Tetrahedron Letters, Vol.33, No.2, pp. 231-234, 1992
Printed in Great Britain

0040-4039/92 $3.00 + .00
Pergamon Press plc

Cyclopropane Ring Location in Linear Aliphatic Compounds by NO^+-Induced Ion-Molecule Reactions

Jacques Einhorn[1*], Alfredo Parrilla[2], Christian Malosse[1] and Angel Guerrero[2]

[1]Station de Phytopharmacie, INRA, route de St Cyr, 78000 Versailles, France
[2]Department of Biological Organic Chemistry, CID (CSIC), 08034 Barcelona, Spain

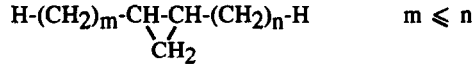
Key Words: cyclopropane location, aliphatic compounds, NO^+, ion-molecule reactions, mass spectrometry.

Abstract: NO^+-induced gas phase ion-molecule reactions allow unambiguous cyclopropane ring location in linear aliphatic compounds through (NO)-containing diagnostic ion products.

Gas-phase ion-molecule reactions in mass spectrometry have proved to be an efficient and sensitive approach to locate functional groups in long chain aliphatic compounds.[1] For instance, using NO^+ as reagent species, methods for localization of a double bond in mono- or bifunctional olefins[1b, 2] or an epoxide group[3] in similar straight chain compounds have been reported.

Considering the presence of the cyclopropane functionality in many natural products[4] and the lack of direct and specific methods[5] to characterize and to locate the cyclopropane ring, except in the case of certain bifunctional molecules[6], utilization of CI-NO-MS has been investigated in this case.[7]

According to the complete C_8-C_9 series of model compounds and various members from C_{10} to C_{23} examined, NO^+ (produced from NO) again appears as an efficient reagent for the assignment of the position of the cyclopropane function.



$m \leqslant n$

Besides the occurrence of molecular species (i.e: $(M+NO)^+$, $((M+NO)-H_2O)^+$, $M^{+\cdot}$ and $(M-H)^+$ ions) as well as series of alkyl and alkenyl ions, two types of abundant even-mass diagnostic ions can be observed (Figure): i) one (or two complementary) ion(s) (a_1, a_2), for example at m/z 88 and 102 for *trans*-4,5-methylenenonane, ii) a series of ions (b_1, b_2..) apparently resulting from the $(M+NO)^+$ adduct ion by the loss of alkene neutrals of C_xH_{2x} type (x= 2, 3,..n), i.e. at m/z 114 and 128 for the same compound. All these even-mass ions are by their m/z values or distribution patterns clearly correlated to the cyclopropane position.

Exact mass measurements[8] obtained through high resolution CI-NO-MS allowed us to determine the elemental compositions of ions a and b to be $C_xH_{2x+2}NO$ and $C_yH_{2y}NO$,

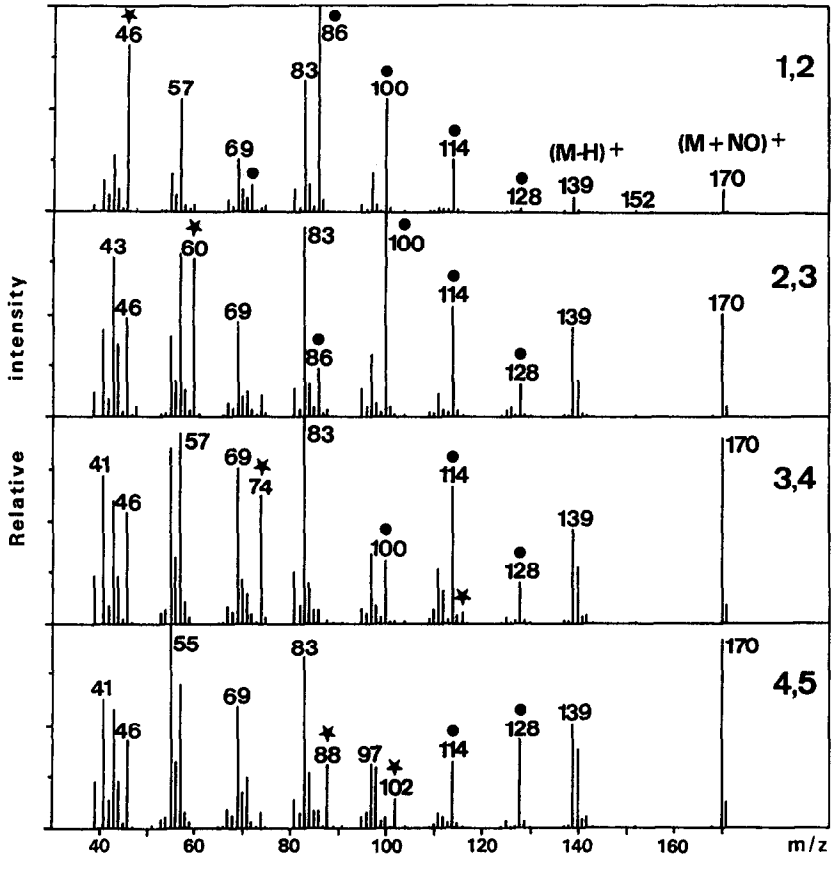


Figure: CI-NO mass spectra of isomeric *trans*-methylenenonanes.
(a (✱) and b (●) diagnostic ions).

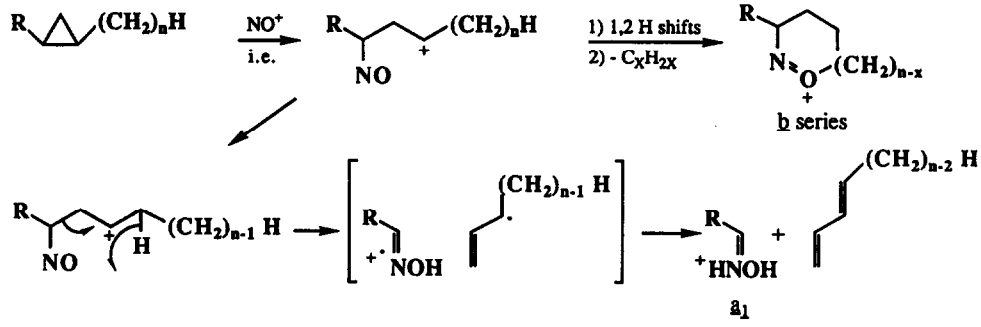
respectively. Preliminary MS-MS studies[9] have been performed to determine the origin and structure of diagnostic ions a and b. Collisional activated dissociation (CAD) spectra obtained under low collision energy conditions from 5,6-methylenedecane (MW=154) as reference indicate the following: i) both types of ions result from the decomposition of the $(M+NO)^+$ adduct ion (cf. CAD daughter ion spectrum of ion m/z 184), ii) ions b and the adduct are homologues as shown by the similarity of the corresponding daughter ion spectra (i.e. loss of alkene neutrals and production of ions NH_4^+ , NO^+ and m/z 46 (likely $CH_2{=}NH^+OH$)) and iii) there is no detectable intermediate involved in the decomposition of $(M+NO)^+$ into a (cf. CAD parent ion spectrum of ion m/z 102 exhibiting only ion m/z 184 as precursor). Furthermore, the CAD daughter ion spectrum of ion m/z 102 giving rise to ions at m/z 69 (loss of NH_2OH) and m/z 46 (see above) as main daughter ions could be interpreted as corresponding to $CH_3(CH_2)_3CH{=}NH^+OH$. This was confirmed by the identical CAD daughter ion spectrum obtained from protonated pentanal oxime (pentanal oxime under CI-NH_3).

compounds	$(M+NO)^+$	$(M-H)^+$	a_1	a_2	b_1	b_2
1,2-methyleneoctane	156 (8)	125 (12)	46 (59)		72 (13)	86 (100)
trans-2,3-meth.-octane	156 (40)	125 (38)	60 (79)		86 (26)	100 (100)
trans-3,4-meth.-octane	156 (94)	125 (66)	74 (74)	102 (11)	100 (42)	114 (64)
trans-4,5-meth.-octane	156 (100)	125 (65)	88 (70)		114 (66)	128 (18)
cis-4,5-meth.-nonane	170 (82)	139 (42)	88 (38)	102 (16)	114 (31)	128 (40)
1,2-meth.-decane	184 (12)	153 (3)	46 (60)		72 (12)	86 (100)
trans-4,5-meth.-decane	184 (100)	153 (36)	88 (38)	116 (8)	114 (29)	128 (34)
trans-5,6-meth.-decane	184 (100)	153 (37)	102 (31)		128 (44)	142 (26)
trans-7,8-meth.-tetradecane	240 (100)	209 (9)	130 (21)		156 (46)	170 (26)
trans-5,6-meth.-hexadecane	268 (57)	237 (4)	102 (24)	186 (1)	128 (26)[a]	142 (21)
cis-5,6-meth.-hexadecane	268 (70)	237 (5)	102 (24)	186 (1)	128 (31)[b]	142 (22)
cis-9,10-meth.-tricosane	366 (100)	335 (3)	158 (1)	228 (<1)	184 (3)[c]	198 (2)

a,b,c Occurrence of a second maximum at m/z 212 (2), 212 (3) and 254 (2), respectively.

Table: Main ion species and their relative abundances from CI-NO-MS spectra of methylenealkanes.

These data and observations from our model compounds (cf. Figure and Table) can then be rationalized as depicted in the following scheme.



Obviously, ions a (e.g. $H-(CH_2)_m-CH=NH^+OH$ and/or $HO^+HN=HC(CH_2)_n-H$) should be sufficient as diagnostic ions to assign the cyclopropane ring position in any linear unknown aliphatic structure. Ions b would be necessarily considered for long chain (i.e., $C \geqslant 20$) and remote end (i.e., position 8,9 or more internal) cyclopropane containing molecules. Ion b distributions are then characterized by 2 maxima regarding the ion relative abundances which formally correspond to α-cleavage (accompagnied by H transfer) on either side of the cyclopropane. Note that in shorter chain (i.e., C_8-C_{10}) unsymetrical compounds allylic cleavage stemming from the longuest alkyl substituent is favoured.

Interestingly, similar (NO)-containing ions as those reported herein can also appear on alkenes although in much lower relative abundances.[1b, 10] However, the highly competitive production of other diagnostic acylium ions under specific experimental conditions[11, 12] make the differentiation between positionally identical aliphatic alkenes and cyclopropanes very easy.

Further studies are in progress to precise the application area of the proposed method, in particular in the frame of bi-(or poly)-functional systems as well as to provide more information on the mechanisms involved.

Acknowledgements: The authors thank P.-H. Lambert, Institut de Recherches Servier, for HRMS measurements and are grateful to H.-E. Audier and J.C. Tabet for fruitful discussions. Financial support from AIFE (N° 259), CICYT (PB 87-0290) and MEC (fellowship to A.P.) is also acknowledged.

References and Notes

1. a) Greathead, R.J.; Jennings, K.R. *Org. Mass Spectrom.* **1980**, 15, 431; b) Budzikiewicz, H.; Busker, E. *Tetrahedron* **1980**, 36, 255; c) Peake, D.A.; Gross, M.L. *Anal. Chem.* **1985**, 57, 115; d) Einhorn, J.; Virelizier, H.; Gemal, A.L.; Tabet, J.C. *Tetrahedron Lett.* **1985**, 26, 1445.
2. Malosse, C.; Einhorn, J. *Anal. Chem.* **1990**, 62, 287.
3. a) Einhorn, J.; Malosse, C.; Wirsta, P.; Tabet, J.C. *Adv. Mass Spectrom.* **1986**, 10 B, 1367; Einhorn, J.; Tabet, J.C. *Spectros. Int. J.* **1987**, 5, 281.
4. Christie, W.W. in *"Topics in Lipid Chemistry"*, F.D. Gunstone ed. Vol. I, 1, John Wiley & Sons, (1970) and references cited therein.
5. Since isomeric aliphatic cyclopropanes are not differentiated by EIMS (Dias, J.R; Djerassi, C. *Org. Mass Spectrom.* **1973**, 7, 753), the only available methods have been based on condensed phase prederivatization: a) McCloskey, J.A.; Law, J.H. *Lipids* **1967**, 2, 225; b) Promé, J.C. *Bull. Soc. Chim. Fr.* **1968**, 655; c) Minnikin, D.E. *Lipids* **1972**, 7, 398; d) Gensler, W.J.; Marshall, J.P. *J. Org. Chem.* **1977**, 42, 126; e) Zaikin, V.G.; Mikaya, A.I. *Mass Spectrom. Rev.* **1984**, 3, 479.
6. Tomer, K.B.; Jensen, N.J.; Gross, M.L. *Anal. Chem.* **1986**, 58, 2429.
7. CI-NO-MS was performed with a Nermag (R10-10 or R30-10) GC-MS instrument with the following source conditions: T 120°C; filament current 80 μA; electron energy 95 eV; nitric oxide (99.9%) pressure 1.4 x 10^{-4} Torr in the source housing. Generally, 50 ng-samples, synthesized by conventional cyclopropanation methods from the corresponding alkenes, were introduced by GC through a 25 m x 0.32 mm i.d. CPSil 5CB capillary column.
8. Data obtained from *cis*-5,6-methylenehexadecane: cald for $C_5H_{12}NO$ m/z 102.0919, found 102.0916; cald for $C_7H_{14}NO$ m/z 128.1075, found 128.1082; cald for $C_8H_{16}NO$ m/z 142.1232, found 142.1230; cald for $C_9H_{18}NO$ m/z 156.1388, found 156.1395.
9. The MS-MS spectra were obtained with a Nermag R30-10 triple quadrupole instrument. Source conditions were those indicated in ref. 7. Laboratory energy was 10 eV and argon was used as collision gas in the second quadrupole at a 3 x 10^{-2} Torr pressure. Samples were introduced *via* direct inlet probe.
10. Hunt, D.F.; Harvey, T.M. *Anal. Chem.* **1975**, 47, 2136.
11. Budzikiewicz, H.; Schneider, B.; Busker, E.; Boland, W.; Francke, W. *Org. Mass Spectrom.* **1987**, 22, 458.
12. Einhorn, J.; Malosse, C. *Org. Mass Spectrom.* **1990**, 25, 49.

(Received in France 14 October 1991)