MASS SPECTROMETRIC STUDIES—II:*

MASS SPECTROMETRIC STUDIES OF MALEIMIDES AND BENZAL-DAZINE ADDUCTS. IDENTIFICATION OF SOLID MIXTURES

S. W. TAM

Department of Chemistry, Chung Chi College, Chinese University of Hong Kong, Shatin, N.T., Hong Kong

(Received 1 August 1972; accepted (revised) 26 October 1972)

Abstract—It has been found by mass spectrometric studies that the so-called '1:1-adduct' formed by N-(*n*-butyl) maleimide and benzaldazine, is in fact a solid mixture of one part *bis*-imide L and one part benzaldazine. *Bis*-imide L is one of the three stereoisomeric products obtained by the addition of two mole of N-(*n*-butyl) maleimide and one mole of benzaldazine. The three stereoisomeric *bis*-imides gave identical mass spectra. Mass spectra of *bis*-imide M and *bis*-imide M- d_2 are discussed, and confirm the proposed structures of perhydropyrazolo-pyrazole derivatives for these 1:2-adducts.

FORMATION of 1,3-2,4-bis-cycloaddition (criss-cross) products of perhydro-pyrazolopyrazoles (I, Ar = aryl; Z = O or N-alkyl) by reacting one mole of aromatic aldazine and two mole of maleic anhydride¹ of N-alkylated maleimides^{2,3} is known. It was also found¹ that at least two stereoisomeric products were obtained from each reaction. Apart from the suggested reaction course which yielded three stereoisomers (I, Ar = C₆H₅; Z = N-Buⁿ) of the 1:2-bis-adducts, (viz: bis-imide L, m.p. 177 to 180°; bis-imide M, m.p. 206 to 207° and bis-imide H, m.p. 226 to 228°), it was reported² that N-(*n*-butyl) maleimide and benzaldazine also gave a '1:1-adduct' (m.p. 141 to 142°), but only in 3% yield. Based on its NMR spectrum, a structure with an azetidine ring (II) was proposed.⁴



Mass spectrometric studies of this '1:1-adduct' revealed that it is in fact a solid mixture of one part *bis*-imide L and one part benzaldazine, rather than a molecular compound.⁵ When the sample was introduced into the cold ion source by the direct insertion method and by slow increase of the ion source temperature up to 100° , a spectrum identical to that of pure benzaldazine⁶ was obtained. Small peaks at m/e 514 and 360 began to appear when the ion source temperature was raised to 105 to 110°. The intensities of these peaks increased with the increase of ion source temperature, and at 160° and above a full spectrum of the *bis*-imide was revealed (Fig. 1).

* For Part I, see S. W. Tam, Org. Mass Spectrom. 2, 729 (1969).



The possibility of labile thermal decomposition of the '1:1-adduct' by a retro-Diels-Alder into benzaldazine and N-(*n*-butyl) maleimide within the ion source has been ruled out. There was no sign of any significant peaks corresponding to that of N-(*n*-butyl) maleimide⁷ (e.g. its base peak at m/e 110 or molecular ion at m/e 153) observed in the spectra obtained at ion source temperature 100° or below. The appearance of the peaks in the m/e 360 region* is always accompanied by peaks of higher intensity in the m/e 514 region. The ratio of m/e 360 to m/e 514 remains between 35 to 37% which is in agreement with the full spectrum of the *bis*-imides (*cf.* Fig. 1).

This result is of significance and shows its superiority over other physical measurements where solid mixtures are concerned. The simultaneous fractional evaporation and ionisation allowed the identification of a solid mixture which would otherwise be difficult to recognise, since other physical measurements would generally include both components in their spectra. A structure of a 1,1'-bis-azetidine, which was at one time⁴ erroneously assigned for the bis-imide L due to the similarities between the methine hydrogen absorption in the NMR spectra of bis-imide L and the so-called '1:1-adduct' becomes obsolete.

The mass spectra of the three isomeric *bis*-imides L, M and H are virtually identical. A representative of their spectra is given in Fig. 1 for *bis*-imide M. The molecular ion[†] appears as the base peak and the first major fragment ion, which was derived via two distinct pathways, is revealed at m/e 360. Direct loss of a molecule of N-(*n*-butyl) maleimide, together with a hydrogen as a one-step process (m/e 514 $\xrightarrow{m^*}$ 360), was supported by the appearance of a pronounced metastable peak at m/e 252·1. Whilst recognising that most of the peak intensity at m/e 361 (9%) is due to the isotopic contribution from m/e 360, part of the peak intensity at m/e 361 (2%) could well be due to the fragment ion generated from the molecular ion through a retro-Diels-Alder process by the expulsion of a N-(*n*-butyl) maleimide molecule. Subsequent loss of a hydrogen from m/e 361 again gives an ion at m/e 360 which was substantiated by a metastable peak at m/e 359·1.

Minor peaks observed between m/e 361 and the molecular ion are m/e 387 (0.5%), 386 (1.5%), 457 (1%) and 471 (1%), and their fragmentations are shown below:



Apart from the retro-Diels-Alder, these modes of fragmentation are in contrast to that for simple N-alkylated maleimides,⁷ where cleavage of a substituent bond α

* The molecular ion of the supposed '1: l-adduct' would be m/e 361.

[†] Throughout the work of this paper, high resolution and elemental mapping techniques⁸ were employed to determine the compositions of all ions. to the nitrogen predominates, giving rise to ion a which is usually the base peak. In the case of our *bis*-imides, similar cleavage only constitutes a very minor fragmenta-



tion, indicating that the initial charge of the molecular ion is preferentially localised at the oxygen rather than at the nitrogen, which is in agreement with the results of Maquestiau and Lejeune⁹ for cyclic imides and cyclic β -diketones.

In competing with the loss of a hydrogen from ions at m/e 387 and m/e 361, loss of a phenyl group in each case gives peaks at m/e 310 and 284, respectively.

The ion at m/e 361 also eliminates a further mole of N-(*n*-butyl) maleimide to give rise to the benzaldazine ion at m/e 208. This process is supported by the observation of a metastable peak at m/e 119.9. Further fragmentation of the benzaldazine ion contributes to the following peaks at m/e 207, 181, 180, 131, 104, 103, 91 and 77, and the relative abundances correspond well with the spectrum for pure benzaldazine.⁶ Similarly, peaks at m/e 153, 111, 110, 99, 98, 82 and 80, represent the molecular and fragment ions of N-(*n*-butyl) maleimide.⁷

The remaining significant peaks to be discussed are m/e 243, 144, 116 and 115. The ion at m/e 243 is represented by the fragment of half a molecule less one nitrogen atom formed by the breaking of two C—N bonds as shown in the partial structure below. Elimination of the amide unit from m/e 243 gives the fragment ion at m/e 144 which could be represented by the partial structure $[C_6H_5$ —CH—CH—CH—CH—CH—CO]⁺. Sequential loss of CO and H from m/e 144 gives rise to ions at m/e 116 and 115, respectively. The former process was substantiated by the observation of a pronounced metastable peak at m/e 93.5.



The above fragmentations gave support to the proposed structure of 'criss-cross' addition. Formation of the 1:2-adducts from benzaldazine and maleimides involving some sort of rearrangement is not anticipated. Since all the three *bis*-imides under discussion have practically identical mass spectra upon electron-impact, their structures should most likely differ only in the configuration of the six asymmetric centres. Mass spectrometry in our present study gives no indication as to the stereochemistry or relative configuration of these compounds, however.

Low ionisation energy (12 eV) spectra are also identical for all these *bis*-imides. They are also indistinguishable in the fragmentation pattern to those obtained at 70 eV, except that the relative abundance of the ions at m/e 207 and 208 are in the reverse order.

Further support for the assignment of structures for the fragment ions was obtained by the study of the spectrum of *bis*-imide $M-d_2$, which was prepared by reacting 1 mole of benzaldazine- d_2 with 2 mole of N-(*n*-butyl) maleimide. The spectrum is shown in Fig. 2.



Loss of a N-(*n*-butyl) maleimide molecule and a hydrogen/deuterium, either directly or sequentially, leads to the formation of ions in the m/e 361 to 363 region. The ratio of the peak intensities at m/e 361 to m/e 362 is approximately 1:1 (after isotopic impurities correction). This indicates that loss of both H and D occurs, which is analogous to that for benzaldazine- d_2 .^{6,10}

On the other hand, peaks at m/e 312 and m/e 286 are each two mass units higher than the corresponding peaks for the unlabelled compound, and this loss of a phenyl group is not accompanied by H/D scrambling.

The ion at m/e 210 becomes the molecular ion of benzaldazine- d_2 , from which both H and D are eliminated, giving rise to ions at m/e 209 and 208. Other peaks, e.g. m/e 182, 181, 180, 133, 132, 131, 105, 104, 103, 92, 91, 77, represent the fragment ions of this compound which are in complete agreement with published data.^{6.10}

The peak at m/e 243 for *bis*-imide M has moved up one mass unit higher in the d_2 compound, which confirms the assignment of its structure. Loss of the amide moiety of 99 mass units gives the ion at m/e 145, which should be represented by the structure $[C_6H_5-CD=CH-CH=C=O]^+$ corresponding to that at m/e 144 for the unlabelled compound. Loss of CO gives the ion at m/e 117, which again expels either H or D in the ratio of 1:6.5. This result indicates that complete scrambling has taken place before H/D expulsion.

EXPERIMENTAL

All mass spectra were obtained with an AEI MS-9 mass spectrometer, with an ion source temperature of ca. 200° and the beam energy at 70 eV. Variation of ion source temperature starting from cold for the study of '1:1-adduct' and low energy (12 eV) spectra for the *bis*-imides were recorded with a CEC-21-104 instrument. High resolution data were obtained by exposure on photoplates with a CEC-21-110 mass spectrometer and the technique of elemental mapping⁸ were employed.

The syntheses and discussion of the stereochemistry of the bis-imides were published elsewhere.³



Acknowledgements—The author wishes to thank Professor K. Biemann of MIT, Cambridge, Massachusetts for providing laboratory facilities, Dr D. H. Williams of Cambridge University for use of the AEI MS-9 mass spectrometer, Professor T. Wagner-Jauregg, research director and Dr L. Zirngibl of Siegfried AG, and Dr H. Günther of Universität Köln for their interest and helpful discussions.

REFERENCES

- (a) T. Wagner-Jauregg, Chem. Ber. 63, 3213 (1930); (b) M. Häring and T. Wagner-Jauregg, Helv. Chim. Acta 40, 853 (1957); (c) W. L. Mosby, 'Heterocyclic Systems with Bridgehead Nitrogen Atoms', in A. Weissberger, The Chemistry of Heterocyclic Compounds, Part I, Interscience Publishers Inc, New York, 1961, p. 216.
- 2. T. Wagner-Jauregg and L. Zirngibl, Chimia (Aarau) 19, 393 (1965).
- 3. T. Wagner-Jauregg, L. Zirngibl, A. Demolis, H. Günther and S. W. Tam, *Helv. Chim. Acta* 52, 1672 (1969).
- 4. T. Wagner-Jauregg, L. Zirngibl and H. Günther, Chimia (Aarau) 20, 442 (1966).
- 5. T. Wagner-Jauregg and L. Zirngibl, Chimia (Aarau) 22, 436 (1968).
- (a) R. G. Cooks and S. W. Tam, Org. Mass Spectrom. 1, 583 (1968);
 (b) B. Zeeh and R. Beutler, Org. Mass Spectrom. 1, 791 (1968).
- 7. W. J. Feast, J. Put, F. C. de Schryver and F. C. Compernolle, Org. Mass Spectrom. 3, 507 (1970).
- 8. K. Biemann and P. V. Fennessay, Chimia (Aarau) 21, 226 (1967).
- 9. A. Maquestiau and P. Lejeune, Bull. Soc. Chim. Belges 78, 309 (1969); 76, 133 (1967).
- S. E. Scheppele, R. D. Grigsby, K. F. Kinneberg, E. D. Mitchell and C. A. Mannan, Org. Mass Spectrom. 3, 557 (1970).