For comparison purposes, 1,8-di-*p*-anisoylnaphthalene was prepared by the method of Bachmann and Chu.[12] It melted at 217–218° (lit.[12] 215–216°). A mixture melting point determination and the infrared spectra showed that this compound was the same as that obtained by oxidation of Vb.

Attempted Benzoylation of Triphenylmethane with Stannic Chloride Catalyst.—A mixture of 1.80 g. of triphenylmethane, 20 ml. of benzoyl chloride, 2.0 ml. of stannic chloride and 30 ml. of carbon disulfide was refluxed for 15 hours and then hydrolyzed with dilute hydrochloric acid. The carbon disulfide was removed by steam distillation and the organic residue taken up in ether. The ether solution was extracted with 5% sodium hydroxide to remove benzoic acid; then it was washed and dried. Removal of the ether and trituration with methanol gave 1.65 g. (92% recovery) of triphenylmethane, m.p. 91° (from methanol). No ketonic product could be detected by testing the ether solution of the neutral products with 2,4-dinitrophenylhydrazine reagent.

EVANSTON, ILL.

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

The Course of Acid-catalyzed Rearrangement of Phenylcyclohexane Hydroperoxide and its Derivatives; Observations on the Properties and Oxidation of 6-Hydroxyhexanophenone

BY HAROLD KWART AND ROBERT T. KEEN[1,2]

RECEIVED MAY 28, 1958

1-Phenylcyclohexyl hydroperoxide (I) rearranged almost quantitatively to cyclohexanone and phenol in acetic–sulfuric solution. The *p*-nitrobenzoate ester of this hydroperoxide gave an entirely analogous result under these conditions. When chromic anhydride–acetic acid solutions of the same acid strength were used to rearrange the hydroperoxide only *w*-benzoylvaleric acid was obtained. The latter reaction has been interpreted as proceeding *via* the chromate ester of the hydroperoxide followed by formation of a highly oxidizable keto-alcohol intermediate. The possible implications these results hold for the mechanism of acid-catalyzed rearrangement of analogous peroxy substances is also discussed. 6-Hydroxyhexanophenone and 1-phenyl-1,6-hexanediol have been synthesized and characterized. The remarkable ease with which these substances undergo chromic acid oxidation to the same product, *w*-benzoylvaleric acid, is considered as a clue to the mechanism of oxidative rearrangement of I.

The acid-catalyzed rearrangement of cumene (and related) hydroperoxides has been extensively investigated by several groups of workers.[3] The similar acid-catalyzed rearrangement of decalyl perbenzoates and various *p*-substituted derivatives thereof have also been studied.[4] The results in all cases are consistent with a mechanism involving concerted ionization of the oxygen–oxygen bond and bond formation at the developing cationic oxygen center.

The parallel to carbonium ion rearrangements has also been drawn[3a,5] on the basis of migration aptitude data[3c] and the correlation of rate with solvent polarity.[4b,c] However, to extend this analogy to carbonium ion rearrangements it seemed desirable to demonstrate the preference for group migration. Such considerations have been well established for rearrangements like the Beckman,[6a] the Pinacol,[6b] the Schmidt[6c] and Wagner–Meerwein,[6d] to name a few. For an examination of the course of migration during acid-catalyzed rearrangement 1-phenylcyclohexyl hydroperoxide (I) and various ester derivatives thereof were chosen as suitable models with which to demonstrate the relationship of an oxygen cation mechanism to ionic rearrangements involving electron deficient carbon and nitrogen.

Results and Discussion

A preparation of phenylcyclohexane hydroperoxide (I) containing a high concentration of the peroxide component has never been attained *via* the air oxidation of phenylcyclohexane.[7] In our hands compound I, available commercially in a *ca.* 20% solution containing both hydrocarbon and alcohol impurity, could be readily concentrated to a useful product assaying at least 95.5% hydroperoxide. The successful method of preparation involved precipitation of the sodium salt[8] and achieved complete separation of any detectable amounts of phenolic or ketonic contamination. It appears that the important point lies in the use of 50% sodium hydroxide since the more dilute base fails to give an easily isolated salt. Indeed, this latter observation was utilized in removing phenolic impurities by extraction with 5% sodium hydroxide.

When a sample of I prepared in this fashion was dissolved in an acetic–sulfuric acid solution and the resulting reaction was worked up after five minutes, the mixed product tested for the presence of both phenolic (Gibbs reagent) and ketonic components. The 2,4-dinitrophenylhydrazone of cyclohexanone could be recovered in nearly quantitative amounts

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[1] Part of this work is taken from the thesis of R. T. Keen submitted to the faculty of the University of Delaware in partial fulfillment of the degree of Master of Science in Chemistry, June 2, 1957.

[2] Presented before the 133rd Meeting of the American Chemical Society, April 14–19, 1958, San Francisco, Calif.

[3] (a) M. S. Kharasch, A. C. Poshkus, A. Fono and W. Nudenberg, *J. Org. Chem.*, **16**, 1458 (1951); (b) F. H. Seabold, Jr., and W. E. Vaughn, THIS JOURNAL, **75**, 3790 (1953); (c) P. D. Bartlett and J. D. Cotman, Jr., *ibid.*, **72**, 3095 (1950).

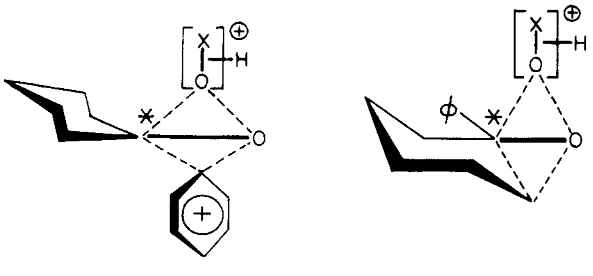
[4] (a) R. Criegee, *Ann.*, **560**, 127 (1948); R. Criegee and H. Dietrich, *ibid.*, **560**, 135 (1948); (b) P. D. Bartlett and J. L. Rice, THIS JOURNAL, **75**, 5591 (1953); (c) H. L. Goering and A. C. Olson, *ibid.*, **75**, 5853 (1953).

[5] (a) J. E. Leffler, *Chem. Revs.*, **45**, 385 (1949); (b) V. von E. Doering and L. Speers, THIS JOURNAL, **72**, 5515 (1950).

[6] (a) B. Jones, *Chem. Revs.*, **35**, 335 (1944); (b) P. I. Pollak and D. Y. Curtin, THIS JOURNAL, **72**, 961 (1950), *et seq.*; (c) P. A. S. Smith, *ibid.*, **70**, 3201 (1948); P. A. S. Smith and J. P. Horwitz, *ibid.*, **72**, 3718 (1950); C. L. Arcus, M. M. Combs and J. V. Evans, *J. Chem. Soc.*, 1498 (1956); (d) D. J. Cram, THIS JOURNAL, **71**, 3863, 3875, 3883 (1949); D. J. Cram and J. D. Knight, *ibid.*, **74**, 5839 (1952); J. D. Roberts, C. C. Lee and W. H. Saunders, Jr., *ibid.*, **76**, 4501 (1954); S. Winstein and D. Trifan, *ibid.*, **74**, 1147, 1154 (1952).

[7] Recently the characteristics of pure I were described for the first time by D. H. Hey, C. J. M. Sterling and C. H. Williams, *J. Chem. Soc.*, 1054 (1957), who prepared it by an entirely different method.

[8] Our results in this regard contrast strongly with reports in the recent literature; R. Foreman and H. Lankelma, THIS JOURNAL, **79**, 409 (1957); R. Criegee, *Ber.*, **77**, 22 (1944), and reference 4a.



IV III

X = p-NITROBENZOYL
OR $-CrO_3R$

Fig. 1.—Possible transition states in PCHP and PCHP ester rearrangement.

indicating a clean rearrangement with the course previously reported for I by Hey and co-workers[7] in dilute aqueous sulfuric acid.

Earlier studies[4] on the mechanism have demonstrated that the transition state structure in acid-catalyzed hydroperoxide rearrangement resembled that of the peroxy reactant, in that the ground state configuration of groups around the oxygen–oxygen bond was still largely intact. The kinetic results of these workers as well as the very informative tracer experiments of Denny[9] clearly show that the ionization products remain associated as a tight ion pair[10] and react covalently with each other more rapidly than with constituents of the solvent cage. It seemed possible, therefore, that by changing the nature of the group on the hydroxylic oxygen some important change in the configuration of the lower energy states as well as the higher energy transition state of the reactant could be effected. Accordingly the *p*-nitrobenzoate ester of I was prepared and subjected to acid-catalyzed rearrangement under precisely the same reaction conditions. A very clean-cut result was again obtained. Besides *p*-nitrobenzoic acid only phenol and cyclohexanone could be identified in a product comprising more than 98% of theoretical. Evidently the change in the nature of the leaving group from H_2O to *p*-nitrobenzoic acid has effected little change in the course of rearrangement.

However, when the hydroperoxide was dissolved in an acetic acid–CrO_3 solution (where we believe the chromic anhydride, by analogy to its behavior with alcohols, rapidly esterifies the peroxy –OH) the course of reaction was dramatically altered. The only product which could be isolated was ω-benzoylvaleric acid (II) in 46% yield after 30 minutes of reaction time and 52% after nearly an hour. Thus instead of the aryl migration noted in the two previous cases, the decomposition of the peroxide now involves ring opening of the cyclohexane moiety.

Cases of rearrangement in oxygen cation mechanisms where alkyl migrates at least as readily or more readily than phenyl have hitherto been noted and received comment.[11] Friess and Farnham, in fact, report that the migration aptitude of cyclohexyl is five times greater than phenyl in the reaction of perbenzoic acid with phenyl cyclohexyl ketone, a rearrangement quite analogous to the present case. A very tentative interpretation of the present case which we have considered may be reached by reasoning from the reaction transition states[9] visualized respectively in Fig. 1 in a few of the possible configurations of the ionizing fragments, where $X = \mathrm{H}-$, $\mathrm{NO_2C_6H_5}\underset{\underset{\mathrm{O}}{\|}}{\mathrm{C}}-$ or $-\mathrm{CrO_3R}$ and R is another peroxy group.

The choice of which of the alternative groups will bridge is obviously determined by the relative stability of the transition state configurations III and IV. The data support the view that III is a lower energy path relative to IV only where X is the $-CrO_3R$ group. This interpretation recalls the mutarotation of cholesteryl dibromide which also shows acid catalysis and has been discussed[12] as involving a concerted movement of groups with minimum charge separation developing in the course of making and breaking bonds. A kinetic study intended to provide further details of the mechanism of this oxidative rearrangement of peroxides and related reactions is presently in progress in these laboratories.

In the chromic acid-catalyzed rearrangement, in view of the fact that the product II represents the original reaction centers at a higher oxidation state than in the reagent, it seems apparent the hexavalent chromium has also functioned to oxidize a reactive intermediate. One possible path for the over-all reaction which identifies this intermediate is shown in Fig. 2.

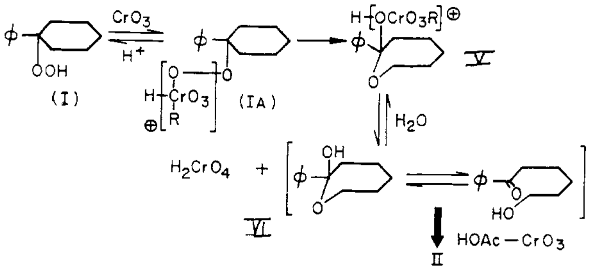


Fig. 2.—Possible route to ω-benzoylvaleric acid.

The failure to isolate any of the intermediate 6-hydroxyhexanophenone (VI) demands that this substance or its less likely[17] ring tautomeric chromate ester be oxidized to product II at a greater rate than the rearrangement of the hydroperoxy chromate ester Ia → V. Some indication that this assumption may be consistent with the facts was obtained by means of crude rate experiments. Thereby, it was realized that both alcohols VI and VIa were at least two and possibly as much as eleven times more rapidly oxidized to the common acid product as the peroxide I.

Finally the remarkable ease with which the 6-hydroxyhexanophenone undergoes oxidation by

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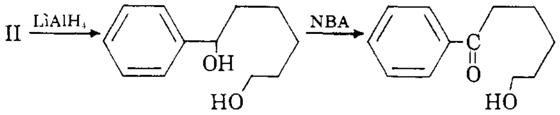
[9] D. B. Denny, This Journal, **77**, 1706 (1955).

[10] Identical with the term "intimate" or "internal" ion pair used originally by S. Winstein, E. Clippinger, A. H. Fainberg, G. C. Robinson, *Chemistry & Industry*, 664 (1954).

[11] (a) See ref. 5b; (b) S. L. Friess and N. Farnham, This Journal, **72**, 5518 (1950).

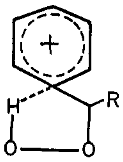
[12] (a) C. A. Grob and S. Winstein, *Helv. Chim. Acta*, **35**, 782 (1952); (b) H. Kwart and L. B. Weisfeld, This Journal, **78**, 635 (1956).

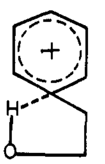
hexavalent chromium deserves some comment. This substance was readily prepared by the synthetic route outlined below, wherein N-bromoacetamide (NBA) selectively oxidizes the secondary carbinol in 1-phenyl-1,6-hexanediol (VIa). Both VIa and VI proved to be at least 5 times more rapidly oxidized than any primary, secondary or tertiary alcohols which, though analogous in carbon chain structure, did not possess a second carbon–oxygen bond along the chain.[13] The greater ease of oxidation of cyclic hemiacetals, as well as mixtures of aldehydes and alcohols which could exist in non-cyclic hemiacetal equilibrium, has been previously noted.[14] In the present case the possible intermediacy of a cyclic hemiketal in the path of oxidation of VIII appears unattractive in view of the reluctance of the seven-membered ring to form, particularly with an exocylic (carbonyl) double bond.[15] Furthermore, the results of a spectral study in the near infrared raise considerable doubt as to the existence of significant amounts of the cyclic hemiketal in equilibrium with the keto-alcohol even in non-polar solvents in which there would be some favor for the cyclic structure. Figure 3 presents the spectra in CCl_4 at high resolution of a number of comparable alcohol structures. The spectrum of VIIIa shows the expected multiplicity of –OH bonds corresponding to the primary and secondary alcohol functions, but the trace of VIII fails to show up even the faintest suggestion of two peaks corresponding to the equilibrium of primary and tertiary hydroxyls.



VIa VI

Figure 3 also illustrates the observation of a multiplicity of hydroxyl peaks for two cases where only a single peak might have been anticipated. Thus the primary –OH peak of 2-phenylethyl alcohol occurs at the lower wave length. The higher wave length peak is probably due to interaction of the –OH and phenyl groups, perhaps even to the extent of forming a hydrogen bond *via* the π-electrons of the benzene ring as depicted by VII. An entirely similar spectral characteristic is found for 1-phenylcyclohexyl hydroperoxide and this is taken to demonstrate a related type of hydrogen bonding as shown by the analogous structure VIII. The absence of a long wave length peak in the 1-phenyl-1,6-hexanediol spectrum supports the contention that such interaction peaks are not to be found in this region when three or more atoms are interposed between –OH and a polar group down the chain.[16]





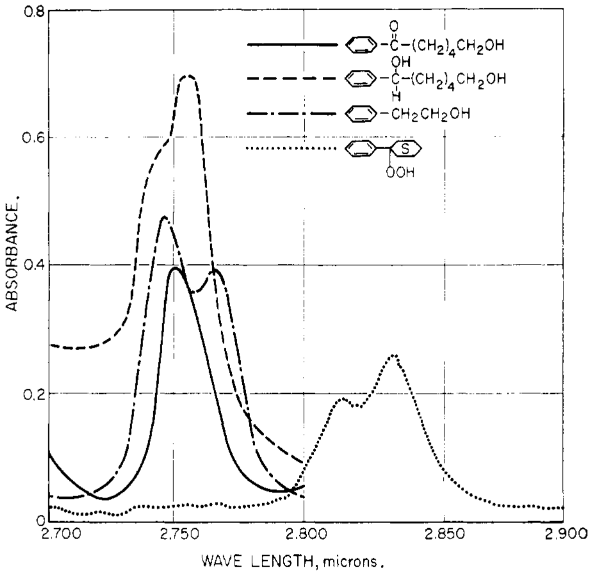


Fig. 3.

Still another indication of a lack of interaction between the carbonyl and carbinol groups is evident in the undimmed properties of the carbonyl group in VI. Typical carbonyl condensations take place without reluctance and the λ_{max} and ϵ_{max} of the carbonyl band in the ultraviolet spectrum compares well with that of acetophenone in all solvents. An entirely opposite characteristic, strong dimming of carbonyl reactions and reduced intensity of the carbonyl absorption near 250 mμ, has been reported as attributable to related psuedo-esterification interactions in *o*-benzoylbenzoic acid derivatives by Newman and co-workers.[17]

It must be pointed out, also, that the present case does not directly resemble the facilitation of the oxidation of hemiacetals reported earlier.[14] Therein the (potential) carbonyl carbon was aldehydic and the end result of reaction was its oxidation to a carboxylic group. In the oxidation of the 6-hydroxyhexanophenone the end product does not represent oxidation of the (potential) carbonyl of the ring-chain tautomer shown as VI, but rather of the carbinol carbon. The fact that oxidation is nonetheless facilitated could mean that it is not the cyclic hemiketal form which is oxidized but rather the open chain form. One possible explanation for the assistance of the carbinol oxidation by the remote benzoyl function may be the following. Since the rate-determining event in the oxidation mechanism[18] is proton abstraction from the chromate esterified carbon, this step can be accommodated by the presence of a conveniently situated proton-acceptor benzoyl

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[13] These results of R. T. Keen will be reported in a forthcoming publication from these laboratories.

[14] (a) See ref. 5a as well as other evidence presented earlier by N. A. Milas, THIS JOURNAL, **50**, 493 (1928); (b) W. A. Mosher and D. M. Preiss, *ibid.*, **75**, 5605 (1953).

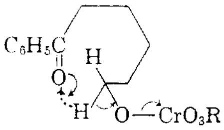
[15] H. C. Brown, J. H. Brewster and H. Shechter, *ibid.*, **76**, 467 (1954).

[16] See also I. M. Goldman and R. O. Crisler, *J. Org. Chem.*, **23**, 751 (1958).

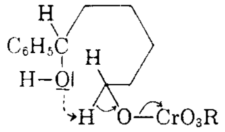
[17] M. S. Newman and C. D. McCleary, THIS JOURNAL, **63**, 1537 (1941); M. S. Newman and B. T. Lord, *ibid.*, **66**, 731 (1944); M. S. Newman and C. W. Muth, *ibid.*, **73**, 4627 (1951).

[18] F. Westheimer, *et al.*, *J. Chem. Phys.*, **11**, 506 (1943); **17**, 61 (1949); THIS JOURNAL, **73**, 65 (1951); **74**, 4383, 4387 (1952); H. Kwart and P. S. Francis, *ibid.*, **77**, 4907 (1955).

group in which a development of positive charge on the carbonyl carbon is diffused over the ring as illustrated in IX. The enhanced oxidative reactivity of the primary carbinol group in the diol VIa may be attributed either to prior formation of VI or to direct reaction of the primary chromate ester *via* the scheme shown in IXa where the secondary alcohol functions as the neighboring group proton acceptor in a fashion that parallels the activity of the carbonyl group in IX.



IX



IXa

To decide between these alternatives an extension of this study of the generality of the keto-alcohol oxidation mechanism is presently in progress in these laboratories.

Experimental

Purification of Phenylcyclohexane Hydroperoxide (I).—A sample of crude I in phenylcyclohexane,[19] containing about 40 g. of active material by titration,[20] was dissolved in one liter of pure acetonitrile and extracted three times with liter portions of isoöctane. The acetonitrile was then removed at the water-pump leaving a residue of 62 g. containing 58% active material, as estimated by titration. Several batches of crude were concentrated by this method; finally 150 g. of concentrate was dissolved in three liters of petroleum ether, scrubbed three times with 200-ml. portions of 5% aqueous sodium hydroxide to remove phenolics, dried by filtration through 100 g. of anhydrous magnesium sulfate and the filtrate cooled to 10° in an ice-bath. Fifty grams of acid-washed Celite analytical filter aid was stirred in. The mixture was then vigorously agitated while 200 g. of 50% sodium hydroxide was added dropwise. The suspension was filtered through a Buchner funnel with a sintered stainless steel mat, and the crude sodium salt was washed four times with petroleum ether, the precipitate being pressed down with rubber dam to squeeze out the residual liquid following each wash. The precipitate was suspended in 1000 ml. of water and maintained at 10° while glacial acetic acid was added slowly with vigorous stirring until *p*H 5 was attained. The aqueous layer was extracted with three 1000-ml. portions of petroleum ether. The combined extracts were washed with water, 5% aqueous bicarbonate and water again; then dried over magnesium sulfate. The petroleum ether was evaporated under aspirator vacuum and the residual solvent removed by use of a vacuum pump (8 hours at 0.5 mm. and 35°). The product weighed 80 g. and assayed 88.5% PCHP (71% yield).

Twenty-five grams of the 88.5% I was purified by repeating the above sodium salt precipitation on a correspondingly reduced scale to yield 18 g. of 95.5% I (78% yield). The product had the garlic-like odor characteristic of hydroperoxides; $n^{20.7}D$ 1.5466.

Preparation of Phenylcyclohexyl *p*-Nitroperbenzoate.—Fifty grams of 90% phenylcyclohexane hydroperoxide was stirred vigorously with 56 g. of *p*-nitrobenzoyl chloride in 500 ml. of pyridine at 0°, for 4 hours. The mixture, on warming to room temperature, was diluted to 200 ml. with ether and washed first with water (twice), then with 5% HCl until the pyridine was removed, then water and aqueous sodium bicarbonate to remove traces of acid. The yield of crude product after drying with magnesium sulfate and removal of ether under aspirator vacuum was 70.5 g. (88%). The crude product was recrystallized three times from benzene–petroleum ether mixtures. The yield of pure perester was 25 g. (32%), m.p. 207–208°. The pure product decomposed slowly at room temperature but could be stored at 0° for several weeks.

Anal. Calcd. for $C_{19}H_{19}O_5N$: C, 66.85; H, 5.61; N, 4.11; O, 23.44. Found: C, 67.24; H, 5.52; N, 3.96 (Dumas); O, 23.64 (Unterzaucher).[21]

Acid-catalyzed Rearrangement of Phenylcyclohexyl *p*-Nitrobenzoate.—To a solution consisting of 0.100 g. of phenylcyclohexyl *p*-nitroperbenzoate in 10 ml. of glacial acetic acid was added 0.10 ml. of concd. H_2SO_4 at 30°. A 1-ml. sample withdrawn after 2 minutes was diluted to 100 ml. with water. An aliquot of this solution gave a strong test for phenol with Gibbs reagent (2,6-dibromoquinonechloroimide) when buffered to *p*H 10 in water–methanol. A second aliquot was treated with 2,4-dinitrophenylhydrazine and gave an immediate, copious precipitate. The hydrazone product was filtered, washed with water and recrystallized from absolute alcohol to orange plates, m.p. 160.5–161°; m.p. of authentic cyclohexanone derivative 161°; mixed m.p. 161–162°. The crude yield of (dry) 2,4-dinitrophenylhydrazone corresponded to 98.1% of theoretical calculated on the basis of complete reaction to cyclohexanone and phenol.

Acid-catalyzed Rearrangement of I.—To 1.004 g. of I (94.5%, 4.88 millimoles active material) in 50 ml. of 99% HoAc was added 1 ml. of concd. H_2SO_4. After standing 5 min. at 30° the solution was treated with 100 ml. of 0.08 *M* 2,4-dinitrophenylhydrazine solution in 3.8 *M* perchloric acid and the total diluted to 1 liter. After standing about an hour the precipitate was filtered into a tared sintered glass crucible and washed until acid free. After drying 4 hours at 105° the precipitate weighed 1.346 g. or 4.85 millimoles calculated as cyclohexanone. This product after one recrystallization from ethanol melted at 160–162° and showed no depression on admixture with a sample prepared above by a similar rearrangement of phenylcyclohexyl *p*-nitrobenzoate.

Crude Rate Study of the Reaction of Chromic Acid with 1-Phenylcyclohexane Hydroperoxide (I), 6-Hydroxyhexanophenone (VI) and 1-Phenyl-1,6-hexanediol (VIA).—A solution containing approximately 14 meq. of the hydroxylic reagent in 765 ml. of 99% acetic acid was rapidly mixed with 12.0 g. of the chromic anhydride while the temperature was maintained at 30°. Aliquots (100 ml.) were withdrawn at 5-, 30-, 60-, 90- and 120-minute intervals, quenched with 2 ml. of hydrazine in 10 ml. of H_2O and finally worked up by diluting to 1000 ml. and extracting four times with a total of 2000 ml. of ether. The combined extracts were washed four times with 50-ml. portions of water. The solution was then evaporated to dryness under a stream of nitrogen. The residue was redissolved in 1000 ml. of ether and extracted three times with a total of 500 ml. of 5% sodium hydroxide. The alkaline extract was acidified with 100 ml. of concd. HCl and extracted four times with a total of 800 ml. of ether. The ether was removed under nitrogen on the steam-bath after drying the solution with magnesium sulfate. The amount of acid constituent could be estimated by titration. Sublimation and recrystallization from methanol gave a product, m.p. 77–78°, neutralization equivalent 205 (calcd. 206), identical with an authentic sample of ω-benzoylvaleric acid in m.p. and infrared spectrum; 2,4-dinitrophenylhydrazone, m.p. 138–139°.

TABLE I

RANGE OF RATE RESULTS

	I	VI	VIa
Half-life, min. min.–max.	2–3	7.5–20	7.5–22
Relative rates	1.0	2.5–10	2.5–11

Preparation of 1-Phenyl-1,6-hexanediol (VIa).—A solution of 125 g. of II in 2 liters of ether was added to 75 g. of $LiAlH_4$ in 500 ml. of ether under good stirring and a double condenser. Rapid refluxing was maintained all during addition and the reaction was permitted to stir overnight after addition was completed. The hydride excess was then destroyed by reaction with 200 ml. of ethyl acetate in 500 ml. of ether and the resulting mixture was made acid with 25% H_2SO_4. The ether layer was decanted after 4 hr. of standing and the aqueous layer extracted with 500 ml. of ether. The combined extracts were washed with two 250-ml. portions of water, 250 ml. of saturated K_2CO_3 and

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(19) Obtained through the courtesy of the Hercules Powder Co.

(20) C. O. Wagner, R. H. Smith and E. D. Peters, *Anal. Chem.*, **19**, 976 (1947).

(21) J. Unterzaucher, *Ber.*, **73**, 391 (1940), and M. Schutze, *Z. anal. Chem.*, **118**, 241 (1939). For further references, see V. A. Aluise, *et al.*, *Anal. Chem.*, **23**, 530 (1941).

finally 250 ml. of water. After drying over $MgSO_4$ the ether solution was evaporated to a yellow oil. The oil was distilled through a 4-inch Vigreux head and 83 g., b.p. 135–139° at 0.02 mm., of a colorless viscous oil was recovered which crystallized on standing at room temperature. The product was readily recrystallized from ether–hexane; m.p. 57–58°.

Anal. Calcd. for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.09; H, 9.37.

Preparation of 6-Hydroxyhexanophenone (VI).—A solution of 7.7 g. of diol VIa in 250 ml. of *t*-butyl alcohol containing 3% H_2O was cooled to 10° and 15 g. of N-bromoacetamide was added under vigorous stirring. A red-orange color developed slowly after the addition was completed. After 4 hours the solution was diluted with 500 ml. of ethyl acetate and 500 ml. of ether and washed twice with 100-ml. portions of 5% aqueous NaOH and finally with 100 ml. of H_2O. After drying with $MgSO_4$ the solvent was removed on a steam-bath, under a dry nitrogen stream, leaving behind 6.5 g. of a pale yellow oil.

A portion of this residue (3.0 g.) was dissolved in ether and hexane added to a point just short of a permanent precipitate. On standing in the cold less than 1.0 g. of a white, waxy solid crystallized, m.p. 28–32°. Recrystallization raised the m.p. to 32–34° with a second crop at 31–33°. This fraction proved to be a side reaction product and was set aside for later examination.

A second 3.0-g. portion of the pale yellow oil was dissolved in 20 ml. of absolute ethanol containing 2 ml. of glacial acetic and 5.0 g. of Girard reagent T (Araphoe Chemical Co.). After 10 minutes of reflux the mixture was diluted with 50 ml. of H_2O and 50 ml. of saturated $NaHCO_3$, then extracted twice with 200-ml. portions of ether to remove non-carbonyl impurities. The aqueous layer was treated with 25 ml. of concd. HCl, warmed for 15 min. on a steam-plate and finally extracted twice with 200-ml. portions of ether. The combined ether extracts were washed once with 50 ml. of H_2O, dried over $MgSO_4$ and evaporated to a clear, colorless oil weighing 1.9 g., $n^{22.8}D$ 1.5324.

Anal. Calcd. for $C_{12}H_{16}O_2$: C, 74.96; H, 8.39. Found: C, 74.90; H, 8.50.

A sample of the crude oil gave an immediate, copious precipitate with 2,4-dinitrophenylhydrazine in perchloric acid solution. The m.p. after washing and drying was 97°, but on recrystallization from ethanol the derivative melted very sharply at 137° and depressed the m.p. of the DNPH derivative of II. Undoubtedly the two melting points correspond to crystalline modifications resembling in this respect the DNPH derivative of acetaldehyde.

TABLE II

ULTRAVIOLET ABSORPTION DATA[b]

Compound	λ_{max}, mμ	ϵ_{max} (10^{-3})
Hexanophenone	240	13.0
Acetophenone[a]	240	13.1
Propiophenone[a]	240	12.9
n-Butyrophenone	240	13.1
i-Butyrophenone	240	12.7
n-Valerophenone	240	12.8
6-Hydroxyhexanophenone	242	12.7
Benzoylvaleric acid	240	13.1
1-Phenyl-1,6-hexanediol	255	0.21

[a] Note that in H_2O solution these substances have a somewhat smaller ϵ_{max} (approx. 11,900) and λ_{max} is bathochromically displaced by more than 5 mμ. L. Daub and J. M. Vandenbelt (THIS JOURNAL, 69, 2714 (1947)) have reported for acetophenone λ_{max} 245.5 and ϵ_{max} 9800 in H_2O.
[b] Solvent, methanol.

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NEWARK, DEL.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF WAYNE STATE UNIVERSITY]

Optical Rotatory Dispersion Studies. XXII.[1] Detection and Stereochemical Implication of Hemiketal Formation[2,3]

BY CARL DJERASSI, L. A. MITSCHER[4] AND B. J. MITSCHER

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The effect of hydrochloric acid upon the shape and intensity of optical rotatory dispersion curves of saturated carbonyl compounds in alcoholic solution was determined. The results are interpretable in terms of hemiketal formation, which was found to be very sensitive to steric and conformational factors. Hemiketal formation is most pronounced in methanol solution and practically inhibited in isopropyl alcohol. It is also affected by ring size, α-alkyl substituents and generation of new 1,3-diaxial interactions, not present in the parent ketone. Since this simple experimental modification—determination of optical rotatory dispersion followed by addition of hydrochloric acid and repetition of the dispersion measurement—offers a valuable means of differentiating between ketones in various steric environments as well as diketones situated in different rings, it is proposed that this be used as a routine adjunct to optical rotatory dispersion measurements.

Hemiketal formation of carbonyl compounds is often difficult to measure by isolation of the actual compound,[5] particularly when the equilibrium lies on the ketone (or aldehyde) side, and recourse is usually taken to physical measurements. Ultraviolet spectroscopy has proved to be particularly useful in this connection[6] by measuring the diminution in extinction of the ultraviolet absorption maximum in the 280–320 mμ region associated with the saturated carbonyl group. Experimentally, this is performed[6] by determining the change in intensity of this maximum in methanol solution produced by the addition of a drop of hydrochloric acid, which is sufficient to catalyze the formation of the hemiketal. Unfortunately, the extinction coefficient of a saturated ketone or aldehyde is of a very low order of magnitude—often completely obscured by absorption of other

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(1) Paper XXI, C. Djerassi and G. W. Krakower, THIS JOURNAL, **81**, 237 (1959).

(2) Supported by the National Cancer Institute (grant No. CY-2919) of the National Institutes of Health, U. S. Public Health Service.

(3) Some of the results were first reported at a Meeting of the Japanese Chemical and Pharmaceutical Societies at the University of Tokyo, March 13, 1958.

(4) U. S. Public Health Service predoctorate research fellow, 1956–1958.

(5) There are, of course, important exceptions, notably in the sugar series.

(6) The most recent detailed study has been carried out by O. H. Wheeler, THIS JOURNAL, **79**, 4191 (1957), who has also reviewed the pertinent literature; see also ref. 15.