acid to maintain solution. When no more iodine was liberated, the mixture was diluted with water, the oil separated, extracted with ether and dried over anhydrous sodium sulfate. Distillation gave, after removal of ether, 2.5 g. of the formylacetate (VII), b. p. 80° (1 mm.), $n^{20}\mathrm{D}$ 1.4715.

5-Allyl-2-thiouracil (VIII).—There was mixed 2.5 g. of the formylacetate (VII), 1.3 g. of thiourea and 30 ml. of anhydrous ethanol. The mixture was warmed to effect solution and 0.5 g. of sodium dissolved in 15 ml. of ethanol added. After refluxing for five hours, the mixture was cooled, neutralized with concd. hydrochloric acid, filtered hot and the volume reduced to one-half by evaporation on the hot-plate. The crude uracil (VIII) separated on cooling and was collected on a filter, m. p. 178–182°. After two recrystallizations from ethanol it melted at 185–186°.

A sample of the uracil (VIII) prepared from ethyl α-allyl-α-formylacetate (IX)[4] in a similar manner melted at 184–186° and gave no depression when mixed with the uracil (VIII) from above. *Anal.* Calcd. for $C_7H_8N_2OS$: C, 50.00; H, 4.82; S, 19.0. Found: C, 49.46; H, 5.12; S, 18.9.

Ethyl α,α,β-Trichloro-β-ethoxypropionate (X).—A solution of 268 g. (1.5 moles) of ethyl α-chloro-β-ethoxyacrylate (III) in 100 g. of chloroform was cooled to 10° and chlorine gas introduced until a faint yellow color persisted. Distillation gave, after removal of chloroform, 340 g. (91%) of the trichloropropionate (X), b. p. 86–90° (2 mm.); $n^{20}\mathrm{D}$ 1.4605. *Anal.* Calcd. for $C_7H_{11}O_3Cl_3$: Cl, 42.7. Found: Cl, 42.5.

Ethyl α,α-Dichloro-β,β-diethoxypropionate (XI).—A mixture of 18 g. (0.07 mole) of the trichloropropionate (X), 40 g. of ethanol and 2 drops of concd. hydrochloric acid was refluxed for eight hours. Fractionation gave, after removal of excess ethanol and 2 g. of forerun, 13 g. (67.5%) of the dichloropropionate (XI), b. p. 85–92° (2 mm.), $n^{20}\mathrm{D}$ 1.4488. *Anal.* Calcd. for $C_9H_{16}O_4Cl_2$: Cl, 27.6. Found: Cl, 27.6.

Ethyl α,α-Dichloro-β-ethoxy-β-phenoxypropionate (XII).—A mixture of 40 g. (0.161 mole) of the trichloropropionate (X) and 16.5 g. (0.164 mole) of phenol was heated on a steam-bath under reduced pressure (70–20 mm.) for six hours during which time hydrogen chloride was evolved. Distillation gave 33 g. (67.5%) of the phenoxypropionate (XII), b. p. 119–122° (1 mm.); $n^{20}\mathrm{D}$ 1.5037; d^{20}_{20} 1.239. *Anal.* Calcd. for $C_{13}H_{16}O_4Cl_2$: Cl, 23.08; *MR* 73.31. Found: Cl, 22.73; *MR* 73.37.

Ethyl α,α-Dichloro-β-ethoxy-β-(2,4-dichlorophenoxy)-propionate (XIII).—In a similar experiment using 2,4-dichlorophenol, the 2,4-dichlorophenoxypropionate (XIII) was obtained in 49% yield, b. p. 171–172° (5 mm.), $n^{20}\mathrm{D}$ 1.5221. *Anal.* Calcd. for $C_{13}H_{14}O_4Cl_4$: Cl, 37.7. Found: Cl, 37.4.

Ethyl α,α-Dichloro-β-(*n*-butylimino)-propionate (XIV).—With cooling there was added to 50 g. (0.2 mole) of the trichloropropionate (X), 29 g. of *n*-butylamine. The temperature was maintained below 50°. To the mixture consisting of a slurry of amine hydrochloride was added 100 g. of methanol to effect solution. Gaseous ammonia was passed into the solution and the ammonium chloride removed on the filter. The filtrate was treated successively with ammonia gas and filtered until no more ammonium chloride precipitated. Distillation gave, after removal of methanol and excess amine, 28.5 g. (60%) of the imine (XIV), b. p. 122–129° (3 mm.), $n^{20}\mathrm{D}$ 1.4705. *Anal.* Calcd. for $C_9H_{15}O_2Cl_2N$: Cl, 29.53; N, 5.8. Found: Cl, 30.07; N, 6.0.

Ethyl α-Chloro-β-ethoxymaleate (XVII).—Ethyl ethoxymaleate (XV) (108 g., 0.5 mole) dissolved in 200 g. of chloroform was cooled to 10–12° and maintained at this temperature while chlorine gas (0.5 mole) was introduced. The chloroform was removed by distillation under reduced pressure to give a residue which was treated with triethylamine by the same procedure used for III. Fractionation gave 87 g. (69.5%) of the chloromaleate (XVII), b. p. 118–122° (3 mm.), $n^{20}\mathrm{D}$ 1.4678.[7] *Anal.* Calcd. for $C_{10}H_{15}O_5Cl$: Cl, 14.2. Found: Cl, 14.2.

Ethyl α,α,β-Trichloro-β-ethoxysuccinate (XVIII).—Chlorination of 70 g. (0.31 mole) of the chloromaleate (XVII) dissolved in 250 g. of chloroform at 10° gave 69 g. (70%) of the chlorosuccinate (XVIII), b. p. 107–110° (2 mm.), $n^{20}\mathrm{D}$ 1.4660. *Anal.* Calcd. for $C_{10}H_{15}O_5Cl_3$: Cl, 33.1. Found: Cl, 31.9.

Summary

The addition of chlorine to ethyl β-ethoxyacrylate (I) and ethyl ethoxymaleate (XV) yields the unstable dichlorides which are readily converted to the stable ethyl α-chloro-β-ethoxyacrylate (III) and ethyl α-chloro-β-ethoxymaleate (XVII). Treatment of III and XVII with chlorine produces the stable ethyl α,α,β-trichloro-β-ethoxypropionate (X) and ethyl α,α,β-trichloro-β-ethoxysuccinate (XVIII). Various reactions of these chlorine derivatives are presented.

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[7] Cope, THIS JOURNAL, **58**, 570 (1936).

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DUQUESNE UNIVERSITY]

Hydrazones and Azines of Diaryl Ketones

BY H. HARRY SZMANT AND CLARE MCGINNIS

In this paper we wish to report convenient procedures for the preparation of hydrazones and azines of diaryl ketones. We also wish to consider the reasons for the distinctive behavior of diaryl ketones in reactions with the common reagents for the carbonyl group when compared to other types of carbonyl compounds.

The reaction of hydrazine with carbonyl compounds proceeds with increasing difficulty as the carbonyl compound varies in the order aldehyde < dialkyl ketone < alkaryl ketone < diaryl ketone. Aldehydes and dialkyl ketones on shaking with hydrazine in a water or alcoholic medium form the hydrazone or azine.[1] When necessary the conversion of the hydrazone to the azine is brought about by the addition of a drop of acid (acetic or hydrochloric) during the crystallization process. The preparation of hydrazones and azines of alkaryl ketones requires heating and, in the case of azine formation, acid catalysis.[2] Examination of the literature reveals that even more vigorous conditions are required to prepare hydrazones and

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[1] (a) Blout and Gofstein, THIS JOURNAL, **67**, 13 (1945); (b) Gerhardt, *Monatsh.*, **41**, 199 (1920); (c) Curtius, *J. prakt. Chem.*, [2] **44**, 161 (1891).

[2] (a) Blout, Eager and Gofstein, THIS JOURNAL, **68**, 1983 (1946); (b) Bruining, *Rec. trav. chim.*, **41**, 655 (1922).

azines of diaryl ketones. Smith[3] used anhydrous hydrazine, absolute ethanol, and a sealed-tube reaction at 150° to prepare benzophenone hydrazone. Grummitt and Jenkins[4] also use a sealed-tube reaction at 150–160° to prepare *p,p*′-dichlorobenzophenone hydrazone, and these authors, as well as Schapiro,[5] mention the failure of the reaction under reflux conditions in isopropyl and ethyl alcohols, respectively. Blout and co-workers[2a] also stress the fact that the preparation of benzophenone azine necessitates the use of a bomb and temperatures of 150–160°.

The present study shows that the hydrazones of typical diaryl ketones can be obtained in satisfactory yields by refluxing a mixture of the ketone, 85% hydrazine hydrate, and 95% ethanol under conditions of continuous removal of water. The conversion of the hydrazone to the azine is brought about by acidifying a mixture of the hydrazone and 95% ethanol with sulfuric acid.

Experimental[6]

Preparation of Hydrazones of Diaryl Ketones.—The extraction thimble of a Soxhlet extractor was filled with 20 g. of freshly heated calcium oxide and the ketone and 85% hydrazine hydrate were refluxed with approximately 150 ml. of 95% ethanol for a period of sixteen to twenty-four hours. The hot alcoholic solution was filtered (to remove any traces of calcium oxide carried over into the flask), and the hydrazone was isolated on concentrating the solution. The results obtained with five diaryl ketones are summarized in Table I.

TABLE I

DIARYL KETONE HYDRAZONE

	Ketone	g.	Weight in g. 85% H_2NN-$H_2 \cdot H_2O$	Yield,[a] %	Hydrazone M. p., °C. found	(lit.)
1	Benzophenone	18.2	17.7	88	97–98	(97–98)[b]
2	*p,p*′-Dichlorobenzophenone	2.3	1.5	45	91–93	(92–93)[c]
3	Michler ketone	2.0	2.0	95	150	(149–150)[d]
4	*p,p*′-Dimethoxybenzophenone	3.1	2.0	50	84–86	(83–85)[e]
5	*p*-Benzenesulfonylbenzophenone[f]	1.0	0.9	50	179–180[g]	

[a] In view of the limited amounts of the ketones available for this study, no efforts were made to increase the reported yields. The yield of benzophenone hydrazone was only slightly improved when the reflux period was extended to forty-four hours. [b] Ref. 3. [c] Ref. 4. [d] Wieland, *Ann.*, **381**, 231(1911). [e] Staudinger and Kupfer, *Ber.*, **44**, 2197 (1911). [f] Szmant, Regan and DeStefano, unpublished work. [g] *Anal.* Calcd. for $C_{19}H_{16}SO_2N_2$: C, 67.83; H, 4.80. Found: C, 67.60; H, 4.54.

Preparation of Azines of Diaryl Ketones.—To a mixture of 0.5 g. of the hydrazone and 30 ml. of 95% ethanol there was added concentrated sulfuric acid until the mixture remained acidic to methyl orange indicator. Usually two to three drops of acid were sufficient. The mixture on standing deposited a white precipitate of hydrazine sulfate. After twelve to fifteen hours the mixture was warmed in order to dissolve the azine and was immediately filtered. The azine was isolated from the filtrate and recrystallized from ethyl alcohol or toluene. The results obtained in the preparation of four diaryl ketones are listed in Table II.

TABLE II

DIARYL KETONE AZINES

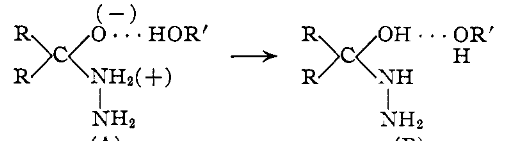
	Hydrazone of	Yield, %	Azine M. p., °C. found	Lit.
1	Benzophenone	85	164	164[a]
2	*p,p*′-Dichlorobenzophenone	33	224.5–225.5[b]	
3	Michler ketone	59	253	253[c]
4	*p,p*′-Dimethoxybenzophenone	72	179–180	124–125[d]

[a] Ref. 2a. [b] *Anal.* Calcd. for $C_{26}H_{16}Cl_4N_2$: C, 62.67; H, 3.24. Found: C, 62.76; H, 3.10. [c] Wieland, *Ann.*, **381**, 232 (1911). [d] We were unable to duplicate the m. p. reported by Staudinger and Kupfer, *Ber.*, 44, 2197 (1911). Our product analyzed correctly: calcd. for $C_{30}H_{28}O_4N_2$: C, 75.19; H, 5.87. Found: C, 75.47; H, 5.42.

Discussion

The mechanism of the formation of hydrazones can be assumed to follow the general scheme of the addition reactions of carbonyl compounds.[7] In view of the fact that no difficulties are encountered in the preparation of semicarbazones, oximes or phenylhydrazones of diaryl ketones, and on the basis of the success of the experimental conditions employed in this study, the following explanation is offered to explain the peculiar difficulties in the formation of diaryl ketone hydrazones.

The high resonance stabilization of benzophenone[8] implies a small contribution of that structure of benzophenone in which the positive charge is located at the carbon atom of the carbonyl group. On this basis one would predict a high potential energy barrier in the formation of the benzophenone-hydrazine transition complex.[9] Furthermore, the relatively high basicity of hydrazine,[10] if carried over to the transition complex would make the proton transfer from A to B more difficult than in the corresponding complex formed from the less basic reagents.[11] Finally, it would seem that the equilibrium in the benzophenone hydrazine reaction is not



(A) (B)

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(3) Smith, "Organic Syntheses," John Wiley and Sons, Inc., New York, N. Y., 1944, Vol. 24, p. 53.

(4) Grummitt and Jenkins, THIS JOURNAL, **68**, 914 (1946).

(5) Schapiro, *Ber.*, **62B**, 2133 (1929).

(6) All melting points are uncorrected. Microanalyses by the Micro-Analytical Laboratory, University of Pittsburgh.

(7) Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, p. 333–334.

(8) The resonance energy of benzophenone is about 10 kcal. in excess of the resonance energy of two benzene rings.

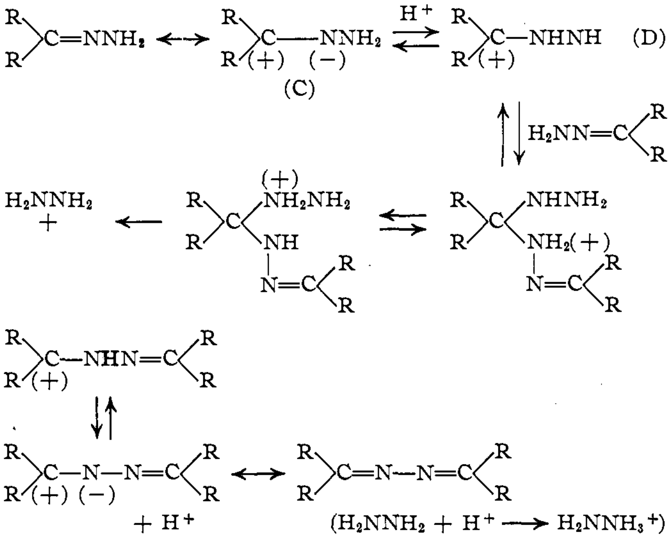
(9) Price and Hammett (THIS JOURNAL, **63**, 2387 (1941)) explain similarly the difference between acetone and acetophenone in the reaction with semicarbazide.

(10) It is noteworthy that the ionization constants of hydrazine, hydroxylamine, phenylhydrazine, and semicarbazide are 3×10^{-6} (25°), 1.07×10^{-8} (25°), 1.6×10^{-9} (40°), and 2.7×10^{-11} (40°), respectively ("Lange's Handbook of Chemistry," Handbook Publishers, Inc., Sandusky, Ohio, 1946, p. 1382–1383).

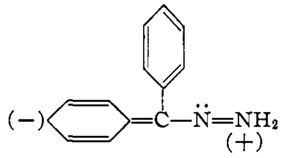
(11) Hammett (ref. 7) considers this phase of the semicarbazone formation to be the rate-determining step.

in favor of the hydrazone. The great ease with which benzophenone hydrazone hydrolyzes was pointed out recently by Pearson and Greer[12] but unfortunately no information is available on the relative hydrolysis rates of hydrazones of the various types of carbonyl compounds. The success of the formation of diaryl ketone hydrazones depends, we believe, on the displacement of the equilibrium (otherwise unfavorable toward hydrazone formation) by the continuous removal of water.[13]

The mechanism of the acid-catalyzed formation of the azines from the corresponding hydrazones is thought to occur as shown



On the basis of postulated mechanism the acid catalyst serves to form a transient carbonium ion (D) which becomes subject to the nucleophilic attack of another hydrazone molecule. It is reasonable to expect that the reaction depends, therefore, on the basicity of the hydrazone molecule. This is particularly significant since during the formation of the azine there is liberated a strong base, namely, hydrazine. While the hydrazones of aliphatic ketones may exist as resonance hybrids (C) and, indeed, structures of this type would be favored by the electropositive nature of the alkyl groups, the introduction of aryl groups permits the existence of


(E)

resonance structures of type (E). The contribution of this type of resonance structure would effectively decrease the basicity of diaryl ketone hydrazones. While information about the basicity of hydrazones is lacking, it was recently reported[12] that benzophenone hydrazone failed to titrate electrometrically with mineral acids in aqueous solution.[14]

Because of the weak basicity of the diaryl ketone hydrazones, the conventional procedure employing a few drops of a weak acid (such as acetic acid) fails to bring about the formation of the azine unless high temperatures are used. The success of the method described in this paper is thought to hinge on the use of sufficient strong acid to provide acid catalysis in spite of the formation of the hydrazine salt.

Summary

Hydrazones of diaryl ketones can be prepared by refluxing a mixture of the ketone, hydrazine hydrate, and ethanol under appropriate dehydrating conditions. The hydrazones can be converted to azines by careful acidification with a strong acid. Theoretical explanations for the distinctive behavior of diaryl ketones in the formation of hydrazones and azine are suggested.

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[12] Pearson and Greer, THIS JOURNAL, **71**, 1895 (1949).

[13] Stieglitz and co-workers (THIS JOURNAL, **56**, 1904 (1934); Chuang, *Abs. of Theses*, The U. of Chicago, Science Series, v. 3, pp. 111 (1924-1925)) seem to have misinterpreted the function of barium oxide in the formation of hydrazones of *p*-methoxy- and *p*-methylbenzophenone. The "condensing agent" was used in quantities in which it was fully capable to dehydrate the reaction mixture.

[14] The determination of the basicities of various hydrazones is in progress in this laboratory.