Cyclic Isoimidium Salts

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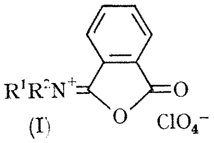
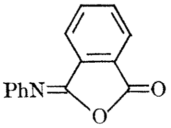
Summary N-Substituted phthalamic, maleamic, and succinamic acids cyclise to isoimidium (iminolactonium) perchlorates on treatment with acetic anhydride–perchloric acid, and with bases give isoimides, imides, or derivatives of amic acids.

ACETIC ANHYDRIDE–PERCHLORIC ACID has recently been shown to effect the cyclisation of diacylhydrazines to 1,3,4-oxadiazolium[1] and of α-acylaminoacids to 5-oxazolonium perchlorates.[2] It has now been found that when this reagent is applied to *N*-substituted monoamides of several dibasic acids stable isoimidium perchlorates (salts of iminolactones) are produced. These appear to be the first well-characterised members of this class with the exception of the isoimidium tetrachloroaurates derived from camphoric acid.[3]

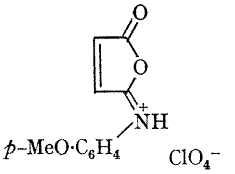


(I)

a; R^1 = Ph, R^2 = H
b; R^1 = R^2 = Et



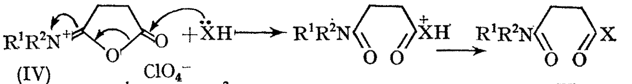
(II)



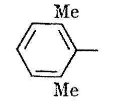
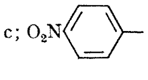
(III)

Phthalanilic acid gave the salt (Ia) (91%), m.p. 152° (decomp.);† i.r. 1690 ($C{=}N^+$) and 1862 cm.$^{-1}$ (this high-frequency absorption appears to be characteristic of γ-lactones containing a positively charged nitrogen atom).[2] The constitution of the salt was established by conversion into *N*-phenylphthalisoimide (II) on treatment with triethylamine. *N,N*-diethylphthalamic acid similarly yielded the immonium perchlorate (Ib) (96%), m.p. 207° (decomp.); i.r. 1690, 1845 cm.$^{-1}$; n.m.r. ($CF_3·CO_2H$) showed the presence of two non-equivalent ethyl groups and four aromatic protons. Both phthalisoimidium salts were converted into *N,N*-diethyl-*N'*-phenylphthalamide,[4] the former by reaction with diethylamine and the latter with aniline. *p*-Methoxymaleanilic acid formed the orange perchlorate (III) (86%), m.p. 125° (decomp.); i.r. 1680, 1860 cm.$^{-1}$; n.m.r., two doublets (*J* 6 Hz.) at τ 1·80 and 2·79 (2 olefinic protons), two doublets (*J* 10 Hz.) at 2·14 and 2·82 (4 aromatic protons), and τ 6·00 (s, OMe), from which the known[5] *N*-*p*-methoxyphenylmaleisoimide was obtained.

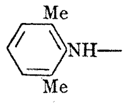
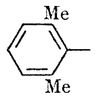
While phthalisoimides[6] and maleisoimides[7] are well known the sole representatives of isoimides derived from saturated dibasic acids remain the camphorisoimides discovered 76 years ago.[6] The failure to prepare such compounds from simpler acids (malonamic to adipamic acids) was attributed[5] to unfavourable conformational effects on ring-closure. It was therefore interesting to find that the action of acetic anhydride–perchloric acid on succinanilic acid readily yielded the stable isoimidium perchlorate (IVa) (92%), m.p. 141° (decomp.). The structure assigned to this salt is in accord with its i.r. spectrum (1690, 1890 cm.$^{-1}$), its n.m.r. spectrum (τ 6·70 [broad, $2CH_2$], 2·52 [Ph]), and its tendency to undergo ring-opening in the presence of nucleophiles, XH (see arrows): water produced succinanilic acid and methanol methyl succinanilate. Reactions with amines proceed in high yield and constitute a useful synthesis of unsymmetrically substituted succinamides. Thus, addition of the salt (IVa) to piperidine, phenylhydrazine, aniline, 2,6-dimethylaniline, *N*-methylaniline and aqueous sodium glycinate gave,

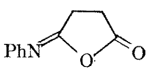


(IV)

	R^1	R^2
a;	Ph	H
b;		H
c;		H
d;	Ph.	Me

(V)

	R^1	R^2	X
a;	Ph	H	$C_5H_{10}N$
b;	Ph	H	PhNH·NH
c;	Ph	H	PhNH
d;	Ph	H	
e;	Ph	H	PhMeN
f;	Ph	H	$HO_2C·CH_2·NH$
g;		H	EtO
h;	Ph	Me	PhMeN



(VI)

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† Satisfactory analyses have been obtained for all new compounds whose melting points are given.

respectively, the piperidide of succinanilic acid (Va), m.p. 122·5—123·5°, its phenylhydrazide (Vb), m.p. 213—214°, succinanilide (Vc), 2′,6′-dimethylsuccinanilide (Vd), m.p. 252—253°, *N*-methylsuccinanilide (Ve), m.p. 152·5—153°, and *N*-carboxymethyl-*N*′-phenylsuccinamide (Vf), m.p. 191·5—192°.

Formation of isoimidium salts from succinamic acids is quite general: 2′,6′-dimethylsuccinanilic acid, m.p. 188—189°, afforded the perchlorate (IVb) (90·5%), m.p. 125° (decomp.), i.r. 1680, 1892 cm.$^{-1}$, n.m.r. τ 6·45—6·95 (m, two non-equivalent CH_2), 7·71 (2Me), 2·76 (m, 3 ArH), which was characterised by conversion into the ethyl ester (Vg)[8] and the mixed amide (Vd) by treatment with ethanol and aniline, respectively. The unstable *p*-nitrophenylisoimidium salt (IVc), m.p. 115° (decomp.), i.r. 1680, 1891 cm.$^{-1}$, was prepared in 61% yield from *p*-nitrosuccinanilic acid, and *N*-methylsuccinanilic acid gave the stable ternary immonium salt (IVd) (100%), m.p. 160° (decomp.), i.r. 1690, 1890 cm.$^{-1}$, n.m.r. τ 6·00—6·80 (m, $2CH_2$), 6·16 (s, Me), 2·47 (m, Ph), which yielded the succinamide (Ve) by reaction with aniline and *N*,*N*′-dimethylsuccinanilide (Vh) with *N*-methylaniline.

When deprotonation of the isoimidium salts (IVa—c) was attempted the normal imides were isolated. The i.r. spectrum of a chloroform solution freshly prepared from equivalent amounts of the perchlorate (IVa) and triethylamine contained only bands attributable to *N*-phenylsuccinimide and triethylammonium perchlorate. Phthalisomides and maleisoimides isomerise to the imides on heating in the absence[9] or presence[7] of bases; the present work suggests that previous failures to isolate succinisoimides from the acid-catalysed dehydration of succinamic acids is due not to conformational inhibition of ring-closure but to the easy isoimide → imide rearrangement within the flexible saturated γ-lactone ring.

While succinisoimides were not directly observed the *N*-phenyl compound (VI) is probably an intermediate in reactions of the perchlorate (IVa) with electrophiles which result in abstraction of the phenylimino moiety: *p*-dimethylaminobenzaldehyde gave the hydroperchlorate of *p*-dimethylaminobenzylideneaniline (87%), and *p*-nitrobenzoyl chloride in the presence of triethylamine yielded *p*-nitrobenzanilide (12%).

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