Electron Ionization Mass Spectra of Some Norbornane/ene-fused 2-*N*-Phenyliminoperhydro-1,3-oxazines

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The 70 eV electron ionization (EI) mass spectra were recorded for eight norbornane/ene-fused 2-*N*-phenyliminoperhydro-1,3-oxazines, and the fragmentation patterns were studied by metastable ion analysis and exact mass measurement. Whereas the stereoisomeric unsaturated compounds could not be distinguished on the basis of their EI mass spectra, the stereoisomeric saturated compounds gave rise to clearly different spectra. The ionized unsaturated compounds decomposed mainly by two consecutive retro-Diels-Alder (RDA) reactions. A methyl substituent on the ring nitrogen strongly influenced the charge distribution on the RDA fragments. The ionized saturated compounds fragmented through several pathways. Loss of cyclopentadiene from the molecular ion was the energetically favoured fragmentation reaction for the saturated di-*endo*-fused compounds but was unimportant for the di-*exo*-fused compounds.

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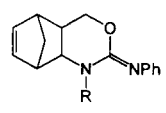
Introduction.

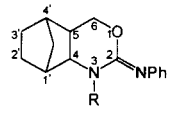
The fragmentation reactions of fused-ring perhydro-1,3-oxazines are strongly influenced by the nature and position of the substituents in the ring system and by the site and stereochemistry of the ring fusion [1-4]. In addition, unsaturation in the fused ring [2,4] sometimes has a marked effect because the retro-Diels-Alder (RDA) reaction has been shown to be the most important fragmentation pathway for a number of unsaturated cyclic compounds [5]. Cyclopentane-, cyclohexane- and cyclohexene-fused 2-*N*-phenyliminoperhydro-1,3-oxazines [3,4] also undergo extensive rearrangement reactions involving intramolecular cyclization between an *ortho* position of the aromatic ring and one of the ring heteroatoms. Such cyclization reactions were first proposed by Bujtás and Tamás [6] in their mass spectrometric study of some 2-arylaminothiazine and 2-arylaminothiazoline derivatives.

As a continuation to our studies on the mass spectrometry of stereoisomeric norbornane/ene [2,7] and 2-*N*-phenylimino-substituted 1,3-oxazine [3,4] derivatives, we recently recorded the electron ionization (EI) mass spectra of norbornene **1-4** and norbornane **5-8** di-*exo*- and di-*endo*-fused 2-*N*-phenyliminoperhydro-1,3-oxazines (Scheme 1). Besides the mass spectrometric behaviour of these compounds, special interest was focused on the stereochemistry of the fused ring and on the differentiation of the stereoisomeric compounds. All the fragmentations discussed were verified through metastable ion analysis and collision-induced dissociation (CID) techniques. The elemental compositions of the principal ions were confirmed by accurate mass measurement. The ion structures indicated are speculative, however, and merely meant to aid in the visualization of the fragmentation pathways.

Scheme 1



1 - 4



5 - 8

Compound	R	Ring fusion	Compound	R	Ring fusion
1	H	di-*exo*	**5**	H	di-*exo*
2	H	di-*endo*	**6**	H	di-*endo*
3	CH_3	di-*exo*	**7**	CH_3	di-*exo*
4	CH_3	di-*endo*	**8**	CH_3	di-*endo*

Results and Discussion.

The 70 eV EI mass spectra are presented in Table 1 and Figure 1. The molecular ion peak was always visible, and for three of the four saturated compounds, *i.e.* compounds **6-8**, it formed the base peak in the spectrum. From the abundances of the molecular ions (% TIC), it can be concluded that the *N*-methyl substituted compounds were always more stable than the respective unsubstituted compounds.

For the stereoisomeric unsaturated oxazines **1, 2** and **3, 4**, respectively, the EI mass spectra were identical (Table 1). Fragmentation of these compounds occurred almost totally through two consecutive RDA reactions, and thus the ionization must mostly have taken place at the double

Table 1

70 eV Mass Spectra of Compounds **1-4**, **8** and **9**. All peaks with Relative Intensities Greater than 7% of the Base Peak are Shown.

Compound	*m/z* (Relative Intensity)
1	240 ($M^{+\cdot}$, 10), 175 (10), 174 (83), 132 (23), 120 (13), 119 (100), 91 (9), 82 (31), 77 (15), 65 (8)
2	240 ($M^{+\cdot}$, 8), 175 (11), 174 (86), 132 (27), 120 (13), 119 (100), 91 (9), 82 (39), 77 (19), 66 (8), 65 (10), 54 (8), 39 (7)
3	254 ($M^{+\cdot}$, 16), 188 (36), 119 (70), 91 (12), 77 (7), 70 (8), 69 (100), 68 (44), 66 (9), 42 (29), 41 (7)
4	254 ($M^{+\cdot}$, 20), 188 (40), 120 (7), 119 (79), 91 (10), 70 (8), 69 (100), 68 (42), 66 (12), 42 (25)
7	257 (19), 256 ($M^{+\cdot}$, 100), 255 (76), 149 (49), 132 (11), 120 (8), 119 (17), 107 (16), 106 (91), 93 (10), 91 (18), 80 (15), 79 (33), 78 (7), 77 (13), 70 (12), 68 (16), 67 (17), 66 (17), 42 (40), 41 (15), 39 (7)
8	257 (18), 256 ($M^{+\cdot}$, 100), 255 (74), 190 (9), 149 (37), 132 (10), 122 (8), 119 (16), 108 (7), 107 (14), 106 (56), 94 (8), 93 (8), 91 (25), 81 (8), 80 (13), 79 (24), 77 (14), 71 (11), 70 (26), 68 (21), 67 (18), 66 (9), 42 (48), 41 (19), 39 (8)

bond (Scheme 2). Norbornene derivatives are known to be ideal for the RDA fragmentation reaction [5], but the extent of the reaction for the present compounds was extraordinary, especially when compared with the corresponding cyclohexene-fused compounds [4]. With the cyclohexene-fused compounds the RDA reaction is dominant only for the unsubstituted compounds, while for the *N*-methyl-substituted compounds the charge is preferentially localized on the nitrogen atom, leading to ring cleavage reactions and extensive rearrangements in the heterocyclic part of the molecule [4]. The absence of the $[M-H]^+$ ion peaks also differentiated the unsaturated compounds from the corresponding cyclohexene-fused compounds [4].

Usually in RDA fragmentations of norbornene compounds the cyclopentadiene fragment retains the charge

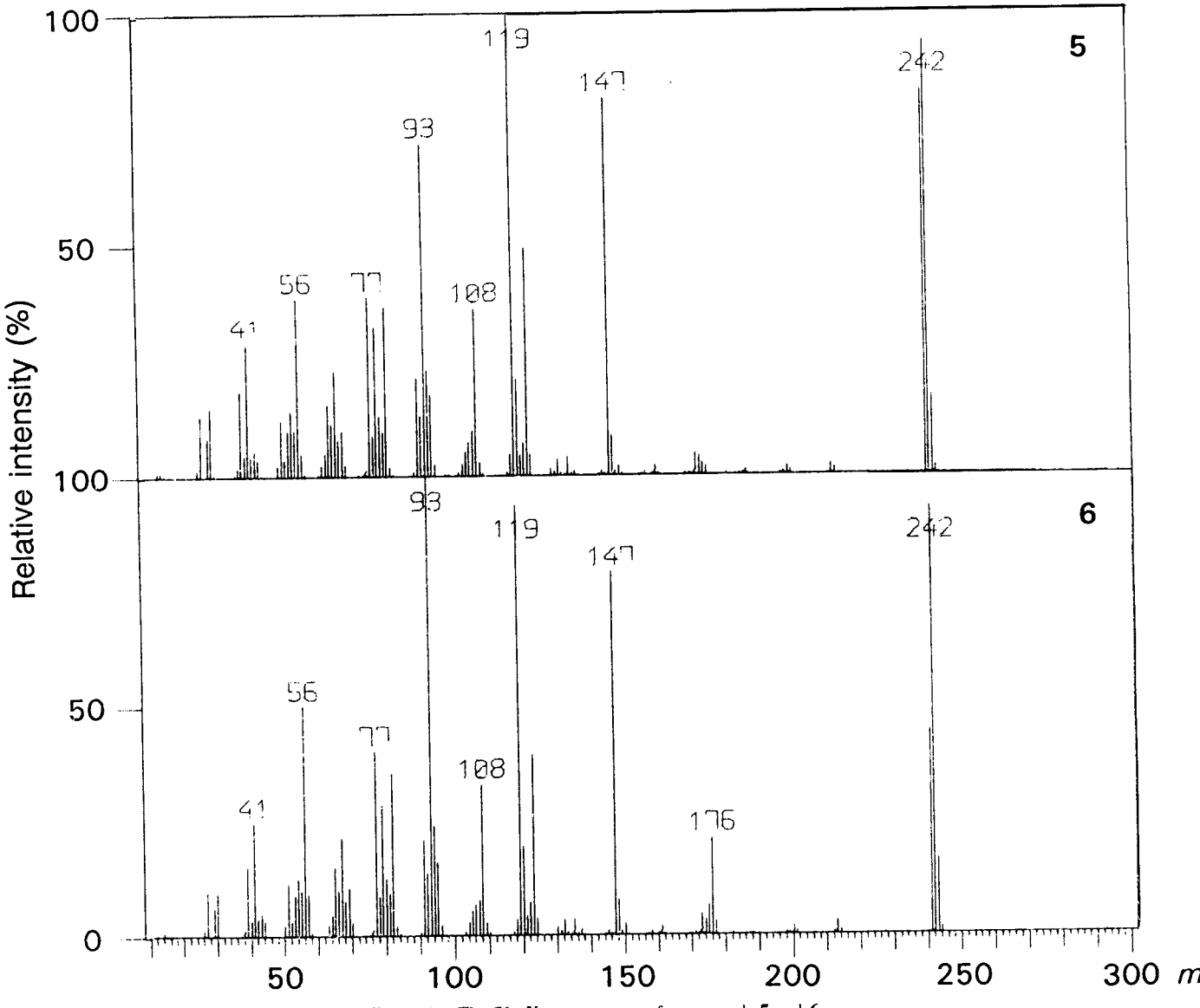
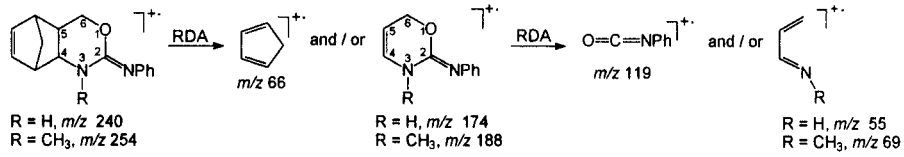


Figure 1. The 70 eV mass spectra of compounds **5** and **6**.

Scheme 2



[5], as it has low ionization energy (IE = 8.56 eV [8]). In the present case the ene fragment contained heteroatoms, which lower the IE of the fragment considerably from that of cyclohexene (8.95 eV [8]), and thus the charge remained almost totally in the heterocyclic part of the molecule (Scheme 2). The heterocyclic ions so formed had a newly created double bond in the ring, and so they decomposed further through a second RDA process (Scheme 2).

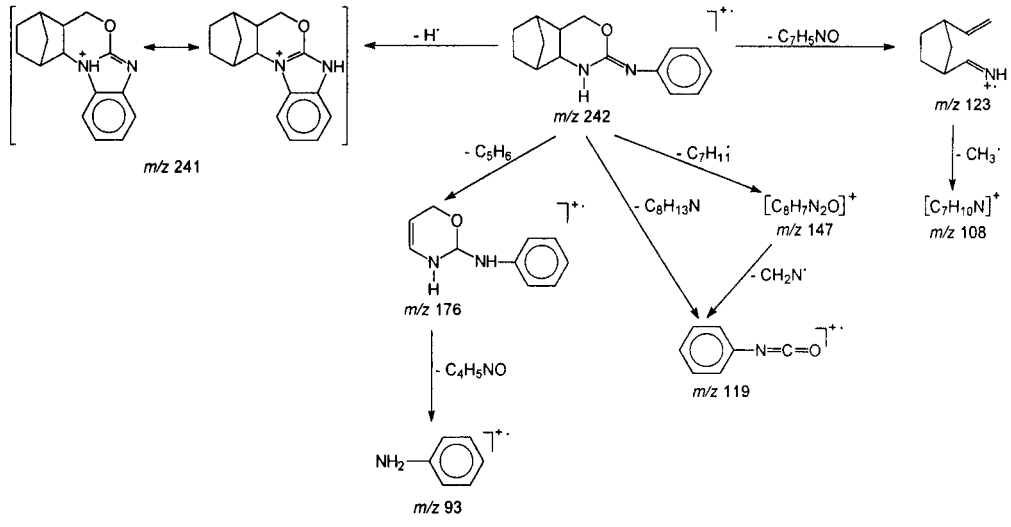
A methyl substituent on the ring nitrogen had a striking effect on the second RDA reaction. For the unsubstituted compounds **1** and **2**, the ene (phenyl isocyanate) fragment ion at m/z 119 gave rise to the base peak in the spectrum, while the diene (2-propen-1-imine) fragment ion peak at m/z 55 was minor. This represents a normal charge distribution, as the IE's of the corresponding neutral species, phenyl isocyanate and 2-propen-1-imine, are 8.8 eV and 9.65 eV, respectively [8]. By contrast, for the *N*-methyl substituted compounds **3** and **4**, both diene (*N*-(2-propenylidene)methylamine) and ene (phenyl isocyanate) fragment ions were abundant and the base peak was formed by the diene fragment ion at m/z 69. The IE of *N*-(2-propenylidene)methylamine is not known, but according to the data obtained, it must be close to that of phenyl isocyanate. An *N*-methyl substituent lowers the IE. For example, the IE's of methanimine ($CH_2=NH$) and the corresponding *N*-methyl substituted compound ($CH_2=N-CH_3$) are 9.9 eV and 9.4 eV, respectively [8]. In the present case a drop of only this size in the IE would not completely explain the greater amount of the *N*-(2-propenylidene)methylamine ion than of the phenyl isocyanate ion.

In the spectra of the unsubstituted oxazines **1** and **2**, the other abundant fragment ions, $[C_9H_{10}N]^+$, $[C_4H_4NO]^+$ and $[C_6H_5]^+$ at m/z 132, 82 and 77, respectively, originated from the first RDA product ion at m/z 174. The formation of the ion at m/z 132 required phenyl group migration to the C4 or C5 position followed by the loss of CNO$^{\cdot}$. Migration of the phenyl group to the radical site has earlier been described for 1,3-oxazolidines [9]; in the present case the unpaired electron of the radical ion of m/z 174 may be located on either C4 or C5.

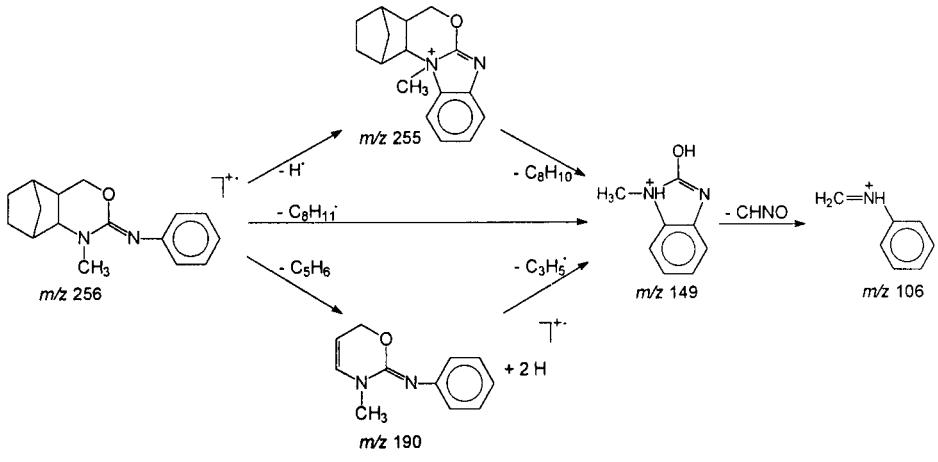
The relative peak intensities of the saturated stereoisomeric compounds **5-8** (Table 1 and Figure 1) were sufficiently different to allow differentiation of the stereoisomers. All the saturated compounds lost hydrogen atom from the molecular ion. Concluding from the 14 eV mass spectra and *B*/*E* spectrum of the molecular ions, the formation of the $[M-H]^+$ ion was the energetically favoured reaction. The loss of H$^{\cdot}$ most probably took place through an intramolecular cyclization reaction as described earlier for the related 2-*N*-phenyliminoperhydro-1,3-oxazines and thiazines [3,4].

The major fragmentation pathways for the unsubstituted compounds **5** and **6** are presented in Scheme 3. The spectra of the two compounds clearly differed in the mo-

Scheme 3



Scheme 4



lecular ion region. From the abundances of the molecular ions (8.9% and 10.0% TIC, for **5** and **6**, respectively), the di-*endo*-fused compound **6** was concluded to be more stable than the corresponding di-*exo*-fused compound **5**, even though the di-*exo* isomer is sterically less hindered. The same trend has been observed for norbornane-fused 1,3-oxazin-2(1*H*)-one [2] and 1,3-amino alcohols [7]. The intensity of the $[M-H]^+$ ion peak was lower for the di-*endo*-fused compound **6** than for the di-*exo*-fused compound **5** (Figure 1), as the cyclization product for the di-*endo*-fused isomer is sterically crowded.

The greatest difference between compounds **5** and **6** was in the peak intensities of the $[C_{10}H_{12}N_2O]^{+\cdot}$ and $[C_6H_7N]^{+\cdot}$ ions at m/z 176 and 93, respectively (Figure 1). For the di-*endo*-fused compound **6** the loss of cyclopentadiene, C_5H_6, from the molecular ion, requiring two hydrogen atoms to move from the norbornane framework to the heterocyclic ring, was the energetically favoured fragmentation reaction. In compound **6** the proximity of the *endo*-hydrogen atoms at C2′ and C3′ to the heterocyclic part of the molecule encourages such migration, whereas in compound **5** the stereochemistry does not allow it. In compound **6** the hydrogens must have migrated to the 2-*N*-phenylimino group (as shown in Scheme 3), because the subsequent decomposition of the ion at m/z 176 included the loss of C_4H_5NO. This neutral loss can best be explained through hydrogen atom migration from the ring nitrogen to the other nitrogen atom. Thus, the ion $[C_6H_7N]^{+\cdot}$ at m/z 93 so formed most probably has the aniline structure. For the di-*exo*-fused compound **5**, by contrast, the loss of C_7H_5NO was the energetically favoured fragmentation reaction. Most probably this elimination starts as an α-cleavage reaction with respect to the ring nitrogen atom, with break of the C4-C5 bond (Scheme 3).

The ionized *N*-methyl substituted compounds **7** and **8** decomposed in approximately the same way as the related cyclohexene-fused compounds [4]. In both cases, low energy fragmentation reactions generated the $[C_8H_9N_2O]^+$ and $[C_7H_8N]^+$ ions at m/z 149 and 106, respectively (illustrated in Scheme 4). This fragmentation pathway was nevertheless more favourable for the di-*exo*-fused compound **7** than for the di-*endo*-fused compound **8**. The formation of the fragment ion at m/z 149 requires that a hydrogen atom move from the norbornane framework to the oxygen atom, and the distance between the oxygen atom and the methano group *syn*-hydrogen atom in compound **7** is much shorter than any of the oxygen-hydrogen distances in compound **8**. This may explain the differences in the mass spectra of **7** and **8**.

The di-*endo*-fused compound **8** also lost cyclopentadiene, with formation of the $[C_{11}H_{14}N_2O]^{+\cdot}$ ion at m/z 190 (Scheme 4), although this pathway was less favourable than for the corresponding unsubstituted compound **6**. Relative to hydrogen atom migration the migration of the methyl group is more difficult, and thus the ion at m/z 190 did not rearrange to the *N*-methylaniline ion; instead $C_3H_5\cdot$ was lost. The mechanism proposed above for the formation of aniline ion from the unsubstituted compounds **5** and **6** is thus further confirmed.

EXPERIMENTAL

The mass spectra were recorded on a Jeol JMS-D300 mass spectrometer (Jeol, Tokyo, Japan) equipped with a combined EI/CI ion source and connected to a Jeol JMA-2000H data system. For all the measurements, samples were introduced through a direct inlet system with heating within 338-438 K. Typical source conditions were: temperature, 443 K; electron energy, 70 eV; accelerating voltage, 3 kV; and ionization current, 300 μA. Accurate mass measurements were made at a resolution of 5000 using the data system. Fragmentation pathways were verified *via* metastable ion analysis and/or collision-induced dissociation

spectra using linked scans at constant *B*/*E*. The syntheses as well as the nmr studies of the compounds have been reported elsewhere [10].

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