

Electron ionization mass spectra of naphthoxazine, naphthpyrrolo-oxazinone and naphthoxazinobenzoxazine derivatives

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Dedicated to Professor Harri Lönberg on the occasion of his 60th birthday

Abstract

Some naphthoxazinobenzoxazines (**1a**, **1b**, **2a–2d**, **3a**, **3b**), naphthoxazines (**4a**, **4b**, **5**, **6a**, **6b**) and naphthpyrrolo-oxazinones (**7**, **8a**, **8b**) were studied using mass spectrometry to find out regioisomeric effects and the effects of substituents. As expected the spectra of regioisomeric pairs **1a–3a** vs **1b–3b** were very different. For example the relative abundances of molecular ions were higher for **1a–3a** and the $[M - OH]^+$ ions were observed only for them. Compounds derived from (1- α -aminobenzyl)-2-naphthol were usually characterized by abundant m/z 231 ions and 1-aminomethyl-2-naphthol derivatives by m/z 156 ions. Ions related or similar to their complementary ions were also observed. Many of the studied compounds exhibited fairly abundant ions $[M - C_{17}H_{11}O_2]^+$ (**1a**, **2a**, **3a**: $[M - 247]^+$), $[M - C_{17}H_{12}O]^+$ (**2b–2d**: $[M - 232]^+$) or ion $[M - C_{11}H_8O]^+$ (**1b**, **5**, **6a**, **7**: $[M - 156]^+$). The results may be useful when making regiochemical conclusions.

Keywords: Electron ionization mass spectrometry, fused heterocyclic compounds, fragmentation pathways, regioisomers

Introduction

Betti bases¹ i.e. (1- α -aminobenzyl)-2-naphthols, are useful synthons in the ring closure reactions.²⁻⁴ They and their analogues commonly contain stereogenic centers and therefore regioselective and diastereoselective syntheses using Betti base synthons is gaining popularity. For example the ligands corresponding to the structure of *N,N*-dialkyl Betti base are becoming important in asymmetric syntheses catalyzed by metallic ions.^{5,6}

(1- α -Aminobenzyl)-2-naphthol and its derivatives can be transformed to naphthoxazino-benzoxazine derivatives via ring-closure reactions.^{3,4} Ring-closure reactions can be also used to synthesize naphthoxazinones and naphthoxazinoisindolones from 1-aminomethyl-2-naphthol.³ These syntheses are usually highly diastereoselective.^{3,4}

To continue our studies on the electron ionization mass spectrometry (EI MS) of condensed isomeric heterocycles,^{7,8} especially molecules containing 1,3-oxazine moiety,⁹⁻²³ a group of naphthoxazine, naphthpyrrolo-oxazinone and naphthoxazino-benzoxazine derivatives were studied. The EI spectra of 16 compounds **1a**, **1b**, **2a-d**, **3a**, **3b**, **4a**, **4b**, **5**, **6a**, **6b**, **7**, **8a**, **8b**, (the formulas are given in Chart 1 and the names^{3,4} in Table 1) were studied. Compounds consisted of three pairs of regioisomers (**1a/b**, **2a/b** and **3a/b**), the mass spectra of which were compared with each other. The other ten compounds were studied to clarify the effects of different substituents. The conformational analysis using NMR spectroscopy, molecular modelling and geometry optimization of selected compounds **2b**, **2c**, **8b** and also **1a**, **1b**, **3a** were reported earlier.^{3,4}

Table 1. The names of the compounds

1a	Naphth[1',2':5,6][1,3]oxazino[3,4- <i>c</i>][1,3]benzoxazine
1b	Naphth[1',2':5,6][1,3]oxazino[3,2- <i>c</i>][1,3]benzoxazine
2a	(8 <i>R</i> *,15 <i>bS</i> *)-8-Phenylnaphth[1',2':5,6][1,3]oxazino[3,4- <i>c</i>][1,3]benzoxazine
2b	(7 <i>aR</i> *,15 <i>S</i> *)-15-Phenyl-7 <i>aH</i> ,13 <i>H</i> ,15 <i>H</i> -naphth[1',2':5,6][1,3]oxazino[3,2- <i>c</i>][1,3]benzoxazine
2c	(7 <i>aR</i> *,13 <i>R</i> *,15 <i>S</i> *)-13-Methyl-15-phenyl-7 <i>aH</i> ,13 <i>H</i> ,15 <i>H</i> -naphth[1',2':5,6][1,3]oxazino[3,2- <i>c</i>][1,3]benzoxazine
2d	(7 <i>aR</i> *,13 <i>R</i> *,15 <i>S</i> *)-13-Ethyl-15-phenylnaphth[1',2':5,6][1,3]oxazino[3,2- <i>c</i>][1,3]benzoxazine
3a	(8 <i>R</i> *,15 <i>bS</i> *)-8-Phenylnaphth[1',2':5,6][1,3]oxazino[3,4- <i>c</i>][1,3]benzoxazin-10-one
3b	(7 <i>aR</i> *,15 <i>S</i> *)-15-Phenylnaphth[1',2':5,6][1,3]oxazino[3,2- <i>c</i>][1,3]benzoxazin-13-one
4a	2,3-Dihydro-1 <i>H</i> -naphth[1,2- <i>e</i>][1,3]oxazin-3-one
4b	1-Phenyl-2,3-dihydro-1 <i>H</i> -naphth[1,2- <i>e</i>][1,3]oxazin-3-one
5	3-Phenyl-1 <i>H</i> -naphth[1,2- <i>e</i>][1,3]oxazine
6a	3-Phenylimino-2,3-dihydro-1 <i>H</i> -naphth[1,2- <i>e</i>][1,3]oxazine
6b	1-Phenyl-3-Phenylimino-2,3-dihydro-1 <i>H</i> -naphth[1,2- <i>e</i>][1,3]oxazine
7	7 <i>a</i> -Methyl-8,9-dihydro-7 <i>aH</i> ,10 <i>H</i> ,12 <i>H</i> -naphth[1,2- <i>e</i>]pyrrolo[2,1- <i>b</i>][1,3]oxazin-10-one
8a	7 <i>aH</i> ,12 <i>H</i> ,14 <i>H</i> -Naphth[1',2':5,6][1,3]-oxazino[2,3- <i>a</i>]isoindol-12-one
8b	(7 <i>aR</i> *,14 <i>S</i> *)-14-Phenyl-7 <i>aH</i> ,12 <i>H</i> ,14 <i>H</i> -naphth[1',2':5,6][1,3]oxazino[2,3- <i>a</i>]isoindol-12-one

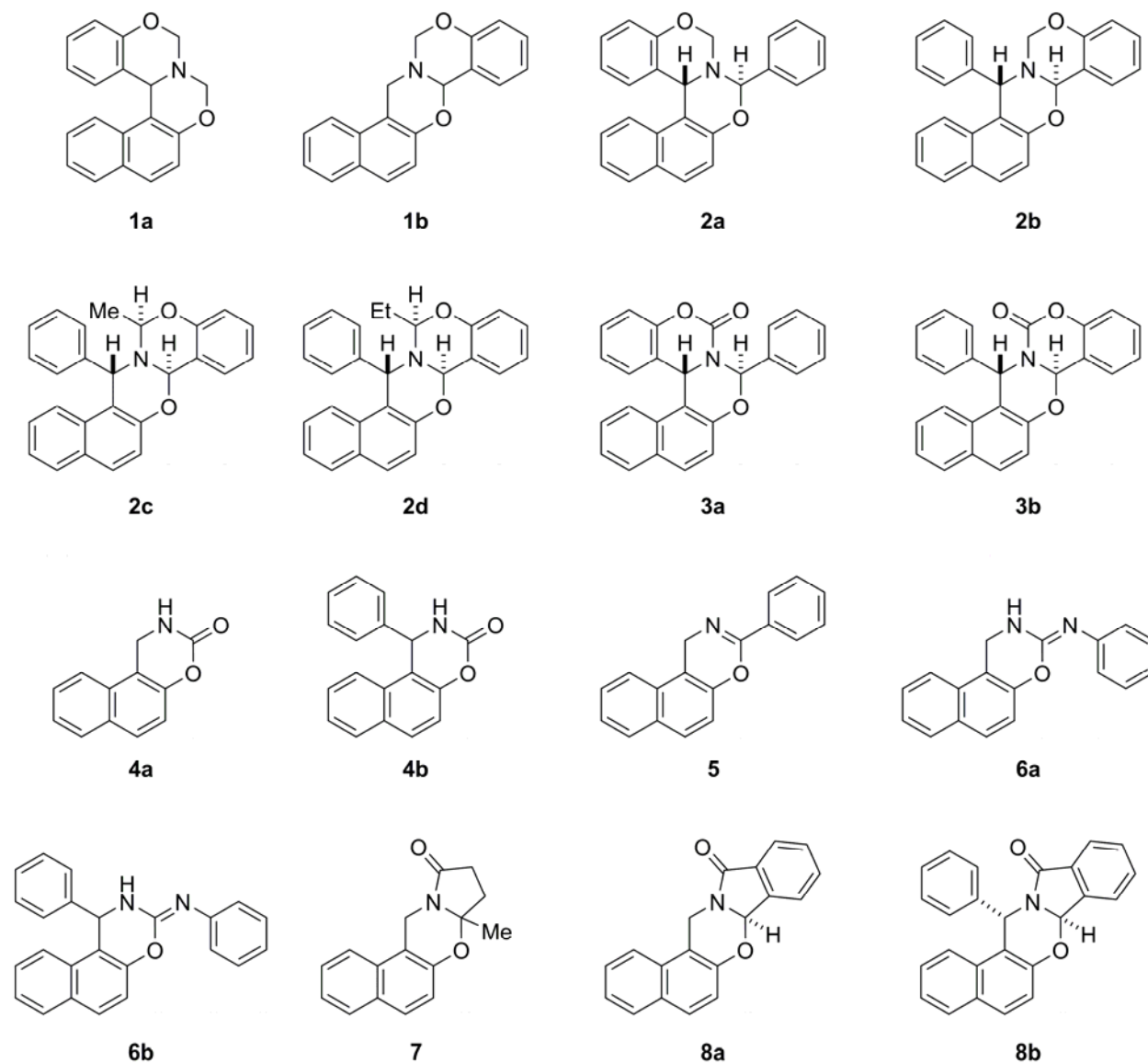


Chart 1. The compounds studied.

The presence of 1,3-oxazine ring gives a possibility to ring-chain tautomeric equilibrium, this tautomerism being widely studied using NMR and MS methods.¹⁴⁻²¹ NMR studies of 1,3-diarylnaphth[1,2-*e*][1,3]oxazines with similar structures to the compounds studied have been stated to show ring-chain tautomeric equilibria.²³⁻²⁵ The ring-openings related to tautomerism require a hydrogen-transfer. However in some ring-openings also a zwitterion can be formed. This does not require any hydrogen-transfer, for example photochromic compounds have been designed based on photoinduced ring opening of 1,3-oxazine ring.^{26,27} Ring opening has not been reported for the sixteen compounds studied now. The ring-chain tautomerism requiring transfer of hydrogen from nitrogen to oxygen is not possible for the studied molecules with tertiary

nitrogen. However mass spectrometric processes involving ring opening have been reported also for 1,3-oxazine compounds with tertiary nitrogen.¹⁶

For 1,3-oxazines the most significant EI MS fragmentations can usually be interpreted based on the charge localisation on the nitrogen.^{10,15,16,20,28} However the charge can also be localized on aromatic rings or oxygen, such is the case with octahydro-1,3-benzoxazines.²⁰

Also the EI MS fragmentations of imino-compounds **6a** and **6b** can be compared with *N*-unsubstituted 4,5-cyclohexane-annelated 1,3-oxazines.²⁹

Experimental Section

General Procedures. The electron ionization (EI) mass spectra were recorded on a VG ZABSpec mass spectrometer (VG Analytical, Division of Fisons, Manchester, UK), that was equipped with Opus V3.3X program package (Fisons Instruments, Manchester, UK). The ionization energy was 70 eV and source temperature 160 °C. Direct insertion probe was used. Perfluorokerosine (PFK) was used for calibration of the mass scale.

The fragmentation pathways were confirmed by B/E-linked scans for metastable ions. Also B²/E-linked scans were used to clarify these pathways. The low resolution, B/E and B²/E spectra were measured using resolution of 3000. The accurate masses were determined by voltage scanning or by peak matching (10% valley definition) using 6000-10000 resolution for small *m/z* values and over 10000 for the larger ones.

Results and Discussion

General fragmentation pathways are described in Scheme 1. Common fragment ions and their relative abundances (*RA*) are listed in Tables 2 and 3 and other fragments in Table 4 and 5. Molecular ions (M⁺) formed the base peaks of **2a**, **7** and **8a**. The ion, *m/z* 128 (C₁₀H₈⁺) was the base peak for **1b** and **4a**. The base peak for **5** was the ion, *m/z* 156 (C₁₁H₈O⁺) and for **6a** the ion, *m/z* 157 (C₁₁H₉O⁺). For compounds derived from (1-*α*-aminobenzyl)-2-naphthol (**1a**, **2b-d**, **3a**, **3b**, **4b**, **6b**, **8b**), the base peak was always the ion C₁₇H₁₁O⁺ at *m/z* 231. This ion was also observed for **2a**, but with much lower *RA* (27%). Due to the multiple bond cleavages required to form this ion C₁₇H₁₁O⁺, some new structures are to be formed, such as 1-(phenylmethylene)-2(1*H*)-naphthalenonyl ion. Possible mechanism is presented in Scheme 2. The ion C₁₇H₁₁O⁺ fragments further by losing CO or HCO, resulting in ions C₁₆H₁₁⁺ (*m/z* 203) of low abundance and C₁₆H₁₀⁺, respectively. The ion C₁₆H₁₀⁺ may have a structure resembling that of (*Z*)-1-ethynyl-2-(2-phenylethenyl)-benzene (Scheme 2). Also the ion C₁₇H₁₂O⁺ at *m/z* 232 was observed for **2b-2d**, **3a**, **3b**, **4b**, **6b**, **8b**. It can lose a hydrogen, HCO[•] or CH₂O.

Table 2. Main electron induced fragmentations and their relative abundances m/z (%RA). Abundances are corrected for ^{13}C isotopes, **1b**, **4a**, **6a** and **8a** have been renormalised. Abundances are rounded to the nearest half percent. (Continued in table 3)

Compound	$\text{M}^{+\bullet}$	$[\text{M} - \text{H}]^+$	$[\text{M} - \text{OH}]^+$	$[\text{M} - \text{CONH}]^+$ $[\text{M} - \text{CONH}_2]^+$
1a	289(82.5)	288(32.5)	272(33)	-
1b	289(6)	-	-	-
2a	365(100)	364(4)	348(67.5)	-
2b	365(5.5)	-	-	-
2c	379(3)	-	-	-
2d	393(2.5)	-	-	-
3a	379(36.5)	-	362(4)	336(9)
				-
3b	379(10.5)	-	-	-
4a	199(46)	-	-	156(96)
				155(4)
4b	275(31)	-	-	232(19)
				231(100)
5	259(54)	258(2)	-	-
6a	274(68)	273(32)	-	-
6b	350(29)	349(4.5)	-	-
7	253(100)	252(1)	236(33)	-
8a	287(100)	286(63)	270(57.5)	-
8b	363(48.5)	362(4.5)	346(8)	-

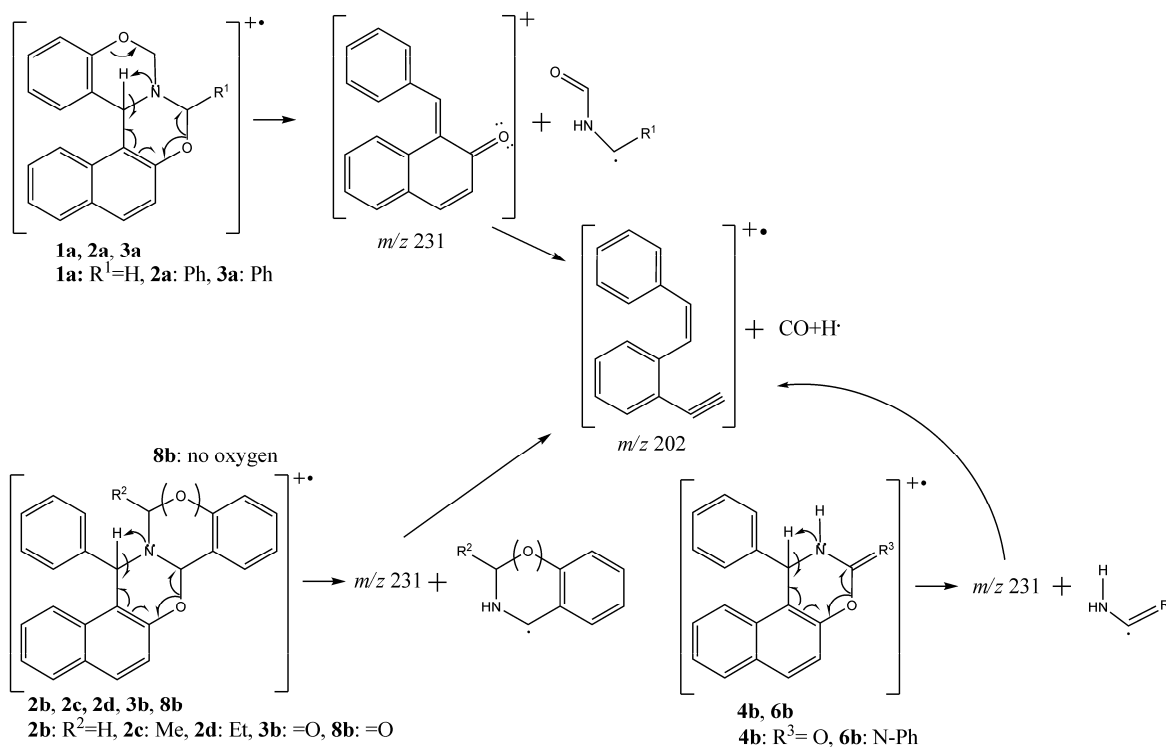
Also $[\text{M} - \text{Ph}]^+$: **4b**: 198(4), **6b**: 273(44), **8b**: 286(3)

Table 3. More main electron induced fragmentations and their relative abundances m/z (%RA). Abundances are corrected for ^{13}C isotopes, **1b**, **4a**, **6a** and **8a** have been renormalised. Abundances are rounded to the nearest half percent

Compound	$\text{C}_{17}\text{H}_{12}\text{O}^{+\bullet}$	$\text{C}_{17}\text{H}_{11}\text{O}^+$	$\text{C}_{11}\text{H}_9\text{O}^+$ $\text{C}_{11}\text{H}_8\text{O}^{+\bullet}$	$\text{C}_{10}\text{H}_8^{+\bullet}$
1a	232(1)	231(100)	-	128(1.5)
1b	-	-	157(2.5) 156(51)	128(100)
2a	232(3)	231(27)	-	-
2b	232(23)	231(100)	-	-
2c	232(22)	231(100)	-	-
2d	232(24)	231(100)	-	-
3a	232(12)	231(100)	-	-
3b	232(24)	231(100)	-	-
4a	-	-	157(4) 156(96)	128(100)
4b	232(19)	231(100)	-	-
5	-	-	- 156(100)	128(70)
6a	-	-	157(100) 156(40)	128(76)
6b	232(16)	231(100)	-	128(2)
7	-	-	157(71) 156(72)	128(95)
8a	-	231(2)	156(26.5)	128(60)
8b	232(14)	231(100)	-	128(0.5)

Table 4. Other fragments (relative abundances mostly > 3%) for compounds **1a**, **1b**, **2a–d**, **3a**, **3b**, **4a**, **4b**, **5**. *RAs* are corrected for ^{13}C isotopes. **1b** and **4a** have been renormalised. Abundances are rounded to the nearest half percent

Compound	<i>m/z</i> (% <i>RA</i>)
1a	260: $\text{C}_{18}\text{H}_{12}\text{O}_2^{++}$ (5)+ $\text{C}_{18}\text{H}_{14}\text{NO}^+$ (1), $\text{C}_{17}\text{H}_{11}\text{O}_2^+$: 247(22), 219(2), $\text{C}_{16}\text{H}_{10}\text{O}^{++}$: 218(11), $\text{C}_{16}\text{H}_{11}^+$: 203(2), $\text{C}_{16}\text{H}_{10}^{++}$: 202(8), $\text{C}_{16}\text{H}_8^{++}$: 200(3), $\text{C}_{15}\text{H}_{11}^+$: 191(4), $\text{C}_{15}\text{H}_9^+$: 189(19), $\text{C}_{13}\text{H}_9^+$: 165(5), $\text{C}_{13}\text{H}_8^{++}$: 164(2), $\text{C}_{13}\text{H}_7^+$: 163(5), 139(4), 101(3), 42(78)
1b	$\text{C}_8\text{H}_7\text{NO}^{++}$: 133(52), $\text{C}_8\text{H}_6\text{NO}^+$: 132(25), $\text{C}_{10}\text{H}_7^+$: 127(16), 126(8), 106(1.5), 105: $\text{C}_7\text{H}_7\text{N}^{++}$ (8)+ $\text{C}_7\text{H}_5\text{O}^+$ (13), $\text{C}_7\text{H}_6\text{N}^+$: 104(14), 103(1), $\text{C}_8\text{H}_6^{++}$: 102(12), C_8H_5^+ : 101(4), 78(32), 77(20), 76(9), 75(10), 74(11), 69(4), 64(7), 63(13), 62(6), 52(9), C_4H_3^+ : 51(32), 50(19), 44(3)
2a	$\text{C}_{18}\text{H}_{12}\text{O}_2^{++}$: 260(12), $\text{C}_{17}\text{H}_{11}\text{O}_2^+$: 247(6), 218(6), $\text{C}_{16}\text{H}_{10}^{++}$: 202(8), $\text{C}_{15}\text{H}_9^+$: 189(6), $\text{C}_8\text{H}_8\text{N}^+$: 118(77), 117(3), C_7H_7^+ : 91(44)
2b	203(3), $\text{C}_{16}\text{H}_{10}^{++}$: 202(21), $\text{C}_{16}\text{H}_9^+$: 201(2), $\text{C}_{16}\text{H}_8^{++}$: 200(4), $\text{C}_8\text{H}_7\text{NO}^{++}$: 133(14), $\text{C}_8\text{H}_6\text{NO}^+$: 132(7), 115.4(metastable, 4), 105(5), 104(4), 101(5), 78(8), 77(6), 76(3), 51(7), 50(4), 45(4)
2c	$\text{C}_2\text{H}_{21}\text{NO}^{++}$ (impurity): 363(4), 203(3), $\text{C}_{16}\text{H}_{10}^{++}$: 202(22), 201(2), 200(4), $\text{C}_9\text{H}_9\text{NO}^{++}$: 147(11), 146(5), $\text{C}_8\text{H}_6\text{NO}^+$: 132(26), 120(4), 115.4(metastable, 4), C_8H_5^+ : 101(5), 91(4), 78(3), 77(5), 76(3), 63(3), 51(8), 50(4)
2d	203(3), 202(22), 201(2), 200(4), $\text{C}_{10}\text{H}_{11}\text{NO}^{++}$: 161(6), $\text{C}_9\text{H}_8\text{NO}^+$: 146(4), $\text{C}_8\text{H}_6\text{NO}^+$: 132(52), 120(4), 116(3), 115.4(4), 101(5), 78(3), 77(7), 76(3), 63(3), 51(10), 50(4)
3a	363(5), $\text{C}_{17}\text{H}_{11}\text{O}_2^+$: 247(13), $\text{C}_{16}\text{H}_{10}\text{O}^{++}$: 218(7), $\text{C}_{16}\text{H}_{10}^{++}$: 202(9), 191(4), $\text{C}_{15}\text{H}_9^+$: 189(10), $\text{C}_8\text{H}_6\text{NO}^+$: 132(52), $\text{C}_7\text{H}_5\text{O}^+$: 105(5), 104: $\text{C}_7\text{H}_6\text{N}^+$ (3)+ $\text{C}_7\text{H}_4\text{O}^{++}$ (1), 77(18), 51(4), 44(5), 40(7)
3b	203(3), $\text{C}_{16}\text{H}_{10}^{++}$: 202(15), $\text{C}_7\text{H}_5\text{NO}^{++}$: 119(2)
4a	272 (impurity, 3), 231 (impurity, 3), $\text{C}_{11}\text{H}_{11}\text{NO}^{++}$ (reactant, impurity): 173(12), 170(3), 160(3), $\text{C}_{11}\text{H}_9\text{O}^+$: 157(4), 129(3), $\text{C}_{10}\text{H}_7^+$: 127(9), $\text{C}_{10}\text{H}_6^{++}$: 126(7), C_9H_7^+ : 115(9.5), $\text{C}_9\text{H}_6^{++}$: 114(3.5), $\text{C}_8\text{H}_6^{++}$: 102(7), 101(4), 100(3.5), 78(3), 77(6), 76(4), 75(4), 74(5), 72(3), 64(5), 63(8), 58(4), 51(8)
4b	$\text{C}_{16}\text{H}_{11}^+$: 203(3), $\text{C}_{16}\text{H}_{10}^{++}$: 202(14), 116(5), C_9H_7^+ : 115(8), C_8H_5^+ : 101(5)
5	129.7(4), 129(2), 127(14), 126(5), $\text{C}_7\text{H}_5\text{N}^{++}$: 103(5), $\text{C}_8\text{H}_6^{++}$: 102(7), C_6H_5^+ : 77(6), 76(4)



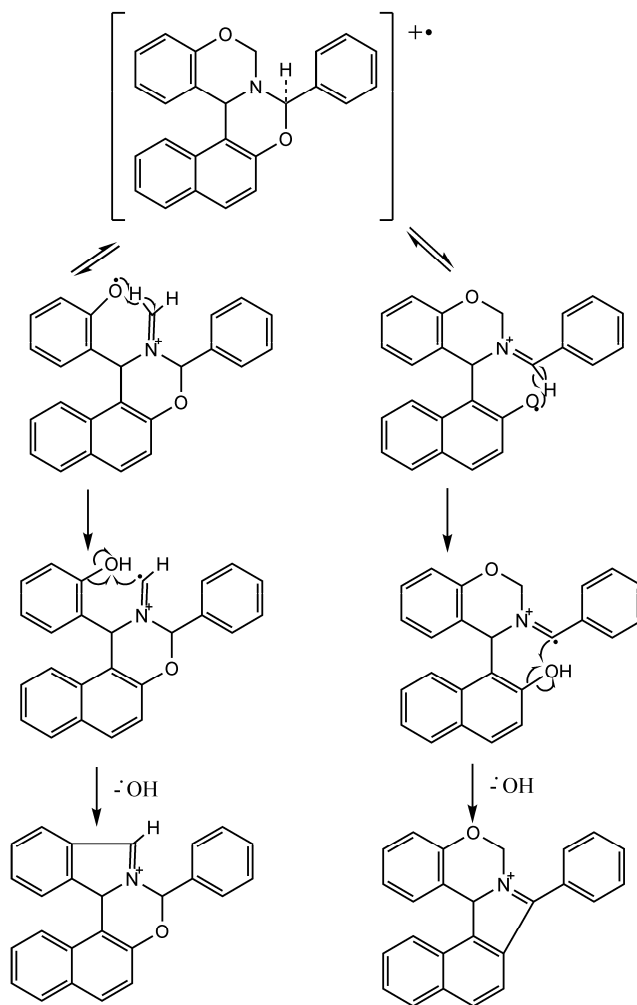
Scheme 2. Suggested mechanism for the formation of ions m/z 231 and m/z 202.

The ion $C_{11}H_8O^+$ at m/z 156 was observed for compounds **1b**, **4a**, **5**, **6a**, **7**, **8a**, i.e. for compounds derived from 1-aminomethyl-2-naphthol. This ion is probably formed via mechanism similar to that presented for the formation of ion m/z 231. The ion m/z 156 loses also CO or HCO, resulting in ions $C_{10}H_8^+$ or $C_{10}H_7^+$. An abundant ion $C_{11}H_9O^+$ at m/z 157 was observed also for **6a** and **7** and a weak one for **4a**.

In the case of **7** ion $C_{11}H_9O^+$ is formed by loss of $C_5H_6NO^+$ from the molecular ion or via the route $M^+ - OH^+ - C_5H_5N$, both of these routes requiring H-transfer. The ion $C_{11}H_9O^+$ in turn loses CO or COH^+ , and forms the ions $C_8H_6^+$ and $C_6H_5^+$.

The ion $[M - OH]^+$ was most abundant for **2a** (*RA* 67.5%) and **8a** (*RA* 57.5%). It was also formed by compounds **1a**, **3a**, **7**, and **8b**. It is questionable which oxygen is lost with the hydroxyl. OH-loss requires hydrogen migration after ionization and ring-opening, possible mechanisms involving distonic ions shown in Scheme 3. The OH-loss from **3a** having a carbonyl group cannot proceed via the first route in Scheme 3; based on steric reasons the carbonyl oxygen may abstract hydrogen from the position bearing the phenyl substituent. Solving the exact mechanism would require complicated deuterium labeling. For **2a** the B/E scans of the $[M - OH]^+$ ion gave no significant signals, so this ion is unusually stable, the positive charge being probably stabilized by the aromatic groups. For **1a** the ion $[M - OH]^+$ may fragment further by loss of C_2H_3N forming the ion m/z 231, and B²/E scan revealed also the $C_3H_4N^+$ loss. If the ion at m/z 231 from **1a** has the structure described in Scheme 2, then the oxygen that is attached to the phenyl group is the one lost with OH and not the oxygen attached to the naphthyl group. Also

based on the geometry⁴ the phenyl oxygen is more likely to be lost as hydroxyl. $[M - OH]^+$ from **7** fragments further by loss of C_3H_5N ($C_{13}H_9O^+$, m/z 181), C_5H_5N ($C_{11}H_9O^+$, m/z 157) or $C_{11}H_7$ ($C_5H_7O^+$, m/z 97) and that from **8b** by loss of C_8H_5N ($C_{17}H_{11}O^+$, m/z 231). For **7** and **8b** (and perhaps also for **8a**) it is probable that the hydroxyl group is formed from the carbonyl group by hydrogen migration. In this case the naphthyl oxygen is not lost as hydroxyl.



Scheme 3. Possible ring openings of **2a** and the consequent OH-loss.

Weak CO loss was observed only for **7** and **8a**. $[M - CONH]^+$ ion was abundant for **4a** (RA 94%) and was also present for **3a** and **4b**. An abundant $[M - Ph]^+$ ion (RA 44%) was exhibited by **6b**, and traces by **4b** and **8b**. The phenyl substituent is axial in **2b-d**,⁴ and hence they are expected to fragment similarly but different from **2a** in which the phenyl group is equatorial.⁴ This may at least partly explain why **2a** gives an abundant $C_7H_7^+$ ion, but **2b-d** not. In contrast to **2a** for which the base peak is that of the molecular ion, compounds **2b-d** all exhibit $M^{+\bullet}$ ions of low abundance and the ions $C_{17}H_{11}O^+$ (m/z 231) form their base peaks instead. Common ions of

similar abundance for **2b–d** are $C_{17}H_{12}O^{+}$ at m/z 232 and $C_{16}H_{10}^{+}$ at m/z 202. Also a metastable transition corresponding to $C_{17}H_{11}O^{2+}$ was observed.

The methyl- (**2c**: R = Me) and ethyl-substituted (**2d**: R = Et) gave very similar spectra. In addition to the common ions mentioned before, both have nearly identical spectra below m/z 120. The greatest differences are as follows: the ion m/z 147 ($C_9H_9NO^{+}$) was obtained only for **2c** and the ion m/z 161 ($C_{10}H_{11}NO^{+}$) for **2d**. Furthermore the ion m/z 132 ($C_8H_6NO^{+}$) was most abundant for **2d**. When the molecular ions lose $C_{17}H_{12}O$, the ions $C_{10}H_{11}NO^{+}$ (**2d**, m/z 161), $C_9H_9NO^{+}$ (**2c**, m/z 147) and $C_8H_7NO^{+}$ (**2b**, m/z 133) are formed. Similar fragment ions have been observed for substituted 1,3-benzoxazino[4,3-*b*][1,3]1,3-benzoxazines¹⁶, where the bond between C-7 and O is cleaved first, resulting to ring-opening of the oxazine ring.

For **2c** and **2d** the ion $C_8H_6NO^{+}$ (m/z 132) is formed via routes $C_9H_9NO^{+} - Me^{\bullet}$ (**2c**) and $C_{10}H_{11}NO^{+} - Et^{\bullet}$ (**2d**). For the other two compounds (**1b** and **3a**) without an alkyl substituent at C-2 or C-2' the ion m/z 132 is formed directly from the molecular ion instead.

The spectra of **4a** (R = H) and **4b** (R = Ph) differ greatly from each other. For **4b** the ion $[M - CONH_2]^+$, i.e. $C_{17}H_{11}O^{+}$, forms the base peak whereas for **4a** the base peak locates at m/z 128 ($C_{10}H_8^{+}$) and it also shows a strong $[M - CONH]^+$ ion. The same is true for **6a** (R = H) and **6b** (R = Ph): **6b** exhibits an abundant ion at m/z 231, $C_{17}H_{11}O^{+}$; based on B^2/E scans it is formed partly via route $M^{+} - NHPH^{\bullet} - HCN$ and partly via route $M^{+} - Ph^{\bullet} - CH_2N_2$. **6a** in turn shows an abundant $[M - NCNPh]^+$ ion, $C_{11}H_9O^{+}$, at m/z 157 and a moderately abundant ion, $C_{11}H_8O^{+}$, at m/z 156; based on B^2/E scans also routes $M^{+} - NHPH^{\bullet} - CN^{\bullet}$ and $M^{+} - Ph^{\bullet} - NHCN^{\bullet}$ are possible. **6a** exhibits a strong ion at m/z 128, $C_{10}H_8^{+}$, but this is very weak for **6b**. For **6b** $[M - Ph]^+$ can be observed, but **6a** exhibits relatively abundant $[M - H]^+$ ion - so it is probable that the Ph-C rather than the Ph-N bond is cleaved. Both **6a** and **6b** gave also weak $[M - NHPH]^+$ ions ($RA < 10\%$).

In addition to the ion m/z 231, $C_{17}H_{11}O^{+}$ or ion m/z 156, $C_{11}H_8O^{+}$ compounds **1a**, **2a–d**, **3a**, **3b**, **4b**, **6b** and **8b** also show ions related or similar to their complementary ion. The ion $[M - C_{17}H_{11}O_2]^+$ was abundant for **1a–3a**. The resulting ions were $C_2H_4N^{+}$ (**1a**), $C_8H_8N^{+}$ (**2a**) and $C_8H_6NO^{+}$ (**3a**). The ions corresponding to $[M - 232]^+$, i.e. $C_8H_7NO^{+}$ (**2b**), $C_9H_9NO^{+}$ (**2c**) and $C_{10}H_{11}NO^{+}$ (**2d**), were moderately abundant. Also **6b** exhibited a weak $[M - 232]^+$, i.e. $C_7H_6N_2^{+}$ ion. $[M - 156]^+$, i.e. $[M - C_{11}H_8O]^+$ was also observed for **1b**, **5**, **6a** and **7**: a very abundant $C_8H_7NO^{+}$ ion for **1b**, a rather abundant $C_5H_7NO^{+}$ ion for **7** and moderately abundant $C_7H_5N^{+}$ ion for **5** and similarly $C_7H_6N_2^{+}$ ion for **6a**. For **3b**, **4b**, and **8b** only traces of $[M - 232]^+$ could be observed, otherwise these compounds and **4a**, **6b** and **8a** did not show ions at m/z (M - 247) and (M - 156). The carbonyl group in **3b** seems to prevent the formation of $[M - C_{17}H_{12}O]^+$ in contrast to structurally similar **2b–d** with alkyl or hydrogen at C-13.

The formation of $C_{11}H_9O^{+}$ from the molecular ion of **6a** is probably initiated by an H-transfer from either NH or phenyl group to oxygen and a subsequent loss of $C_7H_5N_2^{\bullet}$. This fragmentation is different from that found for *N*-unsubstituted 4,5-cyclopentane-fused 1,3-oxazines²⁹ where $C_7H_5NO^{\bullet}$ but no $C_7H_5N_2^{\bullet}$ loss was observed. This may be caused by different annelation

positions. Another difference is the ion $[M - C_6H_6N]^+$ (**6a**, **6b**) which is missing from *N*-unsubstituted 4,5-annelated 1,3-oxazines, exhibiting the ions $C_6H_7N^+$ and $C_6H_6N^+$ instead.²⁹

Comparison of regioisomeric pairs **1a–3a** vs **1b–3b**

The cyclization of the aminonaphthols used to synthesize these compounds are affected by different chemical stabilities of the unsubstituted or phenyl-substituted aminonaphthols.³ Since **1a–3a** were synthesized from derivatives of (1- α -aminobenzyl)-2-naphthol and **1b–3b** from derivatives of 1-aminomethyl-2-naphthol,⁴ the mass spectra of these regioisomeric pairs were expected to be very different. For **1a–3a** M^+ was more abundant than for **1b–3b**. $[M - OH]^+$ was observed only for **1a–3a**. Exclusive ions for **1a–3a** were m/z 247, $C_{17}H_{11}O_2^+$ and m/z 218, $C_{16}H_{10}O^+$. The ion m/z 189, $C_{15}H_9^+$ was also more abundant for **1a–3a** than for **1b–3b**. For **1,2b** $C_8H_7NO^+$, m/z 133, was more abundant than for **1,2a** and the former also gave more abundant ions between m/z values 50 and 78 than the latter. In the case of **1,2b** $C_8H_7NO^+$ may be formed by a mechanism similar to that suggested for 1,3-benzoxazino-1,3-benzoxazines.¹⁶ **1a** gave an abundant ion $C_{17}H_{11}O^+$ at m/z 231 which was missing from **1b**. For **2b**, **3a** and **3b** m/z 231 was the base peak, but for **2a** its *RA* was only 27%. For **1b** the ion $C_{10}H_8^+$ m/z 128 was the base peak, but very weak for **1a**. Compound **2a** gave ions at m/z 91 ($C_7H_7^+$) and m/z 118 ($C_8H_8N^+$) and **3a** at m/z 77 ($C_6H_5^+$), m/z 105 ($C_7H_5O^+$) and m/z 132 ($C_8H_6NO^+$), but these ions were missing from the spectra of **2b** and **3b**, respectively.

$^1H/^{13}C$ NMR analysis has been used to study the conformations of oxazine rings in the studied compounds.⁴ In **1b**, **2b**, **2c**, **2d**, **3b** and the naphtho-bound oxazine ring prefers a 7,15-*twisted-chair* conformation and, in **1a**, **2a**, **3a** a 11,15b-*twisted-chair* conformation. In **1b**, **2b**, **2c**, **2d** the benzo-fused oxazine ring prefers a 7a,12-*twisted-chair* conformation and in **1a** and **2a** a 11,15b-*twisted-chair* conformation.⁴ In **3a** the benzo-fused oxazine ring prefers a 11,15b *boat* conformation. Based on calculations the benzo-fused oxazine ring in **3b** is almost planar and the phenyl substituent is axial.⁴ These conformations possibly cause favored loss of $C_2H_4N^+$ from the molecular ion of **1a** leading to the product ion $C_{17}H_{11}O_2^+$, probably because in the CH_2 groups the hydrogens are sterically less favored in **1a** as compared to **1b**. Also the loss of $C_8H_8N^+$ from **2a** (i.e. $C_6H_5CHNCH_2^+$) corresponds to loss of $C_2H_4N^+$ from **1a**, in both cases the product ion is $C_{17}H_{11}O_2^+$. The ion $C_2H_4N^+$ is observed also for **1a** and $C_8H_8N^+$ for **2a**.

The formation of the $C_7H_5O^+$ ion is easier to explain for **3a**, due to the tertiary α -hydrogen vicinal to phenyl group which can migrate to the carbonyl oxygen. Also the *boat* conformation of benzo-fused oxazine ring in **3a** makes the loss of $C_8H_6NO^+$, i.e. the formation of the $[M - C_6H_5CHNCO]^+$ ion, $C_{17}H_{11}O_2^+$, possible.

Conclusions

Some of the fragmentations such as OH-loss require ring-opening with hydrogen migration. In **7**, **8a** and **8b** the carbonyl group oxygen participates in the loss of a hydroxyl group. Compounds

derived from (1-*a*-aminobenzyl)-2-naphthol were usually characterized by strong or medium strong ions at m/z 231 and 1-aminomethyl-2-naphthol derivatives by ions at m/z 156.

The fragmentations depend on the regiochemistry and geometry of the compounds studied. The formation of fragment ions $[M - C_{17}H_{11}O_2]^+$, $[M - C_{17}H_{12}O]^{+}$ and $[M - C_{11}H_8O]^{+}$ occurred logically from the structures studied. However, these three ions were nearly missing from the spectra of derivatives **3b**, **4a**, **4b**, **6b**, **8a**, **8b** with carbonyl or imino substituents; they favoured the ions $C_{17}H_{11}O^+$ or $C_{11}H_8O^+$ instead.

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References

1. Betti, M. *Gazz. Chim. Ital.* **1900**, *30 II*, 310.
2. Cardellicchio, C.; Ciccarella, G.; Naso, F.; Schingaro, E.; Scordari, F. *Tetrahedron: Asymmetry* **1998**, *9*, 3667 and references cited therein.
3. Szatmári, I.; Hetényi, A.; Lázár, L.; Fülöp, F. *J. Heterocyclic Chem.* **2004**, *41*, 367.
4. Heydenreich, M.; Koch, A.; Klod, S.; Szatmári, I.; Fülöp, F.; Kleinpeter, E. *Tetrahedron* **2006**; *62*: 11081.
5. Dong, Y.; Sun, J.; Wang, X.; Xu, X.; Cao, L.; Hu, Y. *Tetrahedron: Asymmetry* **2005**, *15*, 1667 and references cited therein.
6. Lu, J.; Xuenong, X.; Wang, C.; He, J.; Hu, Y.; Hu, H. *Tetrahedron Lett.* **2002**, *43*, 8367.
7. Ovcharenko, V.; Pihlaja, K.; Stájer, G. *J. Am. Soc. Mass Spectrom.* **2003**, *14*, 1049.
8. Pihlaja, K.; Martiskainen, O.; Stájer, G. *Rapid Commun. Mass Spectrom.* **2007**, *21*, 653.
9. Pihlaja, K.; Ovcharenko, V.; Stájer, G. *J. Am. Soc. Mass. Spec.* **1999**, *10*, 393.
10. Pihlaja, K.; Vainiotalo, P.; Fülöp, F.; Bernáth, G. *Rapid Commun. Mass Spectrom.* **1988**, *2*, 229.
11. Pihlaja, K.; Lötjönen, L.; Fülöp, F.; Bernáth, G.; Vainiotalo, P. *Rapid Commun. Mass Spectrom.* **1990**, *4*, 279.
12. Vainiotalo, P.; Partanen, T.; Fülöp, F.; Bernáth, G.; Pihlaja, K. *J. Am. Soc. Mass Spectrom.* **1991**, *2*, 125.
13. Pihlaja, K.; Liukko-Sipi, S.; Fülöp, F.; Bernáth, G.; Vainiotalo, P. *Rapid Commun. Mass Spectrom.* **1991**, *5*, 230.
14. Fülöp, F.; Pihlaja, K.; Mattinen, J.; Bernáth, G. *J. Org. Chem.* **1987**, *52*, 3821.
15. Vainiotalo, P.; Fülöp, F.; Pihlaja, K.; *Org. Mass Spectrom.* **1991**, *26*, 438.

16. Joutsiniemi, K.; Vainiotalo, P.; Pihlaja, K.; Lázár, L.; Fülöp, F.; Bernáth, G. *Rapid Commun. Mass Spectrom.* **1995**, *9*, 1035.
17. Juhász, M.; Fülöp, F.; Pihlaja, K. *Rapid Commun. Mass Spectrom.* **2007**, *21*, 3701.
18. Fülöp, F.; Pihlaja, K.; Mattinen, J.; *Tetrahedron* **1987**, *43(8)*, 1863.
19. Fülöp, F.; Lázár, L.; Bernáth, G.; Sillanpää, R.; Pihlaja, K. *Tetrahedron* **1993**, *49*, 2115.
20. Vainiotalo, P.; Lehtelä, P.-L.; Fülöp, F.; Bernáth, G.; Vuorilehto, L.; Pihlaja, K. *Rapid Commun. Mass Spectrom.* **1993**, *7*, 465.
21. Neuvonen, K.; Fülöp, F.; Neuvonen, H.; Koch, A.; Kleinpeter, E.; Pihlaja, K. *J. Org. Chem.* **2001**, *66*, 4132.
22. Fülöp, F.; Pihlaja, K.; Mattinen, J.; Bernáth, G. *Tetrahedron* **1987**, *43*, 4565.
23. Szatmári, I.; Martinek, T.A.; Lázár, L.; Fülöp, F. *Tetrahedron* **2003**, *59*, 2877.
24. Szatmári, I.; Martinek, T.A.; Lázár, L.; Fülöp, F. *Eur. J. Org. Chem.* **2004**, 2231.
25. Szatmári, I.; Martinek, T.A.; Lázár, L.; Koch, A.; Kleinpeter, E.; Neuvonen, K.; Fülöp, F. *J. Org. Chem.* **2004**, *69*, 3645.
26. Tomasulo, M.; Sortino, S.; White A. J. P.; Raymo F. M. *J. Org. Chem.* **2005**, *70*, 8180.
27. Tomasulo, M.; Sortino, S.; Raymo, F. M. *J. Org. Chem.* **2008**, *73*, 118.
28. Vainiotalo, P.; Fülöp, F.; Stájer, G.; Bernáth, G.; Pihlaja, K. *Acta Chem. Scand.* **1990**, *44*, 165.
29. Oksman, P.; Pihlaja, K.; Fülöp, F.; Bernáth, G. *Rapid Commun. Mass Spectrom.* **1995**, *9*, 615.