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STEREOCHEMICAL ASPECTS IN THE MASS SPECTRA OF N-Ts-3-AZA-7-CARBETHOXYBICYCLO[3.3.1]NONANES

EVIDENCE FOR ANCHIMERIC ASSISTANCE IN THE EXPULSION OF A TOSYL RADICAL

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Abstract—C_7-Stereoisomers of the title compounds show a markedly different behaviour upon electron impact. The molecular ions of the *exo* series (compounds A and C) appear to lose successively a molecule of ethanol and a tosyl radical (and *vice versa*).

The expulsion of a tosyl radical is rationalized in terms of anchimeric assistance of the radical, produced by transfer of the C_7-H atom in the molecular ion to the charge-localized N atom.

Loss of ethanol is totally absent in the *endo* series (compounds B and D), the expulsion of a tosyl radical being the major observed process. In the *endo* series is inferred that the tosyl radical is eliminated by anchimeric assistance of a carbonyl radical, which is most probably produced *via* migration of the OEt group in the molecular ion to the charge-localized N atom. All these reactions lead to ions, which probably have stable (nor)-aza-adamantane structures.

INTRODUCTION

ALTHOUGH mass spectrometry nowadays is a widely accepted tool for structure elucidation of organic molecules, it has only become apparent very recently that in particular cases this method may also be successful in solving stereochemical problems.[1-11]

The availability of a suitable series of stereoisomers of the N—Ts‡—3-aza-bicyclo [3.3.1]nonane system (Fig 1; compounds A and C *versus* B and D) stimulated therefore a study of their behaviour upon electron impact in terms of stereochemistry.

Both the configuration of the ester groups as well as the conformation of the ring system in *exo* and *endo* series have been reported before.[12,13]

RESULTS AND DISCUSSION

The partial mass spectra of the investigated stereoisomers of the N—Ts—3-aza-bicyclo[3.3.1]nonane system together with those of three related derivatives, relevant to the present study, have been compiled in Table 1.

From the data of this Table the following conclusions may be drawn:

(1) The molecular ions of compounds **A** and **C** eliminate a molecule of ethanol, whereas this decomposition is definitely not observed for the molecular ions of

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* Part of the forthcoming thesis of A. W. J. D. Dekkers.

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‡ Ts = p-CH_3 C_6H_4—SO_2—.

TABLE 1. PARTIAL MASS SPECTRA OF SOME N-Ts-3-AZABICYCLO[3.3.1]NONANES

	A				B			C	D				
Compound^{a}	**1**	**1a**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Mol. wt.	437	438	513	423	437	513	423	351	365	351	393	393	307
Ion source temp. °C	130	90	180	150	100	120	150	120	120	150	130	140	90
Relative intensity of ion^{b}													
[M]	42	12	10	10	2	≪1		14	≪1	≪1	90	≪1	14
[M-EtOH]	70*	14*	20*	48*	—	—	—	69*	≪1*	—	95*	—	—
[M-EtOD]	—	46*	—		—	—	—	—	—	—	—	—	—
[M-Ts]	49	32	75*	40*^{h}	100	100	100	69	100	100	13*	100	83*
[M-CO]	—	—	—	—	—		—	—	—	—	—		21
[M-EtO]	55	29	15	22	12	9	14	5	7	5	21	2	—
[(M-Ts)-EtOH]^{c}	100*	27*	73*	100*	11*	4*	5*	2*	3*	≪1*	13*	≪1*	—
[(M-Ts)-EtOH]^{c}	—	100*	—	—		—	—	—	—	—	—	—	—
[(M-CO)-Ts]^{c}	—	—	—	—	—		—	—	—	—	—		100*
[(M-EtOH-Ts)-CO]^{d}	29*	13*^{g}	21*	15*^{h}	14*	5*	9	100*	6*^{j}	7	6*	—	—
[(M-EtOD-Ts)-CO]^{d}	—	18*^{g}	—	—	—	—	—	—		—	—	—	—
[(M-EtO)-CO]^{d}	18*	11*	3*	18*	5*		—	24*^{i}	—	1*	5*^{k}		—
[(M-EtOH)-CO]^{d}	—	—	—	—	—	—		40*^{i}	≪1*	—	11*^{k}	—	—
[(M-EtOH)-EtOH]	16	—	11*	23*	—	—	—	—		—	—	—	—
[(M-EtOD)-EtOH]	—	12	—	—	—	—	—	—	—	—	—	—	—
[(M-EtOH-EtO)-CO]	22	7	7	9	—	—	—	—	—	—	—	—	—
[(M-EtOD-EtO)-CO]	—	14	—	—	—	—	—	—	—	—	—	—	—
[(M-Ts-EtOH)-EtOH]	9*	—	5	—	—	—	—	—	—	—	—	—	—
[(M-Ts-EtOD)-EtOH]	—	9*	—	—	—	—	—	—	—	—	—	—	—
[(M-EtO-CO-EtOH)-CO]^{d}	3*	2*	<1*	18*	—	—	—	—		—	—	—	—

[(M-EtOH-EtOH)-H]	—	—	12	—	—	—	—	—	—	—	—	—	—
[(M-EtOH-CO)-SO]	—	—	—	—	—		—	19*	—	—	—	—	—
[(M-EtOH-CO)-SO$_2$][e]	—	—	—	—	—	—	—	63*	≪1*	—	—	—	—
[(M-EtOH-CO-SO$_2$)-H]	—	—	—	—	—	—	—	7*	≪1*	—	—	—	—
[(M-Ts)-C$_2$H$_4$][e]	—	—	3*	1*	—	—	—	12*	3*	3*	—	3*	—
[M-H$_2$O]	—	—	—	—	—		—	—	—	—	9*	—	—
[(M-CO$_2$-EtOH)-CO][d, f]	—	—	—	—	—	—		—	—	—	14*	—	—
[M-(EtOH + CO + SO)]	—	—	—	—	—	—	—	—	—	—	8	—	—
[C$_2$H$_5$NTs]	8	9	—	5	—	—	—	12	—		6	—	16
[Ts]	22	30	33	5	12	26	10	19	10	5	19	8	22
[C$_7$H$_7$]	50	83	100	16	36	40	38	81	45	16	100	42	80
m/e 346	—	—	10	—	—	6	—	—	—	—	—	—	—
m/e 180	11	10	—	—	5	—	—	—	—		—	—	—

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[*] Indicates that for the last degradation step a metastable transition is found.

[a] The capitals **A** to **D** and the numbers **1** to **12** refer to those given in Figure 1.

[b] All ions discussed in the text together with the $C_7H_7^+$ (*m/e* 91)-ion, the Ts^+ (*m/e* 155)-ion and those with a *m/e* value ≥ 155 (except for compounds **2** and **5**, where a *m/e* value ≥ 260 has been chosen), showing peaks with a relative intensity ≥ 5%, have been included.
The relative intensities have been corrected for natural ^{13}C contributions

[c] In the mass spectra of compounds **1**, **1a**, **2**, **3** and **10** also a metastable transition is found for the reversed order of reaction, i.e. [(M—EtOH(D)) Ts]. The same is true for compound **12**, but then it refers to [(M—Ts)—CO].

[d] The corresponding diffuse peaks are flat-topped or broadened[23].

[e] The corresponding diffuse peak is not flat-topped; therefore the elimination of C_2H_4 instead of CO has been preferred (see note *d*).

[f] Metastable transitions have also been found for the reactions [M—CO$_2$] (flat-topped diffuse peak) and [(M—CO$_2$) EtOH], but the corresponding peaks appear to have a relative intensity < 5%.

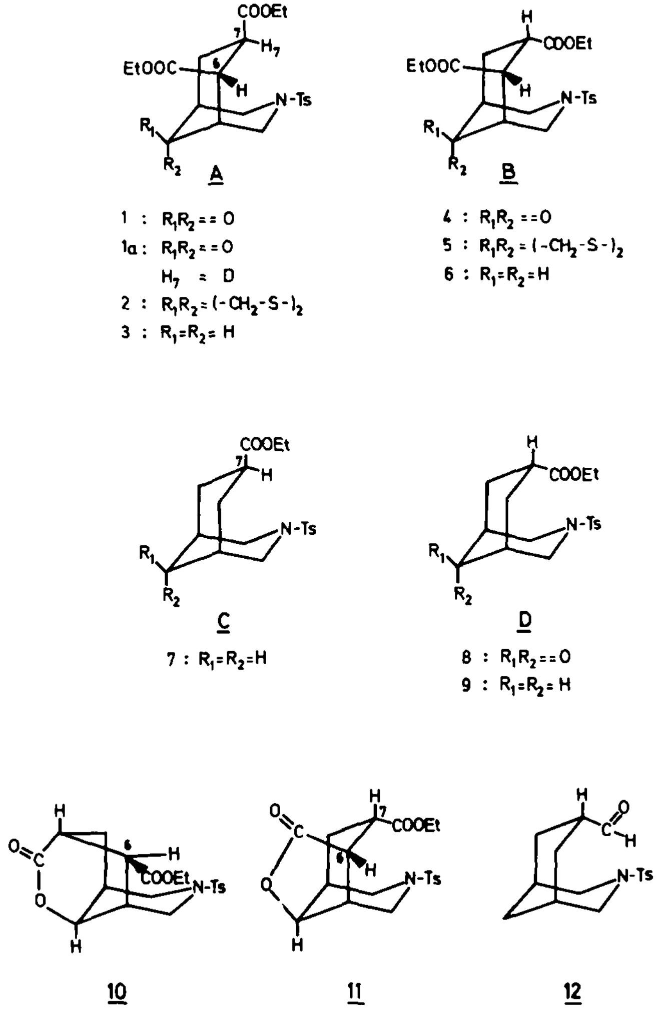
[g] The corresponding diffuse peaks overlap each other partially.

[h] The corresponding diffuse peaks appear to coincide practically.

[i] See note *g*.

[j] The corresponding diffuse peak is not flat-topped or broadened.

[k] See note *g*.



A

1 : $R_1R_2 = O$
1a : $R_1R_2 = O$
$H_7 = D$
2 : $R_1R_2 = (-CH_2-S-)_2$
3 : $R_1 = R_2 = H$

B

4 : $R_1R_2 = O$
5 : $R_1R_2 = (-CH_2-S-)_2$
6 : $R_1 = R_2 = H$

C

7 : $R_1 = R_2 = H$

D

8 : $R_1R_2 = O$
9 : $R_1 = R_2 = H$

10 11 12

Fig 1

compounds B and D.[*] This observation can readily be rationalized on the basis of C_7-configurational differences between *exo* and *endo* series. In the molecular ions of A and C an initial transfer of the C_7-H atom to the charge-localized N[†] atom may occur through a 6-membered transition state, as shown in Scheme 1, sequence *a* → *b*. This transfer is not possible in the molecular ions of the *endo* series. Proton transfer

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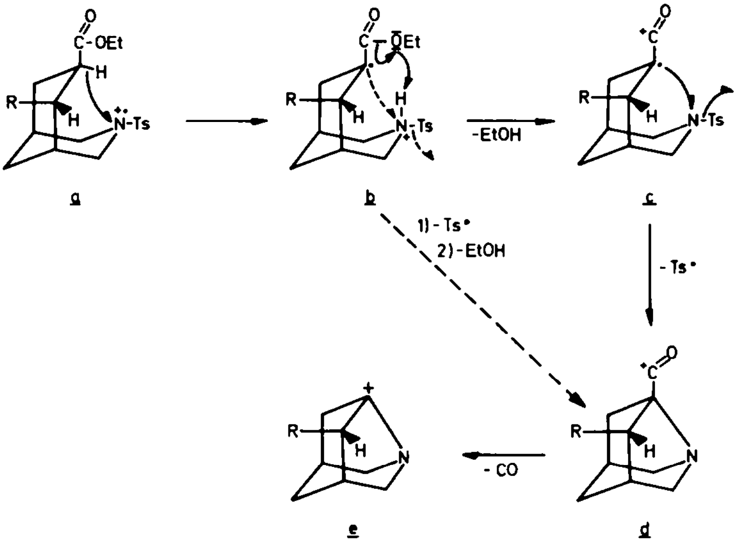
[*] The molecular ion of compound 8 does eliminate a molecule of ethanol to a very small extent, in fact only established by a metastable transition found (*cf* Table 1).

[†] Charge localization in another functional group, present in the molecule, may occur, but the small intensity of the $(M\text{-}EtO)^{+}$ and the absence of a $(M\text{-}CO_2)^{+\cdot}$ peak in the mass spectrum of compound 11 show that this does not give a considerable contribution to peaks in the mass spectrum.

from the N atom to the O atom of one of the OEt groups then results in the loss of a molecule of ethanol, as depicted in Scheme 1, sequence *b* → *c*. The decisive role of the C_7-H atom is further supported by the mass spectrum of C_7-deuterated **1a**. Its molecular ion indeed appears to expel in the ion source predominantly a molecule of deuterated ethanol (77%) besides some unlabeled ethanol (23%).



SCHEME 1. Rationalization of the successive loss of ethanol and tosyl radical and *vice versa* from the molecular ions of stereoisomers **A** and **C** (**A**: R = COOEt and **C**: R = H).

Although the latter result could indicate the existence of an additional mechanism for loss of ethanol, the reaction sequence *a* → *b* → *c* with the extension that in ion *b* a partial exchange between the transferred C_7-H atom on the quaternary N atom and another H atom, presumably C_6-H, occurs prior to or during proton transfer to one of the OEt groups is preferred. This is based on the increased percentage for loss of unlabeled ethanol (35%) from molecular ions of compound **1a**, decomposing in the second field free region of the mass spectrometer, indicating a larger extent of hydrogen exchange in these ions compared with those, decomposing in the ion source. Similar phenomena have been reported[14–16] and explained earlier[17–19] in the literature.

(2) A second distinction between compounds **A** and **C** *versus* **B** and **D** is the fact, that in the spectra of the former compounds appropriate diffuse peaks are found for the loss of a tosyl radical from the $(M—EtOH)^+$-ion, i.e. ion *c* (Scheme 1). At first sight this decomposition of ion *c* is not expected as the radical site therein is located at the C_7-atom, unless homolytic cleavage of the N—Ts bond is assisted by an attack, as depicted in Scheme 1, sequence *c* → *d*.

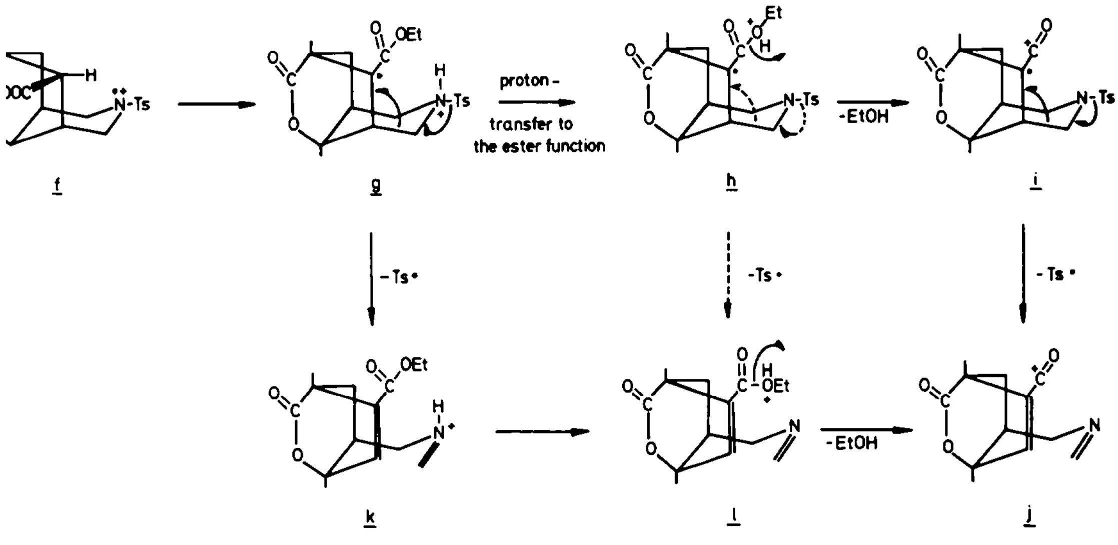
In order to acquire additional information on a possible anchimeric assistance,* the mass spectrum of conformationally rigid **10** has been analyzed.

Firstly it must be noted that elimination of a molecule of carbon dioxide is of very minor importance, thus showing that the δ-lactone ring is not seriously affected. However, the distance between C_7-H and the N atom is too large for being effectively transferred. The relative intensity of the molecular ion being much larger compared with that of the other investigated molecules, confirms this assumption.

The fact that ethanol is expelled rather intensively might be easily explained in terms of an initial transfer of the C_6-H atom to the charge-localized N atom. Models show perfect geometric conditions for this process. Protonation of the OEt group as discussed before induces the loss of ethanol (*cf* Scheme 2, sequence *f* → *g* → *h* → *i*).

This latter reaction is followed only to a small extent by expulsion of a tosyl radical, which supports the assumed reaction path for tosyl elimination as shown by the small relative intensity of the $(M—EtOH—Ts)^+$-peak (*cf* Table 1).

The intermediate C_6 radical *i* may fragment *via* opening of the heterocyclic ring and expulsion of a tosyl radical, as visualized in Scheme 2, sequence *i* → *j*.



SCHEME 2. Rationalization of the successive loss of ethanol and a tosyl radical and *vice versa* from the molecular ion of δ-lactone **10**.

It is evident that a reversed order of reactions in Scheme 1 also may lead to ion *d*, viz. successive losses of a tosyl radical and a molecule of ethanol. Appropriate diffuse peaks for these processes are observed in their spectra. These again can be explained by an initial attack of the C_7-radical upon the N—Ts bond, occurring prior to, during or after protonation of one of the OEt groups, followed by expulsion of ethanol (Scheme 1, sequence *b* → *d*).

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* Neighbouring-group participation reactions in mass spectrometry have been suggested earlier.[20]

To a very minor extent this may also be true for the δ-lactone **10**, where in the rearranged molecular ions *g* and *h* cleavage of the heterocyclic ring, triggered by the C_6-radical, can occur, thus opening the possibility for elimination of a tosyl radical from the molecular ion (*cf* Scheme 2, sequences *g* → *k* and *h* → *l*).

Finally, ion *d* may lose a molecule of carbon monoxide to give ion *e* (Scheme 1). The relative intensities of the corresponding peaks in the mass spectra of compounds **A** however, appear to be much smaller than that of compound **C** (*cf* Table 1). This may be due to a stabilization of the positive charge of the carbon monoxide group by the neighbouring ester group, as shown in Fig 2.

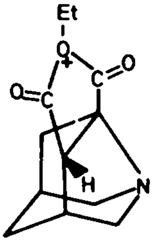

FIG 2. Structure proposed for ion *d* (*cf.* Scheme 1) from stereoisomers **A**.

(3) The only important decomposition of the molecular ions of compounds **B** and **D** appears to be the loss of a tosyl radical (*cf* Table 1; in all cases the $(M—Ts)^+$-peak is the base peak).

In the light of the foregoing discussion this is rather surprising, as in these molecular ions a C_7-H atom, transferable to the charge-localized N atom, is not available. The absence of any loss* of ethanol from the molecular ions further indicates that no other H atom is transferred to the charge-localized N atom.†

The behaviour of compounds **B** and **D** is strongly related, if not similar, to that of the γ-lactone **11** (*cf* Table 1). Its mass spectrum shows neither opening of the lactone ring (No CO_2-expulsion) nor loss of ethanol.

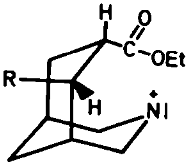

FIG 3
B: R = COOEt
D: R = H

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* See first footnote on page 1832.

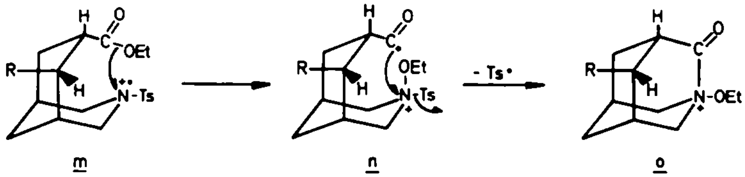
† Compared with the δ-lactone **10** (see above), having the same C_6-stereochemistry but a rigid carbocyclic ring, this may even point to a chair-conformation of the carbocyclic ring in the molecular ions of **B** and **D**, at least in the gas phase.

Thus, the loss of a tosyl radical can not be interpreted in terms of an intermediate C_6-radical, as discussed before for the δ-lactone **10**.

Yet, the $(M—Ts)^+$-peak appears to be the base peak, indicating a stable structure of the corresponding ion. Two ways for its formation could be envisaged:

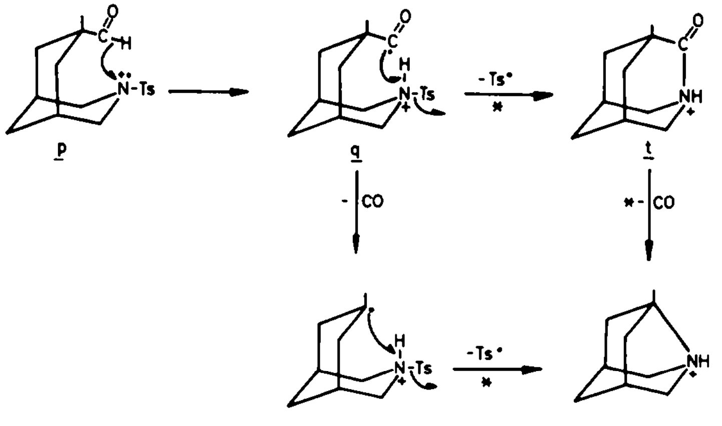
(*a*) A direct cleavage of the N—Ts bond in the molecular ion, leading to a nitrene (Fig 3), followed by a rearrangement to an aza-adamantane structure.

(*b*) In the molecular ion the OEt group may migrate to the charge-localized N atom, followed by an attack of the radical, located at the C-atom of the carbon monoxide group, upon the N—Ts bond. This has been visualized in Scheme 3, sequence *m* → *n* → *o*.



SCHEME 3. Rationalization of the loss of a tosyl radical from the molecular ions of stereoisomers **B** and **D** involving an initial attack of the N atom upon the C_7-carboethoxy group (**B**: R = COOEt and **D**: R = H)

On the basis of the mass spectrum of the aldehyde **12** the second alternative seems most likely. A relatively intense peak for loss of carbon monoxide from the molecular ion is one of the main processes and this reaction is followed by expulsion of a tosyl radical, as supported by an appropriate diffuse peak found in its spectrum and shown in Scheme 4, sequence *p* → *q* → *r* → *s*.*



SCHEME 4. Rationalization of the successive loss of carbon monoxide and of a tosyl radical and *vice versa* from the molecular ion of aldehyde **12**

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[*] It must be recognized that H atoms do migrate more easily than alkoxy groups. In the present case however, the OEt group of C_7-COOR in compounds **B** and **D** has the same position as the aldehydic H atom in compound **12**. Migration of alkoxy groups has been reported earlier.[21]

The structure *q* for the molecular ion can further easily account for the loss of a tosyl radical from the molecular ion, as discussed above (*cf* Scheme 4, sequence *q* → *t* and Scheme 3, sequence *n* → *o**).

Also in this case, an appropriate diffuse peak, found in its spectrum, supports this assumption.

The loss of a molecule of carbon monoxide from the molecular ion of the aldehyde **12** is not observed for the esters **B** and **D**. This phenomenon could be explained by a fast attack of the radical, located at the carbon monoxide group, upon the N—Ts bond to release the sterically crowded ammonium ion from the latter compounds (ion *n* in Scheme 3). This kind of attack could even account for some loss of an OEt radical from the molecular ion, although this can also be explained by charge-localization in the ester groups† (the more intense peaks for the $(M—EtO)^+$-ions of compounds A, C and the δ-lactone **10** are mainly due to the intermediacy of C_7- and C_6-radicals; *cf* Table 1 and Schemes 1 and 2).

Finally, it should be noted, that aza-adamantanes may be synthesized very easily from 7-substituted N—Ts-3-azabicyclo[3.3.1]nonanes, resembling to their behaviour in the mass spectrometer.[22]

EXPERIMENTAL‡

Mass spectra were obtained with an AEI-902 mass spectrometer at an electron beam energy of 70 eV and at ion source temperatures, given in Table 1. All samples were introduced into the ion source by use of the direct insertion probe.

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* Ion *t* loses CO to give ion *s* (Scheme 4), ion *o* however appears to expel EtOH and then CO (*cf* Table 1).

† See second footnote on page 1832.

‡ The syntheses of the compounds **A**, **B**, C, **10** and **11** will be described elsewhere. For compounds **D** and **12**, see refs 12 and 13.

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