted oxidations of the yellow oil by air, silver oxide, or sodium permanganate yielded only small amounts of impure acidic substances. Treatment of the ketol with per-

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(42) A. T. Blomquist and A. Goldstein, *Org. Syntheses*, **36,** 77 (1956).

(43) W. Rigby, *J. Chem. Soc.*, 793 (1951).

(44) H. T. Clarke and E. E. Dreger, *Org. Syntheses*, **Coll. Vol. I,** 87 (1932).

(45) L. F. Somerville and C. F. H. Allen, *Org. Syntheses*, **Coll. Vol. II,** 81 (1943).

acetic acid or Fenton's reagent did not furnish any crystalline materials.

*1,3-Diphenyl-1,2-cyclohexanediol* (VIII). The phenyl Grignard reagent was prepared from 25.2 g. (0.160 mole) of bromobenzene and 3.60 g. (0.150 g. atom) of magnesium in 50 ml. of ether. To this solution, a slurry of 7.34 g. (0.0386 mole) of 2-hydroxy-3-phenylcyclohexanone in 50 ml. of benzene was added. The deep gray-green mixture was heated under reflux for 2.5 hr. (solution temperature 56°). Hydrolysis was effected with an ice–ammonium chloride mixture. The *p*H of the aqueous layer was adjusted to 5–6 with dilute hydrochloric acid. After removal of the solvent from the organic layer, 5.47 g. (53%) of diol, m.p. 126–128°, was obtained. The analytical sample crystallized from a benzene-cyclohexane mixture in large cubic crystals, m.p. 129.5–131°.

*Anal.* Calcd. for $C_{18}H_{20}O_2$: C, 80.56; H, 7.51. Found: C, 80.53; H, 7.58.

Infrared spectral analysis of this diol on a high-resolution instrument demonstrated the existence of two types of O—H stretching absorptions: unassociated hydroxyl (3602 cm.$^{-1}$), and associated hydroxyl (3574 cm.$^{-1}$).[46]

*5-Benzoyl-2-phenylpentanal* (X). A mixture of 0.50 g. (1.9 mmoles) of 1,3-diphenyl-1,2-cyclohexanediol and 1.11 g. (2.5 mmoles) of lead tetraacetate in 15 ml. of benzene was heated under reflux for 1 hr. The mixture was filtered and the solvent removed; 0.41 g. (81%) of solid was obtained, m.p. 80–82°. Three crystallizations from a hexane-benzene mixture furnished the analytical sample, m.p. 84–85°.

*Anal.* Calcd. for $C_{18}H_{18}O_2$: C, 81.17; H, 6.81. Found: C, 81.09; H, 6.86.

The product, which decomposed upon exposure to air for a week, gave positive Tollens' and Benedict's tests. The infrared spectrum exhibited aldehyde absorption bands at 1718 and 2690 cm.$^{-1}$; the conjugated ketone absorption occurred at 1682 cm.$^{-1}$

*5-Benzoyl-2-phenylpentanoic acid* (XII). To a mixture of 0.42 g. (2.47 mmoles) of silver nitrate and 0.26 g. of potassium hydroxide in 5 ml. of water and 2 ml. of ethanol, 0.33 g. (1.24 mmoles) of 5-benzoyl-2-phenylpentanal was added. The reaction mixture was warmed for 0.5 hr. on a steam bath with stirring, then at room temperature for 2 hr. After filtration, the solution was acidified with dilute hydrochloric acid and then refrigerated. The crude acid (120 mg., m.p. 98–102°) was dissolved in base, the basic solution was extracted with benzene, and the acid was reprecipitated from the aqueous layer; 77 mg. (22% yield) of keto acid, m.p. 106–107°, was obtained. The analytical sample was crystallized from a hexane-benzene mixture and melted at 108–109°.

*Anal.* Calcd. for $C_{18}H_{18}O_3$: C, 76.57; H, 6.43. Found: C, 76.65; H, 6.55.

The neutralization equivalent was 286 (theoretical 282); acid bands (1702 cm.$^{-1}$, broad OH) and conjugated carbonyl absorption (1687 cm.$^{-1}$) were present in the infrared spectrum. Oxidation of the aldehyde with potassium permanganate gave the same product in about 8% yield. The neutral fractions from both oxidations were viscous yellow oils which appeared to be mixtures of carbonyl compounds, according to infrared analysis.

*Chromic acid oxidation of 1,3-diphenyl-1,2-cyclohexanediol.* A solution of 0.46 g. (1.71 mmoles) of the diol in 4 ml. of acetic acid was chilled in an ice bath; a solution of 0.37 g. (3.7 mmoles) of chromic anhydride in 2 ml. of water was added dropwise with stirring. The mixture was warmed slowly to 65°, at which temperature it was held for 2 hr. before addition to ice. Following benzene extraction, 0.40 g. of green crystalline material was obtained from which 0.18 g. (37%) of 5-benzoyl-2-phenylpentanoic acid, m.p. 107.5–108.5°, was isolated. This acid did not depress the melting point of a mixture with the product obtained in the previous experiment. The neutral fraction (0.16 g.) from the oxidation was purified by chromatography to yield 0.090 g. (21%) of fluffy platelets, m.p. 65–66°. This material was identified as 1,3-dibenzoylpropane by its infrared spectrum and by comparison with an authentic sample (m.p. 65–66°) prepared by the method of Japp and Michie.[47] That this diketone did not arise from oxidation of the keto acid was demonstrated by an attempted oxidation of the 0.11 g. of keto acid with 0.07 g. of chromic acid. No neutral component was isolated, and the acid fraction was a mixture, m.p. 71–103°, which could not be purified.

*Camphoquinone* was purified by crystallization from petroleum ether; m.p. 199–201°. The infrared spectrum contained two carbonyl bands: 1775 and 1759 cm.$^{-1}$ The 1759 cm.$^{-1}$ absorption was more intense than the 1775 cm.$^{-1}$ band. No hydroxyl absorption was present.

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[46] The authors are grateful to Mr. Page R. Edmondson of the Department of Medicine of the University of Minnesota for this determination on a calibrated Beckmann DK spectrophotometer. The spectrum of a 0.007*M* solution of the diol in carbon tetrachloride was measured in a 1-cm. quartz cell. An identical spectrum was obtained using a 0.0013*M* solution in a 5-cm. cell.

[47] F. R. Japp and A. C. Michie, *J. Chem. Soc.*, **79**, 1010 (1901).

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[CONTRIBUTION FROM THE UNIVERSITY OF CALIFORNIA, LOS ALAMOS SCIENTIFIC LABORATORY]

# α-Nitro Acid Chlorides. Preparation and Properties[1]

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α-Nitro acid chlorides can be prepared in good yields by chlorination of α-nitro acid hydrazides or their salts in inert solvents. They react rapidly with alcohols and ammonia to give α-nitro esters and amides and with sodium azide to give α-nitro acid azides.

Early attempts to prepare nitroacetyl chloride from nitroacetic acid by reaction with thionyl chloride or phosphorus pentachloride[2] failed and the acid chloride was synthesized only much later in small yield by the addition of nitryl chloride to ketene.[3] The higher homologs of nitroacetyl

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[1] (a) This work was performed under the auspices of the U. S. Atomic Energy Commission. (b) Presented before the Organic Section of the American Chemical Society at the 136th Meeting, Atlantic City, September 1959.

[2] W. Steinkopf, *Ber.*, **42**, 3925 (1909).

[3] W. Steinkopf and M. Kuhnel, *Ber.*, **75**, 1323 (1942).