The Mass Spectra of Amino-acid and Peptide Derivatives: Phthaloylamino-acids

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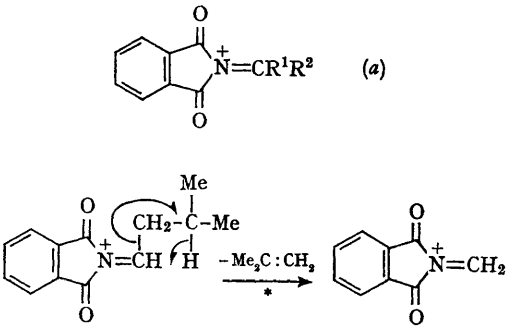
IN the course of our examination[1] of the effect of various amino-protecting groups on the mass-spectral fragmentation of amino-acid and peptide derivatives we have examined several phthaloyl-amino-acids. To facilitate the interpretation of their spectra, we have also investigated some simple *N*-alkylphthalimides, and the current interest[2,3] in the behaviour of cyclic imides on electron impact prompts us to report some of our observations.

All the phthaloylamino-acids examined which had aliphatic side-chains (Table 1) gave molecular ions which lost the carboxyl group to give abundant fragments of type (*a*). The fates of the ions (*a*) were interesting: in the cases of phthaloylglycine and phthaloylalanine loss of hydrogen cyanide occurred; in the case of phthaloyl-leucine and phthaloylvaline, loss of the side chain with hydrogen transfer was observed (*e.g.* Scheme 1),



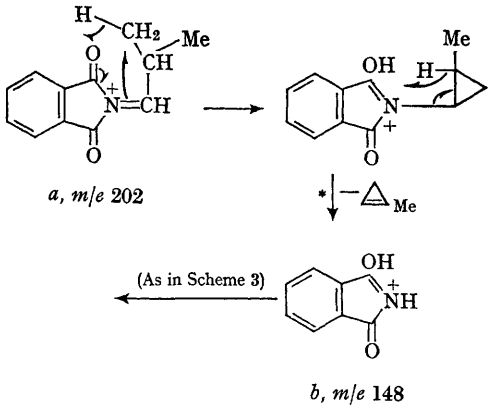
SCHEME 1.

together with loss of the entire carbon chain with double hydrogen-transfer (*e.g.* Scheme 2); and in

TABLE 1.[6] *Phthaloylamino-acids*

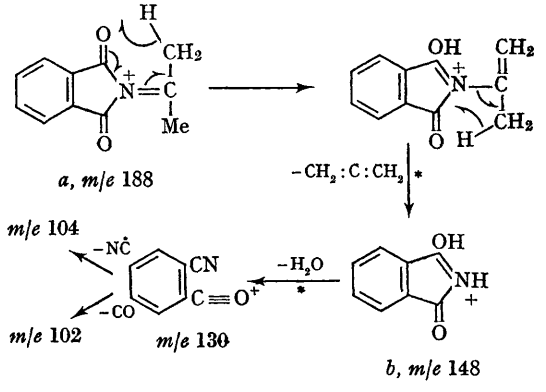
Compound	M^+ *m/e*	M^+ %	R[1]	R[2]	Fragment (*a*) *m/e*	Fragment (*a*) %	Further fragmentation of (*a*)†
Pth.Gly	205	2	H	H	160	100	$160 \xrightarrow{*} 133$ (5%)
Pth.Ala	219	6	H	Me	174	100	$174 \xrightarrow{*} 147$ (6%)
Pth.Leu‡	261	14	H	$CH_2{\cdot}CHMe_2$	216	67	$216 \xrightarrow{*} 160$ (100%); $216 \xrightarrow{*} 148$ (24%) $\xrightarrow{*} 130$ (24%)
Pth.Val‡	247	42	H	$CHMe_2$	202	100	$202 \xrightarrow{*} 160$ (43%); $202 \xrightarrow{*} 148$ (62%) $\xrightarrow{*} 130$ (37%)
Pth.Aib§	233	1	Me	Me	188	100	$188 \xrightarrow{*} 148$ (16%) $\xrightarrow{*} 130$ (18%)

† Transitions indicated by an asterisk (*) were supported by the presence of appropriate metastable peaks.
‡ Other less favoured fragmentations were also observed.
§ The methyl and 1-piperidyl esters gave similar results.



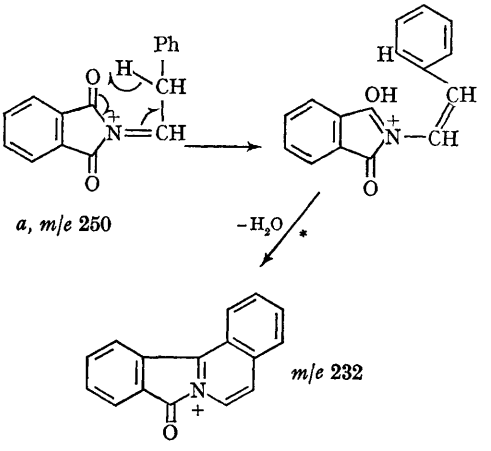
SCHEME 2.[7]

the case of phthaloyl-α-aminoisobutyric acid, the ion (*a*) showed loss of allene to give (*b*), which decomposed as shown in Scheme 3. Phthaloyl-



SCHEME 3.[7]

phenylalanine did not give an abundant ion (*a*) because the preferred cleavage was formation of *m/e* 148 (100%, Ph·CH : CH·$CO_2H^{\cdot+}$) by McLafferty rearrangement. However, when we examined phthaloylphenylalanine thiophenyl ester (with Dr. B. Liberek) the ion (*a*) was the base peak: the subsequent decomposition of (*a*) to *m/e* 232 (23%) is shown in Scheme 4, which is similar to that



SCHEME 4.

suggested for the fragmentation of 2-phthalimidobiphenyl.[3]

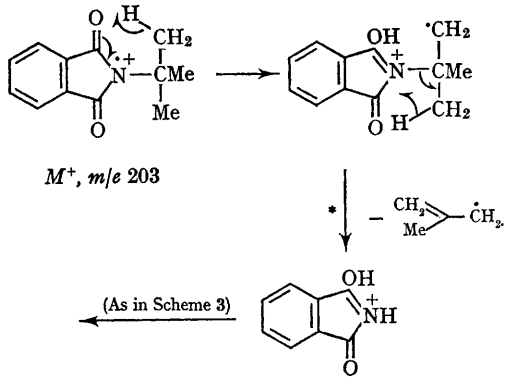
The simple *N*-alkylphthalimides (Table 2) all had ions (*a*) as base peaks, and the subsequent fragmentations were analogous to those observed in the phthaloylamino-acids. In the case of *N*-t-butylphthalimide the ion (*b*) was derived not only from (*a*) according to Scheme 3, but also directly from the molecular ion by expulsion of an allylic radical (Scheme 5).

None of the compounds in Tables 1 and 2 showed $(M-44)$ peaks. Furthermore, we have observed variable relative intensities for the $(M-44)$ peak in the mass spectrum of *N*-methylphthalimide[4]

TABLE 2. N-*Alkylphthalimides*

Alkyl Group	M^+ m/e	%	Base Peak m/e
Ethyl	175	54	160
n-Propyl	189	47	160
Isopropyl	189	20	174
n-Butyl	203	57	160
Isobutyl	203	48	160
s-Butyl	203	23	174
t-Butyl	203	39	188

(10—20%, with different samples: Johnstone *et al.* report a relative intensity of *ca.* 36%). We therefore suggest that the $(M-44)$ peak is due either to an impurity or results from thermal isomerization to 3-methyliminophthalide,[5] which would be expected to lose carbon dioxide readily on electron impact.



SCHEME 5.

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[1] T. R. Aplin, J. H. Jones, and B. Liberek, *Chem. Comm.*, 1966, 794.
[2] R. A. W. Johnstone, B. J. Millard, and D. S. Millington, *Chem. Comm.*, 1966, 600.
[3] J. L. Cotter and R. A. Dine-Hart, *Chem. Comm.*, 1966, 809.
[4] Prepared by the method of F. Sachs, *Ber.*, 1898, **31**, 1225.
[5] The preparation of this compound has been described by S. Hoogewerf and W. A. van Dorp (*Rec. Trav. chim.*, 1894, **13**, 98), but their method has so far been unsuccessful in our hands.
[6] The abbreviated designations for phthaloylamino-acids are as recommended in I.U.P.A.C. Information Bulletin, 1966, No. 25, p. 32.
[7] The composition of the ions in this scheme was confirmed by high-resolution measurements.