[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT, UNIVERSITY OF MICHIGAN]

Azidocarbonyl Compounds. I. A New Synthesis for Certain Substituted Imidazoles from Phenacyl Azides[1]

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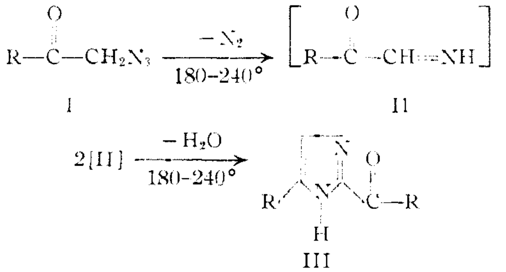
Phenacyl azide (Ia) and structurally related α-azido-ketones (Ib, c, d) underwent the loss of nitrogen when heated between 180 and 240° in an inert solvent. Good yields of the corresponding imidazoles (IIIa, b, c, d) resulted from dimerization and dehydration of the postulated α-imino-ketone intermediate. Both triazoacetone (I, R = CH_3–) and 1-azido-3,3-dimethylbutanone-2 (I, R = $(CH_3)_3C$–) underwent the loss of nitrogen when heated between 180 and 240° in an inert solvent; however, imidazole formation was not detected in either case. Acetylation of 2-benzoyl-4(or 5)-phenylimidazole (IIIa) was brought about by the use of isopropenyl acetate.

As an outgrowth of an investigation on the synthesis of heterocyclic compounds from certain biaryl azides[2] the preparation and properties of phenacyl azide (Ia) were explored. A product obtained by heating 1% solutions of this compound in trichlorobenzene, resorcinol dimethyl ether, or diphenyl ether between 180 and 240° has now been found to be identical with a product previously obtained by several investigators[3–7] from other starting materials. It was first assigned the structure of 2-benzoyl-5-phenylimidazole (IIIa) by Gastaldi[8] who recognized that dimerization followed by dehydration of the imine (IIa) suggested by Pinner[3] from phenylglyoxal and ammonia would lead to IIIa. The proposed formation of imines (II) by the pyrolysis of α-azidoketones (I) is reminiscent to their hydrolytic decomposition into imines.[9]



$$R{-}\overset{O}{\overset{\parallel}{C}}{-}CH_2N_3 \xrightarrow[180-240°]{-N_2} \left[R{-}\overset{O}{\overset{\parallel}{C}}{-}CH{=}NH\right]$$

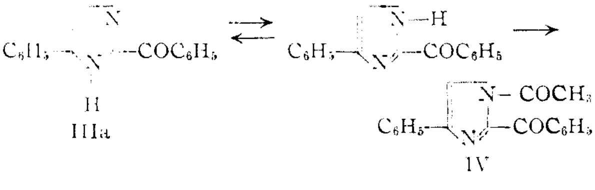
I II

2[II] $\xrightarrow[180-240°]{-H_2O}$

III

a, R = C_6H_5–; b, R = *p*-Br–C_6H_4–;
c, R = *p*-C_6H_5-C_6H_4–; d, R = β-$C_{10}H_7$–

The presence of the carbonyl function in IIIa was established by the formation of the 2,4-dinitrophenylhydrazone, not only from a sample obtained by the action of ammonia upon phenylglyoxal[10] but also from a sample now obtained from phenacyl azide. In the present work the imino group in IIIa was established by the formation of an acetyl derivative, 1-acetyl-2-benzoyl-4-phenylimidazole (IV), by treating the imidazole (IIIa) with either isopropenyl acetate or acetic anhydride in the presence of concentrated sulfuric acid. From additional work, which will soon be reported, upon the acetylation of imidazoles by the use of isopropenyl acetate it is believed that the tautomeric form of (IIIa) is acetylated because of less steric hindrance. Failure to form an acetyl derivative by the use of either acetyl chloride or acetic anhydride under basic conditions is consistent with known reaction failures between imidazoles and these reagents.[11] Basic permanganate oxidation of IIIa gave benzoic acid and apparently destroyed the imidazole nucleus.[12] There was complete recovery of starting material from attempted reduction of IIIa with sodium in boiling ethanol; however, the use of the higher boiling isoamyl alcohol and sodium yielded 2-benzyl-4(or 5)-phenylimidazole.[13]



IIIa IV

Five additional α-azidoketones, as well as phenacyl azide, were prepared from the corresponding α-haloketone and sodium azide. The pyrolysis of *p*-bromophenacyl azide (Ib), *p*-phenylphenacyl azide (Ic), and β-(α-azidoacetyl)-naphthalene (Id) brought about the formation of the corresponding imidazoles (IIIb,c,d) in good yield. Busch had previously prepared 2-*p*-bromobenzoyl-4(or 5)-*p*-bromophenylimidazole (IIIb) from *p*-bromophenacylhydrazine.[5] Apparently an aromatic nucleus adjacent to the carbonyl group is necessary for this transformation since no imidazoles were detected in the pyrolytic products obtained under similar conditions from triazoacetone (I, R = CH_3) and 1-azido-3,3-dimethylbutanone-2 (I, R = $(CH_3)_3C$–).

Experimental[14]

The Halides.—Phenacyl bromide, *p*-bromophenacyl bromide, *p*-phenylphenacyl bromide and chloroacetone were commercially available (Eastman Kodak Co.) and were used without further purification.

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(2) P. A. S. Smith and J. H. Boyer, THIS JOURNAL, **73**, 2626 (1951).

(3) A. Pinner, *Ber.*, **38**, 1531 (1905); H. Muller and H. von Pechman, *ibid.*, **22**, 2556 (1889).

(4) C. Engler and E. Hassenkamp, *ibid.*, **18**, 2240 (1885).

(5) M. Busch and W. Foerst, *J. prakt. Chem.*, **119**, 287 (1928).

(6) S. Minovici, *Ber.*, **32**, 2206 (1899).

(7) F. R. Japp and J. Knox, *J. Chem. Soc.*, **87**, 701 (1905).

(8) G. Gastaldi, *Gazz. chim. ital.*, **51**, 233 (1921).

(9) L. I. Smith, *Chem. Revs.*, **23**, 193 (1938).

(10) J. J. Gallagher, G. T. Newbold, F. S. Spring and J. C. Woods, *J. Chem. Soc.*, 910 (1949).

(11) B. Oddo and F. Ingraffia, *Gazz. chim. ital.*, **61**, 446 (1931).

(12) The instability of the imidazole nucleus toward alkaline permanganate has long been known; *cf.*, G. Wyss, *Ber.*, **10**, 1364 (1877).

(13) The stability of the imidazole nucleus toward reduction is well-known. The failure of sodium in amyl alcohol to reduce imidazoles is reported by H. Biltz and P. Krebs, *Ann.*, **391**, 210 (1912).

(14) Microanalyses by the Clark Microanalytical Laboratory, Urbana, Illinois, and Micro-Tech Laboratories, Skokie, Illinois. Melting points and boiling points are uncorrected.

TABLE I

α-AZIDOKETONES MADE FROM α-HALOKETONES AND SODIUM AZIDE

α-Haloketone	α-Azidoketone	Yield, %	M.p., °C.	Molecular formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
Phenacyl bromide	Phenacyl azide (Ia)[a]	93	17	$C_8H_7N_3O$						
p-Bromophenacyl bromide	*p*-Bromophenacyl azide (Ib)	86	86–87	$C_8H_6BrN_3O$[d]	40.02	40.31	2.52	2.54	17.50	17.56
p-Phenylphenacyl bromide	*p*-Phenylphenacyl azide (Ic)	91	88–88.5	$C_{14}H_{11}N_3O$	70.87	70.69	4.67	4.48	17.72	17.53
β-(α-Bromoacetyl)-naphthalene	β-(α-Azidoacetyl)-naphthalene (Id)	76	66–67	$C_{12}H_9N_3O$	68.23	67.98	4.29	4.18	19.91	19.79
Chloroacetone	Triazoacetone[a,b]	85	...	$C_3H_5N_3O$	...	...	..	..	...	...
1-Bromo-3,3-dimethylbutanone-2	1-Azido-3,3-dimethylbutanone-2	93	...[c]	$C_6H_{11}N_3O$	51.04	50.50	7.86	7.74	29.77	30.58

[a] Prepared by Forster (ref. 17). [b] B.p. 38° (1 mm.); n^{20}_D 1.4520. [c] Purified by evaporative distillation at a jacket temperature of 60–75° (1 mm.); n^{20}_D 1.4530; d^{20}_4 1.0310; MR_D (calcd.) 37.6, MR_D (found) 37.0. [d] Br analysis, calcd. 33.29, found 33.02.

TABLE II

PYROLYSIS OF THE α-AZIDOKETONES

α-Azidoketone	Imidazole	Yield, %	M.p., °C.	Color	Molecular formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
Ia	2-Benzoyl-4(or 5)-phenylimidazole (IIIa)[a]	64	196–198	Pale yellow	$C_{16}H_{12}N_2O$	77.42	77.18	4.84	4.81	11.29	11.10
Ib	2-*p*-Bromobenzoyl-4(or 5)-*p*-bromophenylimidazole (IIIb)	62	245–247	Yellow	$C_{16}H_{10}Br_2N_2O$[c]	47.32	47.61	2.48	2.70	6.90	6.71
Ic	2-*p*-Phenylbenzoyl-4(or 5)-*p*-phenylphenylimidazole (IIIc)	84	254–255	Yellow	$C_{28}H_{20}N_2O$	83.98	83.91	5.03	5.15	7.00	5.40, 5.52
Id	2-β-Naphthoyl-4(or 5)-β-naphthylimidazole (IIId)[b]	46	244–245	Yellow	$C_{24}H_{16}N_2O$	82.73	82.17	4.63	4.65	8.04	8.19

[a] The 2,4-dinitrophenylhydrazone melted at 260–265° (lit.[10] m.p. 265°). [b] Sublimed at 235–240° (3 mm.). [c] Br analysis, calcd. 39.36, found 37.99 (assumed to be in error).

β-(α-Bromoacetyl)-naphthalene was prepared from β-acetonaphthone according to the directions of Immediata and Say,[15] m.p. 78°, 27% yield.

1-Bromo-3,3-dimethylbutanone-2 was prepared according to the general method of Hill and Kropa[16] with certain modifications. Into a 500-ml. round-bottomed flask equipped with a stirrer, thermometer and dropping funnel was placed 250 ml. of anhydrous ether. While the contents of the flask were externally cooled to 0° by an ice–salt-bath, 14 g. (0.14 mole) of pinacolone was added followed by 22 g. (0.14 mole) of bromine. The latter was added dropwise with stirring over a period of 20 minutes. Just as the last of the bromine was added the color changed from dark red to a light yellow. Immediately the reaction mixture was transferred to a separatory funnel and washed with 100 ml. of ice-cold water. Ether extractions of the water layer were added to the organic layer after removal of the ether by evaporation. The product, 15 g. (63%), was then obtained as the main fraction upon distillation, b.p. 59° (4 mm.), n^{25}_D 1.4659, d^{20}_4 1.333; MR_D (calculated) 37.7, MR_D (found) 37.2. There was a small amount of residue which solidified upon cooling.

The Azides.—Certain modifications of the reaction conditions introduced by Forster[17] for the transformation of α-haloketones into α-azidoketones are described in the preparation of phenacyl azide (Ia). Physical constants, yields and analytical data for new azides are summarized in Table I.

Phenacyl Azide (Ia).—A solution of 20 g. (0.1 mole) of phenacyl bromide in 75 ml. of ethanol and 12 ml. (0.2 mole) of glacial acetic acid was cooled to 0–5° in the refrigerator. To this mixture was added a cold solution of 13.0 g. (0.2 mole) of sodium azide in 15–20 ml. of water and the resulting mixture was allowed to stand in the refrigerator for 24 hours with intermittent shaking. The crystalline product, m.p. 16–17°, was collected on a filter and recrystallized from a mixture of diethyl ether and petroleum ether, b.p. 40–60°, wt. 14.9 g. (93% yield), m.p. 17°. An impure product difficult to purify was obtained when the reaction was run at room temperature and unidentified products were obtained when the reaction was carried out in boiling ethanol.

The Imidazoles.—The general conditions for the pyrolysis of the azides (Ia, b, c, d) are described in the preparation of 2-benzoyl-4(or 5)-phenylimidazole (IIIa) from phenacyl azide (Ia). Physical constants, yields and analytical data for the imidazoles are summarized in Table II.

2-Benzoyl-4(or 5)-phenylimidazole (IIIa).—A solution of 8.32 g. (0.052 mole) of phenacyl azide (Ia) in 750 ml. of trichlorobenzene (redistilled), resorcinol dimethyl ether or diphenyl ether was heated between 180 and 240° for 30 minutes or until no more nitrogen and water vapor was evolved. During this time the colorless solution gradually became dark orange in color. Upon cooling in the refrigerator a yellow-orange solid, wt. 2.83 g., m.p. 185–190°, separated and was isolated on a buchner funnel. Distillation of the mother liquor left an oily residue from which an additional 2.00 g. of a solid compound, m.p. 185–193°, was obtained by filtration. The combined product was recrystallized from aqueous ethanol or aqueous pyridine from which it separated as clusters of yellow prisms (a darker product was obtained from ethanol), wt. 4.06 g. (64% yield), m.p. 196–198° alone and when mixed with the 2-benzoyl-4(or 5)-phenylimidazole prepared according to Minovici[6] (see below). The imidazole was also purified by sublimation at 190–200° (1 mm.).

2-Benzoyl-4(or 5)-phenylimidazole (IIIa).—According to the directions of Minovici[6] anhydrous hydrogen chloride was bubbled through a solution of 21.6 g. (0.16 mole) of the cyanohydrin[18] of benzaldehyde in 100 ml. of absolute ether for a period of two hours at room temperature. During this time the yellow solution turned a bright orange and after a few hours standing a precipitate of the crystalline hydrochloride of 2-benzoyl-4(or 5)-phenylimidazole separated. After 24 hours additional ether was added to precipitate the remainder of the hydrochloride, m.p. 215–220° (dec.), which was then isolated by filtration. Addition of dilute

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(15) T. Immediata and A. R. Say, *J. Org. Chem.*, **5**, 512 (1940).

(16) G. A. Hill and E. L. Kropa, THIS JOURNAL, **55**, 2509 (1933).

(17) (a) M. O. Forster and R. Muller, *J. Chem. Soc.*, **97**, 126 (1910); (b) M. O. Forster and H. E. Fierz, *ibid.*, **93**, 72 (1908).

(18) B. B. Corson, R. A. Dodge, S. A. Harris and J. S. Yeaw, "Organic Syntheses," Coll. Vol. I, 2nd edition, John Wiley and Sons, Inc., New York, N. Y., 1947, p. 336.

ammonium hydroxide to the hydrochloride brought about the formation of the free base (IIIa), m.p. 180–190°. Recrystallization from 200 ml. of ethanol gave clusters of yellow-orange prisms, wt. 2.6 g. (13.1% yield based on benzaldehyde), m.p. 196–198°.

1-Acetyl-2-benzoyl-4-phenylimidazole (IV).—A mixture of 4.10 g. (0.016 mole) of 2-benzoyl-4 (or 5)-phenylimidazole (IIIa), 20 ml. of isopropenyl acetate[19] and five drops of concentrated sulfuric acid was refluxed for one hour. Acetone and excess isopropenyl acetate were removed by distillation. Recrystallization of the acetyl derivative (IV), obtained as a solid residue from the distillation, was most successful from isopropenyl acetate from which it separated as light yellow prisms, m.p. 153–155° (softening at 150°), wt. 3.98 g. (83% yield). The compound is very easily hydrolyzed; after four recrystallizations from moist benzene complete conversion to 2-benzoyl-4(or 5)-phenylimidazole occurred.

Anal. Calcd. for $C_{18}H_{14}O_2N_2$: C, 74.47; H, 4.86; N, 9.65. Found: C, 74.34; H, 4.52; N, 9.80.

Oxidation of 2-Benzoyl-4(or 5)-phenylimidazole (IIIa).—A solution of 0.16 g. (0.0006 mole) of the imidazole in 40 ml. of 9% sodium hydroxide was warmed on a steam-cone. To this solution a 6% solution of potassium permanganate was added by a dropping funnel until a purple color persisted after one hour of heating at 70° (about 35 ml. was required). The solution was cooled and the excess permanganate was discharged by the addition of 1 ml. of formalin. The precipitated manganese dioxide was removed by filtration and the filtrate acidified. After a few minutes a copious precipitate of white needles, m.p. 120–122°, was obtained. Ether extraction of the mother liquor followed by evaporation of the ether gave an additional portion of this solid. The total yield was 0.070 g. (49% yield). There was no depression in the melting point when this product was mixed with a known sample of benzoic acid.

Reduction of 2-Benzoyl-4(or 5)-phenylimidazole (IIIa).—To a solution of 1.24 g. (0.005 mole) of the imidazole in 100 ml. of refluxing isoamyl alcohol was added 8 g. of sodium in small pieces over a period of 30 minutes. The solution was kept at reflux temperature an additional half-hour to allow complete dissolution of the sodium. After about 40 minutes the solution had completely lost the yellow-orange color of the benzoyl imidazole. Acidification of the cold reaction mixture with dilute hydrochloric acid was followed by separation of the layers and distillation of isoamyl alcohol from the organic layer. The gummy residue was recrystallized from aqueous ethanol from which the colorless solid, **2-benzyl-4(or 5)-phenylimidazole** precipitated in long, colorless, felt-like needles, m.p. 158–160°, wt. 0.30 g. (26% yield). After several recrystallizations from aqueous ethanol the m.p. became constant at 161–162° with softening at 158°.

Anal. Calcd. for $C_{16}H_{14}N_2$: C, 82.02; H, 6.02; N, 11.96. Found: C, 81.97; H, 5.89; N, 11.20.

Pyrolysis of Triazoacetone and 1-Azido-3,3-dimethylbutanone-2.—Nitrogen evolution was observed when one per cent. solutions of each of these α-azidoketones in trichlorobenzene were heated between 180 and 200°. Cooling the solutions brought about the separation of a high melting (>250°) amorphous solid from the experiments on triazoacetone but only a dark viscous unidentified oil was obtained from the azidobutanone. In neither case could imidazoles be detected.

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[19] A sample of this compound was obtained from Tennessee Eastman Corporation, Kingsport, Tennessee.

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF DOJINDO AND CO., LTD., AND FROM THE LABORATORY OF ORGANIC SYNTHESIS, DEPARTMENT OF APPLIED CHEMISTRY, KYUSHU UNIVERSITY]

Synthesis and Ultraviolet Absorption Spectra of Polyazobenzenes

BY KEIHEI UENO

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The ultraviolet absorption spectra of *p*-, *m*- and *o*-polyazobenzenes have been determined. Both a bathochromic effect and an increase of the extinction coefficient has been observed in the series of *p*-polyazobenzenes. There was observed only an increase of the extinction coefficient without a shift of the absorption peak in the case of *m*-polyazobenzenes. In the case of mixed *p*- and *m*-polyazobenzenes, the para effect is predominant. The results are discussed qualitatively.

Little has been reported about the relation between the structure of polyazobenzenes and their ultraviolet light absorption. A number of polyazobenzenes were synthesized by Ruggli and his co-workers[1] but a comprehensive spectroscopic study was not carried out. Since the discovery of stereoisomerism of azobenzene by Hartley,[2] Cook[3,4] has isolated the stereoisomers of azobenzene and its derivatives and determined their ultraviolet light absorption. Although he also studied the three stereoisomers of 1,4-bis-(phenylazo)-benzene, he did not examine higher members of the polyazobenzene series because of the expected complexity of the stereoisomerism, and his major interest was to study the relationships within his set of stereoisomers.

Since our purpose was to study the relationship between structure and ultraviolet light absorption of polyazobenzenes, our attention was first directed to the *trans* isomers, which are believed to be the more stable and the predominant constituent of the usual preparations. Thus the present paper reports a study of the ultraviolet light absorption of a series of *trans* isomers of *p*-, *m*- and *o*-polyazobenzenes.

In addition to Ruggli's preparations in this series, we synthesized and studied several new members. These new members were prepared by the condensation of nitronitrosobenzene with an amino compound, followed by reduction of the nitro group and condensation with nitrosobenzene. The syntheses of the compounds are illustrated on the chart, and all the compounds investigated in our absorption study are shown in Table I. The substances were purified by recrystallization to constant melting point and by chromatography on activated alumina, and samples obtained in this way were used for the spectrophotometry.

The features of the ultraviolet spectra of *p*-polyazobenzenes are given in Table I. A regular bathochromic shift as well as a regular increase of the extinction coefficient occurs as the number of *p*-phenylazo groups increases, similar to the behavior

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[1] Ruggli and co-workers, *Helv. Chim. Acta*, **17**, 992 (1934); **21**, 711 (1938); **25**, 1533 (1942); **28**, 781 (1945); **30**, 739 (1947).

[2] G. S. Hartley, *J. Chem. Soc.*, 633 (1938).

[3] A. H. Cook, *ibid.*, 876 (1938).

[4] A. H. Cook and D. G. Jones, *ibid.*, 1309 (1939).