Gas Chromatography-Mass Spectrometry of *N*-Trifluoroacetyl Trimethylsilyl Esters of Some Iminodicarboxylic Acids

Katsuhiro Kawashiro,* Shiro Morimoto, and Hideyuki Yoshida
Department of Chemical Engineering, Faculty of Engineering, Tokushima University, Minamijosanjima, Tokushima 770

(Received April 15, 1985)

Synopsis. The simultaneous *N*-trifluoroacetylation and *O*-trimethylsilylation of some iminodicarboxylic acids were studied by the use of a mixture of α,α,α,α′,α′,α′-hexafluoro-*N*-methyldiacetamide and *N*,*O*-bis(trimethylsilyl)trifluoroacetamide, as a derivatizing reagent. The resulting *N*-trifluoroacetyl trimethylsilyl ester derivatives gave rather complicated mass spectra with molecular (M⁺) and M−15 (loss of CH_3) ions upon electron impact at 20 eV.

Previously we reported EI mass spectra of *N*-trifluoroacetyl (TFA) butyl ester[1)] and *N*-trimethylsilyl (TMS) TMS ester[2)] derivatives of some iminodicarboxylic acids (IDCAs). It has been shown that the TMS derivatives had advantages over the *N*-TFA butyl ester derivatives in terms of the simplicity of preparation and the easily recognizable mass spectra containing both molecular (M⁺) and M−15 (loss of CH_3) ions. The major drawback of the TMS derivatives is incomplete trimethylsilylation (formation of both di- and tri-TMS) due to the steric hindrance of *N*-substituent groups. This may be overcome by introducing a TFA group to the imino nitrogen instead of the TMS group, which is less bulky and also a good *N*-masking group for amino acid esters for gas chromatography. Although two groups[3—6)] have reported the preparation of *N*-TFA TMS derivatives of some common amino acids, a convenient single-step derivatization has not been established yet.

We were interested in fast and convenient preparation of *N*-TFA di-TMS esters of some IDCAs on a small scale for gas chromatography-mass spectrometry (GC-MS). This paper deals with a single-step preparation of such volatile derivatives, and also with their mass spectra upon electron impact at 20 eV. The IDCAs include iminodiacetic acid (**1**), 2- and 3-(carboxymethylamino)propionic acids (**2** and **3**), and 2,2′-, 2,3′-, and 3,3′-iminodipropionic acids (**4**—**6**).

Results and Discussion

When a suspension of **3** (50 μmol) in a mixture of

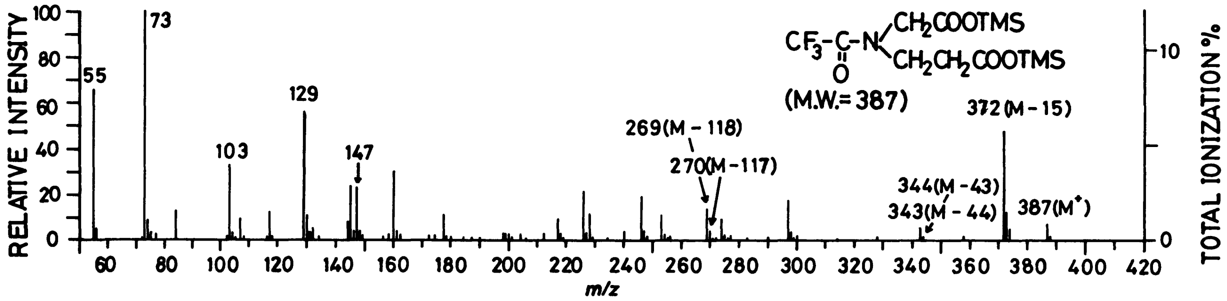

Fig. 1. Mass spectrum of *N*-TFA di-TMS ester of **3**.

Table 1. Some selected ions of *N*-TFA di-TMS esters of **1**—**6**

Parent IDCA	m/z [a)]										
	M⁺	M−15	M−43	M−44	M−117	M−118	M−131	M−189	M−207	Others	
1	373	358	330	329	256	255	—	—	—	147	73
	(3)	(24)	(1)	(4)	(1)	(3)				(44)	(100)
2	387	372	344	343	270	—	—	198	180	147	73
	(1)	(24)	(2)	(8)	(22)			(6)	(34)	(33)	(100)
3	387	372	344	343	270	269	256	198	180	73	55
	(7)	(48)	(2)	(5)	(4)	(14)	(2)	(3)	(2)	(100)	(65)
4[b)]	401	386	358	357	284	283	—	212	194	166	73
	(1)	(37)	(2)	(4)	(27)	(1)		(99)	(50)	(52)	(100)
5	401	386	—	357	284	283	—	212	194	73	55
	(1)	(22)		(1)	(32)	(1)		(14)	(100)	(53)	(69)
6	401	386	358	—	284	283	270	212	194	129	55
	(3)	(30)	(1)		(8)	(33)	(2)	(4)	(13)	(86)	(100)

a) Values in parentheses indicate relative intensity. b) A first GC peak.

equal volumes (0.20 ml) of $\alpha,\alpha,\alpha,\alpha',\alpha',\alpha'$-hexafluoro-*N*-methyldiacetamide (*N*-methyl-bis(trifluoroacetamide), MBTFA)[7], *N,O*-bis(trimethylsilyl)trifluoroacetamide (BSTFA), and acetonitrile was heated at 100 °C for 30 min, a clear solution was obtained. GC analysis showed a single peak, which was determined to be *N*-TFA di-TMS ester of **3** by GC–MS (Fig. 1). Similarly, the other IDCAs except for **4**, gave the corresponding *N*-TFA di-TMS esters on the single-step derivatization (at 100 °C for 30 min). As a typical example, the time course of derivatization of **1** at 100 °C was studied by GC. The peak area ratio of *N*-TFA di-TMS ester of **1** to an internal standard (phenanthrene) became constant after reaction time of 20 min. Although small amounts of both di- and tri-TMS derivatives were present at an early stage of the derivatization (10 min), these two disappeared completely after reaction time of 20 min. These findings indicate that **1** can be converted in a high yield into the *N*-TFA di-TMS ester under the conditions (at 100 °C for 30 min).

In the instance of **4**, however, the derivatization became complicated and gave a mixture of the corresponding *N*-TFA di-TMS ester, TMS derivatives (both di- and tri-), and an unknown by-product[8] under the conditions (at 100 °C for 30 min).

The *N*-TFA di-TMS esters exhibited sharp and symmetrical GC peaks on a packed column. There were no indications of their adsorption on solid supports because of the presence of the stable *N*-TFA group. Retention times of the *N*-TFA di-TMS esters are generally intermediate between those of the corresponding di- and tri-TMS derivatives.[2]

Figure 1 presents the mass spectrum of *N*-TFA di-TMS ester of **3**, as a typical example. Some selected ions for **1**—**6** are listed in Table 1. Both M^+ and M−15 ions characteristic of TMS derivatives are seen for **1**—**6**. These spectra were more complex than those of the corresponding di- and tri-TMS derivatives.[2]

α,α'-IDCAs (**1**, **2**, and **4**) are generally characterized by M−43 (CH_3+CO), M−44 (CO_2), M−117 (COOTMS), M−189 (COOTMS+CH_2=Si$(CH_3)_2$), and M−207 (COOTMS+CH_2=Si$(CH_3)_2$+H_2O). The M−189 and M−207 were absent for **1**. The *N*-TFA group may play an important role for the formation of the M−44 because this ion was not observed for the corresponding TMS derivatives.[2] The M−44 ion[9] can be explained by migration of a TMS group to the carbonyl oxygen of the *N*-TFA group and subsequent elimination of a neutral species CO_2 from the rearranged M^+ ion. Analogous fragmentations are known for *N*-acylglycine TMS esters.[10] The amine fragment, M−117, which constituted a base peak for the corresponding TMS derivatives (both di- and tri-)[2] becomes less abundant.

On the other hand, β,β'-IDCA (**6**) is characterized by a complex spectrum with M−43, M−117, M−118 (COOTMS+H), M−131 (CH_2COOTMS), and M−207. In addition, M−69 (CF_3) and M−97 (CF_3CO) were observed for **6**. The M−44 characteristic of α,α'-IDCAs is not seen in this instance. The structurally most important amine fragment, M−131, which constituted a base peak for the corresponding tri-TMS derivative,[2] becomes far less abundant.

Compound **3** exhibits a complicated spectrum in which both ions characteristic of α,α'- and β,β'-IDCAs are present (Fig. 1). In contrast to **3**, **5** exhibited a similar spectrum to the corresponding α,α'-IDCA, **4**. These facts indicate that either of the fragmentation characteristics of α,α'- or β,β'-IDCAs can take place predominantly depending on the structures of α,β'-IDCAs.

Experimental

Materials. MBTFA was obtained from Gasukuro Kogyo Co. Ltd. BSTFA, acetonitrile, and the IDCAs were the same as previously reported.[2]

Derivatization. About 50 μmol of each IDCA was weighed into a 1 ml mini screw vial (Maruemu MV-1). Acetonitrile (0.20 ml), MBTFA (0.20 ml), and BSTFA (0.20 ml) were added to the vial. It was closed tight with a silicone cap and then heated at 100 °C for different durations in a constant-temperature air bath (Yamato Drying-Oven, DX-58).

GC. GC was carried out with a Hitachi 163 gas chromatograph equipped with a flame ionization detector and a glass column (3 mmϕ×1 m) packed with 1.5% OV-101 on Chromosorb G HP (100/120 mesh) (Shimadzu). The temperature was programmed linearly from 100 °C (5 min hold) to 230 °C at a rate of 5 °C min^{-1}. Nitrogen was the carrier gas flowing at 30 ml min^{-1}. Retention times of the *N*-TFA di-TMS esters: **1** 11.5 min, **2** 12.3 min, **3** 14.0 min, **4** 11.8 and 12.8 min, **5** 14.8 min, **6** 17.4 min. Retention time of phenanthrene: 17.0 min.

GC–MS. GC–MS was carried out with a JEOL JMS-D 300 mass spectrometer connected with a JGC-20 KP gas chromatograph, and mass spectra upon electron impact at 20 eV were obtained. The GC–MS conditions were the same as previously reported.[1]

References

1) K. Kawashiro, S. Morimoto, and H. Yoshida, *Bull. Chem. Soc. Jpn.*, **57**, 1097 (1984).

2) K. Kawashiro, S. Morimoto, and H. Yoshida, *Bull. Chem. Soc. Jpn.*, **57**, 2871 (1984).

3) H. R. Kricheldorf and M. Fehrle, *Synthesis*, **6**, 420 (1974).

4) M. Schwarz and G. Michael, *J. Chromatogr.*, **118**, 101 (1976).

5) G. Michael, *J. Chromatogr.*, **188**, 251 (1980).

6) G. Michael, *J. Chromatogr.*, **196**, 160 (1980).

7) M. Donike, *J. Chromatogr.*, **78**, 273 (1973).

8) Although low-resolution mass spectrum of the by-product (M^+, *m/z* 496) was obtained, its structure could not be determined in the present study.

9) The identity of the M−44 (CO_2) was confirmed for **3** by a high-resolution mass measurement. Found: *m/z* 343.1235. Calcd for $C_{12}H_{24}NO_3F_3Si_2$: M−CO_2, 343.1248.

10) P. V. Fennessey and S. S. Tjoa, *Org. Mass Spectrom.*, **15**, 202 (1980).