Condensation of 2,6-Diphenyl-4-pyrone with Carbanions[1]

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Condensations of 2,6-diphenyl-4-pyrone with sodiodiphenylmethane, sodioacetophenone, disodiobenzoylacetone, and sodium sodiophenylacetate afforded the respective products of nucleophilic attack at the 2 position of the pyrone followed by ring opening. From the diphenylmethane condensation were isolated two isomeric unsaturated β-diketones, which cyclized in hydrogen fluoride to the same naphthyl ketone. The acetophenone and benzoylacetone condensations gave an unsaturated triketone and tetraketone, respectively. However, both products existed primarily as cyclic hemiketals. Aromatic dehydration of the two compounds gave highly substituted phenols. In addition, the acetophenone adduct underwent dehydration in hydrogen fluoride to a highly colored 2-phenacylidenepyran. The unsaturated diketo acid arising from the phenylacetic acid condensation was cyclized to a 2-pyrone by hydrogen fluoride. The reaction of diphenylpyrone with carbanions appears to be a useful method for the preparation of unsaturated β-diketones and particularly compounds containing the heptene-1,3,7-trione moiety.

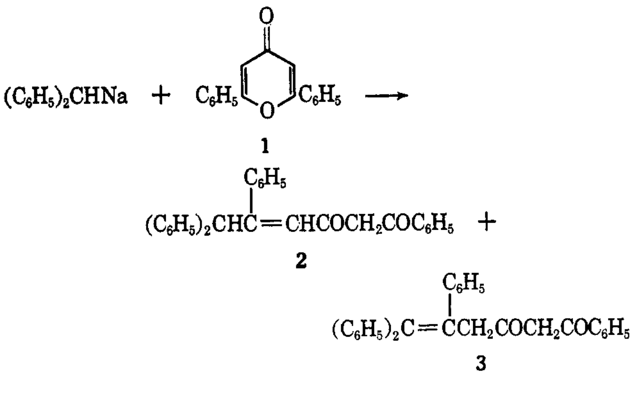
There have been numerous reports of reactions of 4-pyrones with nitrogen and oxygen nucleophiles.[2] The principal site of attack has been the 2 position and, in general, attack at the 4 position has not been observed. On the other hand, with carbon nucleophiles attack has been observed at both the 2 and the 4 positions. Woods has reported that cyanide ion attacks the 4 position of kojic acid to give the corresponding cyanohydrin.[3] Grignard reagents add at the 4 position of 2,6-dimethyl-4-pyrone to afford on acidification 2,4,6-trisubstituted pyrylium ions.[4] The sodium salt of ethyl malonate condenses with 4-pyrone to form ethyl *p*-hydroxybenzoate, presumably by ring cleavage at the 2 position of the pyrone followed by decarboxylation and recyclization.[5] In addition, Schoenberg and Singer have effected ring opening of 2,6-dimethyl- and 2,6-diphenyl-4-pyrone (**1**) with 9-sodiofluorene to afford β,γ-unsaturated diketones.[6]

This paper reports the condensations of four carbanions with 2,6-diphenyl-4-pyrone. Of primary interest was whether attack at the 2 position is a general reaction of sodium salts of carbanions. If the sodium salt of a carbonyl compound were employed this would then afford a polycarbonyl compound containing a heptene-1,3,7-trione moiety. At present there is a need for general methods to prepare such compounds because of the possible involvement of certain of them in the biosynthesis of aromatic compounds, such as the tetracyclines.[7]

Results

Diphenylmethane.—Initially, 2,6-diphenyl-4-pyrone (**1**) was treated with sodiodiphenylmethane[8] in liquid ammonia to confirm and extend the observation by Schoenberg and Singer[6] that a sodium salt of a hydrocarbon would attack **1** at the 2 position. In contrast to their result, not one but two products were obtained after acidification. However, both compounds gave strong red enol tests with ethanolic ferric nitrate indicating that both were β-diketones. One product, 1,5,6,6-tetraphenyl-4-hexene-1,3-dione (**2**), was yellow and showed an absorption maximum at 353 mμ, whereas the other, 1,5,6,6-tetraphenyl-5-hexene-1,3-dione (**3**), was colorless and absorbed at 307 mμ, indicating that in **2** the double bond was α,β to the carbonyl group while in **3** the double bond was β,γ.[9] The nmr spectra of **2** and **3** confirmed this assignment. In the spectrum of **2** the vinylic 4 proton and the allylic 6 proton were weakly coupled (*J* = 1 cps). In the spectrum of **3** the 4-methylene group appeared as a singlet. The spectra indicated that both diketones were essentially completely enolic in deuteriochloroform solution (see Scheme I).

SCHEME I



Alkaline hydrolysis of diketone **2** afforded, in addition to benzoic acid, ketone **4** which exhibited an aliphatic carbonyl stretching band[10] at 1717 cm^{-1}. The ultraviolet and nmr spectra and the elemental analysis were consistent with this assignment. It should be noted that double-bond migration occurred during hydrolysis.

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[1] This work was supported by the National Institutes of Health, U. S. Public Health Service (Research Grant 1-RO1-GM-12848-02).

[2] For reviews, see L. F. Cavalieri, *Chem. Rev.*, **41**, 525 (1947), and H. Meislich in "Pyridine and Its Derivatives," part III, E. Klingsberg, Ed., John Wiley and Sons, Inc., New York, N. Y., 1962, pp 552–560. See also (a) P. Beak and G. A. Carls, *J. Org. Chem.*, **29**, 2678 (1964); (b) D. W. Mayo, P. J. Sapienza, R. C. Lord, and W. D. Phillips, *ibid.*, **29**, 2682 (1964); (c) S. Garratt, *ibid.*, **28**, 1886 (1963); (d) R. N. Schut, W. G. Strycker, and T. M. H. Liu, *ibid.*, **28**, 3046 (1963); (e) D. Cook, *Can. J. Chem.*, **41**, 1435 (1963); (f) P. Yates, M. J. Jorgenson, and S. K. Roy, *ibid.*, **40**, 2146 (1962).

[3] L. L. Woods, *J. Am. Chem. Soc.*, **77**, 1702 (1955).

[4] A. Baeyer and J. Piccard, *Ann.*, **407**, 332 (1915).

[5] R. B. Woodward, unpublished observation, cited by E. D. Bergmann, D. Ginsburg, and R. Pappo, *Org. Reactions*, **10**, 219 (1959).

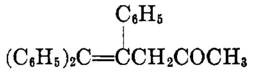
[6] A. Schoenberg and E. Singer, *Chem. Ber.*, **96**, 627 (1963).

[7] See J. H. Richards and J. B. Hendrickson, "The Biosynthesis of Steroids, Terpenes, and Acetogenins," W. A. Benjamin, Inc., New York, N. Y., 1964.

[8] C. R. Hauser and P. J. Hamrick, *J. Am. Chem. Soc.*, **79**, 3142 (1957).

[9] (a) In **3** conjugation of the double bond with three phenyl groups would not significantly contribute to the observed long wavelength absorption maximum since the maximum of 1,1,2-triphenylpropene is 275 mμ (ε 9800): "Organic Electronic Spectral Data," Vol. 1, M. J. Kamlet, Ed., Interscience Publishers, Inc., New York, N. Y., 1960, p 896. (b) The long wavelength maximum of **3** is consistent with that reported for benzoylacetone, 310 mμ (ε 14,000): see reference in 9a, p 321.

[10] See L. J. Bellamy, "The Infrared Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, N. Y., 1958, p 132.



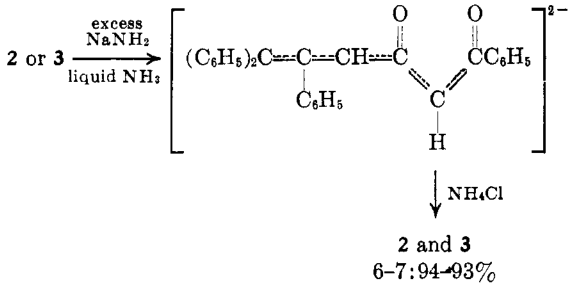
$(C_6H_5)_2C{=}\overset{C_6H_5}{C}CH_2COCH_3$

4

It appears likely that, in the condensation of sodiodiphenylmethane with pyrone **1**, diketone **2** was formed initially and was subsequently converted to diketone **3**. Diketone **2** was the major product when diphenylmethane was employed in excess of sodium amide, but **3** predominated when approximately equal quantities of base and hydrocarbon were employed. One explanation for this result would be that small quantities of amide ion were present in the second case and that amide ion is a more effective reagent for the conversion of **2** to **3** than is diphenylmethide ion. The amide ion might have arisen from losses of diphenylmethane during addition or from ammonolysis of diphenylmethide ion.[8]

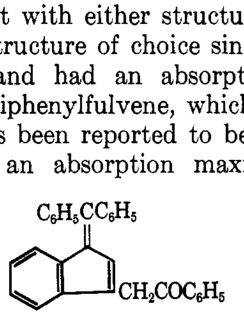
Rearrangement of **2** to **3** was effected under two different sets of conditions. First, solutions of **2** in triethylamine were converted to **3** at least to the extent of 75% by heating at 150° for 10 hr in a sealed tube. On the other hand, **3** was not affected by these conditions. Second, the interconversion could be effected by means of sodium amide in liquid ammonia. Diketones **2** and **3** were dissolved in liquid ammonia containing an excess of sodium amide. Dark violet solutions of the dianion were formed. The color was discharged when the reaction mixtures were poured into a solution of ammonium chloride in liquid ammonia. Ultraviolet analysis indicated that treatment of the two diketones in this fashion led to identical mixtures of them, and that diketone **3** predominated over diketone **2** by more than a factor of 10 (see Scheme II).

SCHEME II



The first of these methods provides information on the thermodynamic relationship of the two isomers. The second does not. Instead, it reflects the relative rate of protonation at two sites in a resonance stabilized anion.[11]

Cyclizations of diketones **2** and **3** were effected by treatment with anhydrous, liquid hydrogen fluoride. The same product (**6**) was obtained in high yield from both diketones. The ketonic structure of **6** was indicated by its infrared spectrum and by conversion to the 2,4-dinitrophenylhydrazone. The nmr spectrum showed a singlet methylene group, which would be consistent with either structure **5** or **6**. However, **6** was the structure of choice since the compound was colorless and had an absorption maximum at 293 mμ. 6,6-Diphenylfulvene, which is a satisfactory model for **5**, has been reported to be a yellow-orange compound with an absorption maximum at about 333 mμ.[12]



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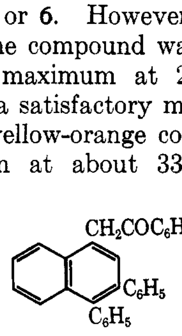
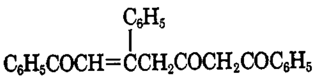


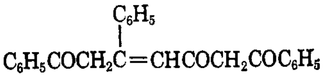
6

Acetophenone.—The condensation of sodioacetophenone with diphenylpyrone (**1**) in liquid ammonia afforded in 60% yield a product of satisfactory analysis for expected triketones **7** and **8**. However, neither the infrared nor the nmr spectrum showed the characteristics of an enolized β-diketone. On the other hand these spectra were consistent with cyclic hemiketal **9**. The ultraviolet spectrum (λ_{max} 287 mμ) which was similar to that reported for 3-ethoxycrotonophenone (λ_{max} 284 mμ)[13] lends additional support to this structure. However, certain other structures such as **10** cannot be rigorously excluded.



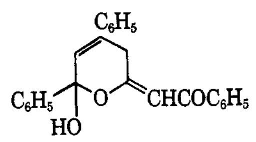
$C_6H_5COCH{=}\overset{C_6H_5}{C}CH_2COCH_2COC_6H_5$

7



$C_6H_5COCH_2\overset{C_6H_5}{C}{=}CHCOCH_2COC_6H_5$

8



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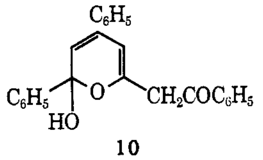
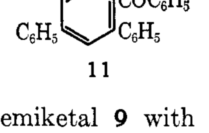


10

Apparently, hemiketal **9** was in equilibrium with traces of **7** since solutions of **9** were not stable over long periods at room temperature. Transformation occurred to aromatic dehydration product **11**. This conversion occurred rapidly in pyridine solution at elevated temperatures. Such dehydration must occur through open-chain tautomer **7** or **8**. The nmr spectrum of **11** supported the assigned structure; the hydroxyl signal appeared at low field (9.7 ppm) indicating the involvement of this group in intramolecular hydrogen bonding. Hemiketal **9** also gave an enol test when warmed with ethanolic ferric nitrate. It is not known whether ferric nitrate assisted in ring opening under these conditions.



11

Treatment of hemiketal **9** with anhydrous, liquid hydrogen fluoride afforded pyran **12**. The hydrogen fluoride solution was a light yellow and the species present was probably a pyrylium ion, such as **13**. However, pyran **12** was a deep red compound (λ_{max} 474 mμ), consistent with an extended system of con-

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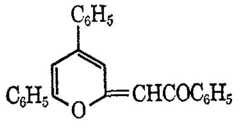
[11] The kinetic result can be predicted by the principle of least motion if the reasonable assumption is made that a major portion of the charge in the anionic species resides on oxygen: J. Hine, *J. Org. Chem.*, **31**, 1236 (1966). For the kinetic and the thermodynamic products to be the same is a violation of the older Hughes–Ingold rule: A. G. Catchpole, E. D. Hughes, and C. K. Ingold, *J. Chem. Soc.*, 8 (1948), and C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, p 565. For a discussion of exceptions to this rule, see D. J. Cram, "Fundamentals of Carbanion Chemistry," Academic Press Inc., New York, N. Y., 1965, p 204.

[12] C. Courtot, *Ann. Chim.* (Paris), [9] **5**, 194 (1916).

[13] R. A. Morton, A. Hassan, and T. C. Calloway, *J. Chem. Soc.*, 883 (1934).

jugation. Intensity enhancement occurred in dilute acid solution, presumably as a result of protonation of the carbonyl group. Pyran **12** provides strong evidence that the initial attack by sodioacetophenone had occurred at the 2 position of diphenylpyrone (**1**). If attack had occurred at the 4 position, pyran **14** would have resulted from hydrogen fluoride treatment. Pyran **14** is a known compound of lower melting point.[14]



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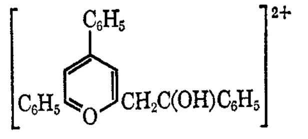

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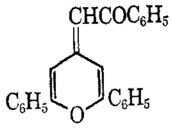
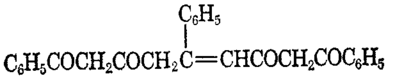


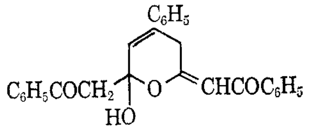
14

Benzoylacetone.—The condensation of the disodio salt of benzoylacetone[15] with diphenylpyrone (**1**) was effected in 56% yield. Although the product was of correct analysis for bisdiketone **15**, the infrared and nmr spectra did not indicate enolic structure. The product was assigned hemiketal structure **16** on the basis of the close similarity between the infrared and ultraviolet spectra of the compound and those of hemiketal **9** derived from acetophenone. The nmr spectrum of **16** was consistent with this structure. A singlet at 5.13 ppm was identified as the hydroxyl proton by facile exchange with deuterium oxide. The spectrum of **16** differed slightly from that of **9**. In **9** the chemical shifts of the two methylene protons were the same, whereas, in **16** the protons were distinguishable and coupled. The methylene protons of the phenacyl group of **16** were also chemically nonequivalent by virtue of the asymmetry of the molecule.



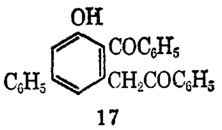
$C_6H_5COCH_2COCH_2\overset{C_6H_5}{\overset{|}{C}}{=}CHCOCH_2COC_6H_5$

15



16

An attempted dehydration of **16** in anhydrous, liquid hydrogen fluoride was unsuccessful and yielded only an intractable red powder, which was not further characterized. Hemiketal **16** was unstable in solution; heating in ethanol at 100° effected aromatic dehydration to phenolic diketone **17**. The structure of **17** was supported by the nmr spectrum, in which the hydroxyl proton produced a signal at low field (9.1 ppm), and the phenacyl methylene group gave a singlet (area 2) at 4.1 ppm.



17

Phenylacetic Acid.—The condensation of sodium sodiophenylacetate[16] with diphenylpyrone (**1**) in liquid ammonia afforded a 65% yield of 5,7-dioxo-2,3,7-triphenyl-3-heptenoic acid (**18**) resulting, as in the other cases, from attack at the 2 position of the pyrone. The nmr spectrum was consistent with the double bond being located β,γ to the carboxyl group and with the dicarbonyl group being highly enolized. The single protons at positions 2 and 4 were coupled slightly (J = 1 cps). Although the compound gave a strong enol test with ethanolic ferric nitrate and was soluble in sodium bicarbonate, neither the enol proton nor the carboxyl proton was apparent in the spectrum. It is possible that the large aromatic multiplet obscured their signals. In the infrared spectrum the stretching mode for the carboxyl group appeared at 1705 cm^{-1}.[17]

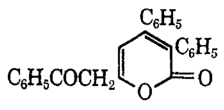
$C_6H_5COCH_2COCH{=}\overset{C_6H_5}{\overset{|}{C}}\underset{\underset{C_6H_5}{|}}{C}HCO_2H$

18

In one experiment the condensation of the pyrone was carried out in a mixture of ether and a small amount of ammonia. An isomer of acid **18**, which was lower melting, was isolated. The infrared spectrum of this adduct indicated that it also was an enolic compound containing a carboxyl group. The compound gave an enol test with ethanolic ferric nitrate, although the color was different from that obtained with the other isomer. The nmr spectrum was highly complex and its appearance was dependent upon the solvent employed. Apparently, the compound existed in solution as a mixture of tautomers. However, the higher melting isomer (**18**) described above was not among the tautomers present in solutions of the lower melting isomer.

It can be concluded that the two compounds differed only by location or configuration of the double bond since treatment of either of them with anhydrous, liquid hydrogen fluoride afforded 2-pyrone **19**.

The nmr spectrum of **19** showed the presence of a methylene group and a vinylic CH. The infrared spectrum contained a single, intense band centered at 1710 cm^{-1}. This is consistent with the spectra of other 2-pyrones.[18] The stretching mode of aromatic ketones is not usually seen at wave numbers this high.[19] However, the width of the band (1690–1740 cm^{-1}) was sufficient to overlap a portion of the usual aromatic carbonyl stretching region. The presence of the keto group was confirmed by conversion of **19** to the dinitrophenylhydrazone derivative.



19

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[14] H. Strzelecka, M. Simalty-Siemiatycki, and C. Prevost, *Compt. Rend.*, **257**, 926 (1963).

[15] K. G. Hampton, T. M. Harris, and C. R. Hauser, *J. Org. Chem.*, **31**, 1035 (1966).

[16] C. R. Hauser and W. J. Chambers, *J. Am. Chem. Soc.* **78**, 4942 (1956).

[17] Reference 10, p 167.

[18] F. M. Dean, "Naturally Occurring Oxygen Ring Compounds," Butterworth and Co. (Publishers) Ltd., London, 1963, p 82.

[19] Reference 10, p 137.

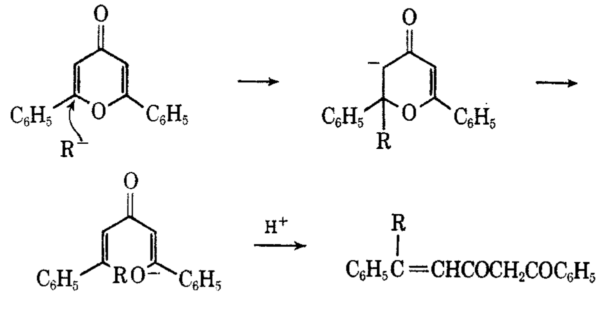
Discussion

Four examples of the addition of carbanions to 2,6-diphenyl-4-pyrone have been presented in this paper. Two different modes of attack were possible in each case, but the products isolated from all four reactions were the result of attack at only the 2 position. Although the yields in these reactions were good, complete accounting was not made for all starting materials. On the basis of the examples presented, the employment of diphenylpyrone (**1**) and perhaps other 4-pyrones in condensations with carbanions appears to be a useful method for the preparation of unsaturated β-diketones. In particular, condensations of the anions of carbonyl compounds can be used advantageously to produce compounds containing the heptene-1,3,7-trione moiety (or a tautomeric equivalent).

The 1,3,7-triketone and the 1,3,7,9-tetraketone resulting from the condensations of acetophenone and benzoylacetone, respectively, differ markedly in their properties from 1,3,5-triketones[20] and the one known 1,3,5,7-tetraketone.[21] Although the latter compounds exist in a number of enol forms, no evidence has been obtained for cyclic hemiketal tautomers. The triketone and the tetraketone prepared in the present study existed essentially completely in hemiketal forms. However, reversion to the open-chain forms occurred readily so that aldol-type cyclizations were observed under mild conditions. In addition, enol tests were obtained with hot, ethanolic ferric nitrate. Aromatic dehydration of a number of polycarbonyl compounds has been observed recently.[22]

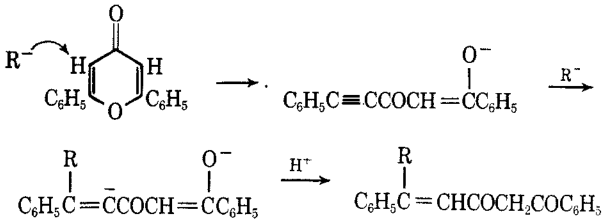
The mechanism of pyrone cleavage by carbanions is unknown. Two pathways are worthy of consideration. The first of these is nucleophilic attack by the carbanion at the 2 position of the pyrone to afford as an intermediate a carbanion stabilized by the 4-carbonyl group. Subsequently, β elimination of the highly stabilized anion of a β-diketone occurs (Scheme III). Such a mechanism has been postulated by Schoenberg and Singer for the anionic attack by 9-sodiofluorene.[6]

Scheme III



The alternative pathway for condensation of carbanions with 4-pyrones involves an elimination–addition sequence. The strongly basic anion might effect a β elimination of the enolate anion of a β-diketone.

Scheme IV



Conjugate addition across the resulting α,β-acetylenic system would follow (Scheme IV).

An addition–elimination mechanism (Scheme III) is supported by the well-documented reaction of nucleophiles with other α,β-unsaturated systems, particularly the base-catalyzed deuterium exchange reactions of cyclic, unsaturated ketones.[23] Acid-catalyzed (but not base) deuterium and oxygen exchange reactions have been reported with 4-pyrone; an acid-catalyzed mechanism similar to Scheme III was postulated by Beak and Carls and by Mayo, *et al.*[2a,b] Support for the second mechanism (Scheme IV) can be obtained from the observation that ring cleavage is merely the reversal of a pathway by which 4-pyrones have been formed from acetylenic β-diketones.[24] Although this reversal has not actually been observed, acetylenic ketones have been formed by the base effected elimination of acyclic β-acyloxy vinyl ketones.[25] More work is necessary to assess the relative importance of these two pathways.

Experimental Section[26]

2,6-Diphenyl-4-pyrone (1).—The condensation of acetone and 2 equiv of methyl benzoate was effected by means of sodium hydride to form 1,5-diphenyl-1,3,5-pentanetrione by the method of Miles, *et al.*[27] The triketone was converted to the pyrone by means of anhydrous, liquid hydrogen fluoride.[28]

Condensation of 1 with Diphenylmethane.—To a solution of 0.025 mole of sodium amide (prepared[29] from 0.575 g of metallic sodium) in 400 ml of liquid ammonia was added 5.04 g (0.030 mole) of diphenylmethane. To the sodiodiphenylmethane was added 2.48 g (0.01 mole) of 2,6-diphenyl-4-pyrone (**1**). After 30 min, the reaction mixture was poured into a solution of 5 g of ammonium chloride in liquid ammonia. The ammonia was evaporated and the residue was slurried with water and filtered. The filter cake was washed with cold pentane to remove unreacted diphenylmethane. Ethanol recrystallization afforded 2.75 g (0.0066 mole, 66% yield) of 1,5,6,6-tetraphenyl-4-hexene-1,3-dione (**2**), yellow plates, mp 96.5–99°, and after further recrystallization from ethanol and from hexane mp 101.5–103°; $\nu_{\max}^{\mathrm{KBr}}$ 1440–1630 cm^{-1} (broad); $\lambda_{\max}^{95\%\ \mathrm{EtOH}}$ 353 mμ (ε 20,000) and 254 mμ (ε 19,600); $\lambda_{\max}^{95\%\ \mathrm{EtOH,\ base}}$ 359 mμ (ε 17,400) and 239 mμ (ε 17,900).

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[20] See R. J. Light and C. R. Hauser, *J. Org. Chem.*, **25**, 538 (1960), and E. Marcus, J. K. Chan, and C. B. Strow, *ibid.*, **31**, 1369 (1966).

[21] M. L. Miles, T. M. Harris, and C. R. Hauser, *J. Am. Chem. Soc.*, **85**, 3884 (1963).

[22] T. M. Harris and R. L. Carney, *ibid.*, **88**, 2053 (1966); T. Money, J. L. Douglas, and A. I. Scott, *ibid.*, **88**, 624 (1966); L. Crombie, D. E. Games, and M. H. Knight, *Chem. Commun.*, 355 (1966); L. Crombie and A. W. G. James, *ibid.*, 357 (1966).

[23] B. W. Rockett, T. M. Harris, and C. R. Hauser, *J. Am. Chem. Soc.*, **85**, 3491 (1963); R. H. Shapiro, J. M. Wilson, and C. Djerassi, *Steroids*, **1**, 1 (1963).

[24] C. R. Hauser, F. W. Swamer, and J. T. Adams, *Org. Reactions*, **8**, 75 (1954).

[25] M. Nakagawa, F. Nakaminami, F. Ogura, and H. Ono, *Bull. Chem. Soc. Japan*, **35**, 1485 (1962).

[26] Melting points were determined in open capillaries and are corrected. Ultraviolet spectra were determined in 95% ethanolic solution with a Beckman DB spectrophotometer; molar extinction coefficients are shown in parentheses. Infrared spectra were determined with a Beckman IR-10 grating spectrophotometer. The nmr spectra were determined with a Varian Model A-60 spectrometer. Unless stated otherwise, deuteriochloroform solutions containing approximately 10% solute were employed. Chemical shifts are expressed in parts per million (ppm) downfield from internal tetramethylsilane. Microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn.

[27] M. L. Miles, T. M. Harris, and C. R. Hauser, *J. Org. Chem.*, **30**, 1007 (1965).

[28] See K. G. Hampton, T. M. Harris, C. M. Harris, and C. R. Hauser, *ibid.*, **30**, 4263 (1965).

[29] J. T. Adams and C. R. Hauser, *J. Am. Chem. Soc.*, **66**, 1220 (1944).

Anal. Calcd for $C_{30}H_{24}O_2$: C, 86.51; H, 5.81. Found: C, 86.71; 6.19.

The nmr spectrum of **2** showed one-proton signals at 5.30, 5.75 (2-CH), and 5.87 ppm. The first and third of these (4- and 6-CH) were coupled (J = 1 cps). A red enol test was obtained with ethanolic ferric nitrate. Concentration of the mother liquors afforded small amounts of colorless isomer **3**.

Diketone **3** became the major product when sodiodiphenylmethane was prepared from stoichiometric amounts of sodium amide and diphenylmethane. Diphenylmethane (3.36 g, 0.02 mole) was added to a suspension of 0.02 mole of sodium amide (prepared from 0.46 g of sodium) in 300 ml of liquid ammonia. To the sodiodiphenylmethane was added 2.48 g (0.01 mole) of **1**. After 20 min, the reaction was stopped with ammonium chloride. The product was isolated as above to yield after washing with ether and with chloroform 1.8 g (43% yield) of colorless diketone **3**, mp 168–170°, and after recrystallization from acetone mp 174–175°; ν_{max}^{KBr} 1600, 1570, 1490, and 1440 cm^{-1}; λ_{max}^{EtOH} 307 mμ (ϵ 20,900) and shoulder 223 mμ (ϵ 23,200); $\lambda_{max}^{EtOH,\ base}$ 327 mμ (ϵ 19,900) and shoulder 230 mμ (ϵ 24,400).

Anal. Calcd for $C_{30}H_{24}O_2$: C, 86.51; H, 5.81. Found: C, 86.53; H, 5.92.

Diketone **3** gave a red enol test with ethanolic ferric nitrate. The nmr spectrum showed singlets at 6.1 (2-CH) and 3.7 ppm (4-CH_2) of areas 1 and 2, respectively.

Hydrolysis of Diketone 2.—A solution of 200 mg of diketone **2** in 5 ml of 10% sodium hydroxide was heated at 140° for 16 hr in a sealed tube. Glpc indicated that the ether soluble portion of the hydrolysate contained traces of acetophenone. Evaporation of the ethereal solution afforded 122 mg (81% yield) of 4,5,5-triphenyl-4-penten-2-one (**4**), mp 145–147°, and 147.5–148.5° after two recrystallizations from ethanol; ν_{max}^{KBr} 1715 cm^{-1} (C=O stretch); λ_{max}^{EtOH} 273 mμ (ϵ 5640) and 226 mμ (ϵ 9070). The nmr spectrum showed two singlets of areas 3 and 2 at 1.97 (1-CH_3) and 3.63 ppm (3-CH_2), respectively.

Anal. Calcd for $C_{23}H_{20}O$: C, 88.43; H, 6.45. Found: C, 88.33; H, 6.28.

The aqueous solution from the hydrolysis yielded on acidification 80 mg of solid having a broad melting range. Recrystallization from water afforded 23 mg (39% yield) of benzoic acid.

Equilibration of Diketones 2 and 3.—Solutions of diketones **2** and **3** in triethylamine were sealed in tubes and heated at 100° for 48 hr without visible change. However, after an additional 10 hr at 150° the colored and highly soluble **2** had been converted largely to the colorless **3**. The solution was homogeneous at 150° but **3** precipitated at room temperature. From diketone **2** was obtained a 75% yield of **3**, mp 167–171°, and 174–175° after recrystallization from acetone. From diketone **3** was recovered an 85% yield of the same compound, mp 169–171° and 174–175° after recrystallization from acetone. No attempt was made to isolate any diketone **2** that might have been present in the reaction products.

Formation and Protonation of the Dianion of Diketones 2 and 3.—Diketone **2** (109 mg, 0.00026 mole) was added to 0.044 mole of sodium amide (prepared from 1.0 g of sodium) in 150 ml of liquid ammonia. After 20 min, the dark purple solution of the dianion was poured into a solution of 3.0 g of ammonium chloride in 100 ml of ammonia. After evaporation of the ammonia and removal of salts with water, the residue weighed 113 mg and melted at 152–160°. Ultraviolet spectral analysis indicated that the material was 85% pure (88% recovery) and consisted of a 94:6 mixture of diketones **3** and **2**. A similar experiment conducted with diketone **3** afforded a 93:7 mixture of diketones **3** and **2**. The analysis was made on the basis of absorbance at 332 and 360 mμ. The former of these is an isosbestic point in the spectra of the two compounds and the latter is a wavelength at which the absorbance of **2** exceeds that of **3** significantly.

Cyclization of Diketones 2 and 3 with Hydrogen Fluoride.—To 0.241 g (0.00058 mole) of diketone **3** in a polyethylene bottle was added 15 ml of anhydrous, liquid hydrogen fluoride. The orange colored solution was allowed to evaporate and the residue was taken up in a mixture of ether and aqueous sodium bicarbonate solution. The ether layer was separated, dried, and evaporated to afford 0.226 g (98% yield) of 1-phenacyl-3,4-diphenylnaphthalene (**6**) as colorless crystals, mp 151–153°, and 154–155° after recrystallization from ethanol; ν_{max}^{KBr} 1690 cm^{-1} (C=O stretch), λ_{max}^{EtOH} 293 mμ (ϵ 11,500) and 245 mμ (ϵ 56,300). The methylene singlet appeared at 4.8 ppm in the nmr spectrum.

Anal. Calcd for $C_{30}H_{22}O$: C, 90.42; H, 5.56. Found: C, 90.55; H, 5.85.

The dinitrophenylhydrazone melted at 236–237.5° after recrystallization from ethanol–ethyl acetate.

Anal. Calcd for $C_{36}H_{26}N_4O_4$: C, 74.73; H, 4.53; N, 9.68. Found: C, 75.04; H, 4.96; N, 9.37.

Cyclization of 0.176 g (0.00042 mole) of **2** was effected similarly to afford 0.155 g (92% yield) of ketone **6**, mp 152–153° and 153–154° after recrystallization from ethanol–acetone. The mixture mp with ketone **6** prepared from diketone **3** was undepressed.

Condensation of 1 with Acetophenone.—Acetophenone (3.6 g, 0.030 mole) was added to a suspension of 0.025 mole of sodium amide (prepared[29] from 0.58 g of sodium) in 300 ml of anhydrous, liquid ammonia, followed after 5 min by 2.48 g (0.01 mole) of pyrone **1** and 150 ml of anhydrous ether. The reaction mixture was neutralized after 1.5 hr with 15 g of ammonium chloride and the ammonia was evaporated. The residue was shaken with a mixture of 100 ml of ether and 100 ml of water and filtered to afford 2.2 g (60% yield) of 2-hydroxy-6-phenacylidene-2,4-diphenyl-5,6-dihydro-(2H)-pyran (**9**), mp 193–195° dec. No more of the adduct was obtained on concentration of the ethereal solution. Recrystallization of **9** from acetone–ethanol gave mp 199.5–201.5° dec (mp 206–208° dec with very rapid heating); ν_{max}^{KBr} 3400 (OH stretch), 1668, 1650, 1610, 1595 and 1575 cm^{-1}; $\nu_{max}^{CHCl_3}$ 3450 cm^{-1} (OH stretch); λ_{max}^{EtOH} (freshly prepared) 287 mμ (ϵ 21,400) and 257 mμ (ϵ 18,000).

Anal. Calcd for $C_{25}H_{20}O_3$: C, 81.50; H, 5.47. Found: C, 81.57; H, 5.61.

Hemiketal **9** gave an enol test with hot ethanolic ferric nitrate. The nmr spectrum of **9** showed, in addition to a complex aromatic multiplet, signals at 3.15 (CH_2), 5.37 and 6.63 ppm of areas 2, 2, and 1, respectively. Treatment of the deuteriochloroform solution with deuterium oxide caused the signal at 5.37 ppm to decrease to one half its original size indicating that it was a composite of the hydroxylic and a nonexchangeable proton.

Aromatic Dehydration of Hemiketal 9.—Solutions of hemiketal **9** in ethanol were unstable at room temperature and over a period of several days underwent cyclization to the corresponding *o*-hydroxybenzophenone **11**. The conversion could be observed by thin layer chromatography and by the change in ultraviolet spectra of solutions. The conversion was conducted preparatively by heating 100 mg (0.00027 mole) of **9** and 4 ml of pyridine in a sealed tube for 2 hr at 140°. The pyridine was removed and the product was recrystallized from ethanol to afford 69.3 mg (73% yield) of 2-hydroxy-4,6-diphenylbenzophenone (**11**), mp 158–160°, and 159–160° after further recrystallization from carbon disulfide; ν_{max}^{KBr} 1625 cm^{-1} (C=O stretch), λ_{max}^{EtOH} 243 mμ (ϵ 38,000) and shoulder 310 mμ (ϵ 6300).

Anal. Calcd for $C_{25}H_{18}O_2$: C, 85.69; H, 5.18. Found: C, 85.92; H, 5.08.

Thin layer chromatography indicated that the product was homogeneous. The nmr spectrum showed a chelated hydroxyl (9.7 ppm) in addition to an aromatic multiplet.

Nonaromatic Dehydration of Hemiketal 9.—Treatment of 61 mg (0.000166 mole) of hemiketal **9** with 15 ml of anhydrous, liquid hydrogen fluoride for 2 hr afforded a dark red residue after evaporation of the hydrogen fluoride. The residue was shaken with a mixture of ether and 5% sodium bicarbonate. The ether layer was separated and the solvent was removed to leave 59 mg of red, crystalline material. Recrystallization from ethanol afforded 47 mg (81% yield) of 2-phenacylidene-4,6-diphenylpyran (**12**), mp 162–163° (Kofler hot stage); ν_{max}^{KBr} 1650, 1580, 1525, and 1500 cm^{-1}; λ_{max}^{EtOH} 474 mμ (ϵ 17,100), 350 (11, 000), 291 (26,400), 236 (20,400), and shoulder 366 (9390); $\lambda_{max}^{EtOH,\ H_2SO_4}$ 476 mμ (ϵ 20,500), 320 (20,300), 236 (16,400), and shoulder 445 (18,900).

Anal. Calcd for $C_{25}H_{18}O_2$: C, 85.69; H, 5.18. Found: C, 85.50; H, 5.26.

The nmr spectrum showed in addition to the aromatic multiplet, three signals of relative areas 1 at 6.5, 6.8, and 8.7 ppm. It is likely that the most deshielded proton is at the 3 position of the pyran ring. No protons were readily exchanged with deuterium oxide.

Condensation of 1 with Benzoylacetone.—Benzoylacetone (4.86 g, 0.03 mole) was added to 0.06 mole of sodium amide (prepared[29] from 1.38 g of sodium) in 300 ml of liquid ammonia. After 20 min, 2.48 g (0.01 mole) of pyrone **1** and 100 ml of anhydrous ether were added. The dark purple solution was neutralized with ammonium chloride after 1.5 hr to give a colorless solution. The ammonia was evaporated and the residue was suspended in a mixture of ether and cold, dilute hydrochloric acid. The suspended solid (**16**) was separated by filtration.

Additional material precipitated when the ether was concentrated to give a total of 2.3 g (56% yield) of 2-hydroxy-2-phenacyl-6-phenacylidene-4-phenyl-5,6-dihydro-(2H)-pyran (**16**), mp 152–155° dec, and after recrystallization from ethanol 156–158° dec; $\nu_{\max}^{\mathrm{KBr}}$ 3400 (OH stretch), 1670, 1640, 1610, 1590, and 1575 cm^{-1}; $\nu_{\max}^{\mathrm{CHCl_3}}$ 3450 cm^{-1} (OH stretch); $\lambda_{\max}^{\mathrm{EtOH}}$ 286 mμ (ϵ 21,900) and 250 mμ (ϵ 29,800).

Anal. Calcd for $C_{27}H_{22}O_4$: C, 79.01; H, 5.40. Found: C, 78.81; H, 5.40.

Hemiketal **16** gave an enol test with hot, ethanolic ferric nitrate. The compound was stable in dilute sulfuric acid at room temperature. The nmr spectrum showed in addition to the aromatic multiplet, three signals of area 1 at 6.55, 5.5, and 5.13 ppm. The last of these was hydroxylic and showed facile exchange with deuterium oxide. The spectra of the two methylene groups were complex because of nonequivalence of the geminal hydrogens. The methylene groups were centered at 3.2 and 3.5 ppm. The hydrogens of the latter were more nearly equivalent.

Attempted dehydration with anhydrous, liquid hydrogen fluoride afforded an intractable, red powder, which was not further characterized.

Aromatic Dehydration of Hemiketal 16.—A suspension of 155 mg (0.00038 mole) of hemiketal **16** in 2.5 ml of ethanol was heated at 100° for 2 hr in a sealed tube. Evaporation of the solvent and washing with 1 ml of ethanol left 128 mg (86%) of 2-hydroxy-6-phenacyl-4-phenylbenzophenone (**17**), mp 174–176°, and 176.5–177° after recrystallization from ethanol–water; $\nu_{\max}^{\mathrm{KBr}}$ 3330 (OH stretch), 1680, and 1655 cm^{-1}; $\nu_{\max}^{\mathrm{CHCl_3}}$ 3300 cm^{-1} (OH stretch); $\lambda_{\max}^{\mathrm{EtOH}}$ 248 mμ (ϵ 35,000), $\lambda_{\max}^{\mathrm{EtOH,\ base}}$ 395 mμ (ϵ 2800) and 245 mμ (ϵ 45,500).

Anal. Calcd for $C_{27}H_{20}O_3$: C, 82.63; H, 5.14. Found: C, 82.43; H, 5.30.

The nmr spectrum showed a sharp singlet (CH_2) at 4.1 (area 2) and a broad singlet (OH) at 9.1 ppm (area 1). The latter exchanged rapidly with deuterium oxide.

Condensation of 1 with Phenylacetic Acid.—Phenylacetic acid (2.72 g, 0.02 mole) was added to a suspension of 0.04 mole of sodium amide (prepared[29] from 0.92 g of sodium) in 400 ml of liquid ammonia. After 30 min, 2.48 g (0.01 mole) of pyrone **1** was added. A purple solution was formed. After 45 min, the ammonia was evaporated and ether was added to the residue. The resulting suspension was poured into a mixture of ice and 40 ml of 12 *N* hydrochloric acid. The layers were separated and the ether layer was washed rapidly with 5% sodium bicarbonate,[30] dried, and evaporated. The residue crystallized upon readdition of a small amount of ether to give 2.50 g (65% yield) of 2,3,7-triphenyl-3-heptene-5,7-dionoic acid (**18**), mp 156–158° dec, and 165–165.5° dec after recrystallization from benzene; $\nu_{\max}^{\mathrm{KBr}}$ 1705 and 1510–1640 cm^{-1} (broad); $\lambda_{\max}^{\mathrm{EtOH}}$ 354 mμ (ϵ 19,200) and 252 mμ (ϵ 10,000).

Anal. Calcd for $C_{25}H_{20}O_4$: C, 78.11; H, 5.24. Found: C, 78.41; H, 5.29.

The compound gave a strong greenish black enol test with ethanolic ferric nitrate and was soluble in aqueous sodium bicarbonate. The nmr spectrum of **18** in acetone showed in addition to an aromatic multiplet, three signals of equal area at 4.93, 5.88, and 6.13 ppm. Coupling (J = 1 cps) was observed between the first and third of these. The spectrum was not materially different in deuteriochloroform solution; equilibration with deuterium oxide caused no observable change in the spectrum. The signal arising from the hydroxylic protons could not be detected but may have been obscured by the aromatic multiplet.

In a similar experiment in which the phenylacetic acid dianion was in a mixture of ether and a small amount of ammonia, the addition of pyrone **1** afforded 2.25 g (58% yield) of another isomer, mp 121–124° dec, and 125–126° dec after recrystallization from benzene–hexane, $\lambda_{\max}^{\mathrm{EtOH}}$ 310 mμ (ϵ 14,100) and 246 mμ (ϵ 16,000).

Anal. Calcd for $C_{25}H_{20}O_4$: C, 78.11; H, 5.24. Found: C, 78.25; H, 5.21.

The compound gave a brick-red enol test with ethanolic ferric nitrate. The infrared spectrum showed a stronger band at 1700 cm^{-1} than had **18** and weaker enol absorption in the 1500–1650-cm^{-1} region. A sharp, medium strength band was superimposed on the enol band at 1610 cm^{-1}. The nmr spectrum was complex and solvent dependent. This probably reflected varying mixtures of tautomers that were present in solution. Acid **18** did not appear to be a part of this mixture.

Cyclization of 18 and Its Isomer with Hydrogen Fluoride.—Anhydrous, liquid hydrogen fluoride (15 ml) was added to 1.0 g of **18** in a polyethylene bottle. The solution was allowed to stand overnight, during which time the hydrogen fluoride evaporated to leave 0.86 g (90%) of 6-phenacyl-3,4-diphenyl-2-pyrone (**19**) as yellow crystals, mp 152–160°, and 164.5–166° after recrystallization from benzene–hexane; $\nu_{\max}^{\mathrm{KBr}}$ 1710 cm^{-1} (carbonyl) but no enol band; $\lambda_{\max}^{\mathrm{EtOH}}$ 328 mμ (ϵ 9600), 284 (7900), and 242 (27,900).

Anal. Calcd for $C_{25}H_{18}O_3$: C, 81.95; H, 4.95. Found: C, 81.64; H, 5.13.

The nmr spectrum showed, in addition to the aromatic multiplet, singlets of areas 2 and 1 at 4.17 (CH_2) and 6.28 ppm (ring CH), respectively.

The dinitrophenylhydrazone melted at 227–229° after recrystallization from ethyl acetate.

Anal. Calcd for $C_{31}H_{22}N_4O_6$: C, 68.13; H, 4.06. Found: C, 67.92; H, 4.20.

The low-melting condensation product underwent cyclization in 88% yield under similar conditions to afford 2-pyrone **19**, which was identical in all respects with that prepared from the high-melting acid.

Registry No.—**1**, 1029-94-3; **2**, 7593-07-9; **3**, 7593-08-0; **4**, 7593-09-1; **6**, 7593-10-4; dinitrophenylhydrazone of **6**, 7593-11-5; **9**, 7593-12-6; **11**, 7593-13-7; **12**, 7593-14-8; **16**, 7593-15-9; **17**, 7593-76-0; **18**, 7593-17-1; **19**, 7593-18-2; dinitrophenylhydrazone of **19**, 7593-19-3.

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(30) Phenylacetic acid was removed from the ether rapidly by this treatment. The product (**18**) extracted more slowly.