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THE ISOLATION AND REARRANGEMENT OF SIMPLE ISOIMIDES (IMINOANHYDRIDES (1))

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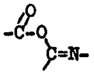
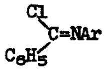
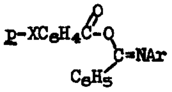
Not surprisingly, the isoimide (or iminoanhydride) functional group (A) has been observed rarely in organic chemistry and has been limited to those relatively few molecules where it has been stabilized by special structural features (2, 3). Reactions which should have produced this functional group have generally led instead to the imide; for example, the reaction of the imidoyl chloride (I) with silver benzoate gave dibenzoylimide (IV) and attempts to isolate the suspected intermediate isoimide III have been unsuccessful (3, 4).

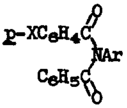


A



I [Ar = C_6H_5]
II [Ar = 2,4-$(NO_2)_2C_6H_3$]
VIII [Ar = 2-$NO_2C_6H_4$]

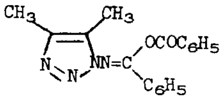




Ar = C_6H_5; X = H	III	IV
Ar = 2,4-$(NO_2)_2C_6H_3$-		
X = H	H-V	H-VI
X = CH_3O	CH_3O-V	CH_3O-VI
X = Br	Br-V	Br-VI
X = NO_2	NO_2-V	NO_2-VI

This implied rearrangement of III to IV which involves a 1,3-benzoyl migration was of interest in connection with our studies (5) of 1,3-acyl migrations in other systems. We have therefore investigated the possibility of placing substituents on the molecule III which might slow its rearrangement to IV and permit its isolation.

The reaction of N-(2,4-dinitrophenyl)-benzimidoyl chloride (II) (prepared from benz-2,4-dinitroanilide and phosphorous pentachloride) gave with silver benzoate in dry ether a 47% yield of isoimide (H-V, Ar = C_6H_5, Ar' = 2,4-dinitrophenyl), which, purified by crystallization at 0° from hexane-toluene, had m.p. 90° (resolidified at 100° and remelted at 171.5-173°). All new compounds described here had satisfactory carbon, hydrogen and nitrogen analyses. The structure was suggested by the infrared absorption at 1750 $cm.^{-1}$ attributed to the ester C=O and at 1680 $cm.^{-1}$ attributed to the C=N. Although no infrared data are available for strictly comparable functional groups these frequencies are in agreement with structure H-V as judged by a comparison with the enol benzoate $C_6H_5COOC(C_6H_5)=C(COC_6H_5)-N=NC_6H_5$ with carbonyl absorption (5) at 1745 $cm.^{-1}$ The more closely related isoimide VII has been shown (6) to have absorption at 1750 $cm.^{-1}$ (C=0) and at 1639 $cm.^{-1}$ (C=N) in good agreement with the present work. Finally the N-arylmaleisoimides and N-arylphthalisoimides with reported (3) carbonyl absorption at 1800 $cm.^{-1}$ and C=N absorption at 1700 $cm.^{-1}$ are in reasonable agreement when allowance is made for the fact that the functional groups are exocyclic in a five-membered ring. The isoimide structure H-V was confirmed by hydrolysis of the compound with concentrated hydrochloric acid for five minutes at room temperature



VII

to dinitrobenzanilide in 96% yield. On heating to 90° it melted and rearranged to the imide H-VI, characterized by its carbonyl absorption at 1685 and 1655 cm.$^{-1}$ (sh.) in the infrared (chloroform solution). In contrast to the isoimide the imide H-VI was stable to treatment for five minutes with concentrated hydrochloric acid but was hydrolyzed rapidly to the benzanilide by treatment with boiling ethanolic potassium hydroxide. The p-methoxy, p-bromo, and p-nitro derivatives of V (CH_3O-V, Br-V and NO_2-V) were obtained from the imidoyl chloride II and the appropriate silver benzoate. The melting behavior and most significant infrared maxima for these compounds and the imides (CH_3O-VI, Br-VI and NO_2-VI) formed from them by rearrangement are summarized in Table I.

Table I

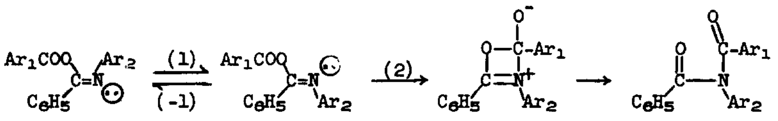
Isoimide or Imide	m.p. (°C.)		Infrared Maxima (cm.$^{-1}$)		$k_1 \times 10^4$(sec.$^{-1}$) (Acetonitrile at 42.86°)
	Initial	Final			
CH_3O-V	142-143.5	---	1740	1675	0.589 ± 0.028[b]
CH_3O-VI	171.5-173	---	1700	1670	
H-V	90	171.5-173	1750	1680	1.18 ± 0.16[a]
H-VI	173.5-174.4	---	1685	1655 (sh)	
Br-V	128-132	Not det.	1750	1685	1.52 ± 0.31[b]
Br-VI	166-167	---	1710	1695	
NO_2-V	135	198-199.5°	1755	1690	3.34 ± 0.05[b]
NO_2-VI	198-199.5	---	1710	1680	

[a]Average of 3 kinetic runs. [b]Average of 2 kinetic runs.

The rearrangement of H-V to H-VI in benzene, followed quantitatively using the absorbance of the developing imide carbonyl peak of H-VI, obeyed good first order kinetics to 95% completion and the rate was unaffected by the addition of a small amount of calcium hydride (suspended) or of 0.022 M acetic acid. The first order rate constants at 42.86° were calculated by a modified least squares method (7) and the mean of five independently determined rate constants was 6.06×10^{-5} sec.$^{-1}$ The rate constant in acetonitrile at the same temperature was 1.18×10^{-4} sec.$^{-1}$ which leads to a value of "a" (measure of sensitivity of the reaction to change in solvent polarity) (8) of 0.36. Rates of rearrangement of H-V, Br-V, and NO_2-V, measured in acetonitrile at 42.86°, are presented in Table 1. A plot of log k against Hammett's sigma constant permits a straight line to be drawn through the points corresponding to the bromo, nitro and unsubstituted compounds but with the point for *p*-methoxyl well below the line. Rho calculated from the line drawn without the methoxyl point is +0.59 and that from a least squares line through all of the points is +0.69. Whether the apparent curvature in the plot is due to a change in reaction mechanism (9) or to some other cause has not been determined.

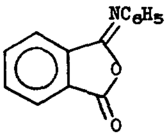
Although there is no direct quantitative measure of the effect of substituents on the aromatic ring attached to the nitrogen atom of the isoimide III the previous failure of attempts to isolate such compounds without the two nitro-substituents suggests that they play a major part in retarding the rearrangement of isoimide to imide. Substantiation of this conclusion came when an attempt was made to isolate an isoamide without the *p*-nitro group from the reaction of N-(2-nitrophenyl)-benzimidoyl chloride (VIII) with silver benzoate; only the imide resulting from 1,3-benzoyl migration could be obtained. This observation implies that rho is negative with respect to variation of substituents on the phenyl ring attached to nitrogen.

These and other results to be described are best considered in terms of the following mechanism.

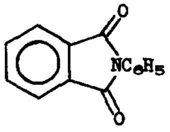


anti-V *syn*-V (Transition state) VI

Such a mechanism, which offers a ready explanation of the observed substituent effects, suggests that the stereochemistry of the isoimides V is of prime importance because of the likelihood that only the *syn*-isoimide can undergo ring-closure to the proposed four-membered transition state (which may or may not be followed by an intermediate with a four-membered ring). Such steric requirements for the rearrangement are supported by the previous work (2, 3) showing that molecules such as IX, in which nucleophilic attack by the imino nitrogen atom at the carbonyl group is sterically prohibited, are relatively stable. The phthalisoimide IX was prepared and its rearrangement to the imide X examined. IX was quite stable at 178° in chlorobenzene solution and at 250° the half-time for the reaction was about twenty-four hours. In dioxane or nitrobenzene at 178.23° rates were erratic and it seems likely that we may have been measuring the rate of an unrelated rearrangement catalyzed by traces of acid or base. In any case it is clear that the 1,3-benzoyl migration is tremendously retarded by incorporation of the isoamide functional group into such a cyclic structure, as is predicted by the mechanism above.



IX



X

It has been found that the rate constants for the *syn*-*anti*-interconversion of N-phenylbenzophenone imines in non-polar solvents are of the order of 10 sec.$^{-1}$ and augmented by substituents with a positive sigma constant (10) so that this represents a probable lower limit for k_{-1} in the present reaction sequence. It is possible and even likely then that the isoimides being considered here are, in solution, rapidly interconverting equilibrium mixtures of the *syn*- and *anti*-isomer. (Examination of the n.m.r. spectra of the isoimides V at 25° failed to give any indication of the presence of a second isomer and irradiation of Br-V in isoöctane for ten minutes with a medium pressure Hanovia ultraviolet lamp followed by immediate measurement of the ultraviolet spectrum showed evidence of a certain amount of irreversible change but no further change in the spectrum occurred on standing.) If reaction (-1) has a velocity which is much greater than that of reaction (2) and if the equilibrium between anti- and syn-V is well toward the side of the anti-isomer because of the instability introduced in the syn-isomer by the unfavorable steric interaction of the two cis-aryl groups (11), application of the steady state approximation shows that the experimental rate constant is k_2K and the experimental value of rho is the sum of rho for the equilibrium plus rho for reaction (2), where k_2 is the rate constant for the isomerization of syn-V (reaction 2) and K is the equilibrium constant for the interconversion of anti- and syn-V. In view of previous work on imine isomerizations (10) it seems reasonably certain that the effect of substituents on Ar_1 has an effect on the equilibrium constant K which is small enough to make rho for the equilibrium unimportant compared to rho for reaction (2). Even with possible stereochemical complications of the sort visualized, then, the experimental rho is primarily a measure of the effect of substituents on the rate of reaction (2). This analysis suggests another important point; it is probable that the relative stability of isoimides of the type being considered here is due both to the low nucleophilicity of the imide nitrogen atom and to storage of the isoimide in solution as the unreactive anti-compound to an extent determined by the magnitude of the equilibrium constant K.

The 1,3-benzoyl migration of V described here differs in several important respects from the 1-3 rearrangements of acyl groups from carbon to oxygen and from carbon to nitrogen shown by benzeneazotribenzoylmethane and its derivatives (5). The effects of substituents (sign of rho) are the reverse in one set of reactions of those in the other. The effect of solvent polarity in the present reaction ("a" value) is significantly larger than with the rearrangements from carbon to oxygen or nitrogen. These observations and detailed consideration of the stereoelectronics of the reactions suggest that the mechanisms are different in the two cases and that the requirement for a facile 1,3-migration of the type being discussed here is that the benzoyl group both leave from and migrate to an atom with one or more pairs of unshared electrons. The mechanism of the rearrangement of V to VI seems to be related to the rearrangement of phenylimino ethers with migration of aryl rings from oxygen to nitrogen, investigated in detail by Wiberg and his associates (12); and to one step of the N-nitrosoamide decomposition (13).

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