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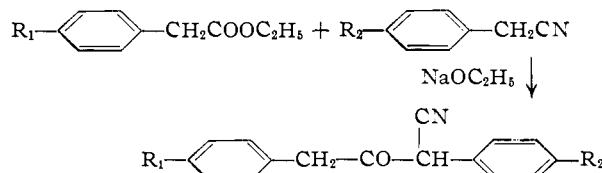
Synthesis of Unsymmetrical 1,3-Diphenyl-2-propanones

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RECEIVED AUGUST 31, 1953

The synthesis of six new unsymmetrically *p*-substituted 1,3-diphenyl-2-propanones has been carried out by condensing ethyl phenylacetate with phenylacetonitrile—the substituent being in either the ester or the nitrile—and hydrolyzing and decarboxylating the intermediate acetoacetonitrile. 1-(2',4'-Dinitrophenyl)-3-benzyl-4-phenyl-2-aminopyrazoles have been used to characterize the acetoacetonitriles and oximes and 2,4-dinitrophenylhydrazones for the 1,3-diphenyl-2-propanones.

In the course of our studies on the synthesis and absorption spectra of tetracyclones,² it was necessary to prepare unsymmetrically substituted 1,3-diphenyl-2-propanones as intermediates. It appeared expedient to us to modify and attempt to standardize the reported Claisen condensation³⁻⁵ whereby a phenylacetonitrile is condensed with an ethyl phenylacetate in the presence of sodium ethoxide; the isolated disubstituted acetoacetonitrile being ultimately hydrolyzed and decarboxylated to yield the desired ketone.



of the intermediate acetoacetonitriles. Derivatives of the β -ketonitriles were prepared in the form of their 2,4-dinitrophenylhydrazones. It was necessary to allow the mixture of ketonitrile and

TABLE I

Acetoacetonitrile		Yield, %	M.p., °C.	Empirical formula	Analyses, %				Found			
R ₁	R ₂				C	Calcd. H	N	Hal. or S	C	H	N	Hal. or S
DIPHENYLACETOACETONITRILES $R_1-\text{C}_6\text{H}_4-\text{CH}_2-\text{CO}-\overset{\text{CN}}{\text{C}}\text{H}-\text{C}_6\text{H}_4-R_2$												
From phenylacetonitrile and an ethyl 4-substituted phenylacetate												
H	H	82	79.4–80.0 ^a	C ₁₆ H ₁₃ NO	81.68	5.57	5.96	...	81.98	5.35	5.82	...
CH ₃	H	84	88.0–89.0	C ₁₇ H ₁₅ NO	81.90	6.06	5.62	...	82.02	6.29	5.36	...
CH ₃ O	H	81	69.5–70.4	C ₁₇ H ₁₅ NO ₂	76.96	5.70	5.28	...	77.24	6.00	5.25	...
Br	H	80	94.0–95.0	C ₁₆ H ₁₂ BrNO	61.16	3.85	4.46	25.44	61.62	4.13	4.28	25.24
CH ₃ S	H	85	85.0–85.2	C ₁₇ H ₁₅ NOS	72.56	5.37	4.98	11.40	72.39	5.27	5.02	11.25
From a 4-substituted phenylacetonitrile and ethyl phenylacetate												
H	Cl	59	31.0–31.2	C ₁₆ H ₁₂ ClNO	5.19	13.14	5.28	13.08
H	F	75	111.8–112.0	C ₁₆ H ₁₂ FNO	75.87	4.77	5.53	...	76.00	4.75	5.83	...

^a Reported m.p. 85–86°, see reference 4.

TABLE II

1-(2',4'-DINITROPHENYL)-3-BENZYL-4-PHENYL-2-AMINOPYRAZOLES		M.p., °C.	Empirical formula	Analyses, %				Found			
R ₁	R ₂			C	Calcd. H	N	Hal. or S	C	H	N	Hal. or S
H	H	127.2–128.2	C ₂₂ H ₁₇ N ₃ O ₄	63.61	4.13	16.84	..	64.14	3.86	17.08	..
CH ₃	H	140.0–141.0	C ₂₃ H ₁₉ N ₃ O ₄	64.33	4.46	16.31	..	64.52	4.50	15.95	..
CH ₃ O	H	113.8–114.5	C ₂₃ H ₁₉ N ₃ O ₅	15.72	15.54	..
Br	H	154.8–155.2	C ₂₂ H ₁₆ BrN ₃ O ₄	14.17	14.17	..
H	Cl	155.0–156	C ₂₂ H ₁₆ ClN ₃ O ₄	58.74	3.59	15.57	7.88	59.21	3.55	15.30	8.12
H	F	175.4–176.4	C ₂₂ H ₁₆ FN ₃ O ₄	16.16	15.56	..

Table I summarizes the results for the preparation

(1) Taken from the Dissertation of S. B. Coan presented to the Graduate Faculty of the Polytechnic Institute in partial fulfillment of the requirements for the Ph.D. degree.

(2) S. B. Coan, D. E. Trucker and E. I. Becker, *THIS JOURNAL*, **75**, 900 (1953).

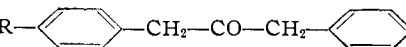
(3) C. von Meyer, *J. prakt. Chem.*, [2] **52**, 115 (1895).

(4) R. Walther and P. G. Schickler, *ibid.*, [2] **55**, 348 (1897).

(5) R. Walther and L. Hirschberg, *ibid.*, [2] **67**, 390 (1903).

2,4-dinitrophenylhydrazone in ethanol-sulfuric acid to stand overnight, after warming, before crystals appeared. The data for these derivatives are shown in Table II.

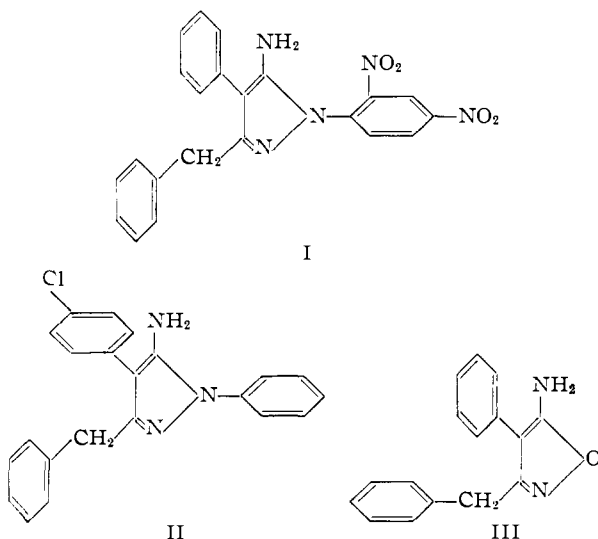
Infrared studies on selected 2,4-dinitrophenylhydrazones invariably showed the absence of a band in the 4.52–4.55 μ region. These results indicate the absence of the $-\text{C}\equiv\text{N}$ group, con-

TABLE III
 1,3-DIPHENYL-2-PROPANONES R-

R	M.p., °C.	Yield	Empirical formula	Analyses, %					
				Calcd. C	H	Hal. or S	Found C	H	Hal. or S
CH ₃	30.8-31.2	66	C ₁₆ H ₁₆ O	85.67	7.19	...	85.49	7.30	...
CH ₃ O	46.6-47.4	19 ^a	C ₁₆ H ₁₆ O ₂	79.98	6.70	...	80.10	6.96	...
F	36.0-36.5	50	C ₁₅ H ₁₃ FO	78.93	5.74	14.49	79.03	5.83	...
Cl	35.9-36.5	71	C ₁₅ H ₁₃ ClO	73.62	5.35	...	74.00	5.47	13.97
Br	53.8-54.2	50	C ₁₅ H ₁₃ BrO	62.30	4.53	...	62.59	4.67	...
CH ₃ S	43.9-44.2	40	C ₁₆ H ₁₆ OS	74.96	6.29	12.51	75.18	6.39	12.26
CH ₃ SO ₂ ⁻	104.6-105.2	70	C ₁₆ H ₁₆ O ₃ S	66.64	5.59	11.12	66.89	5.80	11.03

^a Prepared by refluxing a solution of 5 ml. of glacial acetic acid and 5 ml. of 20% aqueous hydrochloric acid with 1.0 g. of the β-ketonitrile until evolution of carbon dioxide ceased.

firming the suspicion that the dinitrophenylhydrazone was an aminopyrazole (I), rather than a simple hydrazone.



This conclusion corroborates the suggestion of Walther, *et al.*,⁵ who noted the stability of the phenylhydrazone of α-(p-chlorophenyl)-γ-phenylacetoacetonitrile to acid hydrolysis and suggested that the derivative was II. Further analogy for this cyclic structure is taken from Walther and Schickler⁴ who reported that the compound obtained by treating α,γ-diphenylacetoacetonitrile with hydroxylamine hydrochloride was III.

Hydrolysis and decarboxylation in one step was conveniently effected by refluxing the ketonitrile with 60% aqueous sulfuric acid. However, in the preparation of 1-(p-methoxyphenyl)-3-phenyl-2-propanone low yields (see Table III) were obtained even when milder conditions such as acetic acid-aqueous hydrochloric acid were employed. Invariably substantial quantities of dark colored tarry matter formed along with the ketone. On the basis of the work done by Zaugg,⁶ it is likely that after hydrolysis of the nitrile cyclization occurred.

Experimental

Materials.—The known intermediary substituted ethyl phenylacetates and phenylacetamides were prepared ac-

(6) H. E. Zaugg, R. T. Rapala and M. T. Leffler, *THIS JOURNAL*, **70**, 3224 (1948). These authors cyclized α,γ-diarylacetoacetonitriles with concentrated sulfuric acid to yield the corresponding 2-aryl-1,3-naphthohydroquinones.

 TABLE IV
 OXIMES OF 1,3-DIPHENYL-2-PROPANONES

R	M.p., °C.	Empirical formula	Analyses, %			
			Calcd. N	Hal. or S	Found N	Hal. or S
CH ₃	91.5-93.0	C ₁₆ H ₁₇ NO	5.85	...	5.74	...
CH ₃ O	98.8-99.5	C ₁₆ H ₁₇ N ₂ O ₂	5.49	...	5.60	...
Cl	92.0-93.0	C ₁₅ H ₁₄ ClNO	5.39	13.65	5.17	13.65
Br	87.4-88.2	C ₁₅ H ₁₄ BrNO	4.61	...	4.41	...

 TABLE V
 2,4-DINITROPHENYLHYDRAZONES OF 1,3-DIPHENYL-2-PROPANONES

R	M.p., °C.	Empirical formula	Analyses, %			
			Calcd. N	Hal. or S	Found N	Hal. or S
CH ₃	132.2-132.8	C ₂₂ H ₂₀ N ₄ O ₄	13.85	...	13.58	...
CH ₃ O	132.5-133.5	C ₂₂ H ₂₀ N ₄ O ₆	13.33	...	13.50	...
F	114.5-115.0	C ₂₁ H ₁₇ FN ₄ O ₄	13.72	...	13.90	...
Cl	124.5-125.0	C ₂₁ H ₁₇ ClN ₄ O ₄	13.19	8.36	12.92	7.98
Br	134.8-136.2	C ₂₁ H ₁₇ BrN ₄ O ₄	11.94	17.04	11.50	16.83
CH ₃ S	146.5-147.0	C ₂₂ H ₂₀ N ₄ O ₆ S	12.84	7.34	12.33	7.44
CH ₃ SO ₂	122.0-123.0	C ₂₂ H ₂₀ N ₄ O ₆ S	11.95	6.85	11.78	6.70

ording to methods in the literature. Commercial 2B ethanol was found satisfactory as solvent for the condensation.

The preparations described below are typical of the procedures employed.

Ethyl p-Methylmercaptophenylacetate.—A solution of 27 g. (0.15 mole) of p-methylmercaptophenylacetic acid⁷ and 25 ml. of concentrated sulfuric acid in 250 ml. of absolute ethanol was refluxed for four hours and allowed to stand overnight. After pouring over 300 g. of ice, the mixture was extracted with ether. The ether extracts were washed thoroughly with water and sodium bicarbonate solution and dried over anhydrous sodium sulfate. Removal of the solvent by evaporation on a steam-bath yielded 27 g. (0.13 mole, 86%) of an oil which crystallized upon cooling, m.p. 52.0-53.0°. Recrystallization from 100 ml. of petroleum ether (b.p. 35-50°) yielded 24 g. (0.115 mole, 77%) of white needles, m.p. 55.5-56.2°.

Anal. Calcd. for C₁₁H₁₄O₂S: C, 62.82; H, 6.71; S, 15.25. Found: C, 62.93; H, 6.18; S, 15.20.

α-(4-Chlorophenyl)-γ-phenylacetoacetonitrile.—To a stirred and refluxing solution of sodium ethoxide in ethanol prepared from 11.5 g. (0.5 atom) of sodium and 150 ml. of ethanol was slowly added a mixture of 37.8 g. (0.25 mole) of 4-chlorophenylacetonitrile and 50.8 g. (0.31 mole) of ethyl phenylacetate. After refluxing for three hours, the solution was cooled and poured into 600 ml. of ice-water. The aqueous alkaline mixture was thoroughly extracted with ether and then acidified with cold dilute hydrochloric acid. The acidified mixture was then extracted three times with 200-ml. portions of ether. After extracting the ether solu-

(7) Prepared in 20% yield according to the procedure of J. W. Corse, R. G. Jones, Q. F. Soper, C. W. Whitehead and O. K. Behrens, *THIS JOURNAL*, **70**, 2841 (1948).

