The Base-Catalyzed Self-Condensation of α,β-Unsaturated Ketones. Structure of Heilbron's Styryl Alkyl Ketone Dimers[1]

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The crystalline dimers obtained by base-catalyzed self-condensation of certain styryl alkyl ketones have been shown to be 4-alkanoyl-2-alkyl-3,5-diarylcyclohexanones. They are not 1,3-dialkanoyl-2,4-diarylcyclobutanes, as suggested previously by other workers. Three such dimers have been dehydrogenated to 4-alkanoyl-2-alkyl-3,5-diarylphenols and the latter substances cleaved to 2-alkyl-3,5-diarylphenols and alkanoic acids. 2-Ethyl-3,5-diphenylphenol obtained by this reaction sequence was identical with a sample prepared by an independent synthesis. Dimers have been obtained in 13–22% yield from ketones of the type $ArCH{=}CHCOCH_2R$ where R may be any alkyl group other than methyl and Ar is a phenyl group, unsubstituted or one having electron-releasing groups in the *para* (preferably) or *meta*, but not *ortho* position.

In a previous report[3] it was concluded that the base-catalyzed self-condensation of α,β-unsaturated ketones, $RCH_2CH{=}CHCOCH_2R'$, proceeds initially as a Michael condensation, in all known examples of this reaction, to form as the primary product an acyclic monoolefinic 1,5- or 1,7-diketone. As the final product, four structural types (A–D) were recognized: (A) an acyclic monoolefinic diketone, (B) a cyclic saturated diketone, (C) a cyclic monoolefinic ketol, and (D) a cyclic diolefinic monoketone. Products B–D arise from A by Michael or aldol condensations. Numerous reported examples of these various possibilities are now known.[3,4] In the present study the self-condensation of a group of styryl alkyl ketones to cyclic saturated diketones (product type B) has been examined and the structures of the products established. Throughout the following discussion the term monomer is applied to the styryl alkyl ketones, and dimer to the derived cyclic saturated diketones.

The base-catalyzed self-condensation of certain styryl alkyl ketones ($ArCH{=}CHCOCH_2R$) to form dimeric saturated diketones was first recognized by Heilbron and co-workers,[5–7] who prepared many such compounds. These workers also noted the existence of certain dimers of this type which earlier had been described as monomers by others.[8–11] Since the publication of Heilbron's work, only one other report has appeared describing this reaction.[12] None of the reports describes structure elucidation studies on the dimers.

Studies of reaction conditions were made by Heilbron[5–7] and have been extended by us. The condensation is generally conducted with one mole-equivalent each of aromatic aldehyde and methyl ketone for *in situ* formation of the styryl alkyl ketone monomer, which then self-condenses. Although the pure styryl alkyl ketones may be employed, this procedure usually offers no advantage. Sodium hydroxide catalyst (*ca.* 0.2 mole-equivalent) in *ca.* 97% ethanol (3% water) solvent and a reaction time of two to ten days at room temperature, or four to six hours at reflux temperature, were employed in the present work. Water solvent favors monomer formation.[5–7] (In the preparation of styryl propyl ketone dimer 87% ethanolic sodium hydroxide led to 14.5% yield of dimer, whereas ethanolic sodium ethoxide gave a 17.4% yield.) The reaction is not catalyzed by ultraviolet light or heat in the absence of base. Yields are generally low (13–22%) but the reaction is very easily adapted to large-scale preparations—the dimer crystallizes from the reaction solution and is recovered by simple filtration. Usually a single recrystallization from ethanol or ethanol–ethyl acetate produces a pure product. In the condensation of 4-dimethylaminobenzaldehyde with 2-octanone at room temperature (twenty-two hours, 0.4 mole-equivalent of sodium hydroxide) the product which crystallized from the reaction mixture was the monomer, 4-dimethylaminostyryl hexyl ketone (52% yield); by heating the monomer in ethanolic sodium hydroxide solution (50–78°, twenty-four hours), the dimer V was produced in 17.9% yield. Table I summarizes examples of the present study; yields, seldom mentioned in Heilbron's work, are recorded.

Properties of the various styryl alkyl ketone dimers are entirely similar. They are all colorless and relatively much higher melting than the corresponding monomers. Their solubility in most organic solvents is somewhat low. They may be crystallized from hot ethanol or ethanol–ethyl acetate, often in the form of very long, fine needles. Their infrared spectra reveal no hydroxyl or olefinic stretching bands; strong carbonyl absorption is found, usually two bands near 1700 and 1720 cm.$^{-1}$ in potassium bromide, but only one near 1720 cm.$^{-1}$ in carbon tetrachloride solution. The ultraviolet spectra indicate two unconjugated, independently absorbing aryl groups per molecule; in ethanol λ_{max} near 259 mμ (ϵ_{max} 400–600). The compounds do not decolorize potassium permanganate in acetone solution. It is evident that they are saturated diketones as originally suggested by Heilbron.[5–7]

Although the number of different examples of the dimerization reaction previously reported is large (*ca.* twenty-two)[5–7,9,12] no chemical evidence previously has been presented which establishes the structure of any one. Heilbron[6,7] noted the similarity in certain chemi-

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(1) Presented at the 140th National American Chemical Society Meeting, Chicago, Ill., September, 1961.

(2) Deceased, October 31, 1961.

(3) A. T. Nielsen, D. W. Moore, and K. Highberg, *J. Org. Chem.*, **26**, 3691 (1961).

(4) N. Bacon, S. Brewis, G. E. Usher, and E. S. Waight, *J. Chem. Soc.*, 2255 (1961).

(5) R. Dickinson, I. M. Heilbron, and F. Irving, *ibid.*, 1888 (1927).

(6) (a) I. M. Heilbron and F. Irving, *ibid.*, 2323 (1928); (b) I. M. Heilbron and F. Irving, *ibid.*, 931 (1929).

(7) I. M. Heilbron, R. N. Heslop, F. Irving, and J. S. Wilson, *ibid.*, 1336 (1931).

(8) D. Vorlander, *Ber.*, **30**, 2267 (1897).

(9) H. Rupe and S. Wild, *Ann.*, **414**, 111 (1918).

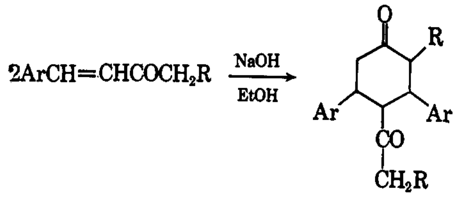
(10) M. Scholtz and W. Meyer, *Ber.*, **43**, 1861 (1910).

(11) H. Carette, *Compt. rend.*, **131**, 1225 (1900).

(12) M. Metayer, *Rec. trav. chim.*, **71**, 153 (1952).

TABLE I

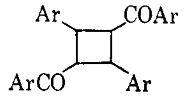
SYNTHESIS OF STYRYL ALKYL KETONE DIMERS



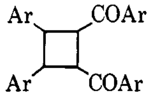
Dimer	Ar	R	Yield, %[a]	M.p., °C.	Formula	Calcd. C	Calcd. H	Calcd. Mol. wt.	Found C	Found H	Found Mol. wt.
I	C_6H_5	Ethyl	14.5[b]	198–199[c]	$C_{24}H_{28}O_2$	82.72	8.10	348.5	82.80	8.29	319
II	C_6H_5	Isopropyl	22.4[d]	205–206[d]	$C_{26}H_{32}O_2$	82.93	8.57	376.5	82.76	8.03	412
III	C_6H_5	Octyl	13.9	116–118[e]	$C_{36}H_{52}O_2$	84.32	10.22	512.8	84.74	10.36	484
IV	4-$CH_3C_6H_4$	Butyl	20.2	165–167[f]	$C_{30}H_{40}O_2$	83.28	9.32	432.6	83.06	9.54	465
V	4-$(CH_3)_2NC_6H_4$	Pentyl	17.9	185–186[f]	$C_{34}H_{50}N_2O_2$[g]	78.51	9.72	518.8	78.56	9.54	492
VI	4-*i*-PrC_6H_4	Hexyl	12.6	161–162[f]	$C_{38}H_{56}O_2$	83.77	10.36	544.8	84.02	10.38	538

[a] Yields of pure recrystallized material. [b] Yield, 17.4% with sodium ethoxide in ethanol, m.p. 196–197°. [c] Reported m.p. 194–195°.[6b] [d] Reported 13.6% yield[6b]; m.p. 202°,[6b] 209°.[12] [e] Reported m.p. 116°.[6a,11] [f] New compounds. [g] Calcd.: N, 5.40. Found: N, 5.21.

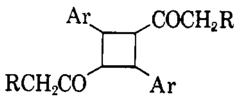
cal and physical properties between his dimers and those obtained by Stobbe[13,14] by photodimerization of chalcones (ArCH=CHCOAr). Stobbe's "truxillic" ketones (VII) are produced by prolonged exposure of chalcones to ultraviolet illumination. They form monocarbonyl derivatives (with difficulty) in contrast to the isomeric 1,2-diaroyl "truxinic" ketones (VIII), which have relatively lower melting points and readily form biscarbonyl derivatives. Heilbron's dimers were described as saturated and relatively inert, forming monoximes with difficulty, and they were arbitrarily assigned the cyclobutane ("truxillic" type) structure (IX). Despite lack of evidence supporting structure IX, the notion has persisted that the dimers are cyclobutane derivatives,[12,15] although an observation has been made that this structure is probably incorrect.[16]



VII



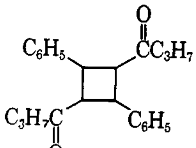
VIII



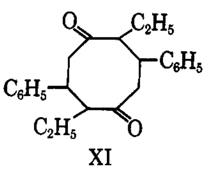
IX

Ar = Aryl; R = Alkyl

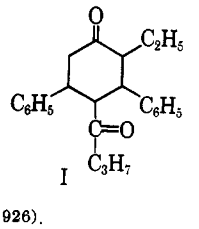
Styryl propyl ketone dimer (I), the simplest known example,[6b,8] was selected for detailed structure elucidation studies. By considering the base-catalyzed dimerization of the monomer to proceed by two successive Michael additions to a cyclic saturated diketone (product type B, discussed previously), three possible structures could be considered (X, XI, and I). These products would arise through anions (XII and XIII) of two possible intermediate acyclic monoolefinic 1,5-diketones.



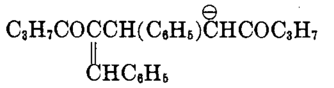
X



XI



I



$$C_3H_7CO\underset{\underset{\displaystyle CHC_6H_5}{\|}}{C}CH(C_6H_5)\overset{\ominus}{C}HCOC_3H_7$$

XII

$$C_2H_5\overset{*}{C}H_2CO\overset{\ominus}{C}HCH(C_6H_5)CH(C_2H_5)COCH{=}CHC_6H_5$$

XIII

Anion XII would seem an unlikely intermediate since its formation would require either prior abstraction of an unreactive vinyl proton from the monomer, or reaction through an anion of a ketol ($C_3H_7CO\overset{\ominus}{C}HCHOHC_6H_5$). It could lead to X or I, but formation of a cyclobutane ring (X) is not favored in Michael condensations.[17] To produce an anion leading to XI would require prior prototropic rearrangement of XIII to place the negative charge on the starred carbon atom. However, XIII is formed directly in the initial Michael condensation of two monomers and could lead directly to the favored six-membered ring product (I) in the second, intramolecular, Michael condensation.

Chemical evidence establishing structure I for styryl propyl ketone dimer was obtained in the following manner. Heating I with palladium-on-charcoal catalyst gave a ketone phenol, $C_{24}H_{24}O_2$, m.p. 172–173°. Strong hydroxyl stretching absorption was present at 3450 cm.$^{-1}$; carbonyl absorption was shifted to 1670 cm.$^{-1}$ (potassium bromide) in the dehydrogenated product. The ultraviolet spectrum was changed from one resembling benzene (in I) to one having a single intense band at 239 mμ (ε 21,500, ethanol). These data support a phenol structure, having an alkanoyl group attached to the aromatic ring, such as compound XIV. Heating the ketone phenol with a catalytic amount of camphorsulfonic acid[18] led to an oily product (not purified) having hydroxyl absorption in the infrared, strong carbonyl absorption at 1740 cm.$^{-1}$ (ester), and practically no absorption near 1670 cm.$^{-1}$. This mixture is believed to be principally ester XVII and phenol XX. It was treated with hot aqueous ethanolic sodium hydroxide solution to yield 3,5-diphenyl-2-ethylphenol (XX), m.p. 82–83° (λ_{max}^{EtOH} 238

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(13) H. Stobbe and A. Hensel, *Ber.*, **59**, 2254 (1926).

(14) H. Stobbe and K. Bremer, *J. prakt. Chem.*, **123**, 1 (1929).

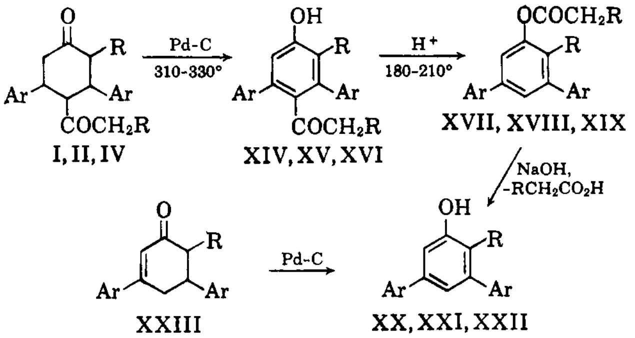
(15) R. A. Raphael in "Chemistry of Carbon Compounds," Vol. IIA; E. H. Rodd, Ed., Elsevier, 1953, pp. 48, 57.

(16) E. R. H. Jones and H. P. Koch, *J. Chem. Soc.*, 393 (1942).

(17) E. D. Bergmann, D. Ginsburg, and R. Pappo, *Org. Reactions*, **10**, 248 (1959).

(18) K. W. Rosenmund and W. Schnurr, *Ann.*, **460**, 56 (1928).

mμ, ϵ 25,300), and butyric acid (identified as its *p*-phenylphenacyl ester). The acid-catalyzed treatment evidently led to a retrograde Fries rearrangement of XIV which produced ester XVII. An authentic sample of XX was synthesized from the known 3,5-diphenyl-6-ethyl-2-cyclohexen-1-one (XXIII)[19] by heating with palladium on charcoal; it was identical with the sample obtained from I.



I, XIV, XVII, XX, XXIII. $R = Et, Ar = C_6H_5$
II, XV, XVIII, XXI. $R = i\text{-}Pr, Ar = C_6H_5$
IV, XVI, XIX, XXII. $R = Bu, Ar = 4\text{-}CH_3C_6H_4$

Preceding degradation sequence also was successful with styryl isobutyl ketone dimer (II)[20] and 4-methylstyryl amyl ketone dimer (IV), leading to ketone phenols XV and XVI, respectively. Heating these substances with camphorsulfonic acid, followed by saponification of the intermediate esters XVIII and XIX, led to phenols XXI and XXII, respectively (the latter compound was a liquid and not characterized). In each saponification reaction the respective aliphatic acid was isolated and identified as its *p*-phenylphenacyl ester. From XIX hexanoic acid itself was isolated. The amount of steam volatile organic acid (isovaleric) obtained by saponification of XVIII was 0.95 mole-equivalent. It is believed reasonable to conclude that other styryl alkyl ketone dimers which have physical and chemical properties like I are also 4-alkanoyl-2-alkyl-3,5-diarylcyclohexanones.

The scope of the dimerization reaction has been examined with respect to structure of alkyl (R) and aryl (Ar) groups in the styryl ketone monomer, $ArCH{=}CHCOCH_2R$. Heilbron determined that the reaction failed with styryl isopropyl and styryl *t*-butyl ketones and thus established the necessity of an RCH_2 group.[6,21] All monomers with alkyl or arylalkyl substituents RCH_2 which have been examined undergo the reaction, including those with R = *n*-alkyl from ethyl through octyl,[6] isopropyl,[6] 2-methylbutyl,[9] benzyl,[7,22] and β-phenylethyl,[7,22] but not methyl.[5,23] The reaction fails when R = hydrogen.[5] It should be noted that R cannot be aryl, for in the condensation of aldehydes with benzyl methyl ketone condensation occurs on the methylene group.[7]

The position and type of ring substituent in the phenyl group of the styryl alkyl ketone monomer affect the dimerization reaction. Successful dimerizations have been realized with phenyl substituents hydrogen, *p*-methyl and *p*-isopropyl reacting at room temperature, and with *p*-dimethylamino, *p*-methoxy, *p*-chloro, 3,4-dimethoxy, and 3,4-methylenedioxy reacting at refluxing ethanol temperature (but not at room temperature). Failures have been reported for *o*-chloro, *o*-methyl, *o*-hydroxy, *m*-chloro, *m*-methoxy, *m*-nitro, and *p*-nitro substituents. The *ortho* substituents prevent the reaction and *para* substitution, relative to *meta*, appears to facilitate it. The effects of ring substitution on certain other Michael reactions fall closely into this pattern of reactivity; *e.g.*, addition of ethyl acetoacetate to various unsymmetrically substituted dibenzylideneacetones, and diethyl malonate to ring substituted benzylidene methyl ketones.[24] For these various Michael reactions, *p*-phenyl substituents affect the yield, to a rough approximation, in the order: CH_3, i-Pr > H > $(CH_3)_2N$ > OH > CH_3O, Cl > NO_2. This order reflects the position of equilibrium, not the rate of Michael addition. Although it follows closely Taft's σ_I values,[25] it is difficult to attach significance to this observation until more is learned of the effects of ring substituents on the forward and reverse Michael reaction. The reaction would be expected to resemble cyanohydrin formation of aromatic aldehydes where electron-withdrawing groups enhance the rate.[26] On the other hand, it should be noted that the effect of ring substituents on the cyanohydrin equilibrium is not profound in degree,[26] and (by comparison) somewhat different reaction constants (ρ) for the forward and/or reverse Michael addition could produce the equilibrium order we observed.

Experimental[27]

4-Butanoyl-3,5-diphenyl-2-ethylcyclohexan-1-one [Styryl Propyl Ketone Dimer (I)].—The procedure of Heilbron and Irving[6b] was used with slight modifications. Benzaldehyde (106 g., 1 mole) and 2-pentanone (86 g., 1 mole) were dissolved in 500 ml. of absolute ethanol. A 10% solution of sodium hydroxide (75 ml.) was added all at once and the mixture was stirred for a few moments. The temperature rose rapidly to 40° and within 20 min. had reached a maximum of 49°. After about 40 min. crystals were noted in the orange solution. The mixture was stored in the dark at room temperature for 6 days before filtering the product and washing with ethanol; the crude product weighed 34.4 g., m.p. 180–193°. The filtrate was chilled and the second crop of crystals was recrystallized from a mixture of ethyl acetate and ethanol to yield 5.0 g., m.p. 193–194°. Recrystallization of the first crop from the same solvent mixture gave 20.0 g., m.p. 198–199°. The total yield of recrystallized material, 25 g., was 14.5%.

The product failed to decolorize potassium permanganate in acetone solution. The ultraviolet absorption spectrum revealed several sharp maxima of low intensity (ϵ_{max} in parentheses): 243

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[19] W. Dieckmann, *Ber.*, **45**, 2703 (1912).

[20] The dimer II has been isolated in three isomeric forms[12] (m.p. 205°, 170°, and 140°) shown in our work to be diastereoisomers. The stereochemistry of these substances will be discussed in a forthcoming publication.

[21] Phenyl *n*-alkyl ketones undergo normal Michael addition to chalcone, whereas isobutyrophenone does not; *cf.* D. B. Andrews and R. Connor *J. Am. Chem. Soc.*, **57**, 895 (1935).

[22] A number of monomers of the type, $ArCH{=}CHCO(CH_2)_nC_6H_5$ (n = 2,3), have been prepared in *ca.* 50% aqueous ethanolic sodium hydroxide [C. M. Clark and J. D. A. Johnson, *J. Chem. Soc.*, 126 (1962)]; no evidence of dimers was found. On the other hand, Heilbron[7] found dimers to form from this monomer type when Ar = C_6H_5 by reaction in *ethanolic* sodium hydroxide. This difference in results confirms the importance of solvent in the reaction.[5-7]

[23] Crystalline products have been obtained by condensation of benzaldehyde and 2-methoxybenzaldehyde with 2-butanone (product formulas $C_{20}H_{20}O_2$ and $C_{24}H_{26}O_5$, respectively). Preliminary evidence indicates their structures to be of a different type from I (unpublished results, this laboratory); *cf.* ref. 5 and C. V. Gheorghiu and B. Arwentiew, *Bull. soc. chim. France*, (4) **47**, 195 (1930).

[24] Ref. 17, p. 219 and pp. 300–327.

[25] R. W. Taft, Jr., and I. C. Lewis, *J. Am. Chem. Soc.*, **80**, 2436 (1958).

[26] J. W. Baker and H. B. Hopkins, *J. Chem. Soc.*, 1089 (1949).

[27] Melting points were determined on a Kofler block and are uncorrected. Ultraviolet absorption spectra were measured in 95% ethanol. Infrared spectra of liquids were determined neat unless otherwise stated.

(285), 248 (354), 253 (469), 258 (596), 265 (555), and 268 mμ (445), and a broad band at 288 mμ (372). The infrared spectrum (potassium bromide) revealed no absorption near 3500 cm.$^{-1}$ but split carbonyl bands (1690 and 1720 cm.$^{-1}$); in carbon tetrachloride solution a single carbonyl band appeared at 1720 cm.$^{-1}$. The other dimers prepared (Table I) were found to have very similar ultraviolet and infrared spectra.

The preparation of I was repeated using sodium ethoxide catalyst (0.2 mole) in 500 ml. of absolute ethanol and a room temperature reaction time of 65 hr. The crude product (40.0 g.) was recrystallized from ethanol to give 30.2 g. (17.4% yield), m.p. 196–197°.

Preparation of Styryl Alkyl Ketone Dimers.—The first procedure described, used for preparing I, was employed for the preparation of other dimers, except that the solvent was *ca.* 97% ethanol rather than 87% [one mole each of aldehyde and ketone were dissolved in 680 ml. of absolute ethanol and 30 ml. of 25% sodium hydroxide solution (aqueous) was added]. The following aldehydes and ketones were condensed at room temperature (reaction times listed in parentheses): benzaldehyde with methyl isobutyl ketone to form II (10 days); *p*-tolualdehyde and 2-heptanone to form IV (12 days); cuminaldehyde with 2-nonanone to form VI (6 days). In these reactions there was an initial rapid exothermic reaction with a temperature rise to *ca.* 40–50°, followed by cooling to room temperature within *ca.* 3 hr. The reaction time selected was somewhat arbitrary and often longer than necessary, since almost all of the crystalline product appeared to form within 1–2 days. Benzaldehyde and 2-undecanone were condensed to form III by initially heating on the steam bath for 4 hr., then allowing to stand at room temperature for 42 hr. The products were recrystallized from ethanol or ethyl acetate or mixtures of these solvents. The preparation of one other dimer (V) is described subsequently. Yields, melting points, elemental analyses, and molecular weights of pure, recrystallized products are summarized in Table I. Reactions, separately, of 4-nitro- and 3-nitrobenzaldehyde with 2-decanone resulted in the formation of dark tarry material from which no crystalline product could be isolated.

4-Dimethylaminostyryl Hexyl Ketone.—To a solution of 74.6 g. (0.5 mole) of 4-dimethylaminobenzaldehyde and 64.1 g. (0.5 mole) of 2-octanone in 340 ml. of absolute ethanol was added 30 ml. of a 25% aqueous sodium hydroxide solution. The aldehyde slowly dissolved as the mixture was agitated and the temperature rose from 22° to 27°. The dark solution on standing at room temperature for 22 hr. deposited yellow crystals which were removed by filtration; yield 86.8 g., m.p. 71–72°. Recrystallization from ethanol gave large yellow needles, 67.6 g. (52% yield), m.p. 77–78°; a second recrystallization from ethanol did not raise the melting point. Infrared bands at 1660 (C=O) and 1640 (C=C) cm.$^{-1}$ (Nujol mull).

Anal. Calcd. for $C_{17}H_{25}NO$: C, 78.71; H, 9.72; N, 5.40; mol. wt., 259.4. Found: C, 78.83; H, 9.42; N, 5.34; mol. wt., 290, 308.

4-Hexanoyl-3,5-bis(4-dimethylaminophenyl)-2-pentylcyclohexan-1-one [4-Dimethylaminostyryl Hexyl Ketone Dimer (V)].—A mixture of 81.8 g. of 4-dimethylaminostyryl hexyl ketone, 300 ml. of absolute ethanol, and 25 ml. of 25% aqueous sodium hydroxide solution was heated to 50–55° to obtain a solution and maintained at this temperature for 17 hr. and at 75–78° for an additional 7 hr. After cooling to room temperature and allowing to stand 24 hr. the mixture was filtered to yield 19.7 g. of crystals, m.p. 173–179°. Recrystallization from ethanol–ethyl acetate gave 14.6 g. (17.9%) of needles, m.p. 184–186°; recrystallization gave 13.9 g., m.p. 185–186°; properties are summarized in Table I.

Attempted Photodimerization of Styryl Isobutyl Ketone.—Styryl isobutyl ketone was prepared by the procedure of Metayer.[12] A 94-g. sample (0.5 mole) was placed in a quartz flask and irradiated for 96.5 hr. using a high-energy ultraviolet lamp while the liquid was stirred continuously. Distillation gave 86.9 g. (92.5%) of recovered ketone and a small amount of dark liquid residue which failed to crystallize.

4-Butanoyl-3,5-diphenyl-2-ethylphenol (XIV).—A 2-g. sample of styryl propyl ketone dimer (I) and 0.3 g. of 10% palladium-on-charcoal catalyst were thoroughly mixed in a test tube and heated (nitrogen atmosphere) with a flame for 30 min. (temp., 310–320° in the liquid). After cooling to room temperature, the volatile materials which had condensed on the walls of the test tube were removed by rinsing out with cold chloroform. The solid residue remaining was extracted with boiling chloroform and filtered and the filtrate concentrated to dryness. From three such runs there was obtained 4.6 g. of a brown solid which was crystallized from benzene to yield 0.95 g., m.p. 168–171°, and 0.25 g., m.p. 152–162°, of crude phenol in successive crops; total yield, 1.20 g. (20%). Recrystallization from benzene gave small prisms, m.p. 172–173°; infrared spectrum (potassium bromide), strong OH stretching band (3500 cm.$^{-1}$) and conjugated carbonyl at 1670 cm.$^{-1}$; ultraviolet spectrum, λ_{max} 239 mμ (ϵ 21,500) and shoulder at 290 mμ (ϵ 4000). No color change was noted when the phenol was added to ethanolic ferric chloride solution.

Anal. Calcd. for $C_{24}H_{24}O_2$: C, 83.69; H, 7.02. Found: C, 83.64; H, 7.19.

3,5-Diphenyl-2-isopropyl-4-(3-methylbutanoyl)phenol (XV).—The procedure used for preparing XIV was employed with styryl isobutyl ketone dimer (II), m.p. 205–206°; temp., 310–320°, 15-min. heating. From three 2-g. batches there was obtained 5.44 g. of yellow solid which was crystallized first from ethanol to yield 1.88 g. of recovered dimer, m.p. 198–207°. The mother liquor was concentrated to dryness and the residue crystallized from benzene to yield 1.38 g. (23%) of phenol XV, m.p. 193–200°; recrystallization gave small rhombic crystals, m.p. 202–203°. Infrared bands at 3500 (OH) and 1670 (conjugated C=O) cm.$^{-1}$ (potassium bromide); ultraviolet spectrum showed shoulders near 240 mμ (ϵ 23,000) and 290 mμ (ϵ 4000). No change in color in ferric chloride solution was observed.

Anal. Calcd. for $C_{26}H_{28}O_2$: C, 83.83; H, 7.58. Found: C, 84.13; H, 8.20.

2-Butyl-3,5-bis(4-methylphenyl)-4-hexanoylphenol (XVI).—The procedure used for preparing XIV was employed with 4-methylstyryl amyl ketone dimer (IV); temp., 320–330°, 20-min. heating. The crude residue (5.15 g.) was crystallized first from ethanol to yield 0.83 g. of recovered dimer, m.p. 160–164°. The mother liquor was concentrated to dryness and the residue crystallized from heptane to yield 1.65 g. (28%) of phenol XVI, m.p. 101–105°. Two recrystallizations from hexane gave 1.2 g., m.p. 105.5–107°; further recrystallization gave prisms, m.p. 106–108°; infrared bands at 3500 (OH) and 1670 cm.$^{-1}$ (conjugated C=O) (potassium bromide); ultraviolet spectrum, broad maximum near 237 mμ (ϵ 28,000) and shoulder at 290 mμ (ϵ 4950). No color was produced in ethanolic ferric chloride solution.

Anal. Calcd. for $C_{30}H_{36}O_2$: C, 84.07; H, 8.47. Found: C, 83.57; H, 8.07.

Deacylation of 4-Butanoyl-3,5-diphenyl-2-ethylphenol to 3,5-Diphenyl-2-ethylphenol (XX).—A mixture of 0.344 g. (1 mmole) of ketophenol XIV, 0.094 g. (1 mmole) of phenol, and 4.5 mg. of camphorsulfonic acid was heated in a test tube immersed in an oil bath at 180° for 1 hr. The residue was distilled to yield 0.15 g., b.p. 160–180° (700 mm.), $n^{25}D$ 1.5221, believed to be a mixture of phenol (major constituent) and phenyl butyrate [infrared bands at 3600 cm.$^{-1}$ (OH) and 1730 cm.$^{-1}$ (ester C=O)]. The residue remaining (0.31 g.) revealed strong infrared bands at 3600 cm.$^{-1}$ (OH) and 1750 cm.$^{-1}$ (ester C=O); practically none of the carbonyl absorption of the starting material at 1670 cm.$^{-1}$ was evident and the material is believed to be a mixture of 3,5-diphenyl-2-ethylphenol (XX) and its butyrate ester (XVII). The entire residue (0.31 g.) was treated with 10 ml. of water, 10 ml. of ethanol, and 10 g. of sodium hydroxide and the mixture refluxed for 18.5 hr. The mixture was diluted with water and extracted with ether; the combined extracts were dried and concentrated to leave 0.28 g. of residue. Crystallization from hexane gave 0.066 g. of **3,5-diphenyl-2-ethylphenol (XX)**, m.p. 82–83°; when mixed with an authentic sample (preparation is described later, m.p. 83–83°), the melting point was not depressed; the infrared and ultraviolet spectra of the two samples were identical. The deacylation could be carried out effectively with camphorsulfonic acid alone (phenol absent) with similar results (mixture of XX and its butyrate ester produced). Aluminum chloride was much less effective as a reagent for this reaction. An attempt to separate the 3,5-diphenyl-2-ethylphenyl butyrate from the mixture by distillation was ineffective since the distillate was contaminated with the phenol (XX); ester XVII could not be crystallized.

The aqueous alkaline portion remaining from this saponification was made acidic with sulfuric acid, diluted with water, and distilled; 3.4 l. of distillate was collected. The distillate was neutralized with sodium hydroxide solution, concentrated to a volume of 10 ml., and then treated with 0.2 g. of *p*-phenylphenacyl bromide and 10 ml. of ethanol. After refluxing 1.3 hr. and cooling, the mixture was filtered to yield 0.24 g. of crude *p*-phenylphenacyl butyrate, m.p. 60–80°; recrystallization from dilute ethanol gave prisms, m.p. 80–81°; when mixed with a authentic sample (m.p. 78–80°), the melting point was not depressed.

Deacylation of 3,5-Diphenyl-2-isopropyl-4-(3-methylbutanoyl)-phenol to 3,5-Diphenyl-2-isopropylphenol (XXI).—A 0.5-g. sample of ketophenol XV and 5 mg. of camphorsulfonic acid were heated at 205° for 4 hr. The residue, which had an isovaleric acid odor, was dissolved in ether and washed with sodium bicarbonate solution; the ether solution was dried and concentrated to dryness. The residue (0.42 g.) had hydroxyl (3600 cm.$^{-1}$) and carbonyl (1750 cm.$^{-1}$, ester) absorption and is believed to contain principally the phenol XXI and its isovalerate ester (XVIII). A 0.36-g. portion of the residue was saponified by refluxing for 24 hr. with a mixture of 10 g. of sodium hydroxide, 10 ml. of water, and 10 ml. of ethanol. There was obtained 0.30 g. of crude phenol XXI which was crystallized from hexane to yield 0.21 g., m.p. 112–115°. Recrystallization gave colorless prisms of **3,5-diphenyl-2-isopropylphenol (XXI)**, m.p. 114–115°; infrared band (potassium bromide) at 3500 cm.$^{-1}$ (OH) (carbonyl absent).

Anal. Calcd. for $C_{21}H_{20}O$: C, 87.46; H, 6.99. Found: C, 87.54; H, 6.94.

The aqueous alkaline portions (including the sodium bicarbonate extracts) were combined, acidified with sulfuric acid, diluted with water, and distilled. The first 1200 ml. of distillate contained 0.00119 equivalent of acid (by direct titration with 0.1 *N* sodium hydroxide) and the next fraction (700 ml.) contained 0.0008 equivalent; total, 0.00127 equivalent (94.5%) of isovaleric acid. The neutralized distillate was concentrated and the *p*-phenylphenacyl ester prepared; 0.16 g., m.p. 76–77°, was obtained; the melting point was not depressed when the material was mixed with an authentic sample (m.p. 73–75°).

Deacylation of 2-Butyl-3,5-bis(4-methylphenyl)-4-hexanoylphenol.—A 0.5-g. sample of the ketophenol XVI and 5 mg. of camphorsulfonic acid were heated at 200–210° for 3.5 hr. The residue was saponified by the procedure described previously; reflux time, 24 hr. The product, believed to be mainly 2-butyl-3,5-bis(4-methylphenyl)phenol (XXII), was obtained as an oil which failed to crystallize from hexane on chilling to −15°.

The aqueous alkaline portion was concentrated to near dryness and diluted with water to a volume of 25 ml. The solution was acidified with sulfuric acid and extracted with ether. After drying the solution and removing the ether the residue was distilled to yield 0.08 g. of hexanoic acid, b.p. 185° (690 mm.), $n^{25}D$ 1.4165, neut. equiv.. 120 (calcd. 116.2). The *p*-phenylphenacyl ester was prepared, m.p. 63–64°; when mixed with an authentic sample, m.p. 63–64°, the melting point was not depressed.

3,5-Diphenyl-2-ethylphenol (XX) from 3,5-Diphenyl-6-ethyl-2-cyclohexen-1-one (XXIII).—A 1.0-g. sample of 3,5-diphenyl-6-ethyl-2-cyclohexen-1-one (XXIII) (prepared by the procedure of Dieckmann[19]) was mixed with 0.3 g. of 10% palladium-on-charcoal catalyst and the mixture heated gently with a flame for 15 min. (until bubbling ceased). The combined product of two such runs was extracted with boiling chloroform several times and the extracts were filtered. Concentration of the filtrate gave 1.43 g. of orange oil which was crystallized from hexane to yield 0.45 g. of crude XX, m.p. 76–81°; two recrystallizations from hexane raised the melting point to 82–83° (colorless prisms); infrared bands (Nujol) at 3500 and 3600 cm.$^{-1}$ (hydroxyl); carbonyl absorption was absent; λ_{max} 238 mμ (ε 25,300), shoulders at 260 mμ (ε 15,600) and 300 mμ (ε 4400).

Anal. Calcd. for $C_{20}H_{18}O$: C, 87.56; H, 6.61. Found: C, 88.06; H, 6.68.

Reactions of Enamines with Electrophilic Sulfur Compounds

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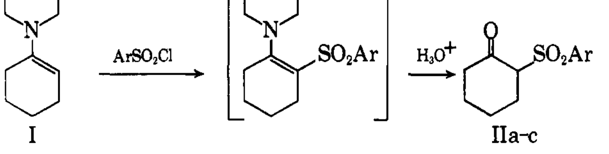
The reaction of 1-pyrrolidinocyclohexene and arylsulfonyl chlorides led, on hydrolysis, to 2-arylsulfonylcyclohexanones. With *o*-, *m*-, or *p*-nitrobenzenesulfenyl chloride, 2-mono- and 2,6-bis(*o*-, *m*-, and *p*-nitrophenylsulfenyl)cyclohexanones were obtained. Intermediate bisnitrophenylsulfenyl enamines were isolated. Only monosubstitution products were obtained from 1-pyrrolidinocyclohexene and *m*- or *p*-nitrophenyl disulfides and from 6-methyl-1-pyrrolidinocyclohexene and *o*-nitrobenzenesulfenyl chloride. From propane-1,3-dithiol-di-*p*-toluenesulfonate and 1-pyrrolidinocyclohexene, the 1,2-cyclohexanedione mono-1,3-propanedithiol ketal was obtained.

Since the initial work of Stork and his collaborators on the alkylation and acylation of enamines,[1] this class of compounds has gained increasing recognition as reactive intermediates in organic synthesis. While previous interest focused mainly on the use of enamines in the formation of carbon to carbon bonds, this report describes some reactions of enamines with electrophilic sulfur derivatives.

A few other studies in this area were indicated recently. Thus the reaction of 1-piperidinopropene with benzenesulfonyl chloride gave 2-benzenesulfonyl-1-piperidinopropene,[2] but alkylsulfonyl chlorides and enamines led to 3-aminotrimethylene sulfones.[2,3] These may arise either from cyclization of initially formed α-sulfonylimmonium intermediates, postulated in analogy to precursors of arylsulfonyl enamines, or from addition of a sulfur analog of ketene to the enamines. A third example is the reaction of sulfur dichloride with the bispyrrolidine enamine of bicyclo[3.3.1]nonane-2,6-dione which gave 2-thiaadamantane-4,8-dione on hydrolysis.[4]

We have found that the pyrrolidine enamine of cyclohexanone I reacts with *p*-acetamidobenzenesulfonyl chloride, *p*-nitrobenzenesulfonyl chloride, and *p*-toluenesulfonyl chloride[5] to give the corresponding arylsulfonyl ketones IIa–c on hydrolysis.



I

IIa–c

a, Ar = *p*-acetamidophenyl
b, Ar = *p*-nitrophenyl
c, Ar = *p*-tolyl

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[1] (a) G. Stork, R. Terrell, and J. Szmuszkovicz, *J. Am. Chem. Soc.*, **76**, 2029 (1954); (b) G. Stork, A. Brizzolara, H. Landesman, J. Szmuszkovicz, and R. Terrell, *ibid.*, **85**, 207 (1963).

[2] G. Opitz and H. Adolph, *Angew. Chem.*, **74**, 77 (1962).

[3] G. Stork and I. Borowitz, *J. Am. Chem. Soc.*, **84**, 313 (1962).

[4] H. Stetter, H. Held, and A. Schulte-Oestrich, *Ber.*, **95**, 1687 (1962).

[5] Also indicated by G. Stork, Abstracts, 16th National Organic Symposium, June, 1959, pp. 44–52.