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Fragmentation of Some 4*H*-Pyran-4-one and Pyridin-4-one Derivatives under Electron Impact

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Abstract—Fragmentation of 13 compounds of the 4*H*-pyran-4-one and pyridin-4-one series under electron impact involves formation of rearrangement ions stabilized by multiple bonds and oxygen atoms (mostly $[RC{\equiv}O]^+$ and $RCH{=}OR'^+$), as well of neutral molecules with low enthalpies of formation (CO, H_2O, CH_2O, CO_2, $CH_2{=}C{=}O$, C_3O_2, and RCOOH; R = H, Me, HC≡C, HOC≡C).

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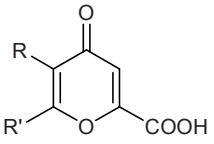
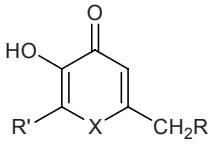
Functionally substituted compounds of the 4*H*-pyran-4-one series exhibit versatile biological activity [1–4]. Unlike 2*H*-pyran-2-ones whose mass spectra have been extensively studied [5], only a few publications are available on the fragmentation of 4*H*-pyran-4-ones [6–9]. Among these, studies on the fragmentation of unsubstituted γ-pyrone [6] and comenic acid [7] may be noted. The fragmentation paths of comenic acid were confirmed by analysis of the corresponding metastable ion peaks. However, our interpretation based on the general structure–fragmentation relations and thermochemical parameters of fragment ions and their neutral analogs [10] somewhat differed from that proposed in [7].

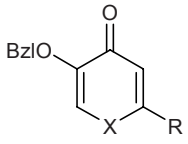
In the present work we examined fragmentation under electron impact of substituted 4*H*-pyran-4-one and pyridine-4-one derivatives **Ia**–**Id**, **IIa**–**IId**, **IIIa**–**IIIc**, **IV**, and **V**. Fragmentation paths of pyranones **Ia**–**Id** having a carboxy group turned out to be the most interesting. The presence in their molecules of a large number of oxygen atoms and little hydrogen gives rise to unusual fragmentation processes. Replacement of the hydroxy group in position *5* of **Ia** by methoxy group (compound **Ib**) does not change the fragmenta-



Ia–Id

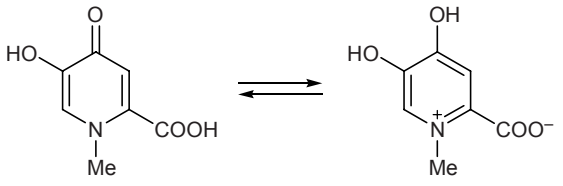


IIa–IId

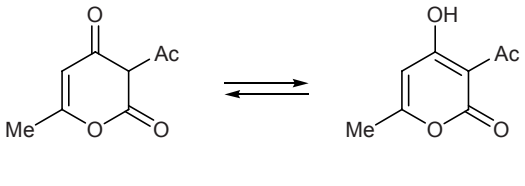


IIIa–IIIc

I, R = HO (**a**, **c**, **d**), MeO (**b**); R′ = H (**a**, **b**), HO (**c**), Br (**d**); **II**, R = HO (**a**, **b**, **d**), Cl (**c**); R′ = H (**a**, **c**, **d**), I (**b**); **III**, R = HOCO (**a**), $HOCH_2$ (**b**, **c**); **IIa**–**IIc**, **IIIa**, **IIIb**, X = O; **IId**, **IIIc**, X = NH.

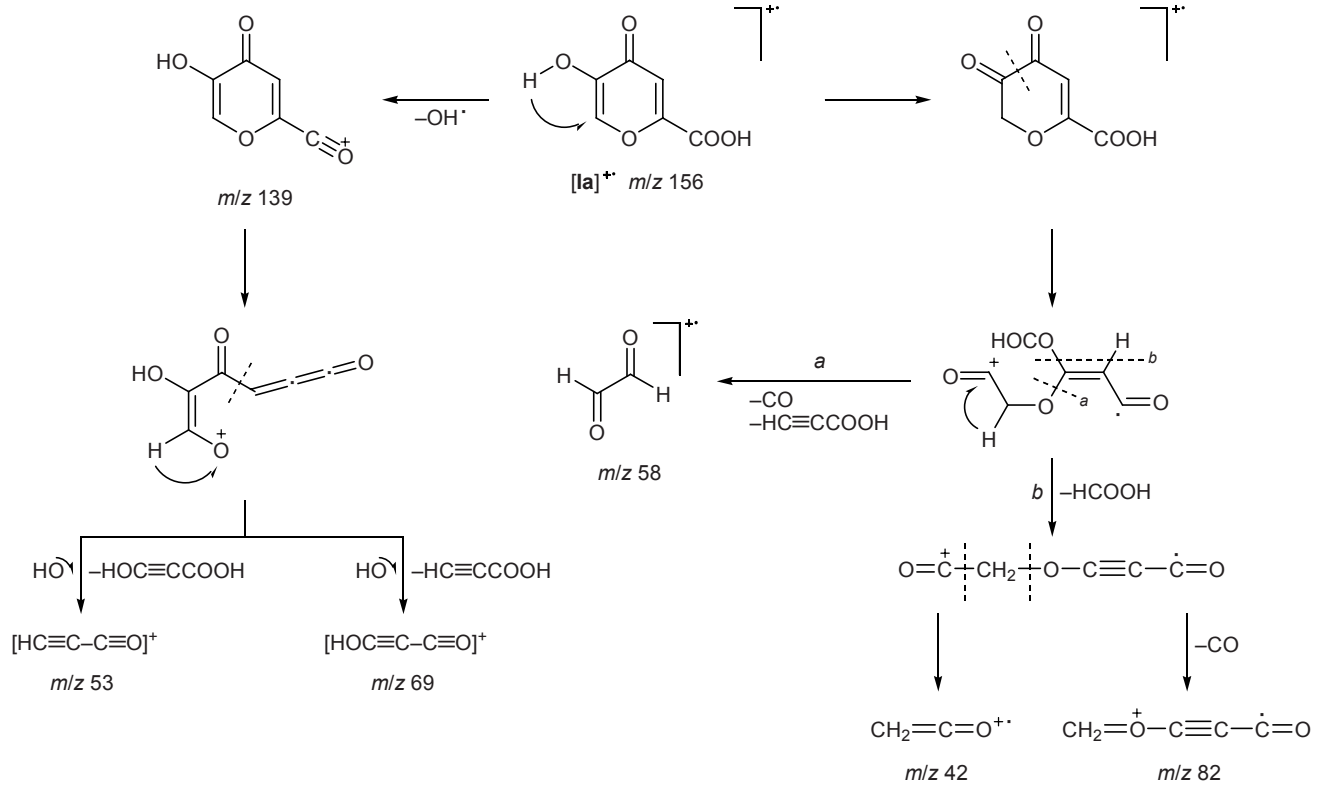


IVa **IVb**



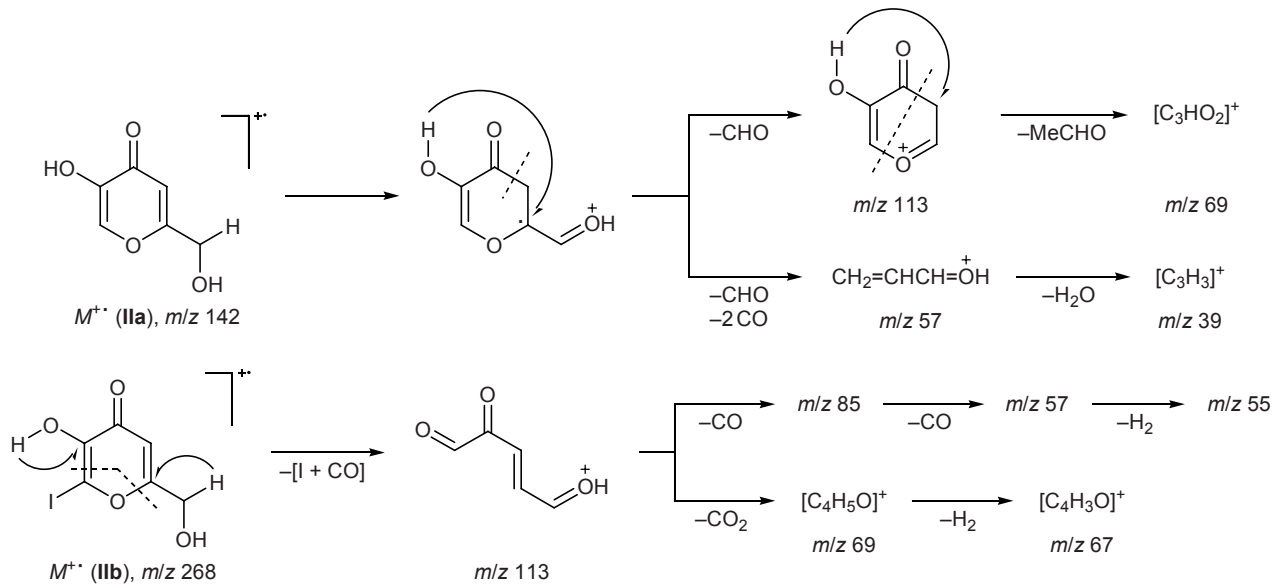
Va **Vb**

Scheme 1.

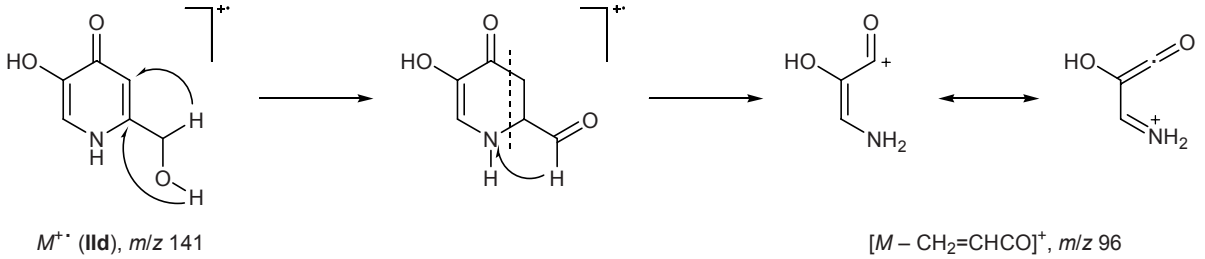


tion pattern to a considerable extent. The mass spectra contain the following ion peaks $[M - COOH]^+$ (**A**), $[\mathbf{A} - CH_2O]^+$, $[\mathbf{A} - CH_2O - CH_2{=}C{=}O]^+$, $[\mathbf{A} - 2CO]^+$, $[\mathbf{A} - C_3H_4O]^+$. Introduction of the second hydroxy group into the 6-position (acid **Ic**) leads to appearance of $[M - COOH]^+$, $[M - 2CO]^{+\cdot}$, $[M - COOH - CO]^+$ or $[M - 2CO - OH]^+$ (*m*/*z* 99), $[M - 2CO - H_2O]^{+\cdot}$, and $[M - 3CO]^{+\cdot}$ ion peaks in the mass spectrum. Apart from elimination of CO molecules, bromo-substituted pyranone **Id** is characterized by new fragmentation paths, including liberation of thermodynamically stable bromine atom and HBr molecule. The formation

Scheme 2.



Scheme 3.



$M^{+\cdot}$ (**IId**), *m*/*z* 141 $[M - CH_2{=}CHCO]^+$, *m*/*z* 96

of HCO and CH_2O species was also unusual. The following ion peaks were detected in the mass spectrum of **Id**: $[M - CO]^{+\cdot}$, $[M - 2CO]^{+\cdot}$, $[M - 3CO]^{+\cdot}$ (**B**), $[M - Br]^+$ (**C**), $[\mathbf{B} - CH_2{=}O]^{+\cdot}$, $[\mathbf{B} - Br]^+$, $[\mathbf{B} - HBr]^{+\cdot}$, $[\mathbf{A} - BrO]^+$ (*m*/*z* 55^+), $[\mathbf{C} - CO]^+$, $[\mathbf{C} - CO - CHO]^{+\cdot}$, $[\mathbf{C} - CO - CH_2{=}C{=}O]^+$. The mass spectra of all compounds **Ia**–**Id** characteristically contained $[C_3HO_2]^+$ ion peak with *m*/*z* 69. The formation of $[C_3HO_2]^+$ ion is typical of acyclic 1,3-diketones [11]. All fragment ions are formed after opening of the pyran ring. The fragmentation process also involves hydrogen shifts and skeletal rearrangements (Scheme 1).

In going from carboxylic acids **Ia**–**Id** to alcohols **IIa**–**IId**, the intensity of the molecular ion peak increases, and new fragmentation pathways appear (Scheme 2). The ion with *m*/*z* 69 derived from compound **IIb** has a different composition, $[C_4H_5O]^+$ rather than $[C_3HO_2]^+$ formed from acids **I**. This follows from the fact that the $[C_4H_5O]^+$ ion undergoes subsequent dehydrogenation, which is impossible for $[C_3HO_2]^+$. An unusual process is simultaneous elimination of iodine radical and CO. Iodine atom is a very stable species; therefore, the value $\Sigma\Delta H_f^o[I^{\cdot} + CO]$ is as low as –2.9 kJ/mol [10], whereas the enthalpy of formation of $I{-}C^{\cdot}{=}O$ as a single species is about 25 kJ/mol (estimated on the basis of the $\Delta H_f^o[BrC^{\cdot}{=}O]$ value equal to 10.5 kcal/mol [10]), so that elimination of ICO is less thermodynamically favorable.

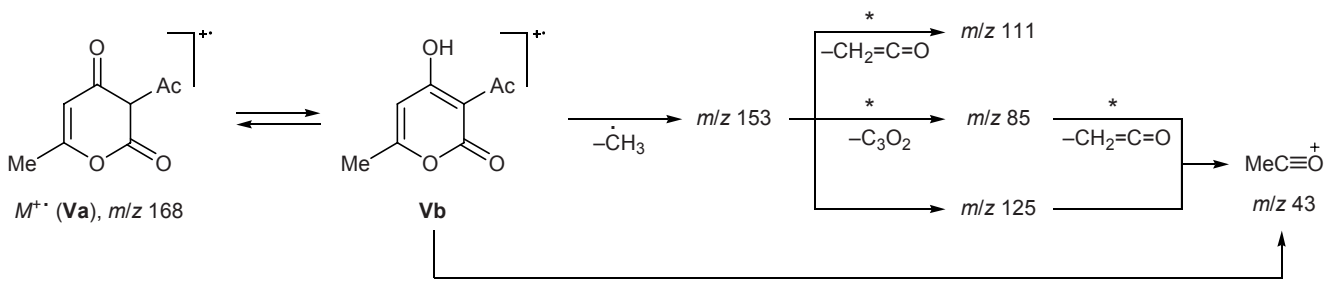
Compound **IIc** was the only among the examined ones where a weak CH_2–Cl bond is present in the side chain, and fragmentation of its molecular ion begins with elimination of chlorine. All other ions are formed from the $[M - Cl]^+$ ion (**D**): $[\mathbf{D} - CO]^+$, $[\mathbf{D} - 2CO]^+$, $[\mathbf{D} - 2CO - H_2]^+$, $[\mathbf{D} - 3CO]^+$ or $C_3H_5^+$, $[C_3H_5 - H_2]^+$ (*m*/*z* 39), $[\mathbf{D} - CH_2{=}C{=}O]^+$, $[\mathbf{D} - CO - CH_2{=}C{=}O]^+$, and $[\mathbf{D} - CO - C_3H_3]^{+\cdot}$ or $[CHOCHO]^{+\cdot}$ (*m*/*z* 58).

Decomposition of the molecular ion of pyridin-4-one **IId** involves initial migration of two hydrogen atoms from the side chain (Scheme 3), which is well known for nucleotides [10]; therefore, the subsequent fragmentation of the ring differs from that observed for pyranones **IIa** and **IIb**. In addition, unlike other derivatives of kojic acid, $[M - H]^+$ ion ($RCH{=}O^+H$) is formed.

Compounds **IIIa**–**IIIc** having a benzyloxy group in the 5-position displayed radically different mass spectra. In these cases, no ring cleavage occurs, but the main fragmentation pathway is that leading to the $C_7H_7^+$ ion; the contribution of this pathway (together with subsequent decomposition of the $C_7H_7^+$ ion) amounts to 80% of the total ion current.

The behavior of the nitrogen-containing analog of comenic acid (compound **IV**) under electron impact resembles its thermal or thermocatalytic decomposition: its undergoes decarboxylation, followed by ionization of the resulting fragments to give ions with *m*/*z* 125 and 44 ($CO_2^{+\cdot}$). Analogous process is not typical of pyranones containing a carboxy group. Presumably, pyridinone **IVa** on heating is transformed into zwitterionic structure **IVb**.

Scheme 4.



$M^{+\cdot}$ (**Va**), *m*/*z* 168 **Vb**

On the whole, fragmentation of the examined compounds under electron impact demonstrates many interesting rearrangement processes leading to ions stabilized by multiple bonds and oxygen atoms (ions like $RC{\equiv}O^+$ are formed most frequently) and neutral species with low enthalpies of formation (CO, C_3O_2, CO_2, $CH_2{=}C{=}O$, R′COOH, R″CH=O, H_2O) or such radicals as $I^{\cdot}$, $Br^{\cdot}$, $^{\cdot}CHO$, and $^{\cdot}COOH$.

Dehydroacetic acid (**V**) may be regarded as both 4- and 2-oxopyran, and it can exist as two tautomers **Va** and **Vb**. The mass spectrum of **V** contained no ion peaks assignable to structure **Va** (Scheme 4). Here, the most important was the absence of peak from the $[M - CH_2{=}C{=}O]^{+\cdot}$ ion which is typical of keto esters having an acetyl moiety [12]. On the other hand, abundant $[M - CH_3]^+$ ion was detected, which is more consistent with structure **Vb** (cf. the data for compound **IIc** having a weak bond in the side chain).

Metastable ion peaks (*m**) providing information on the corresponding mother and daughter ions were also observed in the mass spectra (see Experimental). Unfortunately, *m** ion peaks relating $CH_3C{\equiv}O^+$ ions to parent heavier ions could not be detected, for the corresponding *m*/*z* values are too low. The $CH_3C{\equiv}O^+$ ion originates from the ring fragment including the C^6 atom rather than from separate acetyl group. Such process is typical, e.g., of 2-methylfurans [10]. The absence of structure **Va** may be rationalized assuming that (1) sample vaporization is accompanied by isomerization of neutral molecule **Va** to structure **Vb** or (2) this transformation occurs with ionized species.

To conclude, it should be noted that, except for benzyloxy-substituted compounds **IIIa**–**IIIc**, the fragmentation patterns of 4*H*-pyran-4-one and pyridin-*4*-one derivatives are determined by decomposition of the heteroring. The mass spectra of such compounds are quite specific. Even small structural variations, e.g., replacement of carboxy group in position *2* by hydroxymethyl group, give rise to a different fragmentation pathway. The fragmentation of compounds **Ia** and **Ic** is accompanied by skeletal rearrangement with migration of the hydroxy group, while rearrangement in the fragmentation of **Id** leads to the formation of $BrO^{\cdot}$ species. Elimination of a neutral species with a molecular weight of 155 a.m.u. from the molecular ion of **IIb** was interpreted in terms of simultaneous formation of $I^{\cdot}$ radical and CO molecule rather than of a single $IC^{\cdot}{=}O$ radical, for the latter process is less thermodynamically favorable by about 28 kJ/mol.

EXPERIMENTAL

Comenic acid (**Ia**, 5-hydroxy-4-oxo-4*H*-pyran-2-carboxylic acid) was synthesized according to the procedure described in [13] from kojic acid in three steps (protection of the hydroxy group in position *5* of the pyran ring, oxidation of the benzyloxy derivative with Jones' reagent, and deprotection in acid medium). 5-Methoxy-4-oxo-4*H*-pyran-2-carboxylic acid (**Ib**) [14], 5,6-dihydroxy-4-oxo-4*H*-pyran-2-carboxylic acid (**Ic**) [15], and 6-bromo-4-oxo-4*H*-pyran-2-carboxylic acid (**Id**) [16] were synthesized by known methods.

Kojic acid (**IIa**, 5-hydroxy-2-hydroxymethyl-4*H*-pyran-4-one) was a commercial product (Avocado, UK). 5-Hydroxy-2-hydroxymethyl-6-iodo-4*H*-pyran-4-one (**IIb**) [17], 2-chloromethyl-5-hydroxy-4*H*-pyran-4-one (**IIc**) [1], 5-hydroxy-2-hydroxymethylpyridin-4(1*H*)-one (**IId**) [18], 5-benzyloxy-4-oxo-4*H*-pyran-2-carboxylic acid (**IIIa**) and 5-benzyloxy-2-hydroxymethyl-4-oxo-4*H*-pyran-2-carboxylic acid (**IIIb**) [19], 5-benzyloxy-2-hydroxymethylpyridin-4(1*H*)-one (**IIIc**) [20], 5-hydroxy-1-methyl-4-oxo-1,4-dihydropyridine-2-carboxylic acid (**IV**) [21], and 3-acetyl-4-hydroxy-6-methyl-2*H*-pyran-2-one (**V**, dehydroacetic acid) [22] were synthesized by known methods.

The mass spectra (electron impact, 70 eV) were recorded on an MKh-1330 mass-spectrometer coupled with a gas chromatograph. The mass spectrum of dehydroacetic acid (**V**) was also recorded at a high resolution using an AEI MS-9 instrument. Below are given *m*/*z* values and relative intensities (I_{rel}, %) of ions with I_{rel} no less than 5%. The intensity of the base peak relative to the total ion current (%∑) is also given.

Ia: 156 (71) $[M]^{+\cdot}$, 139 (23), 128 (92), 110 (42), 82 (46), 69 (100, 14.1%∑), 58 (20), 55 (56), 53 (33), 45 (65), 42 (90), 41 (71).

Ib: 170 (52) $[M]^{+\cdot}$, 152 (13), 125 (22), 95 (100, 35.2%∑), 83 (9), 69 (33), 53 (35), 41 (10), 39 (10).

Ic: 172 (46) $[M]^{+\cdot}$, 127 (5), 116 (16), 99 (41), 98 (10), 88 (45), 71 (100, 20.0%∑), 70 (35), 69 (35), 60 (19), 54 (10), 53 (68), 44 (29), 42 (15), 40 (25).

Id: 236/234 (42/42) $[M]^{+\cdot}$, 208 (4.5), 206 (4.4), 155 (26), 152 (6.0), 150 (6.3), 127 (5.5), 122 (4.5), 120 (5.0), 99 (30), 98 (13), 85 (7.4), 71 (45), 70 (13), 69 (50), 56 (5.0), 55 (18), 54 (16), 53 (100, 19.7%∑), 45 (26), 42 (15), 41 (21).

IIa: 142 (100, 27.0∑) $[M]^{+\cdot}$, 113 (41), 85 (9), 69 (69), 57 (34), 55 (25), 53 (9), 39 (53), 30 (31).

IIb: 268 (100, 43.7%∑) $[M]^{+\cdot}$, 127 (5.5), 113 (5.5), 85 (17), 69 (11), 67 (16), 59 (5.0), 57 (24), 55 (17), 53 (6.2), 45 (7.1), 43 (10), 42 (5.2).

IIc: 162/160 (16/55) $[M]^{+\cdot}$, 125 (74), 97 (45), 69 (39), 68 (13), 67 (39), 58 (13), 55(16), 42 (13), 41 (64), 40 (13), 39 (100, 25.0%∑).

IId: 141 (100, 25.8%∑) $[M]^{+\cdot}$, 140 (57), 123 (36), 96 (57), 91 (8.1), 80 (4.8), 68 (54), 55 (12), 39 (34).

IIIa: 246 (7.0) $[M]^{+\cdot}$, 95 (4.5), 92 (6.0), 91 (100, 80.0%∑), 65 (8.3).

IIIb: 232 (16) $[M]^{+\cdot}$, 126 (8.0), 95 (8.2), 92 (8.1), 91 (100, 62.9%∑), 65 (11), 39 (7.8).

IIIc: 231 (8.0) $[M]^{+\cdot}$, 92 (7.3), 91 (100, 79.4%∑), 65 (7.6).

IV: 169 (42) $[M]^{+\cdot}$, 141 (15), 125 (100, 32.6%∑), 108 (4.5), 97 (31), 82 (13), 67 (11), 55 (18), 44 (73).

V: 168 (63) $[M]^{+\cdot}$, 153 (40), 125 (40), 111 (8.0), 98 (13), 85 (47), 69 (20), 55 (7.3), 43 (100, 30.0%∑), 42 (8.0), 39 (8.7); high-resolution mass spectrum: 168 (100) $[M]^{+\cdot}$, 153 (63), 125 (33), 111 (15), 99 (10), 98 (19), 85 (80), 84 (17), 69 (30), 55 (10), 43 (93), 42 (10), 39 (10).

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