Tetrahedron Vol. 38, No. 1, pp. 161 to 164, 1982
Printed in Great Britain.

0040-4020/82/010161-04$03.00/0

THE ELECTRON IMPACT INDUCED FRAGMENTATIONS OF THE FOUR ISOMERIC 7-t-BUTYLBICYCLO[3.3.1]NONANE-3-CARBOXYLIC ACIDS

J. A. PETERS,* B. VAN DE GRAAF, P. J. W. SCHUYL, A. H. KNOL-KALKMAN, A. M. VAN LEERSUM and H. VAN BEKKUM
Laboratory of Organic Chemistry, Delft University of Technology, Julianalaan 136, 2628 BL Delft, The Netherlands

(*Received in UK* 13 *April* 1981)

Abstract—The mass spectral fragmentation of the four isomeric 7-t-butylbicyclo[3.3.1]nonane-3-carboxylic acids is presented and discussed. Characteristic differences in the mode of the expulsion of the t-Bu group allow configurational assignment. The fragmentation of the *endo-endo* isomer as well as that of the related compound *trans*-4-t-butylcyclohexanecarboxylic acid was studied in more detail using deuterium labeling. It is shown that the expulsion of $C_4H_7^{\cdot}$ takes place with a direct hydrogen transfer from the t-Bu to the COOH group.

The geometry of the bicyclo[3.3.1]nonane system allows interesting transannular interactions,[1] which may be reflected in H-transfers during electron impact induced fragmentations. Previously, as a first example, we reported that the t-Bu group in 7-*exo*-t-butyl-3-oxabicyclo[3.3.1]nonane is eliminated exclusively as $C_4H_9^{\cdot}$, whereas in the *endo* isomer this fragmentation is accompanied by the loss of $C_4H_7^{\cdot}$ and C_4H_8.[2] Similar stereoselectivity has been observed in the mass spectral fragmentation of the t-butylcyclohexanecarboxylic acids: here also the mode of elimination of the t-Bu group is dependent on the geometry of the molecule.[3] Apparently, in the compounds mentioned, a fragmentation leading to loss of $C_4H_7^{\cdot}$ and C_4H_8 depends on the ability of the t-Bu group to interact with the radical cation site on oxygen.

In this paper the mass spectral fragmentation of the four 7-t-butylbicyclo[3.3.1]nonane-3-carboxylic acids (**1**–**4**) is reported. The conformation of the compounds under investigation have been studied previously[4] and are depicted schematically in Fig. 1. In compounds **1** and **2** an approach of the t-Bu and the COOH group seems impossible without preceding isomerization, whereas in compound **3** such an approach requires a highly unfavorable double-chair conformation. Inspection of molecular models shows that in compound **4** an interaction of the t-Bu group and the radical cation site on the COOH group is possible in the most stable conformation (chair–boat). Therefore, the mass spectrometry of these compounds might be helpful in obtaining further understanding of the phenomena described above. The genetic connection between the ions was studied using metastable scan techniques. Some of the fragmentation pathways were studied by means of specific labeling in compound **1** and in the related *trans*-4-t-butylcyclohexanecarboxylic acid (**5**).

RESULTS AND DISCUSSION

The mass spectra of compounds **1**–**4** show substantial differences: the elimination of the t-Bu group is indeed strongly dependent on the configuration (Table 1). In compound **2** the expulsion of $C_4H_9^{\cdot}$, yielding the ion at *m/z* 167, is by far the most important mode of elimination of the t-Bu group, whereas in the spectra of the other compounds, in addition to the peak at *m/z* 167, relatively intense peaks are found at *m/z* 168 and 169 (loss of C_4H_8 and $C_4H_7^{\cdot}$, respectively). Remarkably, this is also the case for compound **1**, in which an interaction of the t-Bu group and the COOH group seems to be excluded. The contrast in the mass spectral behaviour of compounds **1** and **2** seems at variance with a simple cleavage mechanism for the expulsion of $C_4H_9^{\cdot}$. Evidence that this fragmentation is indeed more complex is obtained from a B/E linked scan of the molecular ion of **1** which shows that loss of $C_4H_9^{\cdot}$ competes quite effectively with other rearrangement reactions in the metastable time-window (Table 2). A similar conclusion can be reached for the mechanism of $C_4H_9^{\cdot}$ expulsion from the molecular ion of *trans*-4-t-butylcyclohexanecarboxylic acid (**5**). Metastable scans show an intense metastable for the loss of $C_4H_9^{\cdot}$ from the molecular ion of **5**, but no metastable is observed for the loss of C_4H_8, whereas a large peak at *m/z* 128 (relative abundance 30%)[3] shows that loss of C_4H_8 is an important fragmentation pathway.

It is noticeable that the geometry of compound **2** and that of other compounds, which show loss of $C_4H_9^{\cdot}$ as

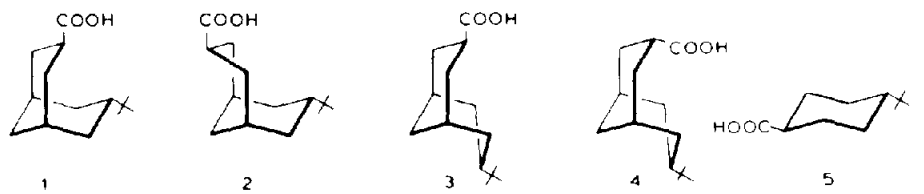


Fig. 1. Compounds studied (in preferred conformation).

Table 1. Relative peak intensities (*m/z* 166–169) in the mass spectra of compounds **1–4** (70 eV)[a,b]

m/z	1[c]	2	3	4
169 (M-55)	54	4	22	39
168 (M-56)	52	4	100	100
167 (M-57)	14	100	7	52
166 (M-58)	30	0	5	2

[a] Corrected for ^{13}C- and ^{18}O-natural abudancies. [b] Complete mass spectra and fragmentation maps may be obtained from the authors. [c] Base peak at m/z 57.

Table 2. Relative metastable abundancies[a] ([m*]) for compound **1**, comparison with abundancies[b] ([m]) in the 70 eV mass spectrum

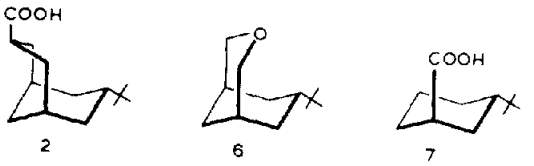
m/z daughter ion	m*	[m*]/[m][c]
169 (M-55)	90	0.50
168 (M-56)	27	0.16
167 (M-57)	27	0.58
166 (M-58)	100[d]	1.00

[a] From a B/E scan of the molecular ion (m/z 224). [b] See Table 1. [c] Relative to the ratio for m/z 166. [d] 0.18% of the main beam.

the dominant t-Bu fragmentation[2,3] have some resemblance (Fig. 2). In these compounds a radical cation site located on oxygen can form a new bond with the C atom carrying the t-Bu group. Therefore, loss of $C_4H_9^{\cdot}$ from the molecular ions of these compounds might well arise from a displacement mechanism.[5]

The mass spectra of compounds **1**, **3**, and **4** as well as data from previous investigations,[2,3] show that the loss of $C_4H_7^{\cdot}$ from the molecular ions is always accompanied by loss of C_4H_8. A rationale is given in Scheme 1. In a first step the radical site migrates to the t-Bu group via one or more hydrogen rearrangements. Loss of C_4H_8 is then possible by a simple cleavage reaction, while a more complex reaction, heterolytic cleavage of the C^2–C^3 bond concerted with or followed by a hydride shift, can account for the loss of $C_4H_7^{\cdot}$. This competition after migration of the radical site explains the relatively low metastable intensity for the loss of C_4H_8 (Table 2). It also accounts for the fact that the $[M-C_4H_7^{\cdot}]^+/[M-C_4H_8]^{+\cdot}$ ratio is lower for the bicyclic compounds—where the conformational freedom is restricted—than for the t-butylcyclohexanecarboxylic acids.[3]

The migration of the radical site to the t-Bu group may occur by a direct H-transfer when the t-Bu group and the COOH group are able to interact. Such an interaction is not possible for compounds **1** and **5**. For these compounds H-transfer must occur either via a multistep mechanism or after an isomerization. To obtain more information the labeled compounds **1–9**, **9-d_2**, **1-COOD**, **1-3-d**, **5-COOD**, and **5-t-Bu-d_9** were investigated. The loss of H_2O vs HDO from the ions $M^{+\cdot}$–$C_4(H,D)_{7-10}$ was used as a probe for H-transfers preceding the expulsion of the t-Bu group (Table 3).The data for **1-COOD** and **5-COOD** show extensive H/D scrambling in the ions $[M-C_4H_8]^{+\cdot}$ and $[M-C_4H_9]^+$. For the $[M-C_4H_7]^+$ ions, however, H/D scrambling is limited. Comparison of the data for **5-COOD** with those for **5-t-Bu-d_9** show that for the latter compound a D-atom is transferred† to the COOH group in the formation of the $[M-C_4D_7]^+$ ions. This seems more in line with an isomerization preceding the transfer than with a multistep mechanism. Moreover, comparison of the data for **1-COOD** with those for **1-3-d** and **1-9,9-d_2** shows that hydrogens at the positions 3 and 9 are probably not involved in multistep mechanisms for the required H-transfers for loss of $C_4H_7^{\cdot}$ from the molecular ion of **1**.[9]



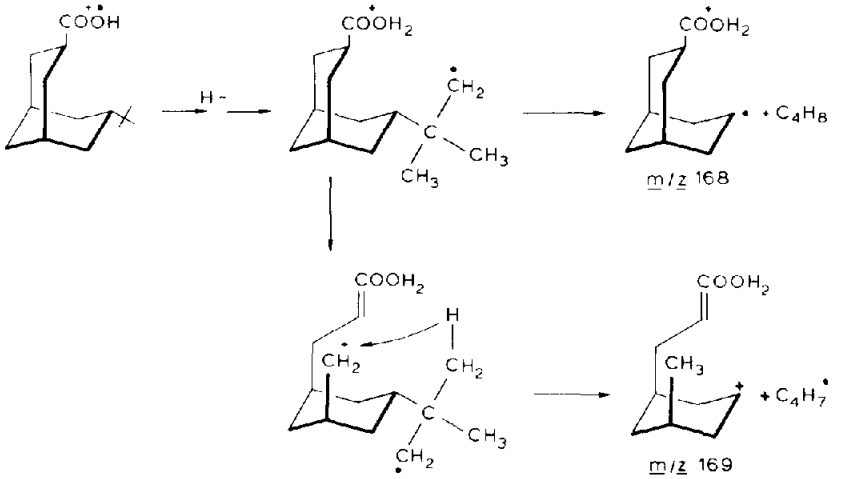
2 6 7

Fig. 2. Compounds showing t-Bu expulsion via loss of $C_4H_9^{\cdot}$.

EXPERIMENTAL

Mass spectra were recorded on a Varian-MAT 311A mass spectrometer, operating at 70 eV and 1 mA emission current. Samples were introduced via a direct insertion probe. The DADI scans were carried out by varying the analyzer voltage from 500–50 V. The metastable defocussing scans were carried out by varying the accelerating voltage from 1–3 kV.

†Ion intensities in the mass spectrum indicate a sizable isotope effect for the formation of $M-C_4D_7^+$ from **5-t-Bu-d_9**.



Scheme 1.

Table 3. Ratio of the -H_2O and -HDO peaks in the DADI spectra of the ions M-55, M-56, M-57, and M-58

	1-COOD[a]	1-3-d[b]	1-9,9-d_2[c]	5-COOD[d]	5-t-Bu-d_9[e]
M-55	34/66	100/0	100/0	31/69	29/71
M-56	88/12	88/12	80/20	78/22	--[f]
M-57	87/13	96/4	91/9	84/16	100/0
M-58	93/7	94/6	75/25		

[a] 48% d_0, 50% d_1, 2% d_2; [b] 10% d_0, 86% d_1, 4% d_2; [c] 2% d_0, 10% d_1, 88% d_2; [d] 20% d_0, 80% d_1; [e] 6% d_3, 12% d_4, 22% d_5, 26% d_6, 19% d_7, 11% d_8, 4% d_9; [f] Not observed, as a result of the incomplete D-labeling of the t-Bu group.

The syntheses of the 7-t-butylbicyclo[3.3.1]nonane-3-carboxylic acids (unlabeled) have been described previously.[4,6]

7-Exo-*t-butylbicyclo*[3.3.1]*nonane*-3-exo-*carboxylic acid*-COOD (1-COOD). The unlabeled compound[4] (5 mg) in 2 ml ether was shaken with five portions of 1 ml D_2O. The soln obtained was dried over $MgSO_4$. Evaporation of the solvents yielded the deuterated compound.

7-Exo-*t-butylbicyclo*[3.3.1]*nonane*-3-exo-*carboxylic acid*-3-*d* (1-3-*d*). Compound 2 (184.4 mg), 10 ml triethylene glycol-d_2 and 2.5 ml 40% NaOD in D_2O were heated. Water was distilled off until a bottom temp of 200° was reached. Then the mixture was heated at 190° for 4 hr. After cooling the mixture was diluted with 15 ml H_2O and subsequently acidified with 10 ml 6N HCl. The dispersion obtained was extracted with ether (5 × 15 ml). The ether soln was washed with H_2O (3 × 15 ml) and dried over $MgSO_4$. After evaporation of the solvents the residue was recrystallized from EtOH–H_2O and then sublimed at 100° 10.5 mm yielding compound 1-3-*d* (87.7 mg); m.p. 138–139°.

7-Exo-*t-butylbicyclo*[3.3.1]*nonane*-3-exo-*carboxylic acid*-9,9-d_2 (1-9, 9-d_2). A soln of 7-*exo*-t-butyl-9-oxobicyclo[3.3.1]nonane-3-*endo*-methanol[4] in 70 ml dry diethyl ether was washed with D_2O (3 × 10 ml). After drying over $MgSO_4$ and evaporation of the solvent the residue was boiled with 50 ml triethylene glycol-d_2, 5 ml hydrazine hydrate-d_6 (Merck Sharp & Dohme Canada Ltd) and 12 ml 40% NaOD in D_2O for 1 hr. Then the mixture was distilled until a bottom temp of 150° was reached (after 4 hr). The residue was diluted with 200 ml H_2O and then extracted with ether (4 × 50 ml). The ether soln was washed with sat NaCl aq (2 × 50 ml) and dried over $MgSO_4$. After evaporation of the solvents 6.50 g 7-*exo*-t-butylbicyclo[3.3.1]nonane-3-*endo*-methanol-9,9-d_2 was obtained. This compound was oxidized to the corresponding carboxylic acid by chromic acid.[4] The product obtained was epimerized according to the procedure described under 1-3-*d*. Now unlabeled triethylene glycol, NaOH and H_2O were used. After this reaction compound 1-9,9-d_2 was obtained. Purification was achieved by recrystallization from EtOH–H_2O and sublimation at 110°/0.5 mm; m.p. 137–137.5°.

Triethylene glycol-d_2. A mixture of 50 ml triethylene glycol and 10 ml D_2O was distilled until a bottom temp of 160° was reached. This procedure was repeated three times. The residue was distilled under vacuo; b.p. 155–157°. The product obtained was contaminated with a small amount D_2O.

4-*t-Butyltoluene-t-Bu*-d_9.[8] To a mixture of D_3PO_4 (212 g, 2.1 mol) and 64 g toluene (0.7 mol) t-BuOH (37 g, 0.5 mol) was added dropwise with stirring (30 min) at 80°. The mixture was stirred at 80° for another 7 hr. After cooling 250 ml of H_2O was added and the layers were separated. The aqueous layer was extracted with toluene (3 × 50 ml). The combined organic layers were dried over $MgSO_4$. After filtration the solvent was distilled off. The residue was distilled under vacuo twice to yield 3.7 g of a

mixture containing 4-t-butyltoluene-t-Bu-d_9; mass spectrometry showed the following deuterium distribution: 4% d_9, 11% d_8, 19% d_7, 26% d_6, 22% d_5, 12% d_4, and 6% d_3.

Trans-4-*t-butylcyclohexanecarboxylic acid-t-Bu*-d$_9$ (5-t-Bu-d_9). The product of the preceding step was converted with the use of the procedures, described successively in Refs. 7, 8, and 3 to give 7 mg of chromatographically pure 5-t-Bu-d_9; m.p. 172.4–174.6°.

Acknowledgement—Thanks are due to Mr. P. R. Crabbendam for experimental assistance.

REFERENCES

[1]See e.g. J. Murray-Rust, P. Murray-Rust, W. C. Parker, R. L. Tranter and C. I. Watt, *J. Chem. Soc.* Perkin 2 1496 (1979).
[2]J. A. Peters, B. van de Graaf, P. J. W. Schuyl, Th. M. Wortel and H. van Bekkum, *Tetrahedron* **32**, 2735 (1976).
[3]H. van Bekkum, B. van de Graaf, G. van Minnen-Pathuis, J. A. Peters and B. M. Wepster, *Recl. Trav. Chim. Pays-Bas* **89**, 521 (1970).
[4]J. A. Peters, J. M. van der Toorn and H. van Bekkum, *Tetrahedron* **31**, 2273 (1975).
[5]F. W. McLafferty, *Interpretation of Mass Spectra*, 2nd Edn, p. 63. Benjamin, Reading (1973).
[6]J. A. Peters, J. M. A. Baas, B. van de Graaf, J. M. van der Toorn and H. van Bekkum. *Tetrahedron* **34**, 3313 (1978).
[7]P. J. Schlatter and R. D. Clark, *J. Am. Chem. Soc.* **75**, 361 (1953).
[8]D. Nightingale and J. R. Janes, *Ibid.* **66**, 154 (1944).
[9]A referee proposed the following alternative hypothesis for the observations: except where the activation energy for t-Bu$^{\cdot}$ loss is relatively low due to product stabilization (e.g. compounds **2**, **6**, **7**), a complex is formed between the $[M-C_4H_9]^+$ ion and the departing t-Bu$^{\cdot}$ radical. This complex would be bound by an ion-dipole and/or ion-induced dipole attraction. The rearrangements would then occur within this complex.[10]
[10]R. D. Bowen and D. H. Williams, *J. Am. Chem. Soc.* **102**, 2752 (1980).