

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT, UNIVERSITY OF MICHIGAN]

Azidocarbonyl Compounds. III. The Preparation and Pyrolysis of Certain Ortho-Substituted Phenacyl Azides¹BY J. H. BOYER² AND D. STRAW

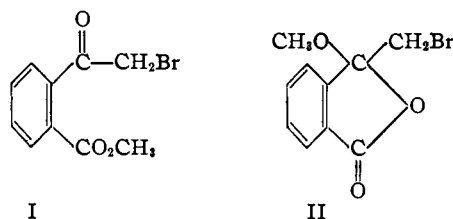
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From the corresponding halides *o*-nitro-, *o*-amino-, *o*-azido-, *o*-hydroxy- and *p*-hydroxyphenacyl azides were prepared. *o*-Carboxyphenacyl bromide and both the normal and pseudo forms of *o*-carboxyphenacyl bromide failed to react with sodium azide or hydrazoic acid to produce the corresponding azides. Pyrolysis of *o*- and *p*-hydroxyphenacyl azides resulted in the formation of the corresponding 2-hydroxybenzoyl-4(or 5)-hydroxyphenylimidazoles; however, pyrolysis of *o*-aminophenacyl azide brought about the formation of indigo.

The rearrangement which occurs upon pyrolysis of α -azidocarbonyl compounds has previously been demonstrated.³ The synthesis of *o*-hydroxy-, *o*-amino- and *o*-carboxyphenacyl azides has now been undertaken with the consideration that upon pyrolysis, interaction of these functional groups with the imino groups, which results from the rearrangement, might occur.

Displacement of halogen by the azido group provided a convenient synthesis for *o*-hydroxy-, *p*-hydroxy-, *o*-amino- and *o*-nitrophenacyl azides. The failure to obtain an azide from *o*-carboxyphenacyl bromide and sodium azide or hydrazoic acid at temperatures up to 80° is reminiscent of observations previously reported on the lack of reactivity of this bromide and closely related derivatives.⁴ Since δ -ketoacids and esters tend to exist in the lactol and *pseudo ester* forms, respectively, the normal methyl ester of acetylbenzoic acid was prepared from the silver salt and methyl iodide. Bromination then afforded *o*-carboxyphenacyl bromide (normal ester, I). For comparison the pseudo methyl ester (II) was prepared by esterification of *o*-bromoacetylbenzoic acid with methyl alcohol in the presence of hydrochloric acid.⁴ Infrared absorption at 5.8 μ by the normal ester is characteristic of the conjugated ester and keto carbonyl groups, while absorption at 5.55 μ by the pseudo methyl ester agrees with the values reported for carbonyl groups in lactones.⁵

Surprisingly enough, not only the pseudo form but also the normal ester failed to react with sodium azide or hydrazoic acid to produce the corresponding azides.



Pyrolysis of the azides occurred at 180–210° with the evolution of nitrogen and rearrangement.

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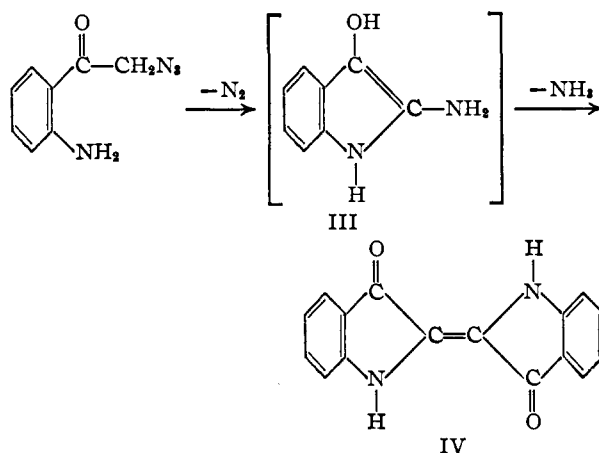
(2) Chemistry Department, Tulane University, New Orleans, Louisiana.

(3) J. H. Boyer and D. Straw, *THIS JOURNAL*, **75**, 1642 (1953).

(4) H. de Diesbach and O. Klement, *Helv. Chim. Acta*, **24**, 158 (1941).

(5) H. M. Randall, R. G. Fowler, N. Fuson and J. R. Dangi, "Infrared Determination of Organic Structures," D. Van Nostrand Co., Inc., New York, N. Y., 1949, pp. 21–25.

Dimerization of the imines thus formed from the hydroxyphenacyl azides followed by dehydration led to the corresponding 2-hydroxybenzoyl-4(or 5)-hydroxyphenylimidazoles in accordance with previous results.³ A similar reaction failed to occur with the imine which resulted from *o*-aminophenacyl azide. In this case ring closure through interaction with the amino group presumably resulted in the formation of 2-amino-3-hydroxyindole (III). Under the conditions of its formation, however, dimerization with elimination of ammonia provided a nearly quantitative yield of indigo (IV).⁶ That initial formation of indoxyl by displacement of the azido group did not occur was established by collecting the gas evolved over water and by detecting the ammonia formed in the reaction.

Experimental⁷

Preparation of the Halides. *o*-Aminophenacyl Bromide.—Commercially available *o*-nitrotoluene was oxidized⁸ to *o*-nitrobenzoic acid in 36% yield. Transformation into the acid chloride⁹ by thionyl chloride (86% yield) was followed by a reaction with ethoxymagnesium malonic ester which resulted in the formation of *o*-nitroacetophenone (83% yield).¹⁰ Attack by an equimolar quantity of bromine in chloroform afforded *o*-nitrophenacyl bromide¹¹ (95% yield), which was reduced by copper powder in sulfuric acid to *o*-aminophenacyl bromide (52%).¹¹

(6) The dimerization with elimination of ammonia of 5-methoxy-2-amino-3-hydroxyindole which resulted in the formation of the corresponding dimethoxyindigo was reported by H. Wieland, L. Semper and E. Gmelin, *Ann.*, **367**, 52 (1909).

(7) Melting points are uncorrected. Microanalyses by Micro-Tech Laboratories, Skokie, Illinois.

(8) L. A. Bigelow, *THIS JOURNAL*, **41**, 1559 (1919).

(9) M. Boëtius and H. Römisch, *Ber.*, **68**, 1924 (1935).

(10) G. A. Reynolds and C. R. Hauser in *Org. Syntheses*, **30**, 70 (1950).

(11) P. Ruggli and H. Reichwein, *Helv. Chim. Acta*, **20**, 913 (1937).

TABLE I
 NUCLEAR-SUBSTITUTED PHENACYL AZIDES

Phenacyl azides			M. p., °C.	Yield, %	Empirical formula	Carbon		Analyses, % Hydrogen		Nitrogen	
	R'	R				Calcd.	Found	Calcd.	Found	Calcd.	Found
<i>o</i> -Amino	H	NH ₂	66-67	90	C ₈ H ₉ ON ₄	54.53	54.76	4.58	4.58	31.81	31.88
<i>o</i> -Hydroxy	H	OH	73-74	89	C ₈ H ₇ O ₂ N ₃	54.23	54.45	3.99	4.03	23.72	23.76
<i>o</i> -Nitro	H	NO ₂	62-62.5	81	C ₈ H ₆ O ₂ N ₄	46.60	46.60	2.93	3.04	27.18	27.35
<i>o</i> -Azido	H	N ₃	37-38	88	C ₈ H ₈ ON ₆	^b	^b	^b	^b	^b	^b
<i>p</i> -Hydroxy ^a	OH	H	139-140	80	C ₈ H ₇ O ₂ N ₃	54.23	54.12	3.99	4.13	23.72	23.71

^a Previously reported by K. Fries and K. Saftien, *Ber.*, **59**, 1246 (1926). ^b Not attempted.

o- and *p*-Hydroxyphenacyl chlorides resulted from rearrangement of phenyl chloroacetate (Eastman Kodak Co.) in 29 and 50% yields, respectively.¹²

o-Carboxyphenacyl bromide, m.p. 126-127°, was obtained by the bromination¹³ of *o*-acetobenzoic acid¹⁴ in 83% yield. Esterification by methanol saturated with hydrogen chloride produced the pseudo methyl ester (II),⁴ m.p. 59-60° (63% yield).

o-Carbomethoxyphenacyl Bromide (Normal Ester, I).—The silver salt of *o*-acetobenzoic acid was prepared by dissolving 19.6 g. (0.119 mole) of *o*-acetobenzoic acid in 60 ml. of 2 *N* sodium hydroxide, followed by the addition of a solution of 26.3 g. (0.119 mole) of silver nitrate dissolved in 50 ml. of water, with vigorous shaking. The white, curdy precipitate of the silver salt formed immediately, was separated by filtration, washed twice with water and pressed as dry as possible. The crude silver salt was placed in a 200-ml. round-bottomed flask equipped with dropping funnel and condenser and a threefold excess of methyl iodide (51 g., 0.36 mole) added dropwise. After cooling to room temperature, the contents of the flask were extracted with ether, the combined extracts dried over anhydrous magnesium sulfate and the ether removed in an air stream. The slightly yellow liquid residue was distilled, giving 18.6 g., b.p. 155-159° (21 mm.) (88%). By successive distillations an analytical sample was prepared, b.p. 152-153° (18 mm.),¹⁵ n_{D}^{25} 1.5252.

Anal. Calcd. for C₁₀H₁₀O₃: C, 67.40; H, 5.66. Found: C, 67.38; H, 5.78.

The semicarbazone derivative, prepared according to the standard method, on recrystallization from 50% aqueous methanol separated as white needles, m.p. 196-197°.

Anal. Calcd. for C₁₁H₁₃N₃O₃: C, 56.16; H, 5.57; N, 17.87. Found: C, 54.92; H, 5.79; N, 17.58.

o-Carbomethoxyphenacyl bromide was obtained by direct bromination of 4.1 g. (0.023 mole) of methyl *o*-acetobenzoate with an equimolar portion of bromine in a chloroform solution, yield 5.2 g. (87%) of white needles, m.p. 90-92°, after recrystallization from aqueous methanol.

(12) K. Fries and W. Pfaffendorf, *Ber.*, **43**, 214 (1910).

(13) S. Gabriel, *ibid.*, **40**, 72 (1907).

(14) H. L. Yale, *THIS JOURNAL*, **69**, 1547 (1947).

(15) H. de Diesbach and O. Klement, ref. 4, report the preparation of this ester, b.p. 158° (12 mm.). They give no additional data and make no analyses.

Anal. Calcd. for C₁₀H₉BrO₃: C, 46.71; H, 3.53; Br, 31.09. Found: C, 46.35; H, 3.71; Br, 31.62.

Preparation of the Azides.—According to procedures previously described,³ the azides described in Table I were prepared from the corresponding halides. *o*-Azidophenacyl azide resulted from treating a dilute acid solution of diazotized *o*-aminophenacyl azide with a slight molar excess of aqueous sodium azide.¹⁶ The diazide recrystallized from aqueous ethanol as white needles (see Table I). Analysis was not attempted since the compound immediately showed signs of decomposition which would be complete after several days.

All attempts failed to prepare the corresponding azides from *o*-carboxyphenacyl bromide, its normal and pseudo methyl esters by treating the halides with aqueous sodium azide or hydrazoic acid at temperatures ranging from 0-80° for lengths of time ranging from a few hours up to several weeks.

Pyrolysis of *o*- and *p*-hydroxyphenacyl azides was carried out in diphenyl ether.⁵ Nitrogen evolution was vigorous at 190-200°. Identification of the products as imidazoles is based on elementary analyses, general physical properties, and conformity with previous syntheses of imidazoles from phenacyl azides.¹⁷ A 19% yield of 2-*o*-hydroxybenzoyl-4 (or 5)-*o*-hydroxyphenylimidazole as yellow needles, m.p. 210-211°, was obtained.

Anal. Calcd. for C₁₅H₁₂N₂O₃: C, 68.56; H, 4.32. Found: C, 67.99; H, 4.21.

Similarly a 69% yield of 2-*p*-hydroxybenzoyl-4 (or 5)-*p*-hydroxyphenylimidazole as a yellow powder, m.p. 290-292°, was obtained.

Anal. Calcd. for C₁₅H₁₂N₂O₃: C, 68.56; H, 4.32; N, 10.00. Found: C, 68.37; H, 4.42; N, 10.01.

Pyrolysis of *o*-aminophenacyl azide was also carried out in diphenyl ether. Nitrogen evolution was vigorous at 205-215°. Removal of diphenyl ether left a purple residue of indigo, m.p. 390-392°, in 85% yield after recrystallization from acetone.

ANN ARBOR, MICHIGAN

(16) In a similar manner *o*-azidoacetophenone was obtained from *o*-aminoacetophenone and by identification of its DNP derivative, m.p. 183-185°, proved to be the same compound previously obtained from the oxime of diazotized *o*-aminoacetophenone and dilute acid by J. Meisenheimer, O. Senn and P. Zimmerman, *Ber.*, **60**, 1736 (1927).

(17) J. H. Boyer and D. Straw, *THIS JOURNAL*, **74**, 4506 (1952).