Mass Spectrometry of Organic Compounds of the Group V Elements

VI†—A New Type of Amine Fragmentation Under Electron Impact

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A new type of amine fragmentation under electron impact is elucidated for proline, sarcosine and aspartic acid derivatives and aminomethylphosphines of the general formula R_2NCH_2X. Ordinary α-cleavage affording the $R_2\overset{+}{N}{=}CH_2$ ion is suppressed by elimination of a neutral HX particle and $[M-HX]^+$ ion formation, or M–HX neutral particle ejection and generation of an $[HX]^+$ ion from $[M]^{+\cdot}$. Such fragmentation is ensured by the presence of an α-heteroatom (N, O, P, S) in one substituent (X) and a CO_2R type delocalizing group in the α-position of the other substituent (R_2N).

Amines usually undergo fragmentation with α-cleavage and generation of even electron amine fragments $\begin{matrix} R'' \\ R' \end{matrix}\!\!>\!\overset{+}{N}{=}CHR$, their peaks being very abundant in the mass spectra. We have found a new type of amine fragmentation of the α-amino acid derivatives proline (**1–8**, Figs. 1–4, Scheme 1), aspartic acid (**9–11**, Fig. 5) and sarcosine (**12**), for which the unusual odd electron amine fragments *a* and *b* are of high abundance in the spectra.[2] In the case of **5–8** (Figs. 3 and 4) the new fragmentation competes successfully with the normal one, the amine fragment *c* peak being dominant (*m/z* 142) only in the spectrum of **6**.

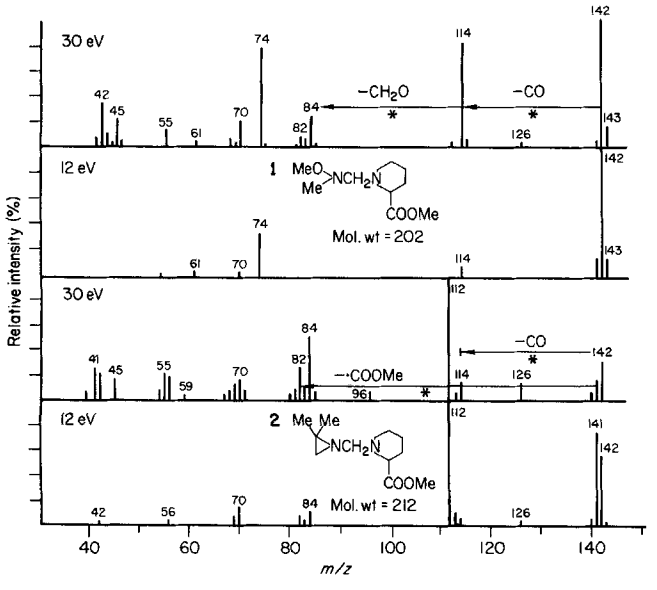

Figure 1. Mass spectra of **1** and **2**.

† For Part V, see Ref. 1.
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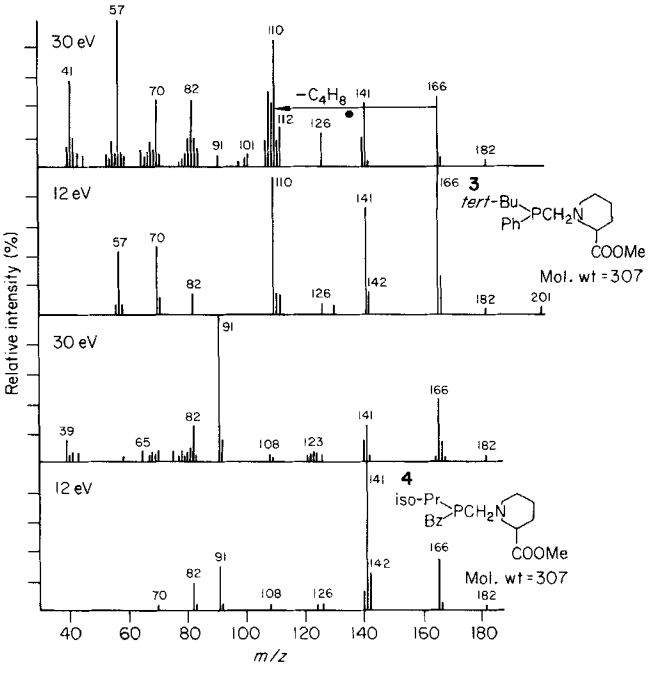

Figure 2. Mass spectra of **3** and **4**.

Similar fragmentation routes are observed for compounds **1** and **2** (Fig. 1 and Scheme 1). In these compounds the +M-ability of the nitrogen atom is reduced by electronegative substituents. On the other hand, for aminomethylphosphines **3** and **4** (Fig. 2 and Scheme 1) the observed $[M]^{+\cdot}$ fragmentation into *a* and *b* ions almost totally suppresses the amine peaks, which are weak (6% at 30 eV, 18% at 12 eV) and the ester group cleavage is absent altogether. It should be noted that such fragmentation is in agreement with the principal rule of phosphine fragmentation yielding odd electron fragments.[3]

For elucidating the effect of the proline ring upon tertiary carbon hydrogen lability and the generation of

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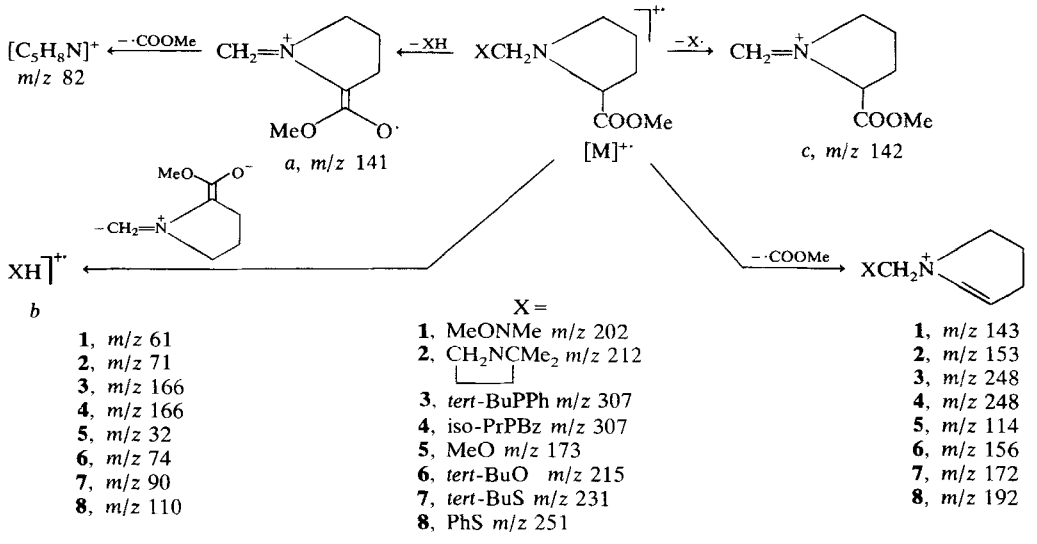
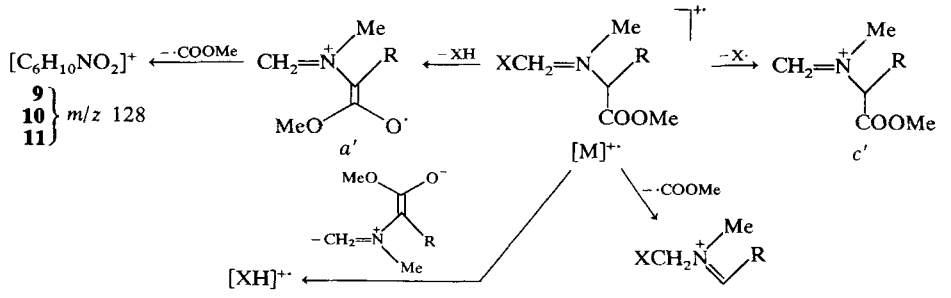


X =
1, MeONMe *m/z* 202
2, CH_2NCMe_2 *m/z* 212
3, *tert*-BuPPh *m/z* 307
4, iso-PrPBz *m/z* 307
5, MeO *m/z* 173
6, *tert*-BuO *m/z* 215
7, *tert*-BuS *m/z* 231
8, PhS *m/z* 251

b
1, *m/z* 61
2, *m/z* 71
3, *m/z* 166
4, *m/z* 166
5, *m/z* 32
6, *m/z* 74
7, *m/z* 90
8, *m/z* 110

c
1, *m/z* 143
2, *m/z* 153
3, *m/z* 248
4, *m/z* 248
5, *m/z* 114
6, *m/z* 156
7, *m/z* 172
8, *m/z* 192

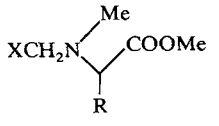
Scheme 1



b'	*X* =	*R* =	*c'*
9, *m/z* 32	**9**, MeO	CH_2COOMe *m/z* 219	**9**, *m/z* 160
10, *m/z* 90	**10**, *tert*-BuS	CH_2COOMe *m/z* 277	**10**, *m/z* 218
11, *m/z* 110	**11**, PhS	CH_2COOMe *m/z* 297	**11**, *m/z* 238
12, *m/z* 32	**12**, MeO	H *m/z* 147	**12**, *m/z* 88

Scheme 2

the *a*–*c* fragments we investigated the acyclic derivatives **9–12** (Fig. 5, Schemes 2 and 3):



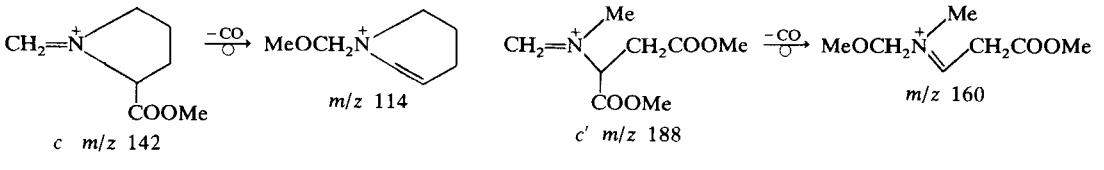
R = CH_2COOMe, X = MeO (**9**); *tert*-BuS (**10**); PhS (**11**)

R = H X = MeO (**12**)

As could be expected a complete analogy was observed for the fragmentation of these compounds and proline derivatives.

However, the peak intensities of the *a* and *b* type ions are 2–3 times lower.[2] The maximum intensity of the *b* peak in the case of **11** is explained by the high stability of the PhS^+H ion. The peak intensity of the amine fragment *c* is the same as for the proline analogues. Structural identity of the *a*, *c* and *a'*, *c'* fragments is confirmed by their fragmentation. This may serve as evidence that the model (aspartic acid) chosen for the study of the role played by the proline ring in the fragmentation is adequate.

In the proline *c* and aspartic acid *c'* derivatives the amine fragment undergoes further degradation with CO ejection from an ester group. A flat-topped metastable peak is observed for this transition. In accordance with Ref. 4 it is testimony of an energetically favourable rearrangement. The latter appears to include the double bond migration in the amine fragment:



Scheme 3

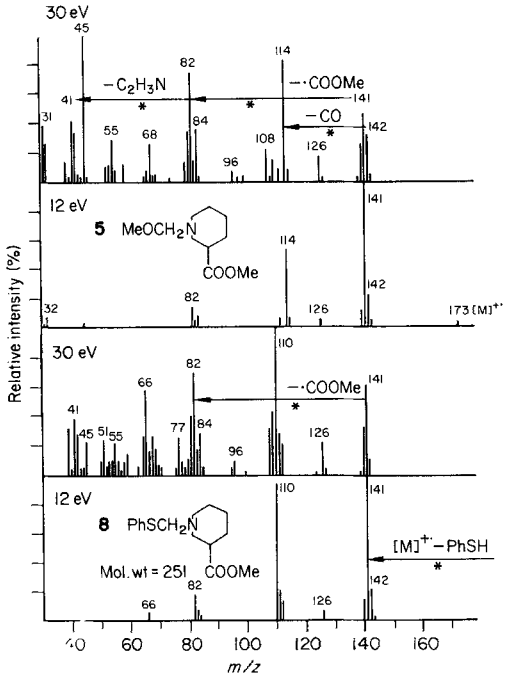
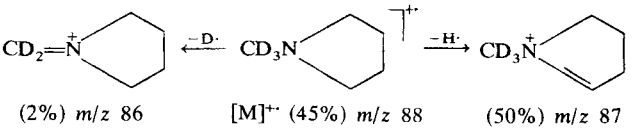


Figure 3. Mass spectra of **5** and **8**.

In this case an internal energy decrease T found from the flat-topped metastable peak width[4] is $T = 0.78$ eV for proline derivatives and $T = 0.74$ eV for aspartic acid derivatives. For proline derivatives the assumption of the favoured new rearrangement structure of the amine fragment is confirmed by dominant formation of a fragment with an endocyclic rather than exocyclic bond in the model compound *N*-trideuteromethylpyrrolidine (**13**). It should be noted that for N-Et, -iso-Pr and -*tert*-Bu azetidine-2-carboxylic esters[5] the amine fragment generated by α-cleavage in the nitrogen atom substituent undergoes slight fragmentation only for *tert*-butyl derivatives,

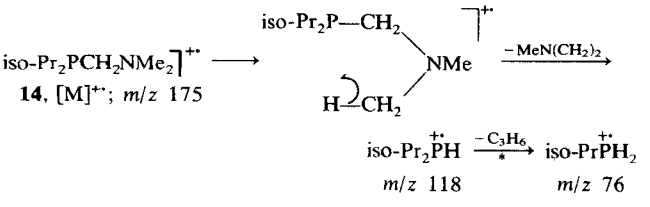


(The relative intensities at 30 eV are given in parentheses)

Scheme 4

with the ejection of ethylene. The metastable ion peak has the usual diffuse pattern. For **3**, **4** and **8** no flat-topped metastable peak is observed since the amine fragment generation is suppressed completely by competitive fragmentations producing *a* and *b* ions.

Thus, the new fragmentation is ensured by the presence of an α-heteroatom (N, O, P, S) in one substituent and a CO_2R type delocalizing group in the α-position of another substituent. If only one of these conditions is fulfilled the fragmentation is poor or is suppressed by competitive processes, e.g. for aminomethylphosphines (**14–16**) (Figs. 6 and 7; Schemes 5 and 7) along with ordinary $[M]^{+\cdot}$ amine cleavage only one of the fragmentation routes found is observed. This can be explained by elimination of a neutral nitrogen-containing particle from $[M]^{+\cdot}$ and involves a 5-membered transition state similar to that for olefinic fragmentation of $[M]^{+\cdot}$ alkylphosphines with long chain substituents.[6] For the oxide (**15**) and the methylol derivative (**20**) (Fig. 6 and Scheme 6)



Scheme 5

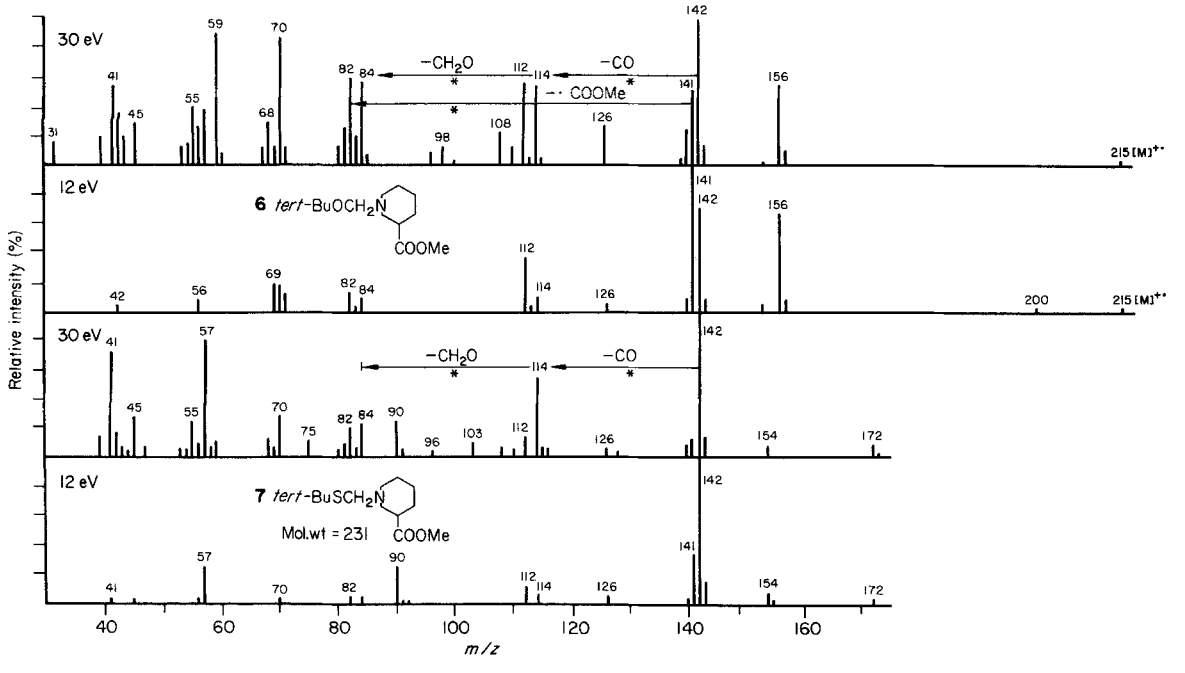
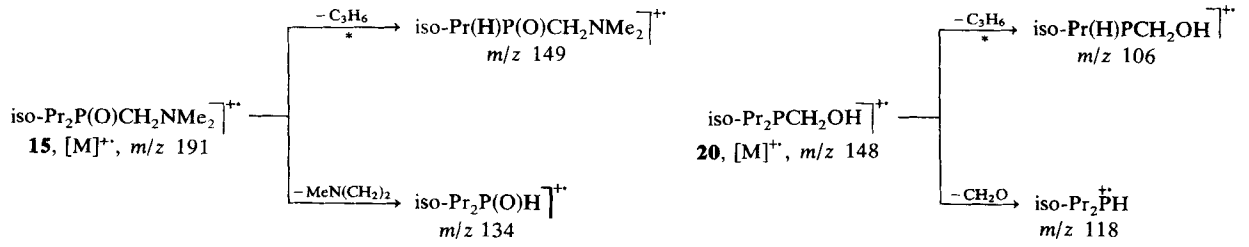


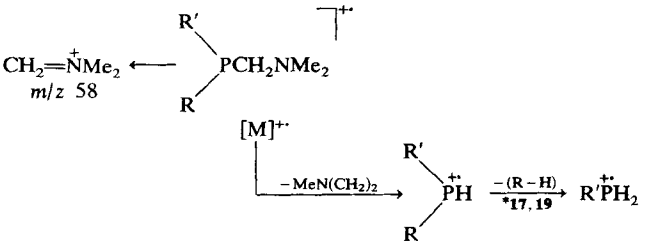
Figure 4. Mass spectra of **6** and **7**.



Scheme 6

olefinic $[M]^{+\cdot}$ fragmentation is observed along with the process described above:

Thus, the absence of olefinic fragmentation and primary elimination of a neutral nitrogen-containing particle from $[M]^{+\cdot}$ are specific for the fragmentation of the aminomethylphosphines and their principal fragmentation routes are described by Scheme 7:



16, R = iso-Pr; R¹ = *tert*-Bu, *m/z* 189 **16**, *m/z* 132
17, R = *tert*-Bu; R' = Ph, *m/z* 223 **17**, *m/z* 166 **17**, *m/z* 110
18, R = iso-Pr; R¹ = Bz, *m/z* 223 **18**, *m/z* 166 **18**, *m/z* 124
19, R = *tert*-Bu; R' = Bz, *m/z* 237 **19**, *m/z* 180 **19**, *m/z* 124

Scheme 7

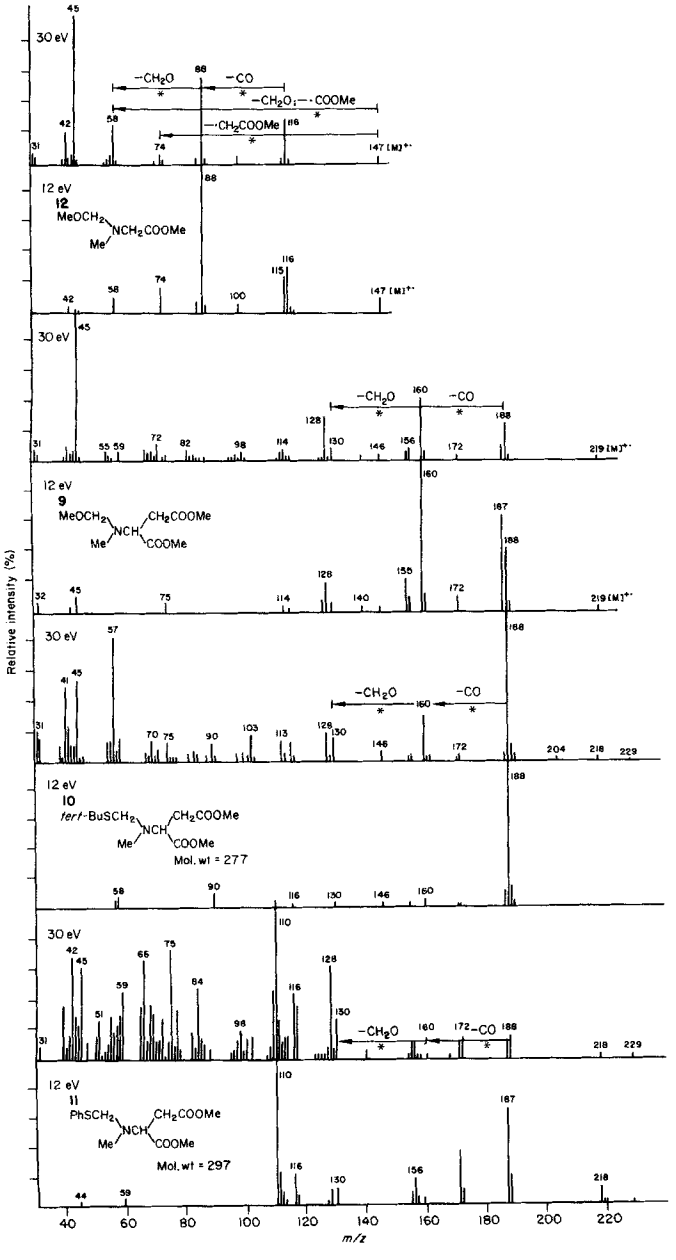


Figure 5. Mass spectra of **9–12**.

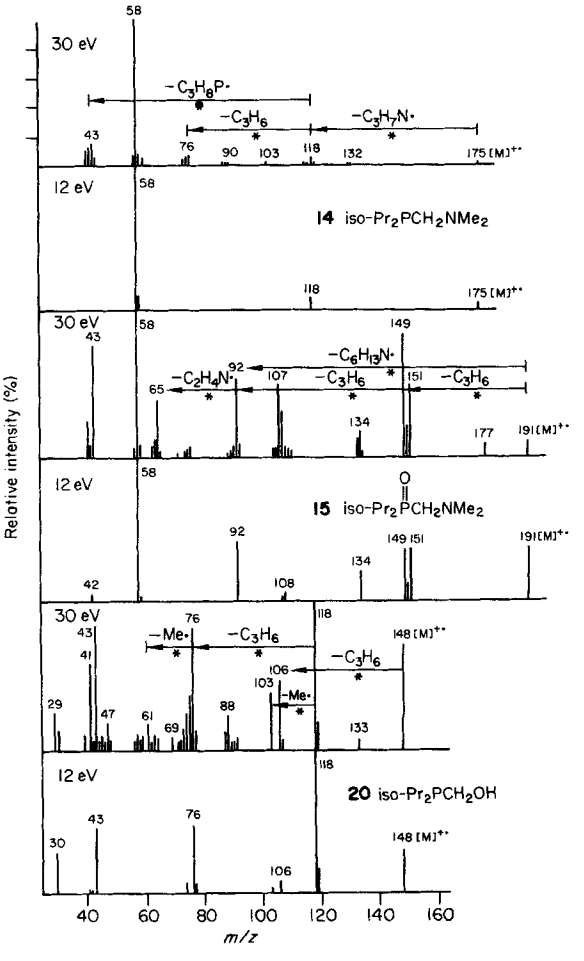


Figure 6. Mass spectra of **14**, **15** and **20**.

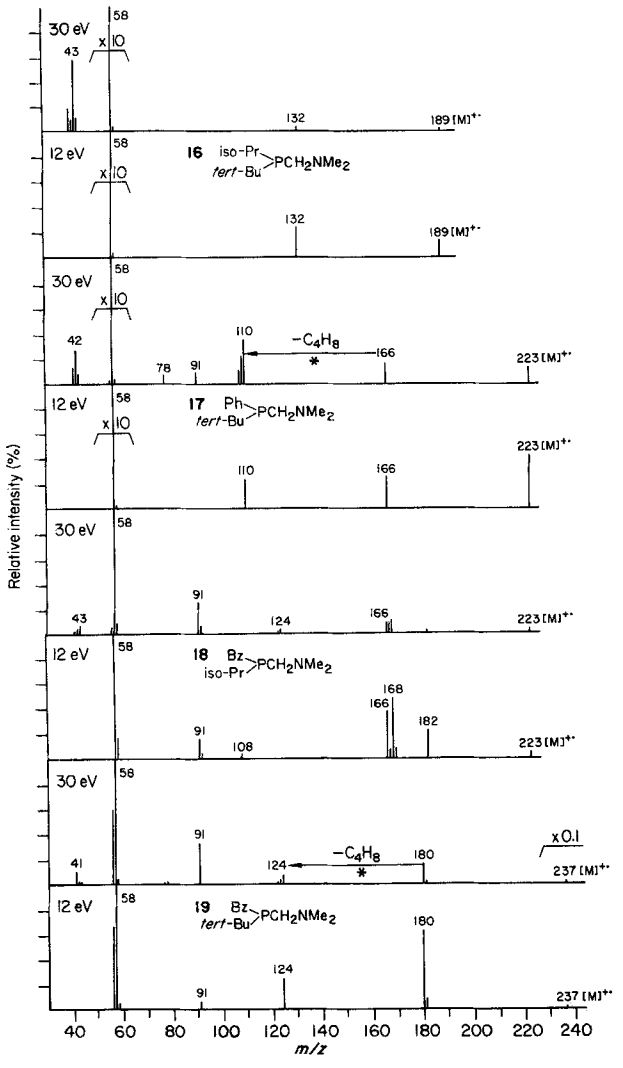
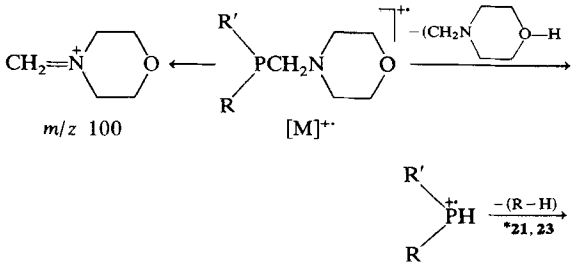


Figure 7. Mass spectra of **16–19**.

In the case of morpholinomethylphosphines (**21–23**) (Fig. 8 and Scheme 8) the fragmentation observed is



21, R = R′ = *tert*-Bu, *m/z* 217 **21**, *m/z* 188 **21**, *m/z* 76
22, R = *tert*-Bu; R′ = iso-Pr, *m/z* 231 **22**, *m/z* 132 **22**, *m/z* 76
23, R = *tert*-Bu; R′ = Ph, *m/z* 165 **23**, *m/z* 166 **23**, *m/z* 110

Scheme 8

more intense with respect to aminomethylphosphines (**14–20**). Fragmentation of compounds **21–23** is the same as that of **16–19** (Scheme 7). The total fragmentation of aminomethyl- and morpholinomethylphosphines investigated can be described by Scheme 9:

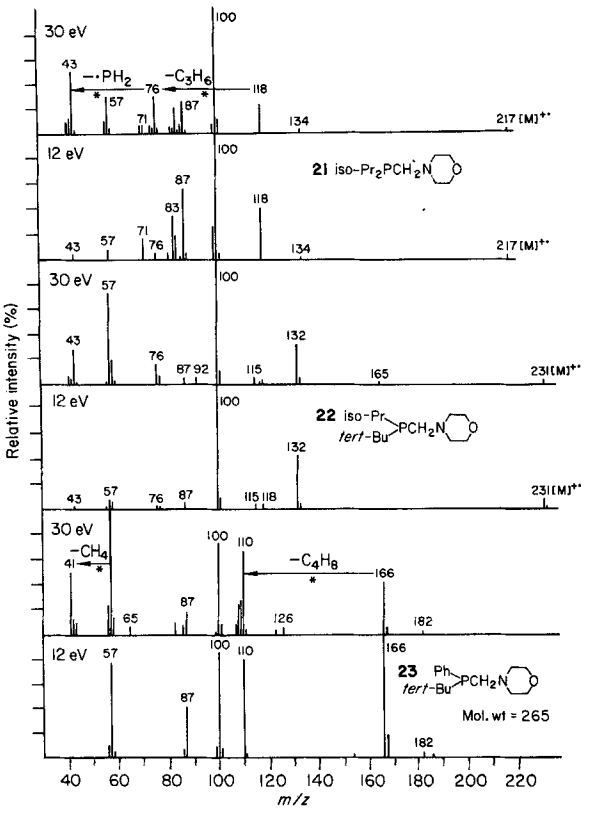
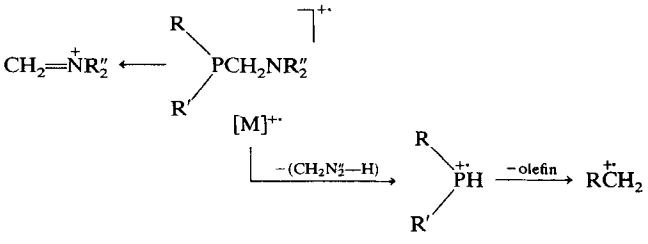


Figure 8. Mass spectra of **21–23**.



Scheme 9

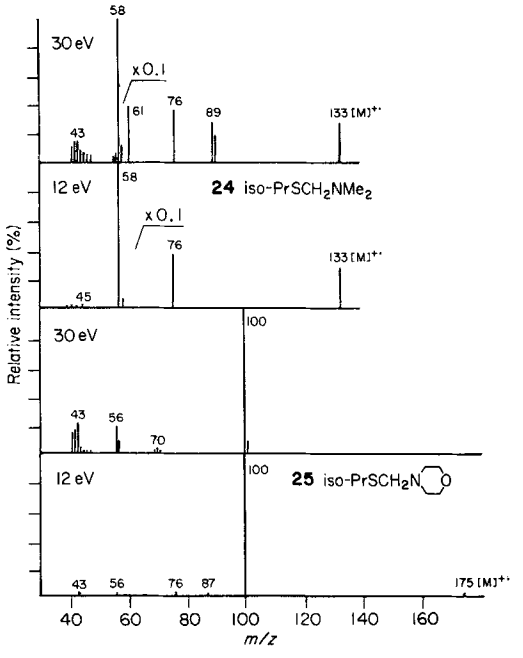
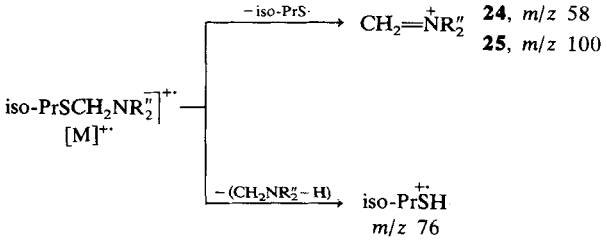


Figure 9. Mass spectra of **24** and **25**.

A decrease in the ionizing energy leads to higher abundance of the $[M-(CH_2NR_2-H)]^+$ ion. This is testimony that the latter is a rearrangement ion.

It should be noted that this unusual fragmentation path is also observed for thioanalogues **24** and **25** (Fig. 9 and Scheme 10):



24: $NR_2''=NMe_2$, *m/z* 133

25: $NR_2''=N$ O, *m/z* 175

Scheme 10

EXPERIMENTAL

The mass spectra were taken on a MX-1303 mass spectrometer with balloon inlet system at ionizing energies of 30 and 12 eV and a temperature of 20–100 °C. The nuclear magnetic resonance spectra were recorded on JEOL JNM-C-60 HL (60 MHz), Tesla BS-487C (80 MHz) and Varian HA-100 (100 MHz) spectrometers. Chemical shifts were referenced from hexamethyldisiloxane (HMDS) δ in ppm, $\Delta\nu$ and J in Hz. Syntheses of phosphines and mercaptans were performed under argon atmosphere. Compound **2** is described in Ref. 7. Compounds **3–5**, **14**, **17–19**, **21** and **23** are reported in Ref. 8.

***N*-Methoxy-*N*-methylaminomethyl-(*S*)-proline methyl ester (1).** B.p. 65 °C (1 mm) (V. F. Rudchenko, unpublished results).

***N*-*Tert*-Butoxymethyl-(*S*)-proline methyl ester (6).** A solution of 1.5 g (13.8 mmol) of *tert*-butylhypochlorite in 30 cm³ of EtCl was added to a solution of 2.88 g (13.6 mmol) of (**2**) in 60 cm³ of EtCl at −35 °C and kept for 12 h. After solvent removal the residue was distilled. 0.8 g (27%) of (**6**) was obtained, b.p. 95–97 °C (4 mm), n_D^{20} 1.4528. ^{1}H NMR (CCl_4), δ: 1.12 (Me_3C), 1.75 (β-CH_2), 2.91 (α-CH_2), 3.54 (CH), 3.62 (MeO), 4.24 (CH_2N, $\Delta\nu = 10$, J *gem* = 9).

***N*-*tert*-Butylthiomethylproline *S*-(−)-methyl ester (7).** 0.85 g (5 mmol) of **5** was added dropwise to 0.45 g (5 mmol) of *tert*-butylmercaptan. The mixture was kept for 12 h, methanol produced was evaporated, and the residue distilled. 0.6 g (52%) of **7** was obtained, b.p. 80 °C (1 mm), $[\alpha]_{546}^{20} = -86.8°$ (*c*. 1.15 MeOH) Found: C, 57.1; H, 9.13; N, 5.91%. $C_{11}H_{21}O_2NS$. Calc: C, 57.14; H, 9.09; N, 6.06%. ^{1}H NMR (CCl_4), δ: 1.25 (Me_3C), 1.86 (β-CH_2), 2.65 (α-CH_2), 3.39 (CH), 3.59 (MeO), 4.03 (CH_2N, $\Delta\nu = 20$, $J_{gem} = 13$).

***N*-Phenylthiomethylproline *S*-(−)-methyl ester (8).** Similarly 0.75 g (6.8 mmol) of thiophenol and 1.2 g (6.9 mmol) of **5** gave 1.29 g (75%) of **8**, b.p. 124–125 °C (1 mm), $[\alpha]_{546}^{20} = -36.4°$ (*c*. 1.48 MeOH). Found: C, 61.88; H, 6.75; N, 5.51%. $C_{13}H_{27}O_2Ns$. Calc.: C, 62.15; H, 6.77; N, 5.57%. ^{1}H NMR (C_6F_6), δ: 1.78 (β-CH_2), 2.70 (α-CH_2), 3.42 (CH), 3.51 (MeO), 4.48 (CH_2N, $\Delta\nu = 14.4$, $J_{gem} = 13$).

***N*-Methyl-*N*-methoxymethyl aspartic acid dimethyl ester (9).** A solution of 13.3 g (76 mmol) of the dimethyl ester of *N*-methylaspartic acid was prepared analogously to **2**, b.p. 92 °C (3 mm), n_D^{20} 1.4372. ^{1}H NMR (CCl_4), δ: 1.44 (NH), 2.28 (MeN), 2.48 (CH_2, $\Delta\nu = 17$, $J_{gem} = 15$), 3.35 (CH, $J(H_ACH) = 7.5$, $J(H_BCH) = 6.5$), 3.58 (MeO^1), 3.63 (MeO^2)) in 15 cm³ of abs. MeOH was added to 2.3 g (76 mmol) of α-polyoxymethylene in 30 cm³ abs. MeOH at −30 °C. The mixture was kept at 15 °C for 15 h, MeOH evaporated and 12 cm³ of benzene added. After removal of benzene the residue was distilled. 10.2 g (61%) of **9** was obtained, b.p. 86 °C (1 mm), n_D^{20} 1.4410. ^{1}H NMR (CCl_4), δ: 2.34 (MeN), 2.6 (CH_2, $\Delta\nu = 22$, $J_{gem} = 16$), 3.09 (MeO), 3.56 ($COOMe^1$), 3.6 ($COOMe^2$), 3.74 (CH, $J(H_ACH) = J(H_BCH) = 7.5$), 3.97 ($CH_2N$).

***N*-Methyl-*N*-*tert*-butylthiomethyl aspartic acid dimethyl ester (10).** Analogously to the synthesis of **7** 0.61 g (6.8 mmol) of *tert*-butylmercaptan and 1.5 g (6.8 mmol) of **9** gave 1.4 g (74%) of **10**, b.p. 135–137 °C (1 mm). ^{1}H NMR (C_6H_6), δ: 1.14 (Me_3C), 2.16 (MeN), 2.51 (CH_2, $\Delta\nu = 28$, $J_{gem} = 16$), 3.22 (MeO^1) 3.23 (MeO^2), 3.75 (CH_2N, $\Delta\nu = 15.5$, $J_{gem} = 14$), 4.08 (CH, $J(H_ACH) = 7$, $J(H_BCH) = 8$).

***N*-Methyl-*N*-phenylthiomethyl aspartic acid dimethyl ester (11).** Similarly 0.7 g (3.2 mmol) of **9** and 0.35 g (3.2 mmol) of thiophenol gave 0.9 g (96%) of **11**, b.p. 167 °C (1 mm). ^{1}H NMR (CCl_4), δ: 2.32 (MeN), 2.54 (CH_2, $\Delta\nu = 24$, $J_{gem} = 16$), 3.46 (MeO^1) 3.59 (MeO^2), 3.83 (CH, $J(H_ACH) = J(H_BCH) = 7.5$), 4.2 ($CH_2N$), 7.2 (Ph). Found: C, 56.4; H, 6.23; N, 4.69%. $C_{14}H_{19}O_4$ NS, Calc.: C, 56.5; H, 6.39; N, 4.71%.

***N*-Methoxymethyl sarcosine methyl ester (12).** Analogously to the synthesis of **9** 1.95 g (65 mmol) of α-polyoxymethylene in 25 cm³ of abs. MeOH and 6.7 g (65 mmol) of sarcosine methyl ester (b.p. 33–34 °C (13 mm). ^{1}H NMR (CCl_4), δ: 1.39 (HN), 2.27 (MeN), 3.16 (CH_2), 3.6 (MeO)) gave 3.8 g (40%) of **12**, b.p. 44–46 °C (1 mm), n_D^{20} 1.4242. ^{1}H NMR (CCl_4), δ: 2.39 (MeN), 3.15 (MeO), 3.26 (CH_2), 3.57 (MeOOC), 3.94 (O—CH_2—N).

***N*-Trideuteromethylpyrrolidine (13).** 2.25 g (15.5 mmol) of CD_3I was added to 1.1 g (15.4 mmol) of pyrrolidine in 5 cm³ of ether at −30 to −40 °C. The precipitate was treated with 3 cm³ of 50% KOH solution. The ethereal layer was decanted, dried over KOH, ether evaporated and the residue distilled. 0.1 g (7%) of **13** was obtained, b.p. 79 °C.

Oxymethyldiisopropylphosphine (20). A mixture of 3.28 g (28 mmol) of iso-Pr_2PH and 0.83 g (28 mmol)

of paraform was heated (bath temp. 90 °C) until the latter dissolved completely. After evaporation 2.7 g (66%) of **20** was obtained, colourless liquid, b.p. 59 °C (3 mm), n_D^{20} 1.4928. ^{1}H NMR (Freon 113), δ: 1.06 (Me, J(MeH) = 7, J(MeP) = 12.5), 1.83 (HCP, J(HCP) = 2.5), 3.74 (HO), 3.91 (CH_2).

Dimethylaminomethylisopropyl(*tert*-butyl)phosphine (21). By the method given in Ref. 8, 3 g (23 mmol) of iso-*Pr*(*tert*-Bu)PH and 2.5 g (29.7 mmol) of bis-dimethylaminomethane gave 3.5 g (82%) of **21**, b.p. 45 °C (1 mm). ^{1}H NMR (C_6F_6), δ: 1.02 (Me_3C, J(HCCP) = 11.8), 1.1 (Me_A, $J(Me_AH) = J(Me_BH) = 7$ $J(Me_AP) = 16.8$), 1.04 (Me_B, $J(Me_BP) = 11.5$), 1.63 (CH, J(HCP) = 2.5), 2.33 (MeN), 2.54 (CH_2, J(HCP) = 2.5).

***N*-Morpholinomethylisopropyl(*tert*-butyl)phosphine (22).** Similarly 3.6 g (27 mmol) of iso-Pr(*tert*-Bu)PH and 4.1 g (31 mmol) of methoxymethylmorpholine gave 5.6 g (89%) of **22**, b.p. 86 °C (1 mm). ^{1}H NMR (C_6H_6), δ: 0.96 (Me_3C, J(HCCP) = 11), 0.99 (Me_B, $J(Me_BCH) = 7$, $J(Me_BP) = 7.5$), 1.08 (Me_A, $J(Me_ACH) = 7$, $J(Me_AP) = 12.5$), 1.49 (CH), 2.34 (CH_2, J(HCP) = 2.5), 2.37 (CH_2N), 3.5 (CH_2O).

Dimethylaminomethylisopropylsulfide (24). By the method given in Ref. 8, 0.8 g (10 mmol) of iso-PrSH and 1.07 g (10 mmol) of bisdimethylaminomethane gave 0.52 g (37%) of **24**, b.p. 43–45 °C (20 mm). ^{1}H NMR (C_6H_6), δ: 1.08 (Me, J(MeCH) = 6.5), 2.05 (MeN), 2.61 (CH), 3.62 (CH_2).

***N*-Morpholinomethylisopropylsulfide (25).** By the method given in Ref. 8 0.6 g (7 mmol) of iso-PrSH and 0.92 g (7 mmol) of methoxymethylmorpholine gave 0.59 g (43%) of **25**, b.p. 100 °C (10 mm). ^{1}H NMR (C_6H_6), δ: 1.07 (Me, J(MeCH) = 6.5), 2.22 (CH_2), 2.51 (CH), 3.42 (CH_2O), 3.47 (CH_2).

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