ture over a period of 10 minutes. The reaction mixture was refluxed for 1.5 hr., then carbonated by pouring into a stirred slurry of Dry Ice and ether and subsequently hydrolyzed with 10% hydrochloric acid. The ether layer from the hydrolysis, combined with two ether washings of the aqueous layer, was extracted with 8% sodium bicarbonate and 5% sodium hydroxide.

The sodium bicarbonate extract was made strongly acidic to give 0.83 g. (38%) of 5-bromosalicylic acid (II) having a melting point of 165.5–167.5°, identified by a mixed melting point and infrared analysis. After concentration of the acid mother liquor, 0.16 g. (12%) of impure *p*-hydroxybenzoic acid (III) melting at 197.5–199° separated. An infrared analysis identified the material beyond doubt.

The sodium hydroxide extract yielded, upon acidification, 0.10 g. of boron-containing crystals melting at 85–87°. The product was recrystallized from ethylene dichloride, but the material obtained decomposed before any test could be effected. The crude product gave no color with ferric chloride, and its infrared analysis showed the presence of an alkyl group, borono group and hydroxyl group and the absence of a phenyl ring and a carboxy group. This spectrum was identical to that of an authentic specimen of *n*-butaneboronic acid. The reported melting point for *n*-butaneboronic acid is 92–94°. The yield, calculated for this compound, is 10%.

When the mixture was carbonated 18 minutes after the addition, there was obtained 30% of II and 10% of *n*-butaneboronic acid. No III was isolated.

Acknowledgment.—We wish to thank Mr. Robert McCord and Mr. E. Miller Layton of the Ames Laboratory of the Atomic Energy Commission for the infrared spectra.

We also wish to acknowledge the support of the Division of Biology and Medicine of the United States Atomic Energy Commission who have helped make this work possible. The results of the biological testing of these compounds will be reported by Dr. Otho D. Easterday of the Brookhaven National Laboratory.

AMES, IOWA

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, HARVARD UNIVERSITY]

α-Ketoethers. I. The Reaction of α-Phenoxyacetophenone with Sodium and with Sodium Amide[1]

BY PETER YATES, DONALD G. FARNUM AND GEORGE H. STOUT[2]

RECEIVED JUNE 24, 1957

The orange product from the reaction of α-phenoxyacetophenone with sodium in xylene or with sodium amide in ether and methanol is shown to be 1,2,3-tribenzoylpropene (II). The equilibrium between II and its enol IIa is discussed on the basis of infrared and ultraviolet spectral data. The reaction of II with hydrazine is shown to yield the hydrazone of 4-phenacyl-3,6-diphenylpyridazine (V). The mechanism of the formation of II is discussed.

Kostanecki and Tambor,[3] in an attempted synthesis of 3-hydroxyflavone, reacted α-phenoxyacetophenone (I) with ethyl *o*-ethoxybenzoate in the presence of sodium; they obtained, in unreported yield, an orange compound, $(C_8H_6O)_x$, m.p. 120°, which they subsequently showed could also be obtained by the action of sodium in warm xylene on α-phenoxyacetophenone alone.[4] This product was found to be soluble in aqueous sodium hydroxide, from which it was precipitated by passage of carbon dioxide. Reduction with zinc and acetic acid gave a white compound, m.p. 118°, for which no analysis was reported. The only conclusion drawn by these authors was that the orange compound was neither *trans*- nor *cis*-dibenzoylethylene. As part of a general study of the chemistry of α-ketoethers, we have investigated further the nature of this product.

Treatment of I in xylene solution with sodium at 40 to 50° for 40 hr. yielded an orange compound, II, corresponding in properties to Kostanecki's compound. The yield of II, however, was only 7.5% and was improved only slightly by the use of refluxing ether as solvent. It was later found that the same product could be obtained in 48% yield by the reaction of I with sodium amide in ether containing a small amount of methanol at 10° under nitrogen. Several recrystallizations from ethanol gave II as fine, orange needles. On the basis of analysis and titration it was assigned the formula $C_{24}H_{18}O_3$.[6] Its infrared and ultraviolet spectra are characterized by their striking solvent dependence (see Table I). This was early attributed to a mobile tautomeric equilibrium whose operation was also evidenced by the small, but distinct, variations in the melting points of samples with different histories: while all samples normally melted sharply at temperatures between 118° and 123°, it was found that a sample stirred in a slowly heated mineral oil-bath did not melt until the bath temperature reached 138°. Similar phenomena

TABLE I

INFRARED AND ULTRAVIOLET SPECTRA OF II IN VARIOUS SOLVENTS

Solvent	λ_{max}, mμ	log ε	Solvent	λ_{max}, μ
Isoöctane	243	4.45	Carbon tetrachloride	5.93(s)
	248	4.40		6.01(s)
Ethanol	254	4.26		6.20(w)
	406	4.28	Nujol mull	3.10(m)
Ethanolic NaOH (0.5%)	258	4.34		6.14(m)
	487	4.61		6.52(vs)
			Chloroform	5.93(s)[a]
				6.00(s)
				6.18(w)
				6.48(m)

[a] Shoulder.

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[1] A preliminary account of this work has appeared in *Chemistry & Industry*, 821 (1956).

[2] National Science Foundation Pre-doctoral Fellow, 1953-1955.

[3] St. v. Kostanecki and J. Tambor, *Ber.*, **35**, 1679 (1902).

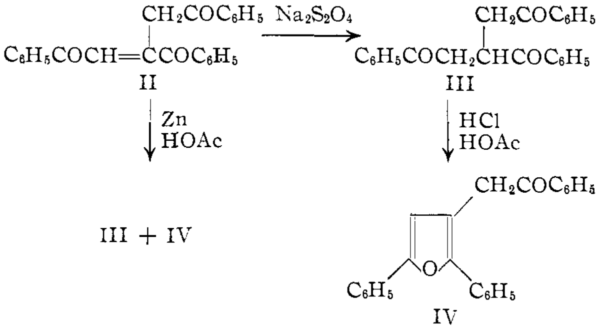
[4] Stoermer and Atenstädt[5] have also treated I with sodium but reported only that no steam-volatile product was formed.

[5] R. Stoermer and P. Atenstädt, *Ber.*, **35**, 3560 (1902).

[6] Since II is a very weak acid the titration values were approximate only; this molecular formula was corroborated by the formulas of the transformation products discussed below.

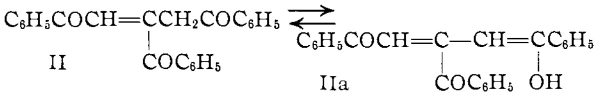
have been observed by Lutz and King[7] in the case of another tautomeric system.

We now propose that II is 1,2,3-tribenzoylpropene, or a tautomer, on the basis of the following evidence.[8] Reduction with sodium hydrosulfite in 50% aqueous ethanolic solution gave, in 85% yield, 1,2,3-tribenzoylpropane (III), identified by direct comparison (mixed melting point and infrared spectrum) with an authentic sample prepared by the condensation of acetophenone with *trans*-1,2-dibenzoylethylene.[9] Reduction with zinc and acetic acid at 80° followed by chromatography yielded two crystalline products in low yield. One of these was identified as III, while the other was shown to be the known dehydration product of III, 2,5-diphenyl-3-phenacylfuran (IV),[9,10] identified by direct comparison (mixed melting point and infrared spectrum) with a sample of the furan prepared by dehydration of III with hydrochloric acid in acetic acid.[9]



This structural assignment is in good accord with the other observed properties and reactions of II. Thus, it would be anticipated that II should behave as a weak acid, consonant with its behavior on titration and with the fact that it is soluble in cold, dilute aqueous sodium hydroxide and is recovered unchanged by saturation of the solution with carbon dioxide. Hydrolysis of II, effected by heating the aqueous basic solution under reflux for 1.5 hr. in a nitrogen atmosphere, yielded benzoic acid (*ca.* 1 molar equivalent) and acetophenone (0.2 molar equivalent), together with a major, neutral fraction, remaining after removal of acetophenone by steam distillation, from which no pure material could be isolated. The benzoic acid could arise readily by cleavage of the vinylogous β-dicarbonyl system of II, while the acetophenone formation might occur by hydration of II followed by a reverse aldol cleavage. Oxidation of II in aqueous acetone with potassium permanganate gave 2.7 molar equivalents of benzoic acid, again clearly compatible with its formulation as 1,2,3-tribenzoylpropene.

We next consider the detailed structure of II on the basis of the spectroscopic data. As previously noted, both the infrared and ultraviolet spectra are remarkably dependent on the medium (Table I). They may be interpreted in terms of a tautomeric equilibrium between the species II and IIa.



$$\underset{\text{II}}{C_6H_5COCH{=}\underset{\displaystyle COC_6H_5}{C}CH_2COC_6H_5} \rightleftarrows \underset{\text{IIa}}{C_6H_5COCH{=}\underset{\displaystyle COC_6H_5}{C}{-}CH{=}\underset{\displaystyle OH}{C}C_6H_5}$$

The infrared spectrum of the carbon tetrachloride solution is in agreement with the structure II, for the carbonyl band at 5.93 μ corresponds in position to that of acetophenone in the same solvent (5.91 μ)[11] while that at 6.01 μ is similar in position to the carbonyl band of *trans*- or *cis*-1-methyl-1,2-dibenzoylethylene (6.05, 6.06 μ).[12] Also, the ultraviolet spectrum of the isoöctane solution is concordant with the triketonic structure, since on subtraction of the spectrum of acetophenone the resultant maximum, 259 mμ (log *e* 4.35), approximates those of *cis*- and *trans*-1-methyl-1,2-dibenzoylethylene, 254 mμ (log *e* 4.39) and 258 mμ (log *e* 4.37), respectively.[12] The small magnitude of the differences between the positions of the infrared and ultraviolet carbonyl bands of *cis*- and *trans*-1-methyl-1,2-dibenzoylethylene does not permit a choice to be made between the *cis* and *trans* forms of II on the basis of the spectral data.

The infrared spectrum in Nujol mull is explicable in terms of the enolic structure IIa if the band at 6.14 μ is assigned to the carbonyl group of the 2-benzoyl substituent and the very intense band at 6.52 μ to the enolized vinylogous β-diketone system[14]; the band at 3.10 μ is compatible with the presence of a highly bonded hydroxyl group. The appearance of the long wave length band at 406 mμ in the visible–ultraviolet spectrum in ethanolic solution also bespeaks the presence of the highly conjugated system of IIa; thus, for example, cinnamalacetophenone absorbs at 345 mμ,[15] and the $\Delta\lambda$ attributed to substitution by a β-[16] or δ-hydroxyl[17] group on a conjugated ketonic system is 40–50 mμ. The bathochromic shift of 81 mμ in basic solution with accompanying hyperchromic shift also finds close analogy in related systems[18] and is attributed to the formation of the enolate ion. The unusually large hyperchromic shift is probably due in this case to the fact that the enolate is formed from a mixture of IIa and II, since it appears from the intensity of the 406 mμ band that in ethanolic solution the compound is only partially in the enolic form.[19] The infrared spectrum in

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(7) R. E. Lutz and S. M. King, *J. Org. Chem.*, **17**, 1519 (1952).

(8) P. F. Devitt, E. M. Philbin and T. S. Wheeler, *Chemistry & Industry*, 822 (1956), have arrived independently at the same conclusion; *cf.* Ref. 1.

(9) R. E. Lutz and F. S. Palmer, THIS JOURNAL, **57**, 1947 (1935).

(10) C. Paal and H. Schulze, *Ber.*, **36**, 2425 (1903).

(11) N. Fuson, M.-L. Josien and E. M. Shelton, THIS JOURNAL, **76**, 2526 (1954).

(12) L. P. Kuhn, R. E. Lutz and C. R. Bauer, *ibid.*, **72**, 5058 (1950). These spectra are of mineral oil mulls; it would be expected that the carbonyl bands would fall at somewhat lower wave lengths in carbon tetrachloride solution.[13]

(13) *Cf.* L. J. Bellamy, "The Infrared Spectra of Complex Molecules," Methuen and Company, London, 1956, p. 117.

(14) *Cf.* C. L. Angell and R. L. Werner, *Australian Chem. J.*, **6**, 294 (1953).

(15) E. Smakula and A. Wasserman, *Z. physk. Chem.*, **A155**, 353 (1931).

(16) E. A. Braude in "Determination of Organic Structures by Physical Methods," E. A. Braude and F. C. Nachod, ed., Academic Press, Inc., New York, N. Y., 1955, p. 154.

(17) C. W. Greenhalgh, H. B. Henbest and E. R. H. Jones, *J. Chem. Soc.*, 2375 (1952).

(18) *Cf.*, for example, the $\Delta\lambda$ of 72 mμ reported for 3,7-diketo-4-cholestene.[17]

(19) This view is corroborated by the change observed in the lower wave length band in basic solution.

TABLE II

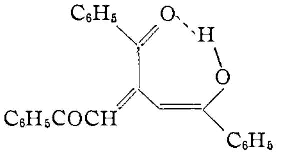
INFRARED AND ULTRAVIOLET SPECTRA OF V AND VI AND RELATED COMPOUNDS

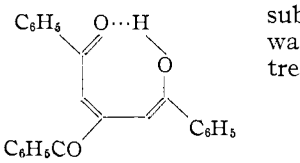
Compound	$\lambda_{\max}^{\text{EtOH}}$, mμ	log ε	$\lambda_{\max}^{\text{CHCl}_3}$, μ
V	263	4.50	2.93(s), 3.03(s), 3.12(m), 6.13(w), 6.29(s), 6.92(s), 7.14(s)
VI	250	4.53	3.00(w), 5.92(s), 6.25(m), 6.32(m), 6.92(m), 7.15(s)
3-Phenylpyridazine[a]	254	4.08	3.00(w), 6.32(s), 6.89(m), 7.00(s)
3,6-Diphenylpyridazine[b]	278	4.46	3.00(w), 6.28(m), 6.90(s), 7.08(s)
3,4,6-Triphenylpyridazine[c]	268	4.49	3.00(w), 6.29(m), 6.91(m), 7.16(s)

[a] S. Gabriel and T. Colman, *Ber.*, **32,** 395 (1899); m.p. 101–102° (rec. m.p. 102–103°). [b] C. Paal and H. Schulze, *ibid.*, **33,** 3795 (1900); m.p. 224.5–225° (rec. m.p. 221–222°). [c] A. Smith, *Ann.*, **289,** 310 (1896); m.p. 172.5–174.5° (rec. m.p. 171°).

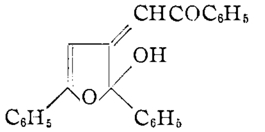
chloroform solution also gives evidence of the presence of both II and IIa together in this medium since the carbonyl region shows bands corresponding to both forms.

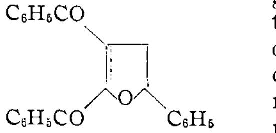
The tendency observed in these cases for the enol/ketone ratio to increase with increasing polarity of the medium is in contradistinction to the case of *chelated* enolic β-dicarbonyl compounds[20] but is reminiscent of the effect of change of basicity of solvent in the case of *non-chelated* enolic β-dicarbonyl compounds involved in intermolecular hydrogen bonding.[14] This solvent effect is therefore in conformance with structure IIa, for which a six-membered chelate ring is impossible.[21] It does not serve to distinguish between intermolecular hydrogen bonding and non-chelated intramolecular hydrogen bonding as in IIb and IIc.[22]


IIb

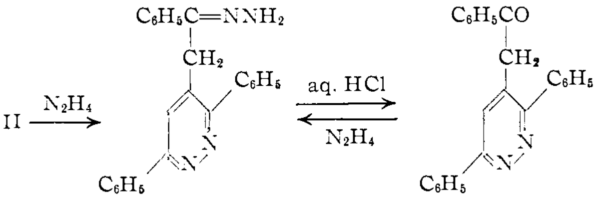

IIc

It must be noted that the possibility of ring-chain tautomerism also exists. The structure IId is analogous to a tautomer postulated for 1,4-diphenyl-1,2,4-butanetrione.[23] However, in the present case, the existence of such a tautomer in significant amount is considered unlikely on the basis of the spectral data, which also appear to exclude other ring tautomers, such as IIe.


IId


IIe

Treatment of II with hydrazine in ethanolic acetic acid gave a white compound, $C_{24}H_{20}N_4$, m.p. 155–156.5° dec., in 74% yield; this was accompanied by a yellow isomer, m.p. 143.5–144°, in small amount. The major product may be assigned the structure V on the basis of the structure found for II and of the following observations. Its infrared spectrum shows bands in the NH stretching region at 2.93(s), 3.03(s) and 3.12(m) μ, similar to those observed in other hydrazones.[24] On hydrolysis with hydrochloric acid it is converted to a compound, $C_{24}H_{18}N_2O$. This hydrolysis product shows a strong band in its infrared spectrum at 5.92 μ, indicating the presence of a carbonyl group conjugated with a single aromatic system and bands at 3.00(w), 6.32(m) and 7.15(s) μ which have been found to be characteristic of the pyridazine ring system (see Table II)[25]; it is therefore formulated as the ketone VI. This assignment is in accord with the ultraviolet spectrum of the hydrolysis product since subtraction of the spectrum of acetophenone left a maximum at 263 mμ (log ε 4.4). This is compatible with the presence of the 3,6-diphenylpyridazine chromophore (Table II), with its maximum shifted by 15 mμ to lower wave lengths because of the presence of an *ortho* type substituent.[26] This relationship between V and VI was confirmed by the regeneration of V from VI by treatment with hydrazine.


V VI

Oxidation of V with potassium permanganate in aqueous acetone gave a product, $C_{24}H_{16}N_2$, together with some benzoic acid. It is proposed that this product has the structure VII and is formed by oxidation of the hydrazone to an aliphatic diazo compound, nucleophilic attack on the pyridazine ring, elimination of nitrogen and oxidation of the resulting dihydrobenzophthalazine derivative. An alternative formulation, VIII, derived by a closely allied mechanistic pathway, is considered less likely in that the oxidation product is white, while arylated cinnoline derivatives, unlike phthalazine derivatives, are usually yellow.[27]

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(20) H. Henecka, "Chemie der β-Dicarbonylverbindungen," Springer Verlag, Berlin, 1950, pp. 7 *et seq.*

(21) In this connection it may be noted that II fails to give a copper complex and a positive color reaction with *methanolic* ferric chloride (*cf.* reference 20, p. 111).

(22) A chelated form of IIc, with a *planar* eight-membered ring, is excluded on the basis of the solvent effect.

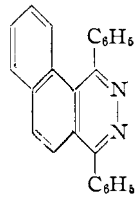
(23) R. E. Lutz and S. M. King, *J. Org. Chem.*, **17,** 1519 (1952).

(24) Thus, for example, the hydrazone of desoxybenzoin has bands in this region at 2.95(s), 3.05(m), 3.10(w) μ.

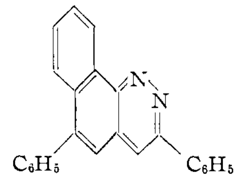
(25) The band in the range 6.28–6.32 μ observed for the pyridazines is distinguishable from the phenyl band which falls in this region by virtue of its considerably greater intensity. It also may be noted that the bands here associated with the pyridazine system are also present in the spectrum of V, although the presence of the hydrazone group adds to the complexity of the spectrum.

(26) *Cf.* the hypsochromic shift of 16 mμ brought about by the introduction of an ethyl or *n*-butyl group into the *o*-position of the biphenyl system: E. A. Braude, F. Sondheimer and W. F. Forbes, *Nature*, **173,** 117 (1954).

(27) J. C. E. Simpson, "Condensed Pyridazine and Pyrazine Rings," Interscience Publishers, Inc., New York, N. Y., 1953, pp. 8, 76.

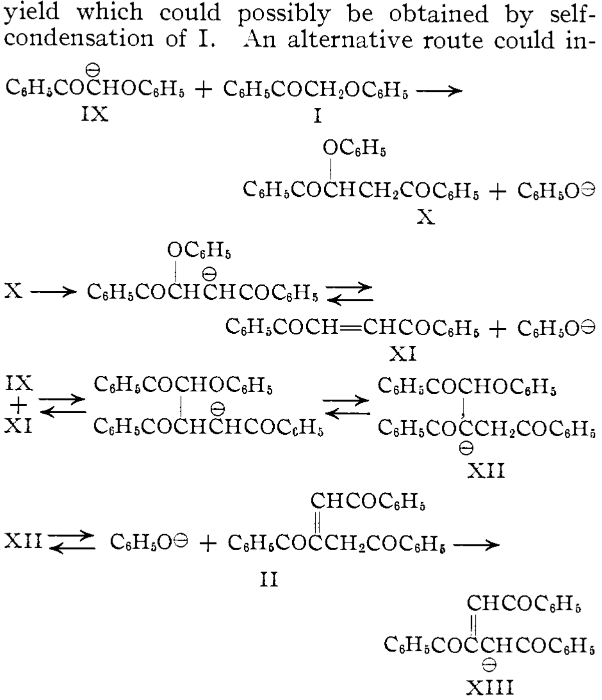


VII



VIII

We turn now to consideration of the mechanism of formation of II from I. It appears likely that I is first attacked by its anion IX with displacement of phenoxide ion to give X, which is converted to 1,2-dibenzoylethylene (XI) by elimination of phenoxide ion. Michael addition of the anion of I to XI followed by tautomerization would then give the anion XII, which, on elimination of phenoxide ion, would give II. The intervention of XI as an intermediate in the formation of II is corroborated by our observation that when *trans*-1,2-dibenzoylethylene (XI) is added to the reaction mixture, II is formed in a yield greater than the maximum yield which could possibly be obtained by self-condensation of I. An alternative route could involve loss of phenoxide ion from IX with formation of the carbene XIV and dimerization of this to XI[28]



$$\underset{\text{IX}}{C_6H_5CO\overset{\ominus}{C}HOC_6H_5} + \underset{\text{I}}{C_6H_5COCH_2OC_6H_5} \longrightarrow \underset{\text{X}}{C_6H_5CO\overset{OC_6H_5}{\overset{|}{C}H}CH_2COC_6H_5} + C_6H_5O^{\ominus}$$

$$\text{X} \longrightarrow C_6H_5CO\overset{OC_6H_5}{\overset{|}{C}H}\overset{\ominus}{C}HCOC_6H_5 \rightleftarrows \underset{\text{XI}}{C_6H_5COCH{=}CHCOC_6H_5} + C_6H_5O^{\ominus}$$

$$\begin{array}{c}\text{IX}\\+\\\text{XI}\end{array} \rightleftarrows \begin{array}{l}C_6H_5COCHOC_6H_5\\ \qquad\;\; |\\ C_6H_5COCH\overset{\ominus}{C}HCOC_6H_5\end{array} \rightleftarrows \underset{\text{XII}}{\begin{array}{l}C_6H_5COCHOC_6H_5\\ \qquad\;\; |\\ C_6H_5CO\underset{\ominus}{C}CH_2COC_6H_5\end{array}}$$

$$\text{XII} \rightleftarrows C_6H_5O^{\ominus} + \underset{\text{II}}{C_6H_5CO\overset{CHCOC_6H_5}{\overset{\|}{C}}CH_2COC_6H_5} \longrightarrow \underset{\text{XIII}}{C_6H_5CO\overset{CHCOC_6H_5}{\overset{\|}{C}}\underset{\ominus}{C}HCOC_6H_5}$$

$$\text{IX} \longrightarrow C_6H_5O^{\ominus} + \underset{\text{XIV}}{C_6H_5CO\ddot{C}H} \longrightarrow \text{XI}$$

The former route is preferred, however, on the following basis. When excess sodium amide was used as the condensing agent, no formation of II occurred, as evidenced by the complete absence of the characteristic deep red color of its anion XIII, until methanol was added to the reaction mixture. This observation is explicable in terms of the first route, since rapid and complete conversion of I to IX by sodium amide would necessitate the addition of a proton source in limited amount in order to regenerate sufficient I for the displacement reaction to proceed.[29] On the other hand, there appears to be no rationale in terms of the second route for the intervention of methanol.

Investigation of the non-acidic fractions from the reaction of I with sodium in xylene showed that other products were formed in addition to II. In one run, after removal of 25% of I by crystallization, acetophenone was isolated by distillation of the residual oil; in addition, the infrared spectrum of the oil showed the presence of an alcoholic component. In another experiment, the non-acidic fraction was distilled and the distillate yielded, after removal of ketonic material by treatment with Girard reagent T, the alcoholic product as a crystalline solid, identified as 2-phenoxy-1-phenylethanol. The reduction of I to acetophenone finds ample analogy in the reductive cleavage of aromatic ethers by sodium in liquid ammonia.[30] Furthermore, the formation of secondary alcohols from ketones by the action of sodium also has been reported previously.[30,31]

Experimental[32]

α-Phenoxyacetophenone (I). (i).—Preparation from aqueous sodium phenoxide and phenacyl bromide according to the method of Möhlau[33] gave 20–30% of product, m.p. 73–74° (rec.[34] 72°, 74°).

(ii).—A solution of freshly recrystallized phenacyl bromide[35] (74 g., 0.37 mole) in anhydrous ether (90 ml.) was allowed to stand in contact with finely powdered potassium iodide (1.0 g.) for 18 hr.[36] This solution was added over a period of 1.5 hr. to a stirred slurry of phenol (40 g., 0.43 mole) and anhydrous potassium carbonate (60 g., 0.44 mole) in anhydrous ether (110 ml.) under vigorous reflux. Refluxing and stirring were continued for an additional 5.5 hr., and the reaction mixture was then cooled, washed with water, dilute aqueous potassium carbonate and saturated aqueous sodium chloride. The ether layer was dried over sodium sulfate, evaporated on the steam-bath, and the yellow solid residue was recrystallized from ethanol. The yield of fluffy, white needles was 60 g. (76%), m.p. 73.5–74.0°.

Self-condensation of I: 1,2,3-Tribenzoylpropene (II). (i).—Following the briefly outlined procedure of Kostanecki and Tambor, a solution of I (8.49 g., 0.040 mole) in warm xylene (45 ml.) was added to granular sodium (0.92 g., 0.040 mole) in xylene (20 ml.). The pale yellow solution of I became wine red upon addition to the sodium, and vigorous gas evolution occurred. The reaction flask was equipped with a drying tube and warmed at 40–50° for 40 hr. Ethanol (2 ml.) was added to decompose unreacted sodium, and the solution was acidified with dilute acetic acid. Ether was added, and the pale yellow aqueous phase was separated from the dark red organic layer. The ethereal layer was washed with water, extracted with two 100-ml. portions of 5% aqueous sodium hydroxide and retained for further investigation. The combined basic extracts were acidified with hydrochloric acid and extracted with ether. Evaporation of the ethereal extract gave a dark brown oil which was crystallized twice from ethanol to give 357 mg. (7.5%) of very small, orange needles, m.p. 119.5–121.0°. The product

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[28] It may be noted that treatment of phenacyl iodide with sodium gives rise to *cis*- and *trans*-1,2,3-tribenzoylcyclopropanes.[10] Their formation may be rationalized in terms of routes in part analogous to either of those discussed here.

[29] In the reactions where sodium was used as the condensing agent, formation of IX was slow and incomplete: this could permit reaction of IX with unreacted I and formation of XII without the addition of a proton source, as observed.

[30] G. W. Watt, *Chem. Revs.*, **46**, 289 (1950); A. J. Birch, *Quart. Revs.*, **4**, 69 (1950).

[31] *Cf.*, for example, W. A. Waters, "The Chemistry of Free Radicals," Clarendon Press, Oxford, 1948, p. 203; A. Drewski and J. Wiemann, *Compt. rend.*, **232**, 1941 (1951).

[32] Melting points and boiling points are uncorrected.

[33] R. Möhlau, *Ber.*, **15**, 2497 (1882).

[34] W. B. Whitney and H. R. Henze, THIS JOURNAL, **60**, 1148 (1938).

[35] Old, discolored samples gave poorer yields (*ca.* 50%).

[36] *Cf.* C. Djerassi and C. R. Scholz, THIS JOURNAL, **69**, 1688 (1947).

was soluble in cold 3% aqueous sodium hydroxide and could be reprecipitated by the passage of carbon dioxide through the solution.

A portion of the ethereal layer containing the non-acidic products of the reaction was fractionally distilled to give a yellow oil, b.p. 165–175° (1.5 mm.), which set to a semi-solid mass; $\lambda_{\max}^{\mathrm{CHCl_3}}$ 2.79, 5.88(shoulder), 5.95 μ. The crude distillate (1.25 g.) was taken up in ethanol (25 ml.), and Girard reagent T (1.25 g.) and glacial acetic acid (1 ml.) were added. The mixture was warmed briefly and allowed to stand at room temperature for 3 hr. The solution was diluted with water, extracted with ether and the ethereal extract washed with 10% aqueous sodium bicarbonate, dried over sodium sulfate and evaporated to give a brown oil which set to a yellow pasty mass. Recrystallization from benzene–ligroin afforded faintly yellow needles (337 mg.), m.p. 62.0–63.5°; $\lambda_{\max}^{\mathrm{CHCl_3}}$ 2.76 μ. This compound was identified as 2-phenoxy-1-phenylethanol by mixed m.p. and infrared comparison with an authentic sample (*vide infra*).

In another run, evaporation of the ethereal layer containing the non-acidic fraction and recrystallization of the semi-solid residue from ethanol gave 25% of I, m.p. 73–74.5°; evaporation of the mother liquors and distillation of the brown oily residue in a molecular still afforded a small amount of colorless liquid, identified as acetophenone by its infrared spectrum and the m.p. and mixed m.p. of its 2,4-dinitrophenylhydrazone.

(ii).—Modification of procedure i by using refluxing ether as solvent and a reaction time of 4 hours increased the yield of orange needles, m.p. 120–121°, to 10%.

(iii).—Sodium amide (12.2 g., 0.315 mole) was gradually added to a stirred slurry of I (50.0 g., 0.248 mole) in anhydrous ether (500 ml.) at 10° under a gentle stream of dry nitrogen.[37] When the evolution of ammonia had ceased, methanol (5 ml., 0.08 mole) was added, the system was allowed to warm to room temperature and stirred under dry nitrogen for 48 hr. The brick-red slurry was poured into ice-water, and the ethereal layer was separated and extracted with cold 3% aqueous potassium hydroxide. The combined aqueous and basic extracts were acidified with iced hydrochloric acid, and the granular orange precipitate was collected and recrystallized from ethanol. The yield of very small, orange needles was 14 g. (48%), m.p. 122–123°. When samples were stirred in a slowly heated mineral oil-bath, the undissolved material did not melt until the bath temperature reached 138°. This product was shown to be identical with those obtained by procedures i and ii by mixed melting point determinations and comparison of their infrared spectra (see Table I).

Three recrystallizations from ethanol afforded an analytical sample, m.p. 118–119°.

Anal. Calcd. for $C_{24}H_{18}O_3$: C, 81.34; H, 5.12; mol. wt., 354. Found: C, 81.34; H, 5.00; neut. equiv. (by potentiometric titration in ethanol with 0.1 *N* ethanolic KOH), 322, 330.

2-Phenoxy-1-phenylethanol.—Sodium borohydride (50 mg., 1.3 millimoles) dissolved in a small amount of water was added to a solution of I (500 mg., 2.40 millimoles) in ethanol (25 ml.). After 3.5 hr. at room temperature, the solution was diluted with water and the ethanol was evaporated on the steam-bath. Extraction of the remaining cloudy solution with ether and evaporation of the ethereal extract gave a yellow oil which solidified when scratched and cooled. Recrystallization from ligroin gave faintly yellow needles (420 mg., 82%), m.p. 62.0–63.5°.[38]

Basic Degradation of II.—A solution of II (500 mg., 1.40 millimoles) in de-aerated 3% aqueous sodium hydroxide (50 ml.) was refluxed under a stream of nitrogen for 1.5 hr. The effluent vapors were led into 2,4-dinitrophenylhydrazine reagent, but no significant amount of precipitate collected in the reagent during the course of the reaction. The reaction mixture was slowly steam distilled for 4 hr. with the volume maintained by continuous addition of water through a dropping funnel. The cloudy, pale yellow-orange reaction mixture was extracted twice with ether. The aqueous layer was acidified with hydrochloric acid and extracted several times with ether; the ethereal extracts were dried over sodium sulfate and evaporated to give 200 mg. of pale yellow crystals. Recrystallization from a small volume of water afforded 150 mg. (1.20 millimoles) of benzoic acid, m.p. 121.0–122.5° (identified by mixed m.p. and infrared spectral comparison with an authentic sample).

The neutral, non-steam-distillable material was obtained as a yellow gum by evaporation of the dried ethereal extracts of the original reaction mixture. The infrared spectrum of the crude material ($CHCl_3$) exhibited maxima at 2.75 and 5.95 μ; neither repeated attempts at crystallization from various solvents nor chromatography afforded a significant amount of crystalline material.

The steam distillate was saturated with salt and extracted several times with ether. The ethereal extracts were dried over sodium sulfate and evaporated to give 30 mg. (0.25 millimole) of a colorless liquid identified as acetophenone by its infrared spectrum and the m.p. and mixed m.p. of its 2,4-dinitrophenylhydrazone with an authentic sample.

Oxidation of II.—A warm, 20% solution of potassium permanganate in 50% aqueous acetone (5 ml.) was added to a solution of II (204 mg., 0.576 millimole) in 50% aqueous acetone (5 ml.). After 0.5 hr., the mixture was acidified with dilute sulfuric acid, and sodium bisulfite was immediately added until the solution became clear. Dilution of the solution with water, several extractions with ether and evaporation of the combined, dried, ethereal extracts gave 206 mg. of pale yellow crystals. After pressing on a porous plate, these afforded white crystals of benzoic acid (190 mg., 1.56 millimoles), m.p. 117–119°, identified by mixed m.p. and infrared spectral comparison with an authentic sample.

Hydrogenation of II.—Hydrogenation of II (114 mg., 0.322 millimole) was carried out in 85% aqueous ethanol (25 ml.) with 10% palladium-on-charcoal (100 mg.) as catalyst. After 3.25 hr., 32.3 ml. (1.31 millimoles) of hydrogen had been absorbed, and the rate of absorption had slowed to about 1 ml. per hour. The catalyst was filtered and washed with ether, and the combined filtrate and washings were diluted with water and extracted with ether. The ethereal extract was dried over anhydrous calcium chloride and evaporated to give 100 mg. of a pale yellow glass; infrared spectrum ($CHCl_3$): bands at 2.80 and 2.95 μ and a very weak band at 5.95 μ. Attempted crystallization from ethanol failed to give a significant amount of crystalline material.

Zinc Reduction of II: 1,2,3-Tribenzoylpropane (III) and 2,5-Diphenyl-3-phenacylfuran (IV).—Zinc dust (10 g.) from a freshly opened bottle was added in small portions to a stirred solution of II (1.65 g., 4.66 millimoles) in glacial acetic acid (80 ml.) at 80° while the reaction mixture was kept under a gentle nitrogen stream. The rich brown coloration formed initially gradually faded, and a permanent, pale greenish-yellow color was present at the end of the reaction. The reaction mixture was filtered through glass wool, and the filtrate was added to concentrated hydrochloric acid (50 ml.) and crushed ice (100 ml.) in a nitrogen atmosphere. The pale yellow precipitate was collected and dried under nitrogen to give 1.3 g. of powder, m.p. 35–47°; the infrared spectrum ($CHCl_3$) had bands characteristic of both products subsequently isolated. The product was chromatographed on alumina (60 g.) under nitrogen in 50% petroleum ether–50% benzene. Two fractions were collected, the second by elution with benzene, which proved to have identical infrared spectra. The combined fractions were evaporated and the yellow, glassy residue was treated in methanol with activated charcoal. Filtration of the hot solution and cooling with vigorous scratching gave 186 mg. (12%) of IV as very pale yellow, fluffy needles, m.p. 116–117°, $\lambda_{\max}^{\mathrm{CHCl_3}}$ 5.93 μ; $\lambda_{\max}^{\mathrm{EtOH}}$ 235 mμ (log ϵ 4.35), 245 mμ (log ϵ 4.30), 313 mμ (log ϵ 4.33), 318 mμ (infl.: log ϵ 4.32). Recrystallization from methanol gave an analytical sample as long, white, fluffy needles, m.p. 116.5–117.0°.

Anal. Calcd. for $C_{24}H_{18}O_2$: C, 85.18; H, 5.36. Found: C, 84.78; H, 5.73.

The column was extruded and the top, dark red band removed. Extraction of the remaining alumina with hot chloroform and evaporation of the chloroform extracts yielded a pale yellow oil which crystallized upon cooling and scratching. After washing with cold ligroin, 151 mg. (9%) of III was obtained as thick, white needles, m.p. 122–124°, $\lambda_{\max}^{\mathrm{CHCl_3}}$ 5.93 μ, $\lambda_{\max}^{\mathrm{EtOH}}$ 245 mμ (log ϵ 4.58) and 280 mμ (log ϵ 3.50), unshifted in 0.4% ethanolic potassium hydroxide. Two recrystallizations from benzene–ligroin gave an analytical sample, m.p. 124.5–125.0°.

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(37) In the presence of air the yield of product was 18%.

(38) C. O. Guss, This Journal, **71**, 3460 (1949), records m.p. 63–64°.

Anal. Calcd. for $C_{24}H_{20}O_3$: C, 80.88; H, 5.66. Found: C, 80.55; H, 5.43.

Sodium Hydrosulfite Reduction of II: 1,2,3-Tribenzoylpropane (III).—Sodium hydrosulfite (2.0 g., 0.012 mole) was added to a hot solution of II (350 mg., 0.99 millimole) in 50% aqueous ethanol (30 ml.). The solution was boiled gently for 1 hr. and poured into ice-water; the yellow precipitate was extracted with ether, and the ethereal extracts were evaporated. The residual oil was crystallized from methanol to give 300 mg. (85%) of thick, white needles, m.p. 123.5–124.5°. This material was shown to be identical with the zinc reduction product, m.p. 124.5–125°, by mixed m.p. and infrared spectral comparison.

Dehydration of III: 2,5-Diphenyl-3-phenacylfuran (IV).—Hydrochloric acid was added to a warm solution of III (20 mg., 0.056 millimole) in glacial acetic acid (2 ml.) until cloudiness appeared. The solution was heated for 0.25 hr. on the steam-bath and cooled in ice; the white crystals which separated were collected and washed with cold methanol. The yield of long, fine, white needles was 15 mg. (79%), m.p. 116.5–117.0°. This material was shown to be identical with the zinc reduction product, m.p. 116.5–117°, by mixed m.p. and infrared spectral comparison.

1,2,3-Tribenzoylpropane (III).—Preparation according to the method of Lutz and Palmer[9] from *trans*-1,2-dibenzoylethylene and acetophenone gave thick, white needles, m.p. 123.0–124.5° (rec. 124.5–125.0°) in 16.5% yield. The infrared spectrum ($CHCl_3$) was identical with that of the zinc reduction product, m.p. 124.5–125°, and a mixture melted at 124–125°. The mother liquors from this preparation were poured into dilute aqueous potassium hydroxide, the red solution was washed with ether and the aqueous layer was acidified with hydrochloric acid. The red, granular precipitate was collected and recrystallized from ethanol, giving orange needles, m.p. 162.0–163.5°[39]; $\lambda_{max}^{CHCl_3}$ 6.00(m), 6.26(s), 6.57(vs), 7.20(s) μ.

Reaction of Hydrazine with II: 4-Phenacyl-3,6-diphenylpyridazine Hydrazone (V).—Hydrazine (1 ml.) was added to a solution of II (1.0 g., 2.8 millimoles) and glacial acetic acid (1 ml.) in absolute ethanol (20 ml.) at room temperature. After 0.5 hr. at room temperature, the mixture was cooled in ice, filtered and the product washed with cold ethanol. The yield of white crystals (V) was 750 mg. (74%), m.p. 151.5–154.0°. Three recrystallizations from ethanol afforded an analytical sample: flat, white needles, m.p. 155.0–156.5° dec. (for spectrum see Table II).

Anal. Calcd. for $C_{24}H_{20}N_4$: C, 79.09; H, 5.53; N, 15.38. Found: C, 78.86; H, 5.36; N, 15.12.

The filtrate and washings from the original isolation of V were diluted with water and extracted with ether; the ethereal extracts were dried over sodium sulfate and evaporated. The residual yellow glass crystallized after long standing, and the yellow cubic crystals obtained were washed with methanol. The yield of yellow cubes was 200 mg. (20%), m.p. 139–141°. Three recrystallizations from methanol gave an analytical sample: yellow cubes, m.p. 143.5–144.0°; $\lambda_{max}^{CHCl_3}$ 3.00(w), 6.31(s), 7.15(s) μ; λ_{max}^{EtOH} 267 mμ (log ε 4.52).

Anal. Calcd. for $C_{24}H_{20}N_4$: C, 79.09; H, 5.53; N, 15.38. Found: C, 78.96; H, 5.28; N, 15.09.

Hydrolysis of V: 4-Phenacyl-3,6-diphenylpyridazine (VI).—Compound V (100 mg., 0.275 millimole) was warmed on a steam-bath with 50% aqueous hydrochloric acid (6 ml.). The brilliant red precipitate initially formed dissolved to give a yellow solution which gradually deposited a pale yellow gelatinous material. After 0.5 hr., the mixture was cooled in ice and the yellow crystals (50 mg.) were filtered. Recrystallization from ethanol afforded 36 mg. (37%) of very pale yellow needles, m.p. 154.0–155.5° (for spectrum see Table II). An analytical sample was obtained by recrystallization from methanol as white needles, m.p. 155.0–155.5°.

Anal. Calcd. for $C_{24}H_{18}N_2O$: C, 82.26; H, 5.18; N, 8.00. Found: C, 82.02; H, 5.25; N, 7.76.

Reaction of Hydrazine with VI: Regeneration of V.—Treatment of a small sample of VI with hydrazine in aqueous ethanol for 0.25 hr. at room temperature gave a white crystalline material which on recrystallization from ethanol afforded white needles, m.p. 150–153°, identified as V by mixed m.p. and comparison of infrared spectra.

Oxidation of V.—A warm 20% solution of potassium permanganate in 50% aqueous acetone (15 ml.) was added to a slurry of V (150 mg., 0.41 millimole) in 50% aqueous acetone (10 ml.). The mixture was warmed on the steam-bath for 0.5 hr., cooled and acidified with dilute sulfuric acid. Sodium bisulfite was added immediately until all the manganese dioxide had dissolved, the mixture was cooled and the white crystalline precipitate (60 mg.) was collected. Recrystallization from methanol gave 32 mg. (23%) of white crystals, m.p. 177.5–178.5°; $\lambda_{max}^{CHCl_3}$ 3.00(w), 6.23(s), 6.31(s), 6.72(m), 6.98(s), 7.16(s), 7.23(s), 11.02(s) μ; λ_{max}^{EtOH} 225 mμ (log ε 4.36), 250 mμ (log ε 4.29), 288 mμ (log ε 4.72); solutions in methanol exhibited a pale green fluorescence. Two recrystallizations from methanol gave an analytical sample, m.p. 179.5–180.5°.

Anal. Calcd. for $C_{24}H_{16}N_2$: C, 86.72; H, 4.85; N, 8.43. Found: C, 86.55; H, 4.77; N, 8.48.

The original mother liquor was diluted with water and extracted with ether: the ethereal extract was washed with dilute hydrochloric acid and extracted several times with 10% aqueous sodium carbonate. The basic extracts were combined, acidified to *p*H 2 with dilute hydrochloric acid and extracted several times with ether. From the ethereal extracts was obtained 50 mg. of pale yellowish-white crystals which on sublimation gave benzoic acid, m.p. 120–121°, identified by mixed m.p. and infrared spectral comparison.

Preparation of II by Condensation of I with *trans*-1,2-Dibenzoylethylene,—Sodium amide (1.6 g., 0.040 mole) was added gradually to a stirred slurry of I (8.5 g., 0.040 mole) in anhydrous ether (100 ml.) at 0° under a gentle nitrogen stream. When the evolution of ammonia had ceased, *trans*-1,2-dibenzoylethylene (9.4 g., 0.040 mole) was added; a dark red color formed immediately. After the reaction mixture had been stirred for 1 hr. at room temperature, more sodium amide (1.6 g., 0.040 mole) was added. Stirring under nitrogen was continued for a further 3 hr. The brick-red slurry was then poured into ice-water, and the ethereal layer separated and extracted with cold 3% aqueous potassium hydroxide. The combined aqueous layer and basic extracts were acidified with hydrochloric acid, and the orange, granular precipitate was filtered and crystallized from ethanol. The yield of very small, orange needles was 6.49 g. (45%), m.p. 120–122°. A mixture with the product from reaction of I with sodium amide alone melted at 121–123°, and the infrared spectra ($CHCl_3$) of the two samples were identical.

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(39) *Cf.*, R. C. Fuson, C. L. Fleming, P. F. Warfield and D. E. Wolf, *J. Org. Chem.*, **10**, 121 (1945).