[Contribution from the Chemistry Department, University of Michigan]

Azidocarbonyl Compounds. II. The Pyrolysis of α-Azidocarbonyl Compounds[1a]

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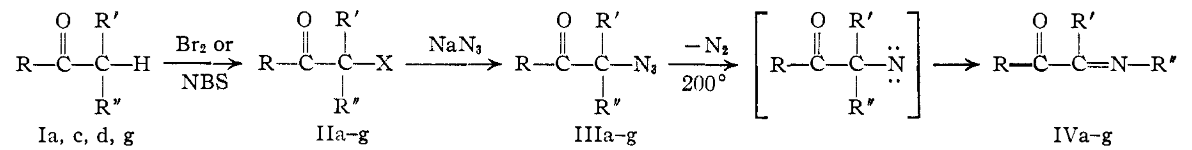
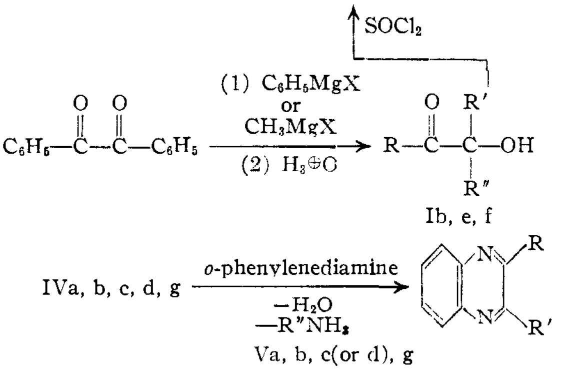
Combinations of H, CH_3 and C_6H_5 as substituents in the α-position of phenacyl azide together with ethyl α-azido-α-phenylacetate provided a series of seven structurally related α-azidocarbonyl compounds (III) for a study of the rearrangement step which accompanied the loss of nitrogen upon pyrolysis. Without exception, migration from the α-carbon to nitrogen followed the pattern H > C_6H_5 > CH_3 and resulted in the formation of α-iminocarbonyl compounds (IV). Condensation of the imines (IVa, b, c, g) as well as the N-methylimine (IVd) with *o*-phenylenediamine and the isolation of the resulting quinoxalines (Va, b, c, g) provided a convenient method for identification of the migrating group in these five cases. Migration of the phenyl group resulted in the formation of anils (IVe, f), neither of which would condense with *o*-phenylenediamine.

In previous work the pyrolysis of phenacyl azide (IIIa) and nuclear-substituted derivatives was assumed to involve the corresponding imines of phenylglyoxal as intermediates which upon dimerization led to imidazoles.[2] This suggested a study of structurally related α-azidocarbonyl compounds in which other groups were also attached to the α-carbon.

With each of the seven azides now under consideration as well as the five additional azides described previously, pyrolysis occurred at a moderate rate at 200 ± 20°. This report describes a study of the migration step which accompanies the loss of nitrogen at this temperature. Since in most cases the products IV could not be isolated in pure state, the pyrolyses were carried out in the presence of *o*-phenylenediamine. Identification of the quinoxalines V formed by the condensation between the diamine and α-iminocarbonyl compounds in most cases provided a convenient method for identification of the migrating group.



Ia, c, d, g IIa–g IIIa–g IVa–g



Ib, e, f

IVa, b, c, d, g

Va, b, c(or d), g

	a	b	c	d	e	f	g
R	C_6H_5	C_6H_5	C_6H_5	C_6H_5	C_6H_5	C_6H_5	OC_2H_5 (OH in V)
R′	H	C_6H_5	CH_3	CH_3	C_6H_5	CH_3	C_6H_5
R″	H	H	H	CH_3	C_6H_5	C_6H_5	H

The azides were prepared either from the corresponding carbonyl compounds (Ia, c, d, g) or from benzil *via* the α-hydroxycarbonyl compounds (Ib, e, f). Transformation into the α-halo derivatives (II) was carried out by standard methods of bromination of carbonyl compounds using bromine[3] or N-bromosuccinimide,[4] or by treating the benzoins with thionyl chloride.[5] The displacement of the halogen by the azido group, according to Forster's preparation for phenacyl azide,[6] readily occurred.

Apparently pyrolysis of the azides in the presence of *o*-phenylenediamine involved initial thermal decomposition of the azido group with rearrangement into an imine followed by condensation, rather than initial displacement of the azido group followed by condensation and dehydrogenation. In test cases nitrogen was collected above water, and ammonia or methylamine was detected by the characteristic odors and reactions to litmus. That α-azidoketones would not alkylate amines, a reaction hitherto not investigated, was expected, since alkali does not displace the azido group attached to the α-carbon atom of carbonyl compounds to an appreciable extent.[7] Nevertheless, a few experiments were carried out to test the ability of phenacyl azide as an alkylating agent. When this azide was heated in quinoline the only reaction observed was decomposition of the azido group and the subsequent formation of 2-benzoyl-4(or 5)-phenylimidazole.[2] In similar experiments displacement of the azido group by other amines such as aniline, *o*-toluidine and *o*-phenylenediamine failed to occur.

The rearrangement which accompanies the loss of nitrogen upon pyrolysis of α-azidocarbonyl compounds is reminiscent of the Curtius reaction,[8a] and the thermal decompositions of ethyl azide[8b] and triarylmethyl azides.[8c] In each case the rearrangement involves the transfer of electrons from the carbon atom attached to the azido group to the adjacent nitrogen atom. In the present study this

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[2] J. H. Boyer and D. Straw, This Journal, **74**, 4506 (1952).

[3] (a) P. G. Stevens, O. C. W. Allenby and A. S. Dubois, *ibid.*, **62**, 1424 (1940).

[4] C. Djerassi, *Chem. Revs.*, **43**, 271 (1948).

[5] A. M. Ward, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1947, p. 159.

[6] M. O. Forster and R. Muller, *J. Chem. Soc.*, **97**, 126 (1910).

[7] M. O. Forster and H. E. Fierz, *ibid.*, **93**, 669 (1908).

[8] (a) P. A. S. Smith, "Organic Reactions," Vol. III, John Wiley and Sons, Inc., New York, N. Y., p. 337; (b) J. A. Leermakers, This Journal, **55**, 2719 (1933); (c) J. K. Senior, *ibid.*, **38**, 2718 (1916); L. A. Pinck and H. E. Hilbert, *ibid.*, **59**, 8 (1937).

would result in the migration of one of three groups $R'-$, $R''-$, or $R-\overset{\overset{\displaystyle O}{\|}}{C}-$. In all possible cases (IIIa, b, c, g) hydrogen migration occurred exclusively. In these examples ammonia was eliminated in the condensation with the diamine. Three examples were studied in which no hydrogen was substituted on the α-carbon. Migration of a methyl group in the case of α-azidoisobutyrophenone (IIId) resulted in the formation of 1-phenyl-1-oxo-2-methyliminopropane (IVd). Subsequent condensation with *o*-phenylenediamine involved the elimination of methylamine and the formation of 2-methyl-3-phenylquinoxaline (Vc). Migration of a phenyl group in the cases of α-azido-α,α-diphenylacetophenone (IIIe) and α-azido-α-phenylpropiophenone (IIIf) allowed the formation of benzil anil (IVe) and 1-phenyl-1-oxo-2-phenyliminopropane (IVf), respectively. Both of these anils were readily isolated; however, neither of them condensed with *o*-phenylenediamine. That migration of the phenyl group predominated over the migration of the methyl group in the latter case is in agreement with the migration aptitudes of these groups.[9] There was no evidence for the N-substituted imines which would have been formed from IIIb, c, f, g by the migration of R′ instead of R″. In two cases, IIIc, f ($R' = CH_3$), subsequent condensation of the N-methylimine of benzil with *o*-phenylenediamine would have produced methylamine which was not detected by odor or litmus.

Insofar as we know, no previous example has been reported in which *o*-phenylenediamine condensed with either the mono- or diimine of a dicarbonyl compound to form a quinoxaline; however, it has been demonstrated that mono- but not dioximes of dicarbonyl compounds will condense with *o*-phenylenediamine in this manner.[10] Our results indicate that this is a general reaction for α-iminocarbonyl compounds and their N-methyl derivatives.

The quinoxalines were identified by their known melting points and in the case of 2-methyl-3-phenylquinoxaline (IVc) by a mixed melting point determination with authentic material prepared from either α-bromopropiophenone (IIc) or 1-phenyl-1,2-propanedione and *o*-phenylenediamine.[11]

Experimental[12]

Preparation of the Ketones.—Benzoin (Ib), propiophenone (Ic), isobutyrophenone (Id) and ethyl phenylacetate (Ig) were obtained from Eastman Kodak Co. and used without further purification.

α-Phenylbenzoin (Ie), m.p. 86–88°, was prepared from benzil and phenylmagnesium bromide in 85% yield by the method of Acree.[13] In a similar manner α-methylbenzoin (If), m.p. 64–67°, was obtained in 81% yield.[14]

Preparation of the Halides.—Phenacyl bromide (IIa), m.p. 49–50°, was obtained from Eastman Kodak Co. Desyl chloride (IIb), m.p. 66–68°, was obtained from the reaction of benzoin and thionyl chloride in 81% yield.[5] In similar reactions α-phenyldesyl chloride (IIe), m.p. 83–84°,[15] 73% yield, and α-methyldesyl chloride (IIf), m.p. 57–58°,[16] 75% yield, were obtained from Ie and If, respectively.

Two general methods were used for the bromination of propiophenone (Ic), isobutyrophenone (Id) and ethyl phenylacetate (Ig). (a) A mixture of 0.2 mole of the carbonyl compound and 0.2 mole of N-bromosuccinimide in 300 ml. of carbon tetrachloride was heated on a steam-cone for 24 hours and allowed to cool. Succinimide separated on top of the liquid and was isolated by filtration. The filtrate was evaporated to approximately 50 ml. on the steam-cone and the residue was distilled. From Ic, α-bromopropiophenone[8] (IIc), b.p. 96° (1 mm.), was obtained in 75% yield and from Ig, ethyl α-bromo-α-phenylacetate[8] (IIg), b.p. 130° (8 mm.), was obtained in 91% yield. (b) A solution of 0.2 mole of the carbonyl compound in 50 ml. of carbon tetrachloride was cooled to 0–5° in an ice–salt-bath. A solution of 0.2 mole of bromine in 30 ml. of carbon tetrachloride was added throughout a period of 30 minutes. For an additional hour the flask was kept at 25°, after which time the bromine color had disappeared. Carbon tetrachloride was then removed by evaporation on the steam-cone and the residue was distilled. From Ic, α-bromopropiophenone was obtained in 88% yield. From Id, α-bromoisobutyrophenone[8] (IId), b.p. 130° (13 mm.), was obtained in 82% yield.

Preparation of the Azides.—Displacement of the halogen by the azido group through the action of sodium azide on the halides occurred in most cases at refrigerator temperature. α-Azido-α-phenylpropiophenone (IIIe) was best prepared in refluxing methanol containing a small amount of acetic acid.[3] The azides, IIIa, b, were purified by recrystallization from aqueous ethanol. Desyl azide (IIIb) completely decomposed upon standing for several months at room temperature in a clear glass bottle not protected from light. When the bottle was opened there was a strong odor of benzaldehyde and an oily solid which failed to show any decomposition in concentrated sulfuric acid. Distillation of IIIc, d, g at reduced pressure proceeded satisfactorily but with some decomposition; however, IIIe, f decomposed to a major extent when distillation was attempted at or under 1 mm. Each of these two azides (IIIe, f) was obtained free from halogen (Beilstein test), gave vigorous decomposition reactions with concentrated sulfuric acid, indicative of the azido group; and upon infrared analysis showed strong absorption peaks at 4.67 μ, also characteristic of the azido group. The yields of crude product were 82% for IIIe and 88% for IIIf. Other yields and physical constants are shown in Table I.

Pyrolysis of the Azides (IIIa, b, c, d, g).—A solution 0.01 mole of the azide and 0.01 mole of *o*-phenylenediamine in 100 ml. of diphenyl ether was heated to 220°. The solution would begin to darken around 150°. Nitrogen evolution usually commenced at 170–180°, became vigorous at 200°, and was completed in about 15 minutes. The solvent was removed *in vacuo* and the residue recrystallized from 50% aqueous ethanol. For yields and physical constants of the corresponding quinoxalines (Va, b, c, g obtained, see Table I.

Trace amounts of 2-phenylbenzimidazole, m.p. 289–290°,[17] were found along with 2-methyl-3-phenylquinoxaline (Vc) when the latter was prepared from IIIc.

Anal. Calcd. for $C_{13}H_{10}N_2$: C, 80.38; H, 5.19; N, 14.43; mol. wt., 194.23. Found: C, 80.14; H, 5.29; N, 14.58; mol. wt., 277 (Rast).

The association of N-unsubstituted benzimidazoles is discussed by Hunter and Marriot.[17]

A similar hydrolytic decomposition of IVc was observed. Upon warming the residue obtained from the distillation of IIIc with aqueous ethanol, a copious precipitate of benzoic acid, m.p. and mixed m.p. 121–122°, was obtained.

Pyrolysis of the Azides (IIIe, f).—Pyrolysis in the presence of *o*-phenylenediamine did not lead to a substituted quinoxaline. In agreement with this observation was the failure to detect methylamine either by odor or by litmus test from this reaction with IIIf.

A solution of 0.01 mole of the azide in 100 ml. of diphenyl ether evolved nitrogen when heated to 180–220°. Purification of the residue left after removal of diphenyl ether by recrystallization from aqueous ethanol brought about the iso-

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[9] G. Wheland, "Advanced Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1949, p. 513.

[10] C. G. Ponzio, *Gazz. chim. ital.*, **63**, 744 (1933).

[11] K. von Auwers, *Ber.*, **50**, 1182 (1917).

[12] Melting points are not corrected. Microanalyses by the Micro-Tech Laboratories, Skokie, Illinois.

[13] S. F. Acree, *Ber.*, **37**, 2758 (1904).

[14] R. Roger, *J. Chem. Soc.*, **127**, 518 (1925).

[15] A. Lowenbein and L. Schuster, *Ann.*, **481**, 114 (1930).

[16] M. Garry, *Ann. chim.*, **17**, 5 (1942).

[17] L. Hunter and J. A. Marriot, *J. Chem. Soc.*, 777 (1941).

TABLE I

THE AZIDES III AND THE CORRESPONDING QUINOXALINES V

Azide, III	Yield, %	Molecular formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found	Quinoxalines, V Yield, %	Quinoxalines, V M.p., °C.
a[a]	93	$C_8H_7N_3O$	...	...	..	..	...	...	47	77[b]
b[c]	39	$C_{14}H_{11}N_3O$	70.87	71.06	4.67	4.64	17.72	17.48	59	125[d]
c[e]	77	$C_9H_9N_3O$	61.70	61.60	5.18	5.34	23.99	23.35	47	64[f]
d[g]	88	$C_{10}H_{11}N_3O$	63.47	63.74	5.86	5.98	22.21	22.22	54	64[h]
g[i]	84	$C_{10}H_{11}N_3O_2$	58.52	58.24	5.40	5.30	20.48	20.72	40	244[j]

[a] M.p. 17°. [b] O. Fischer and F. Romer, *Ber.*, 41, 2350 (1908). [c] M.p. 85°. [d] O. Hinsberg and F. Konig, *Ber.*, **27**, 2181 (1894). [e] B.p. 75° (0.5 mm.), $n^{25}\text{D}$ 1.5484, d^{25}_4 1.1375; MR_D (calcd.) 47.91, MR_D (found) 48.94. [f] Lit.[11] m.p. 58°. See Experimental. [g] B.p. 74° (0.5 mm.), $n^{25}\text{D}$ 1.5309, d^{25}_4 1.0954; MR_D (calcd.) 52.53, MR_D (found) 53.44. [h] No depression in a mixed m.p. determination with Vc prepared from IIIc. [i] B.p. 130° (8 mm.), $n^{25}\text{D}$ 1.5188, d^{25}_4 1.1478; MR_D (calcd.) 54.17, MR_D (found) 54.30. [j] J. Buraczewski and L. Marchlewski, *Ber.*, 34, 4009 (1901).

lation of benzil anil (IVe), m.p. 106–107°,[18] 19% yield from IIIe and the previously unreported anil (IVf), m.p. 170–172°, from IIIf in 14% yield.

Anal. Calcd. for $C_{15}H_{13}NO$: C, 80.69; H, 5.87; N, 6.28. Found: C, 80.80; H, 5.87; N, 6.10.

Preparation of 2-Methyl-3-phenylquinoxaline (Vc).—Following the procedure of von Auwers[11] this compound, m.p. 64–65°, was obtained in 90% yield from acetylbenzoyl[19] and *o*-phenylenediamine. In a similar reaction with α-bromopropiophenone, Vc was obtained in 87% yield. (No condensation product was detected from a mixture of isonitrosopropiophenone and *o*-phenylenediamine in refluxing ethanol.) The product was recrystallized from aqueous ethanol and from carbon tetrachloride.

Anal. Calcd. for $C_{15}H_{12}N_2 \cdot H_2O$: C, 75.61; H, 5.92. Found: C, 75.89; H, 5.86.

After a purified sample was dried in an Abderhalden drying pistol at room temperature, it became a viscous oil which crystallized upon standing and had a m.p. of 40–50°. (Von Auwers[11] reported a m.p. of 57–58°.) Recrystallization of the dried material from aqueous ethanol allowed recovery of the hydrate, m.p. 64–65°.

Hydrolysis of the Anils (IVe, f).—To a solution of 20 ml. of concentrated hydrochloric acid in 5 ml. of water was added 84 mg. (0.295 mmole) of the benzil anil (IVe). The mixture was heated on a steam-cone for 17 hours. After cooling the reaction mixture in an ice-bath, it was thoroughly extracted with ether. The combined ether extracts were evaporated in an air stream and the yellow residue recrystallized from dilute aqueous ethanol. Three recrystallizations yielded 25 mg. (40%) of cream-colored needles, m.p. 93–94°. A mixed melting point determination with an authentic sample of benzil showed no depression.

The aqueous layer from the ether extraction was made basic by adding 20% sodium hydroxide and was then extracted with ether. The combined ether extracts were evaporated in an air stream to a few drops. Ten ml. of acetic anhydride was added and the solution placed on a steam-cone 30 minutes and then evaporated to dryness in an air stream. The crystalline white residue was recrystallized as leaflets from water containing a few drops of ethanol, wt. 27 mg. (68%), m.p. 112–114°. A mixed melting point determination with an authentic sample of acetanilide showed no depression.

In a similar manner, 29 mg. (0.133 mmole) of the anil (IVf) was hydrolyzed. A solution of 0.2 g. of hydroxylamine hydrochloride and 1 ml. of 10% sodium hydroxide was added to the ether extracts. Ethanol was added until a solution was obtained, which was heated 30 minutes on a steam-cone. Upon cooling, white needles separated and were recrystallized from aqueous ethanol yielding 5.4 mg. (25%) of a monoöxime of acetylbenzoyl, m.p. 108–109°. A mixed melting point determination with an authentic sample of α-isonitrosopropiophenone (Eastman Kodak Co.) showed no depression.

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[18] F. X. Bandrowski, *Monatsh.*, **9**, 687 (1888); M. Siegfeld, *Ber.*, **25**, 2600 (1892).

[19] W. W. Hartman and L. J. Roll, *Org. Syntheses*, **23**, 1 (1943).

[CONTRIBUTION FROM THE CHEMISTRY DIVISION OF OAK RIDGE NATIONAL LABORATORY]

Studies in the Wagner Rearrangement. VI. The Directive Effects of the Methyl and Methoxyl Groups[1]

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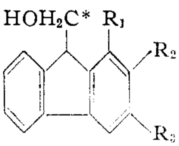
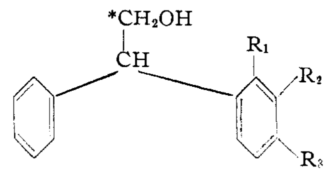
The directive effects of the 3-methyl and 3-methoxyl groups on the rearrangements of their derivatives of 9-fluorenyl (carbinol-C[14]) have now been determined. The 3-methyl group enhances the ability for migration of the substituted benzo moiety in relation to the benzo-ring in the ratio 73:27. The corresponding effect of the 3-methoxyl group is to increase this ratio to 98:2. These results are compared with previous results in the 9-fluorenylcarbinol (A) and in the 2,2-diphenylethanol (B) series.

Introduction

Previous reports[3–7] from this Laboratory have been concerned with the directive influences of various substituents on the dehydration–rearrangement reactions of carbon-14 labeled, unsymmetrically substituted 9-fluorenylcarbinols (A) and 2,2-diphenylethanols (B). We now report the results of the syntheses and rearrangements of two more



A



B

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[1] This paper is based on work performed under contract Number W-7405-eng-26 for the Atomic Energy Commission at Oak Ridge National Laboratory.

[2] That portion of this research concerned with 3-methoxy-9-fluorenyl-(carbinol-C[14]) was abstracted from the Ph.D. Thesis of Ben M. Benjamin, submitted to the Graduate School of the University of Florida, Gainesville, June, 1952.

[3] C. J. Collins, J. G. Burr and B. N. Hess, THIS JOURNAL, **73**, 5176 (1951).

[4] C. J. Collins, D. N. Hess, R. H. Mayor, G. M. Toffel and A. R. Jones, *ibid.*, **75**, 397 (1953).

[5] B. M. Benjamin and C. J. Collins, *ibid.*, **75**, 402 (1953).

[6] C. J. Collins, L. S. Ciereszko and J. G. Burr, *ibid.*, **75**, 405 (1953).

[7] J. G. Burr and L. S. Ciereszko, *ibid.*, **74**, 5426 (1952).