

ZASTOSOWANIA SPEKTROMETRII MAS W CHEMII ORGANICZNEJ I BIOCHEMII

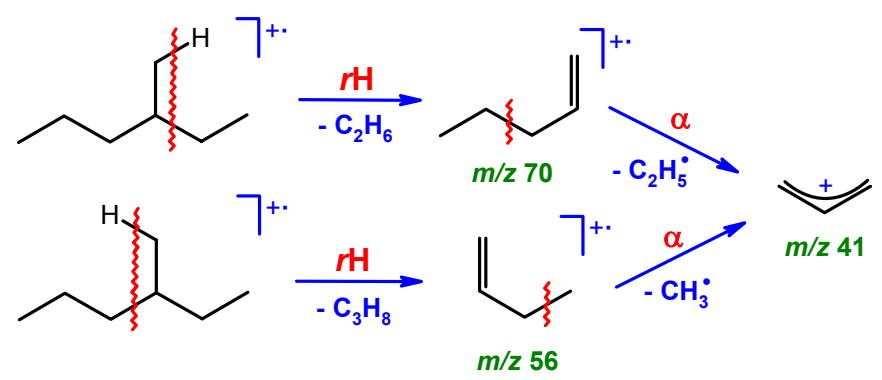
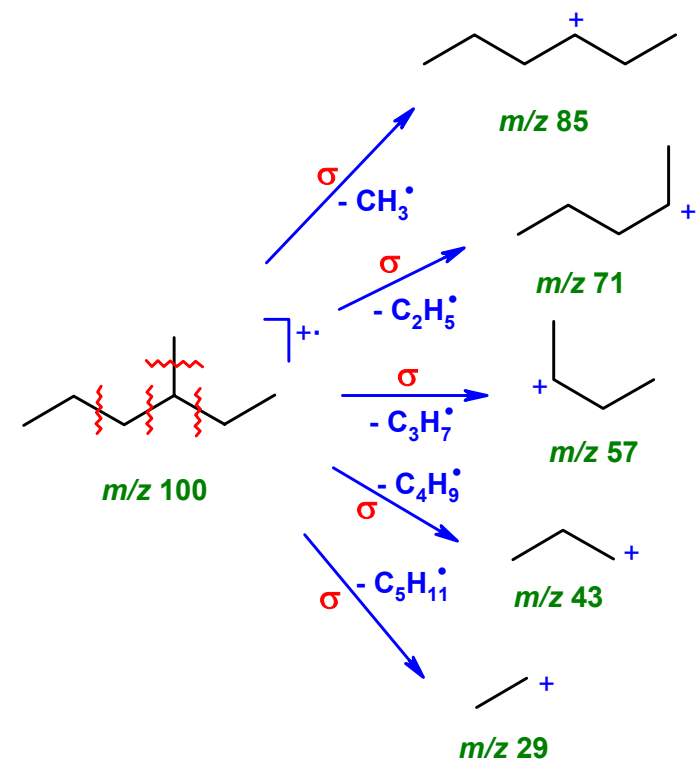
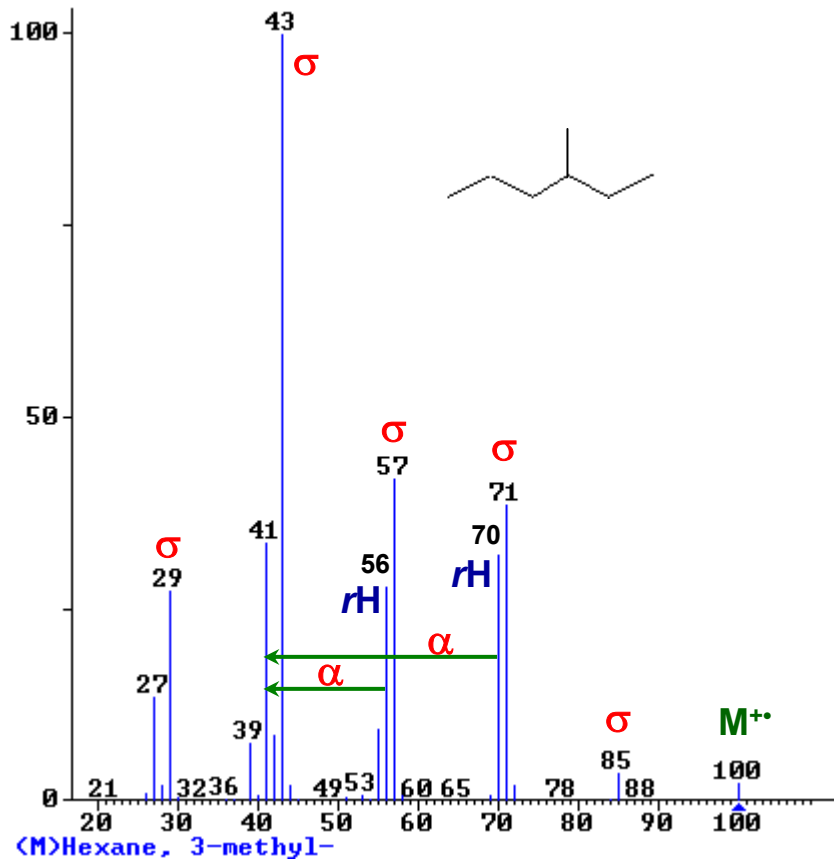
WYKŁADY 13 i 14

ANALIZA FRAGMENTACJI WYBRANYCH ZWIĄZKÓW

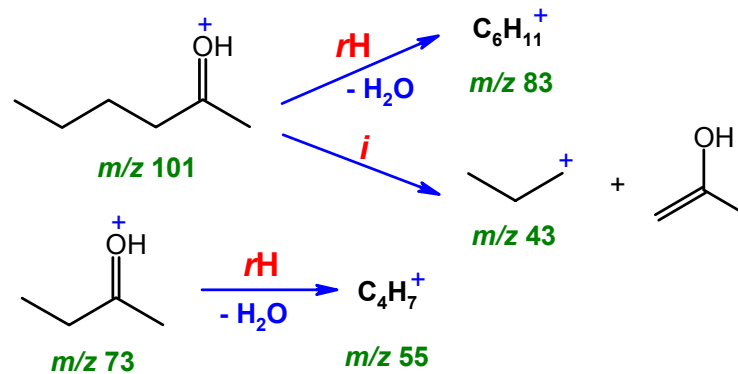
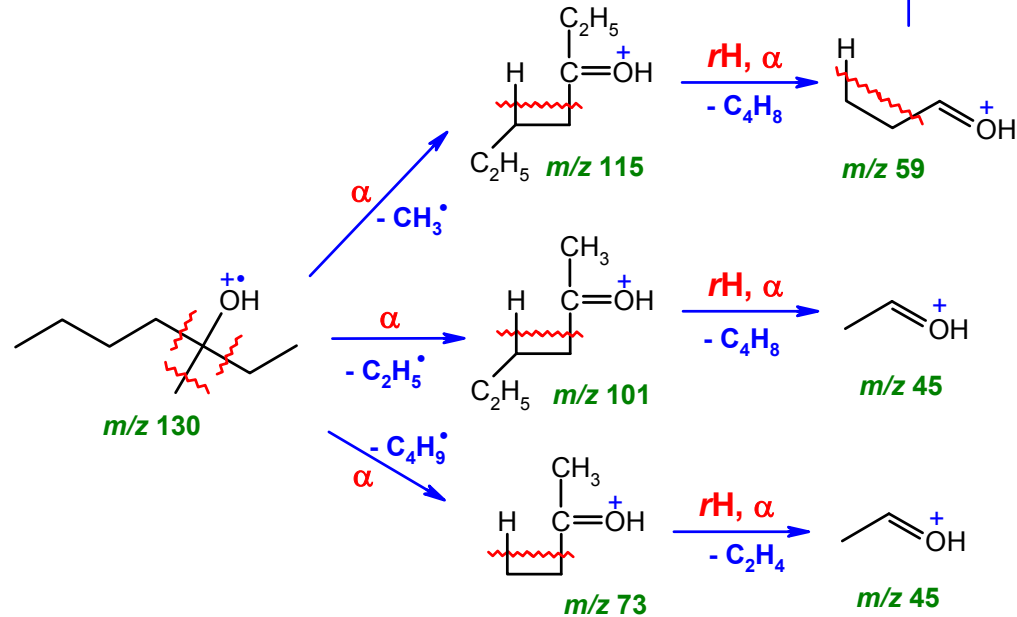
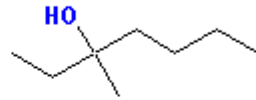
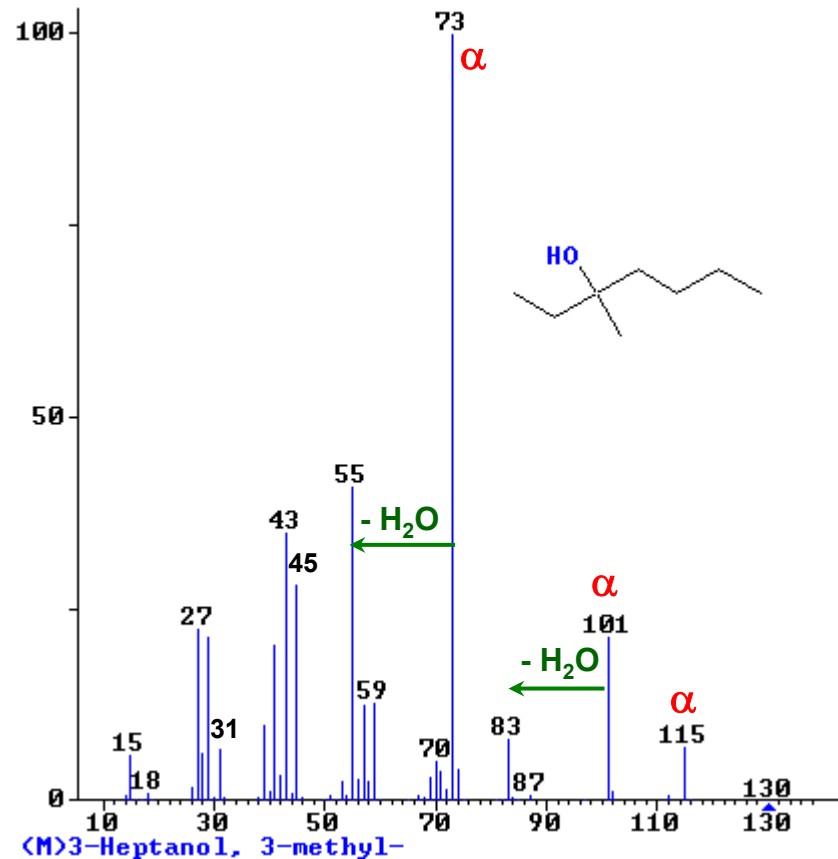
Witold Danikiewicz

Instytut Chemii Organicznej PAN, Warszawa

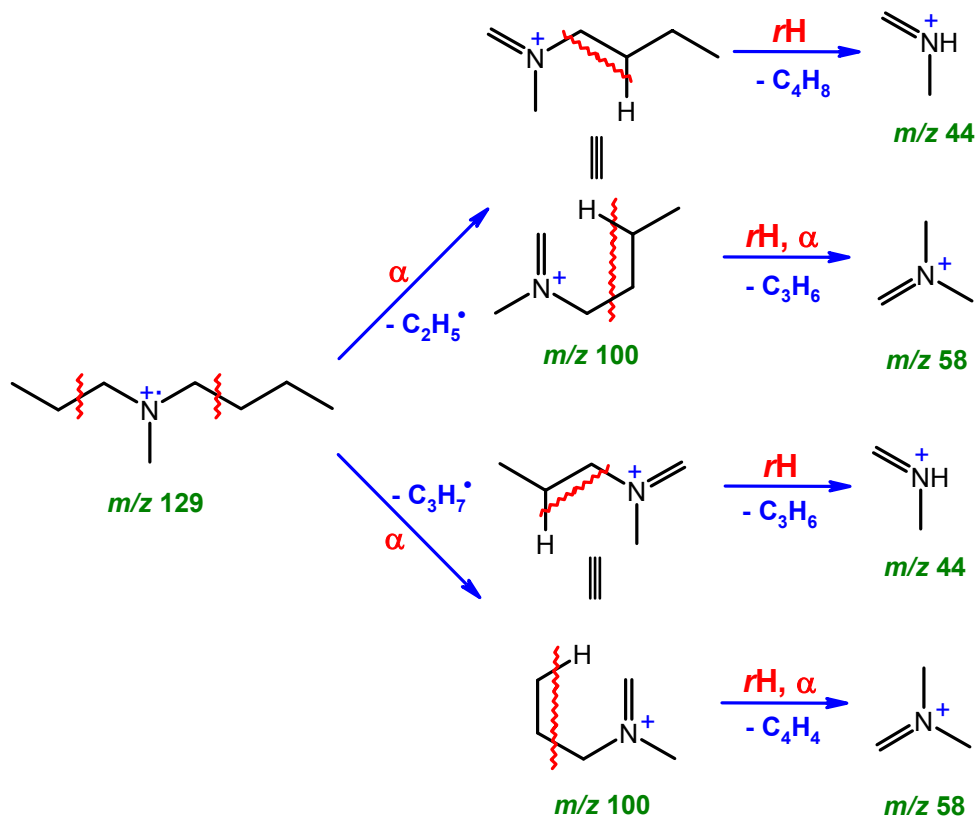
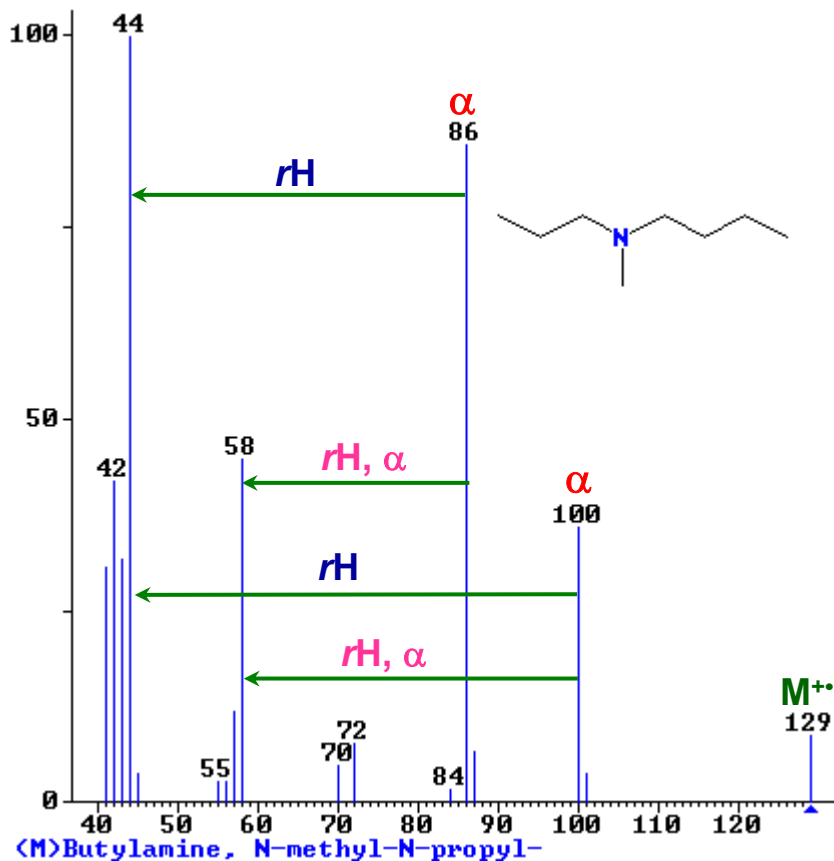
Alkany - 3-metyloheksan



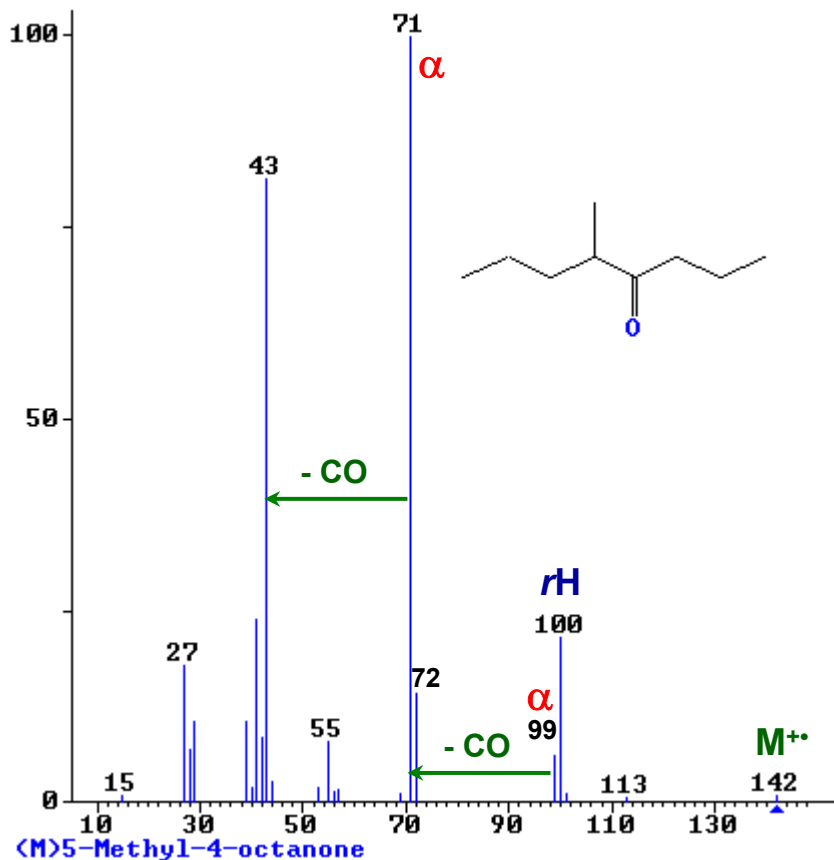
Alkohole - 3-metyloheptan-3-ol



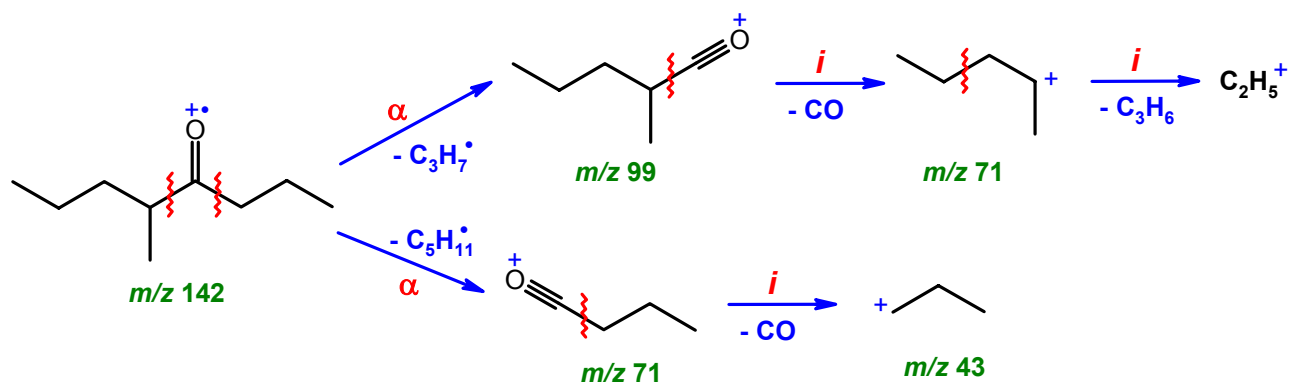
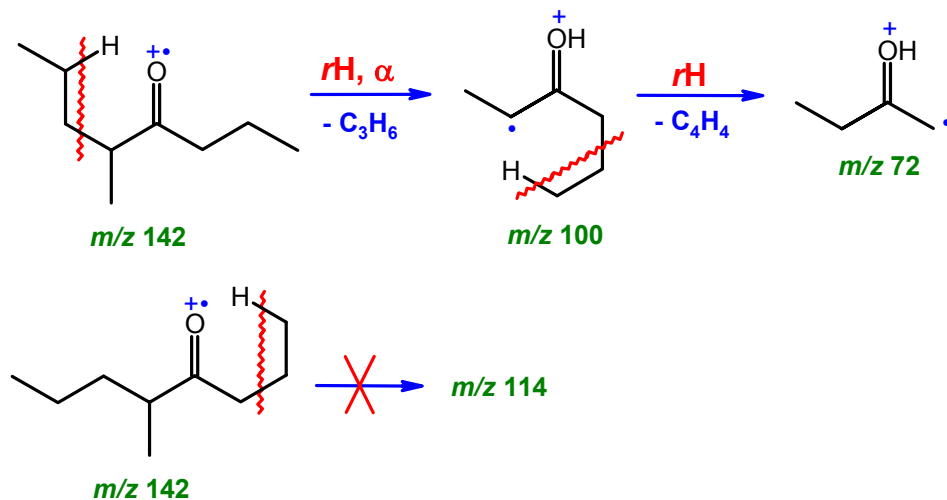
Aminy alifatyczne - *N*-metylo-*N*-propylobutyloamina



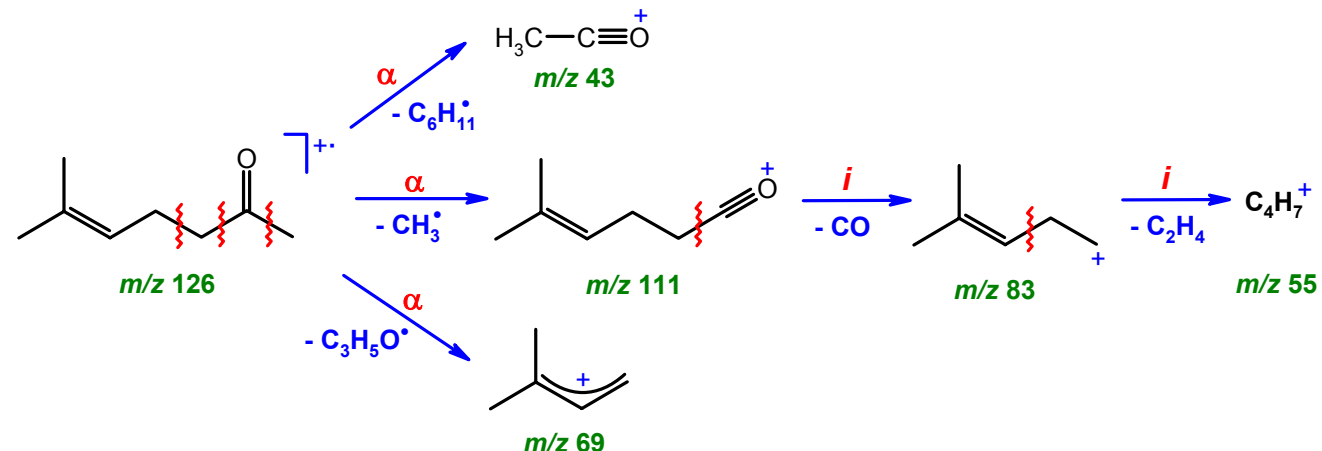
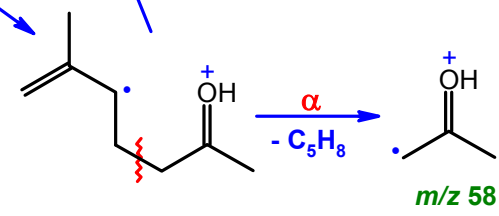
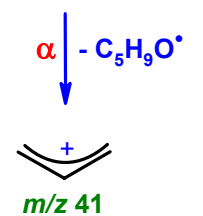
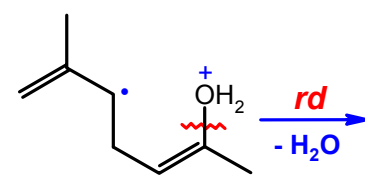
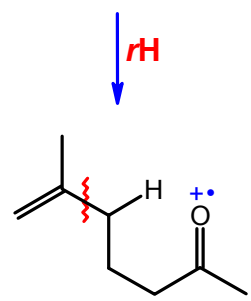
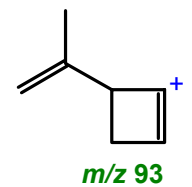
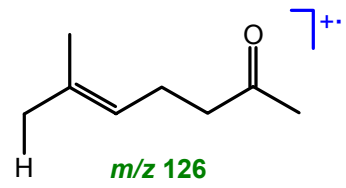
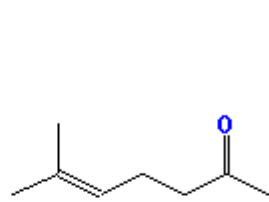
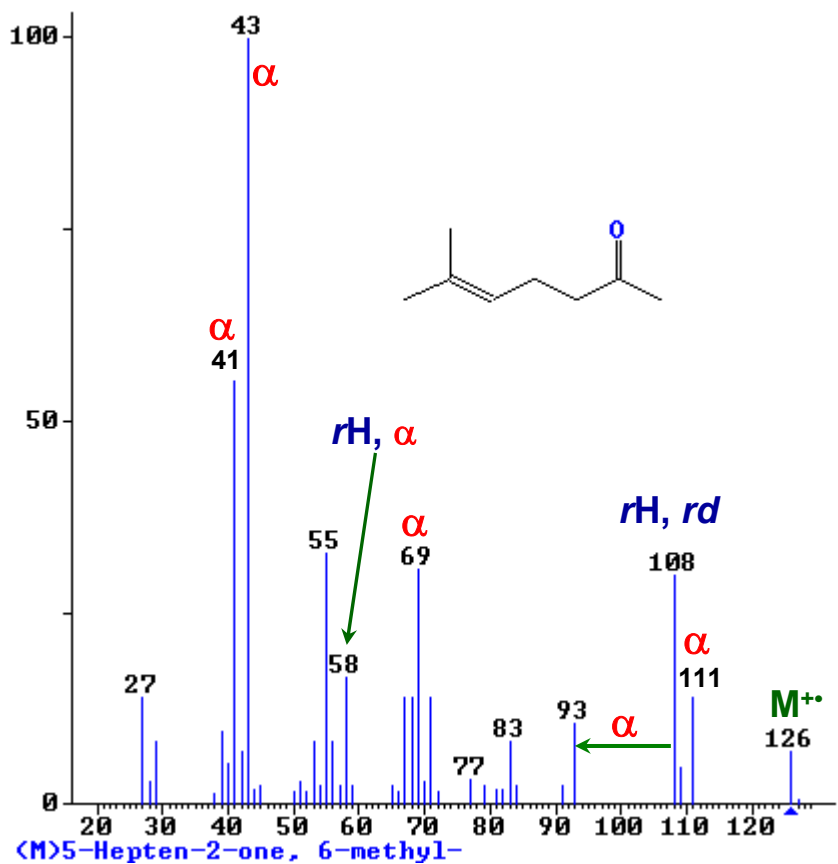
Ketony - 5-metylooktan-2-on



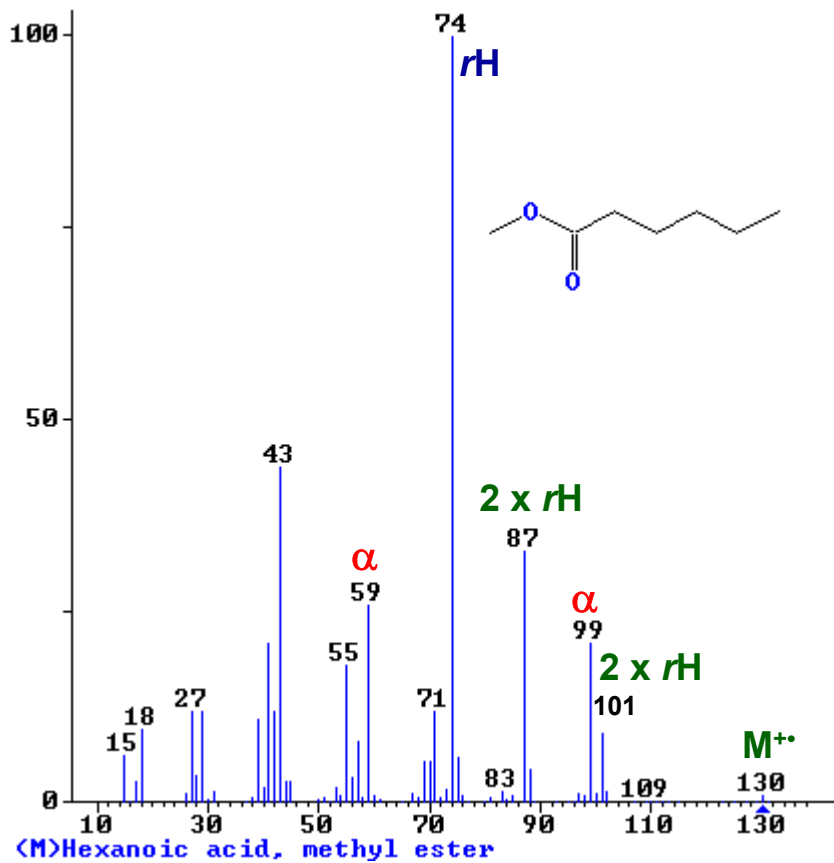
Przegrupowanie McLafferty'ego



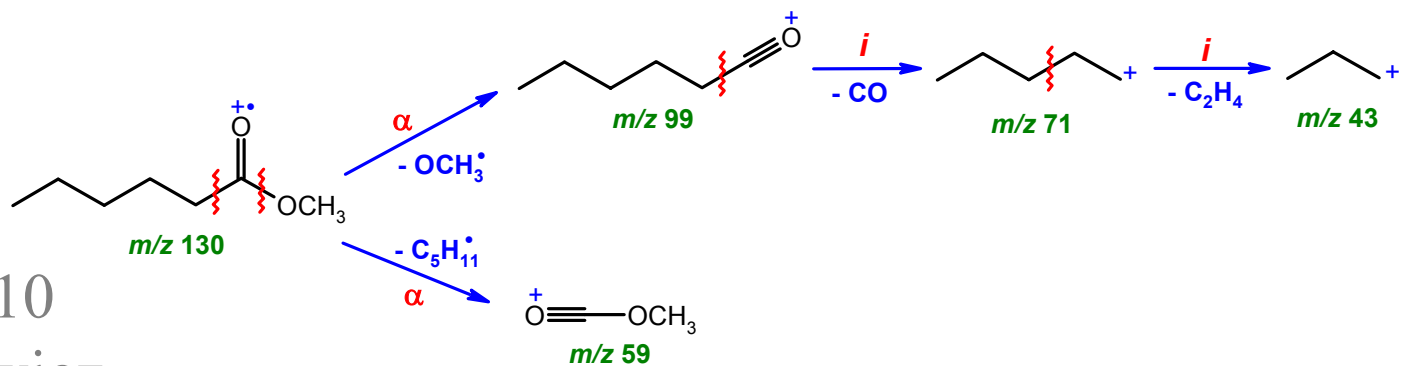
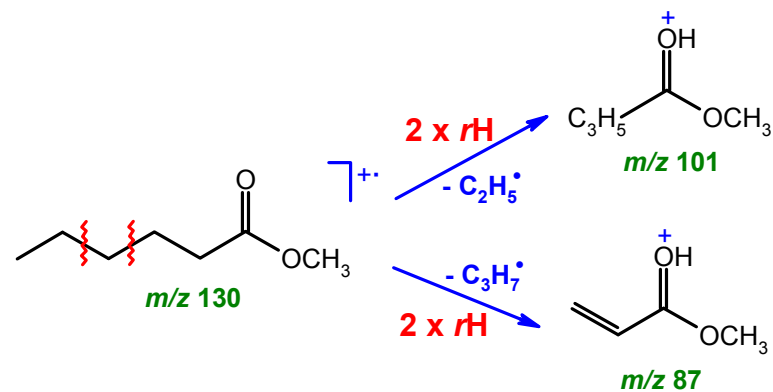
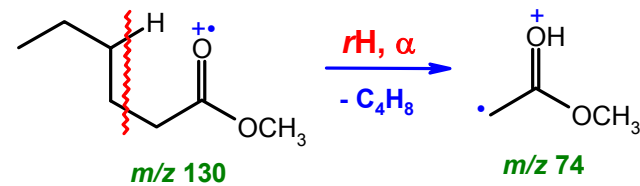
Ketony nienasycone - 6-metylohept-5-en-2-on



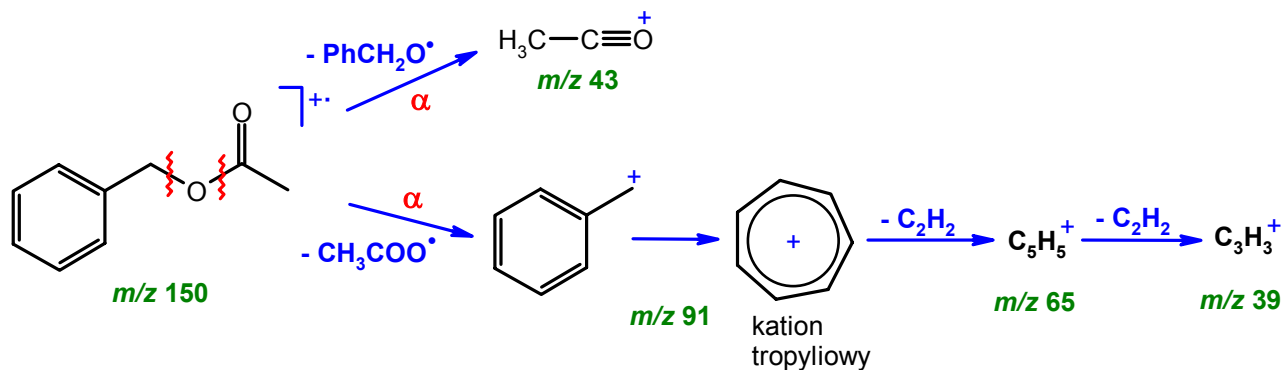
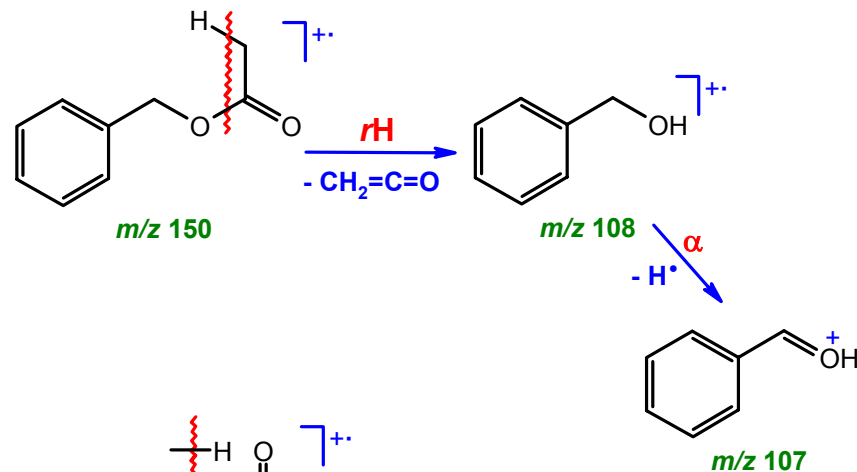
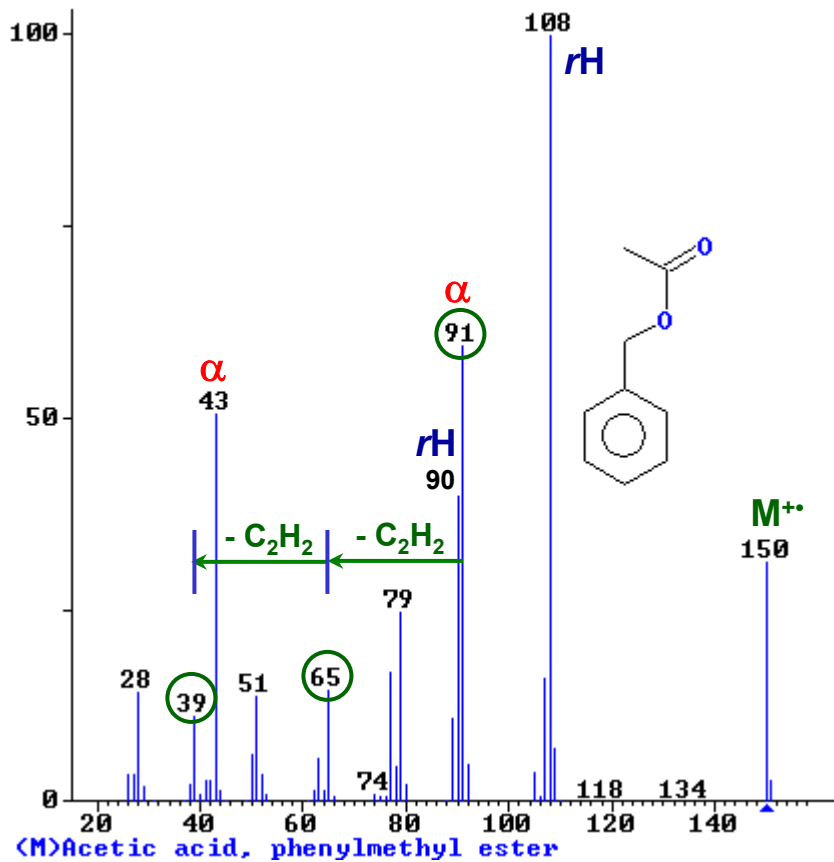
Estry - ester metylowy kwasu heksanowego



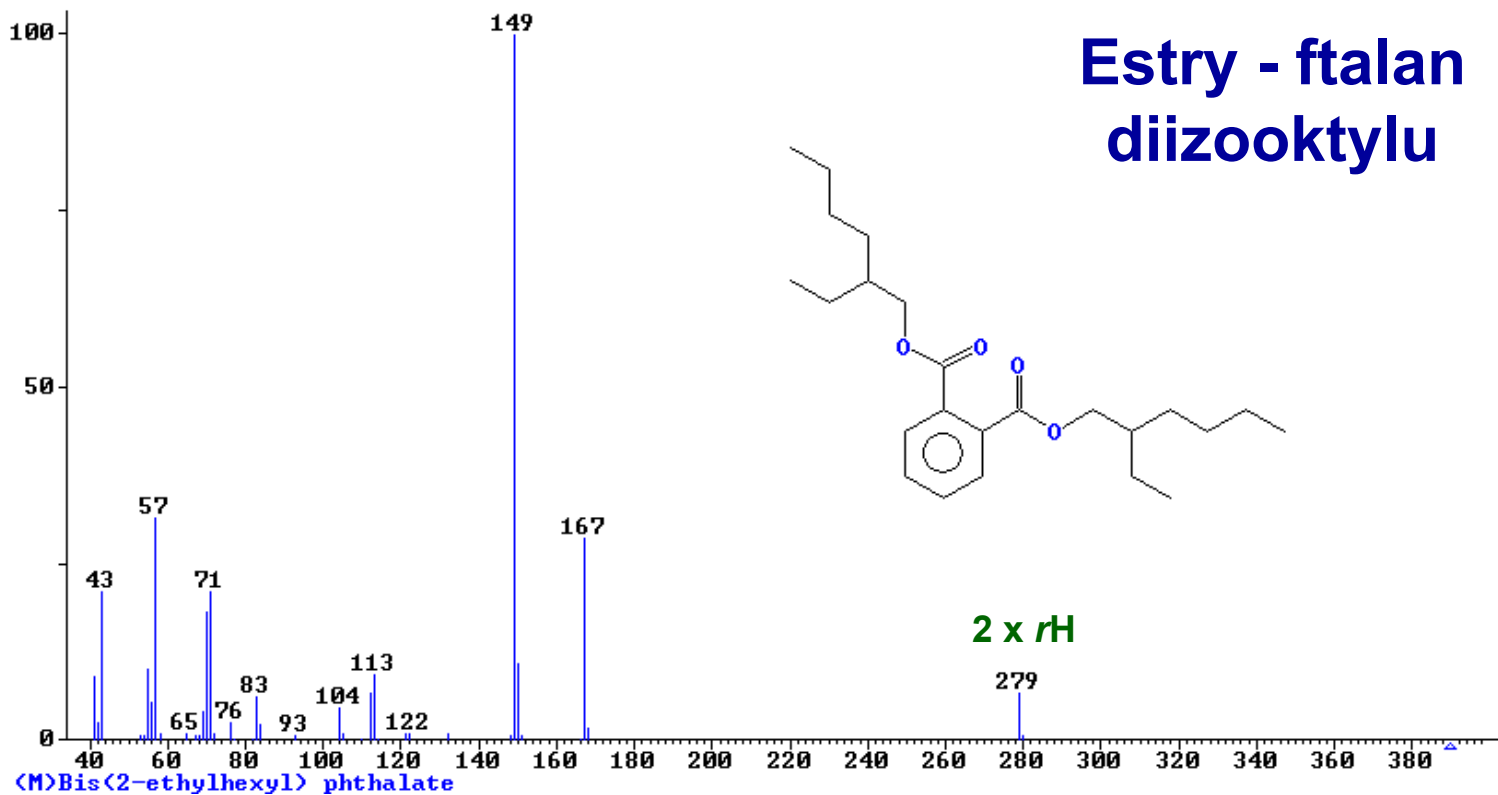
(M)Hexanoic acid, methyl ester



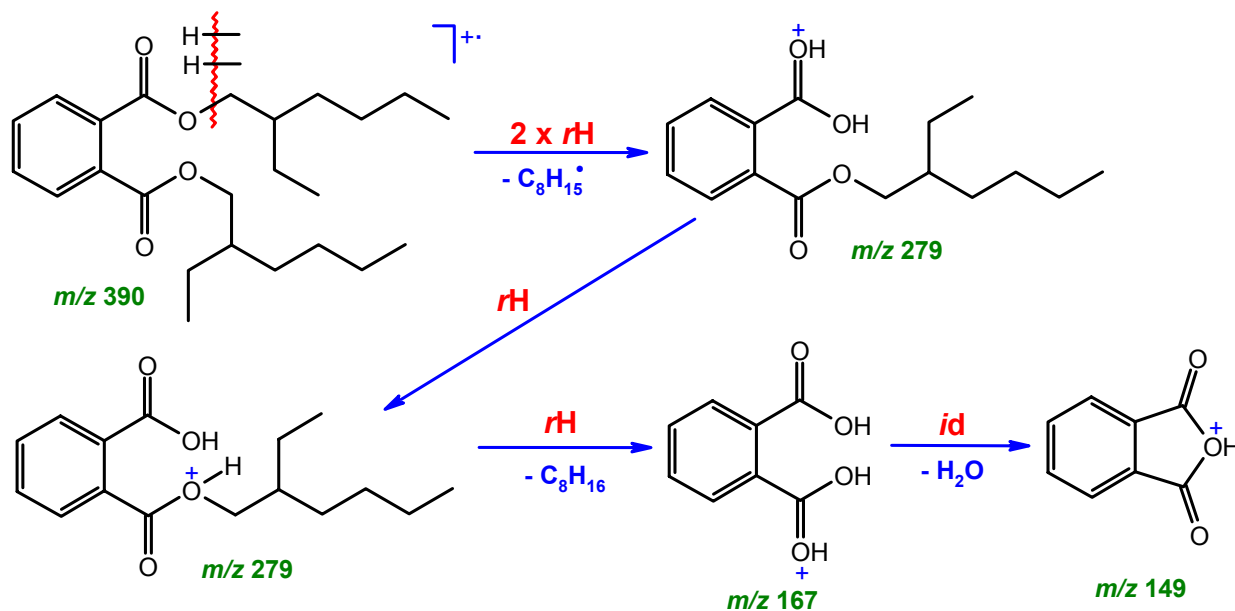
Estry - octan benzylu



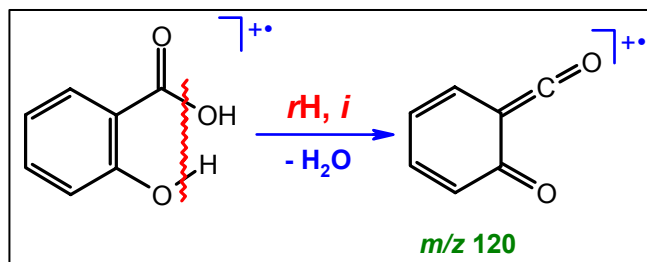
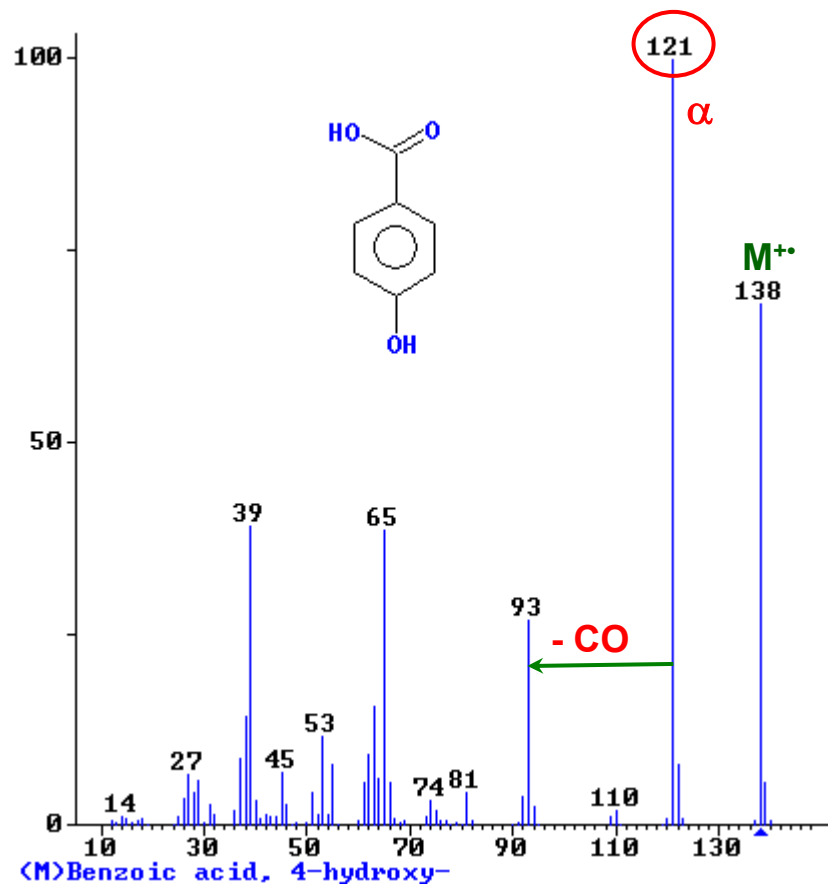
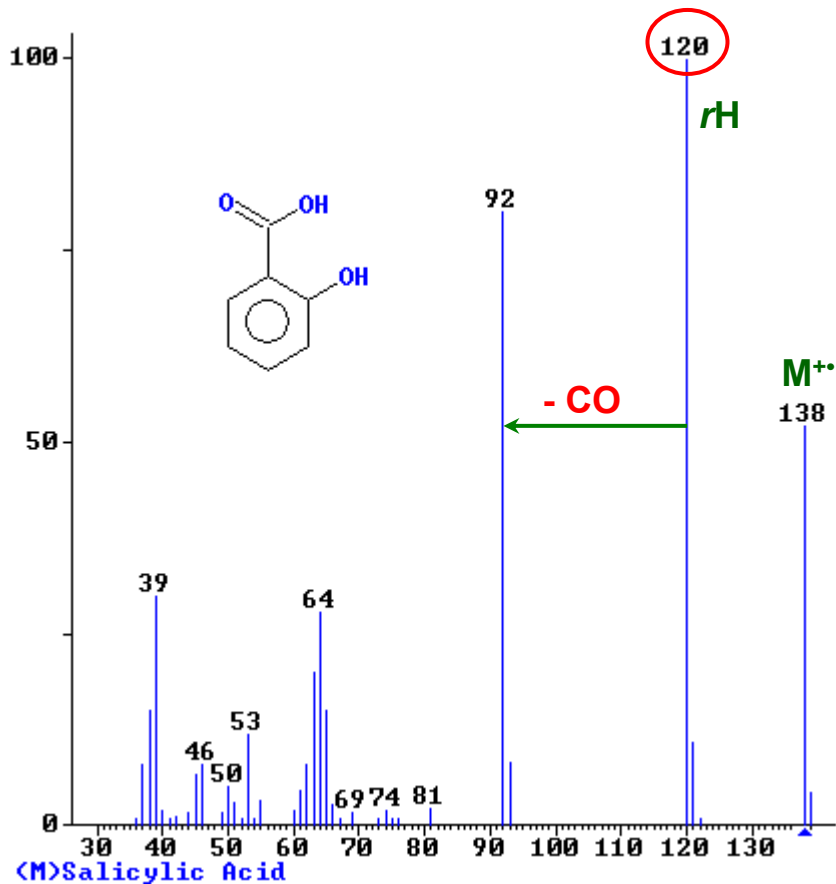
Estry - ftalan diizooktylu



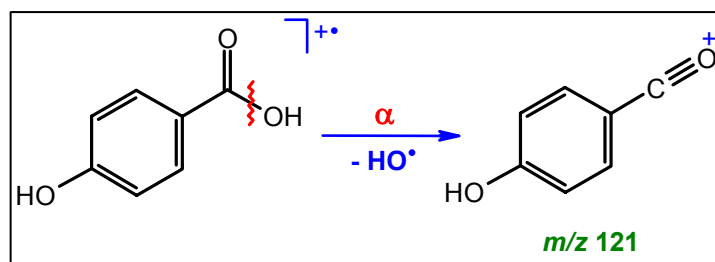
(M)Bis(2-ethylhexyl) phthalate



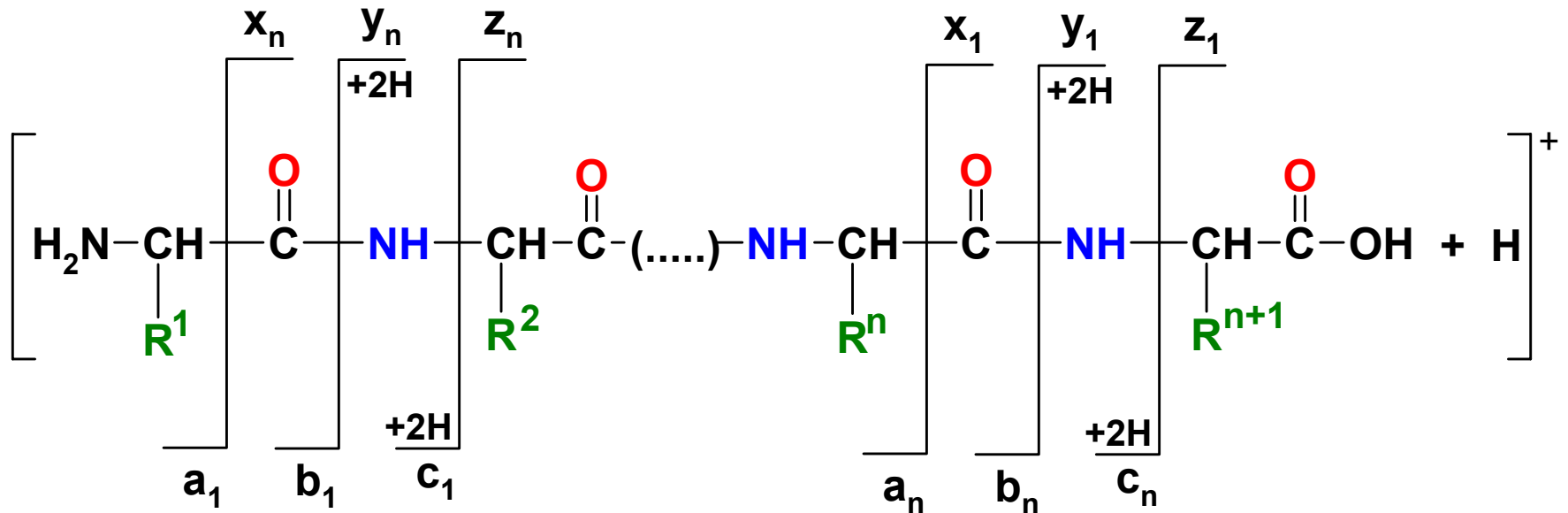
Efekty orto - kwasy orto- i para-hydroksybenzoesowe



efekt orto

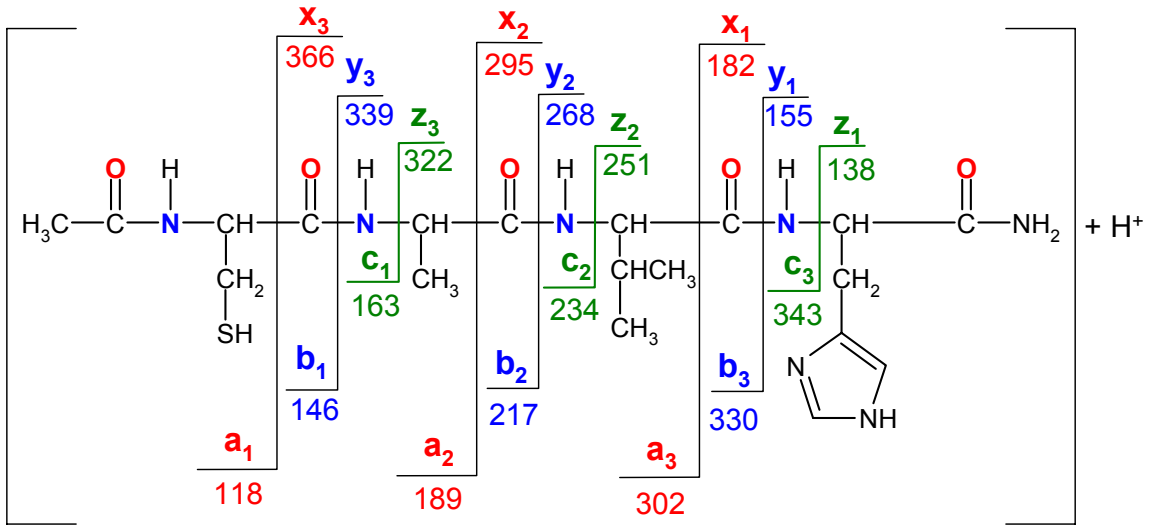


Klasyfikacja podstawowych typów fragmentacji protonowanego łańcucha peptydowego



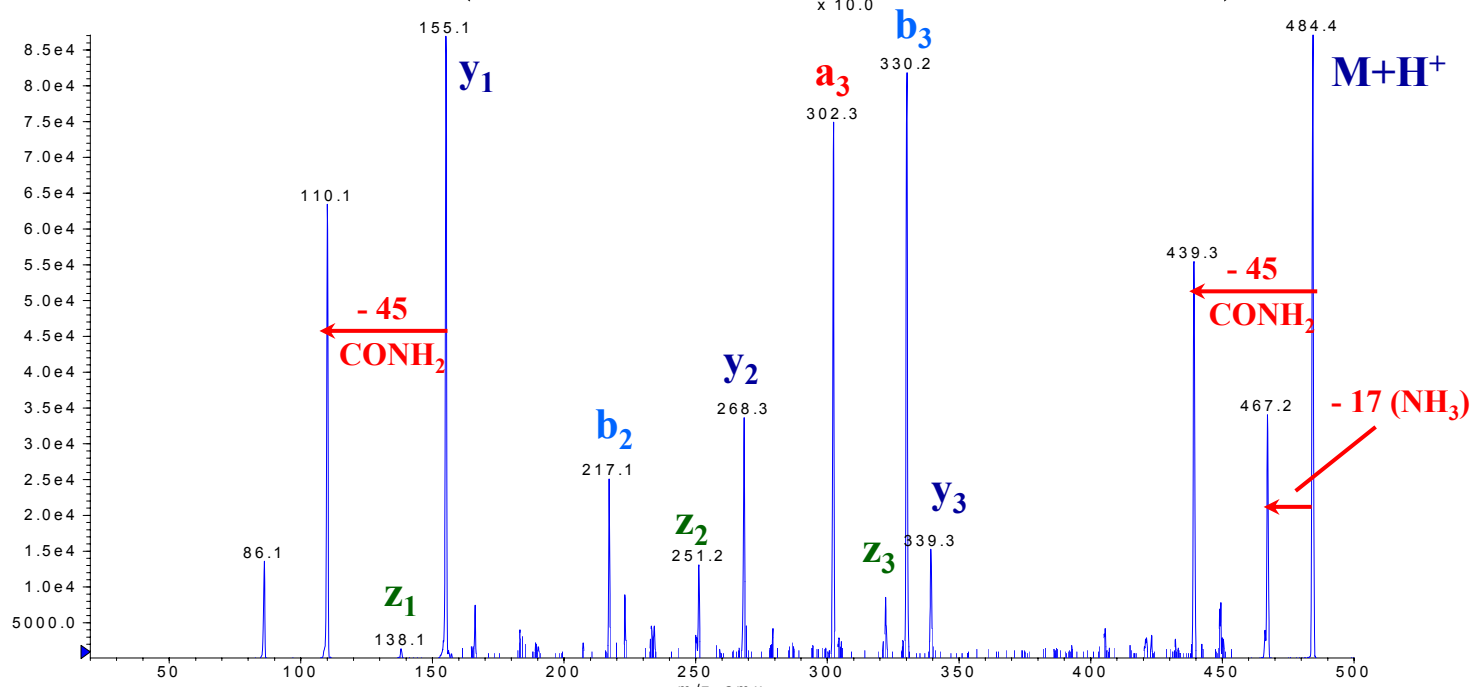
43	103	71	113	137	16
Ac	Cys	Ala	Ile	His	NH ₂

Ustalanie sekwencji peptydu na podstawie widma ESI-CID-MS/MS

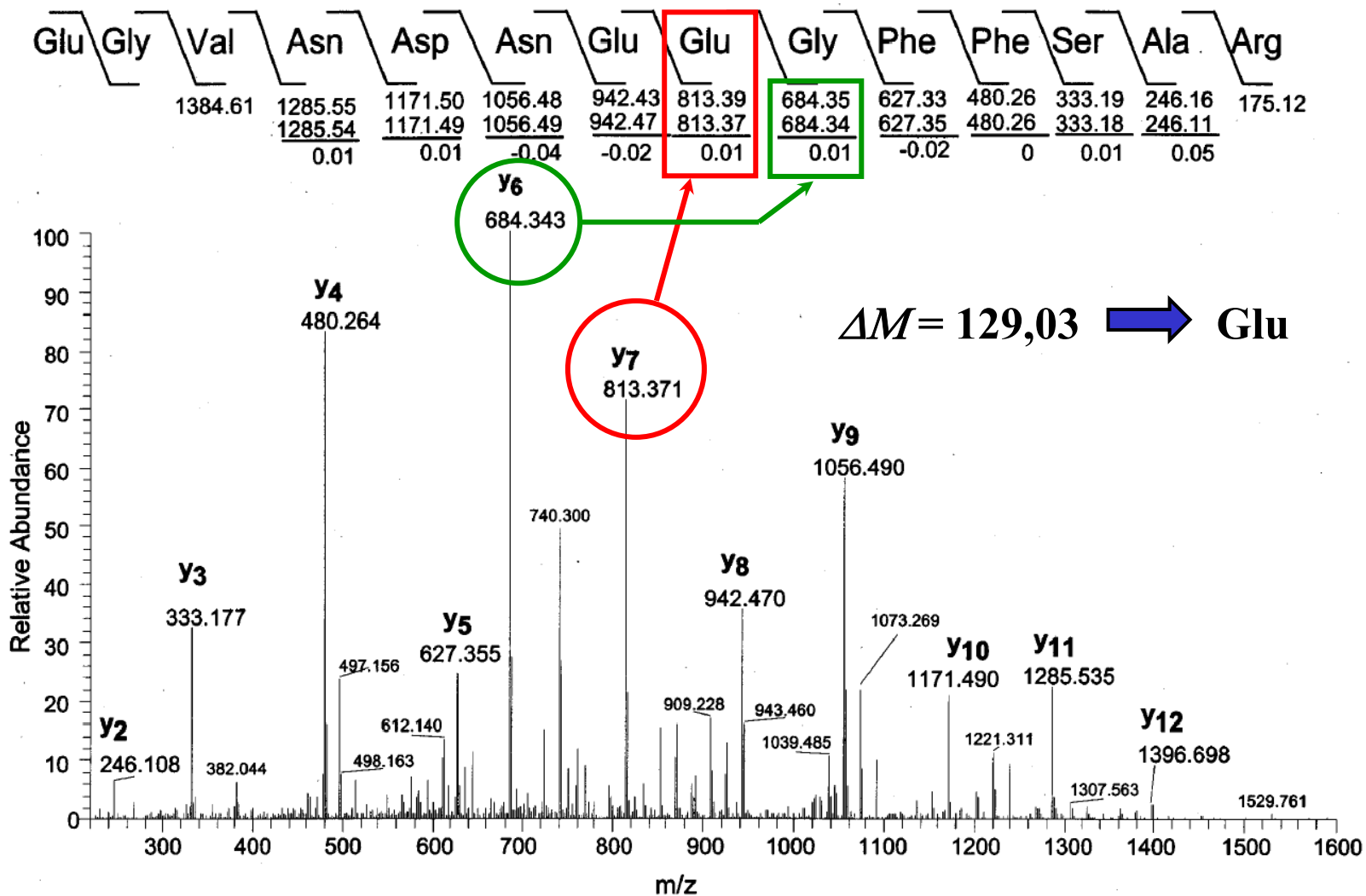


Jony **c** i **y**: +2H⁺

+MS2 (484.30) CE (25): 0.100 to 1.152 min from Sample 1 (CAIHN) of Peptyd.wiff, Smoothe... Max. 8.7e4 cps.

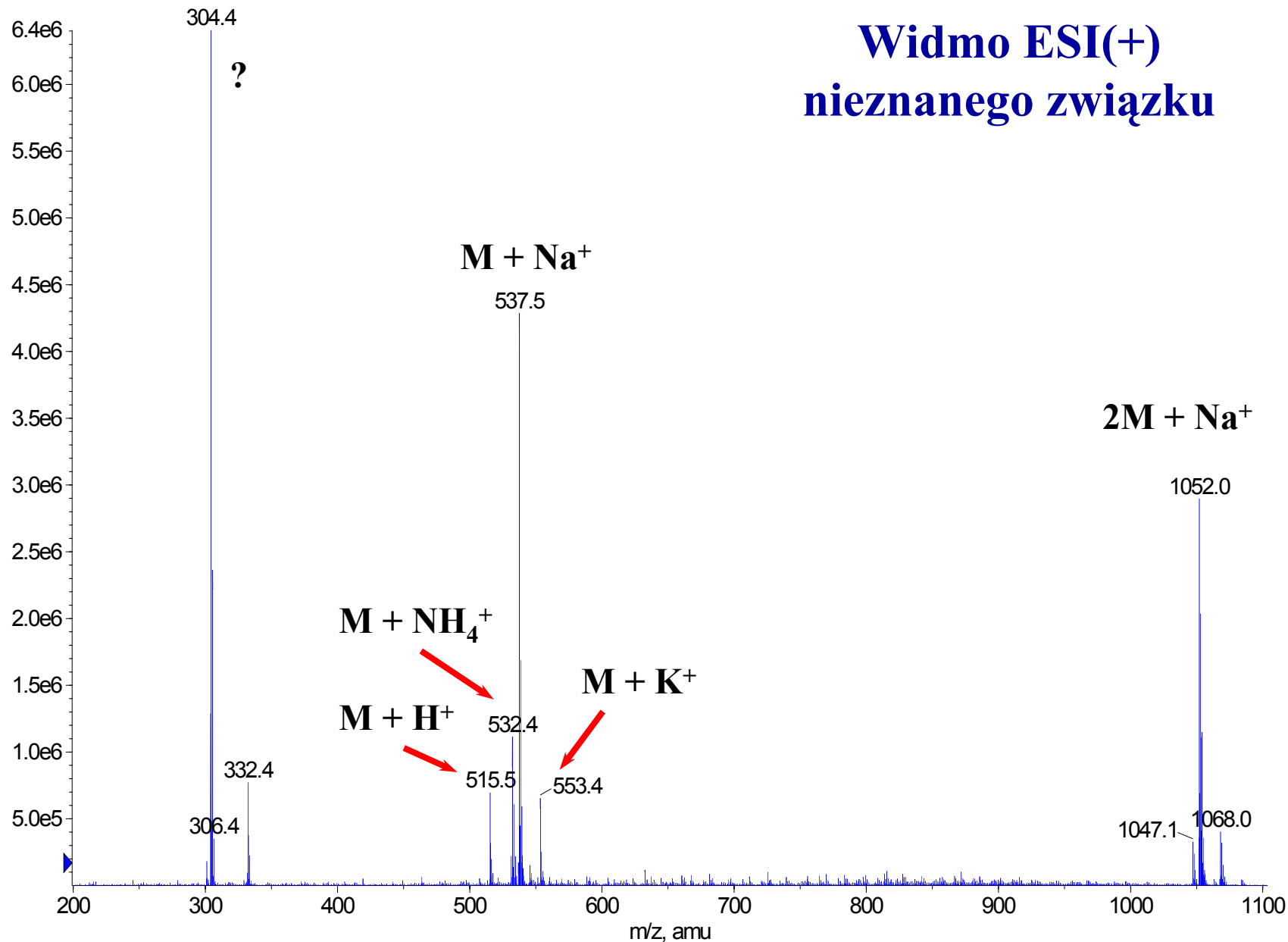


Ustalanie sekwencji peptydu na podstawie widma ESI-CID-MS/MS

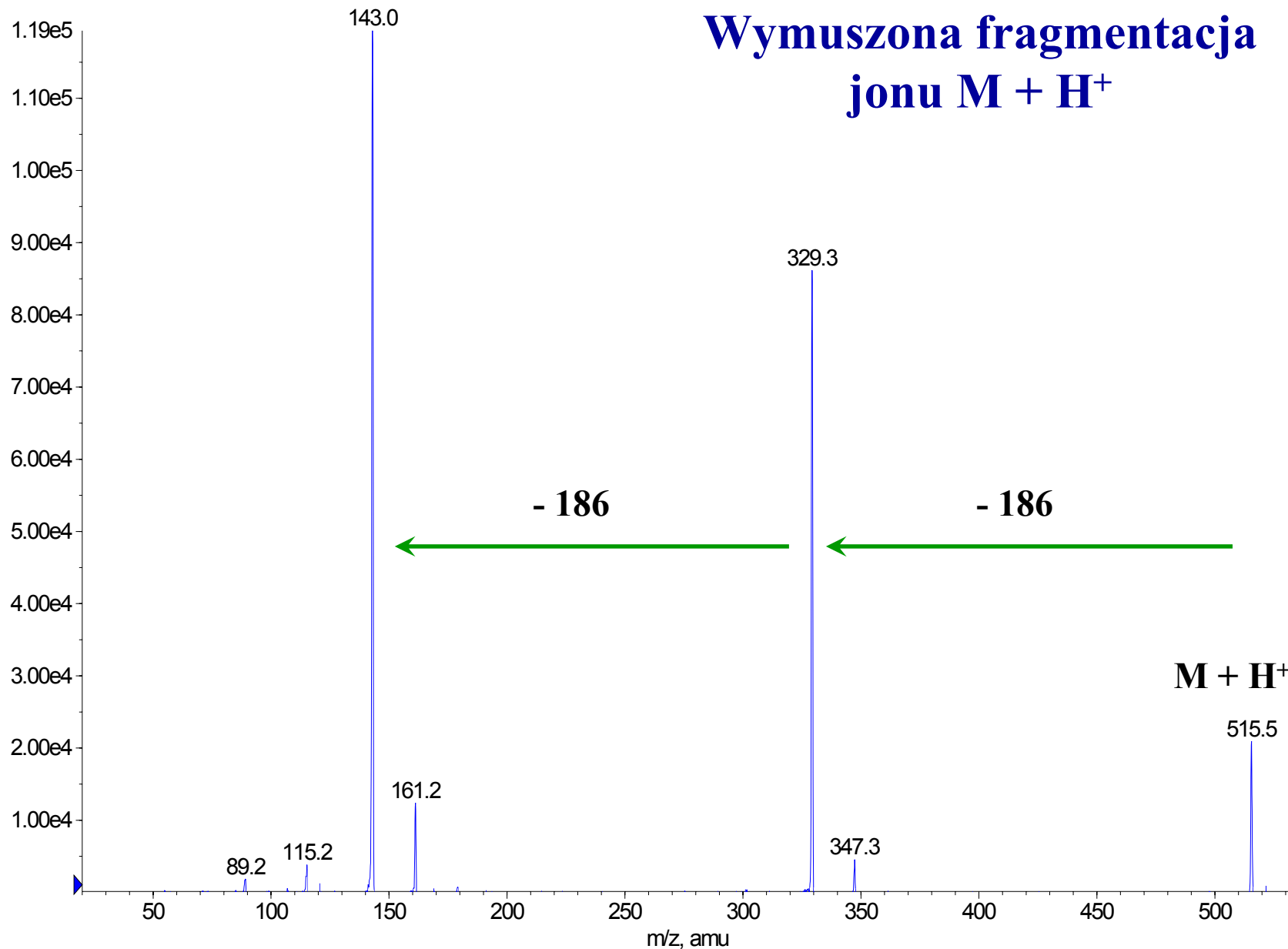


**Próba ustalenia budowy
nieznanego związku za pomocą
ESI-MS i innych technik
spektrometrii mas**

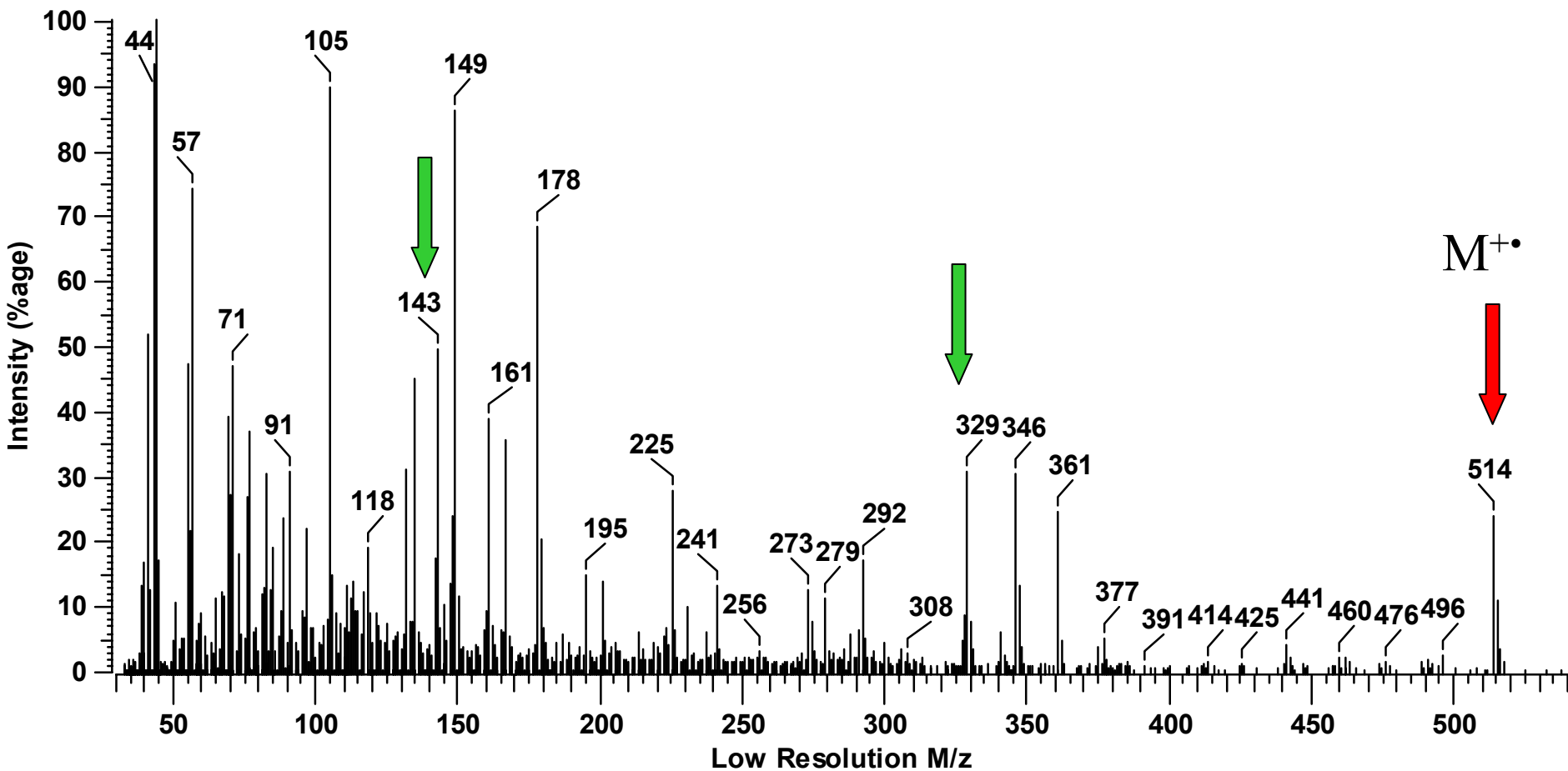
Widmo ESI(+) nieznanego związku



Wymuszona fragmentacja jonu $M + H^+$



Widmo EI nieznanego związku



ATOMIC COMPOSITION REPORT (MANUAL)

Selected isotopes:

Symbol	Min	Max	V'cy	Name
C	0	40	4	Carbon-12
H	0	80	1	Hydrogen-1
O	0	20	2	Oxygen-16
N	0	2	3	Nitrogen-14

Allowable error = minimum of 50.0 ppm, 10.0 mmu.
 Ring/Double Bond limits = [-0.5 : 100.0]

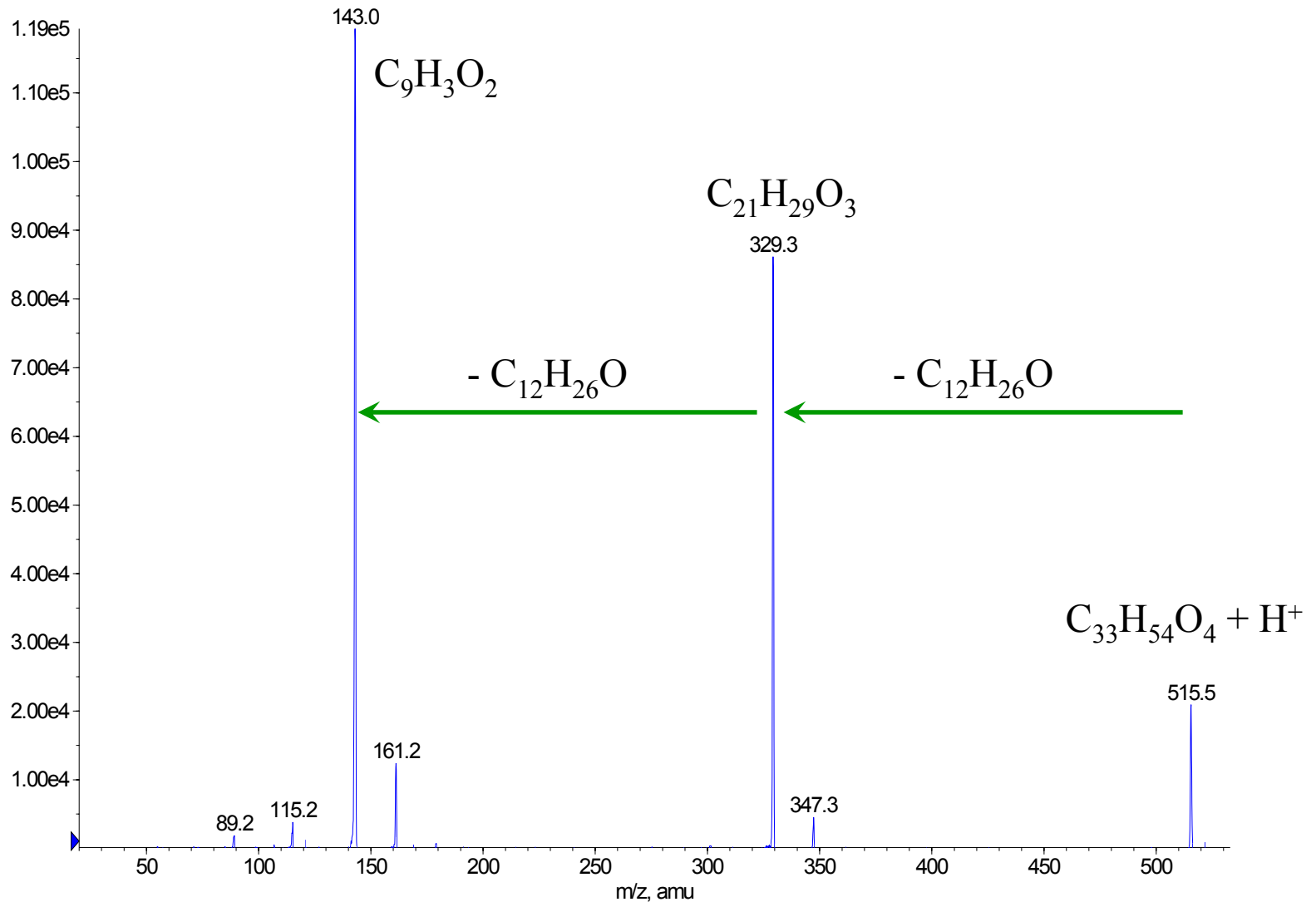
Mass	Calculated	ppm	mmu	R/DB	Formula
514.40617	514.40489	-2.5	-1.3	11.5	C36.H52.O.N
	514.40221	-7.7	-4.0	7.0	C33.H54.O4
	514.41076	8.9	4.6	2.5	C29.H56.O6.N
	514.41344	14.1	7.3	7.0	C32.H54.O3.N2
	514.39819	-15.5	-8.0	3.0	C28.H54.O6.N2
329.21311	329.21435	3.8	1.2	12.0	C24.H27.N
	329.21167	-4.4	-1.4	7.5	C21.H29.O3
	329.20765	-16.6	-5.5	3.5	C16.H29.O5.N2
	329.22022	21.6	7.1	3.0	C17.H31.O5.N
	329.22290	29.7	9.8	7.5	C20.H29.O2.N2
143.01161	143.01330	11.8	1.7	8.5	C9.H3.O2
	143.00928	-16.3	-2.3	4.5	C4.H3.O4.N2
	143.00660	-35.0	-5.0	0.0	C.H5.O7.N

**Wyniki
dokładnych
pomiarów
masy w EI**

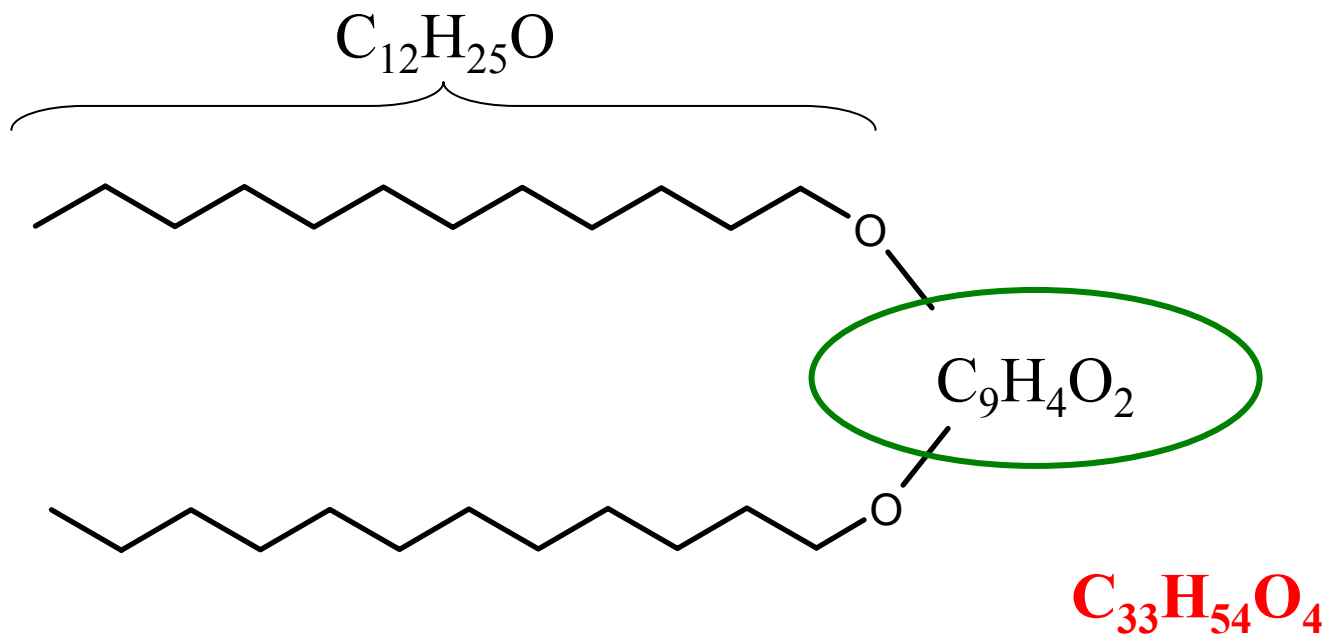
Składy jonów fragmentacyjnych i obojętnych fragmentów

+MS2 (515.40) CE (20): 0.000 to 0.701 min from Sample 2 (1 w MeOH for 515 CE 20) of AS0739....

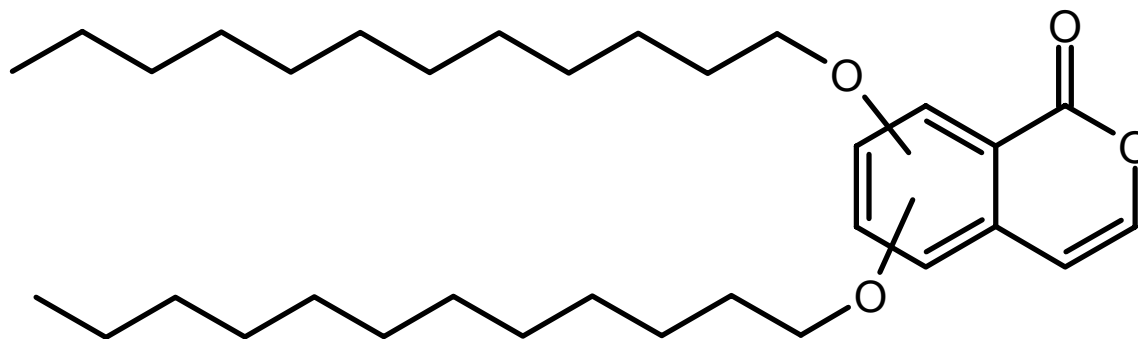
Max. 1.2e5 cps.



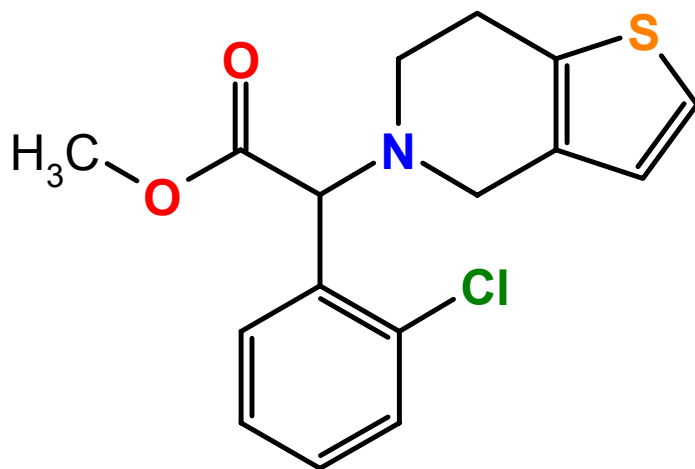
Proponowany wzór badanego związku



Na przykład:



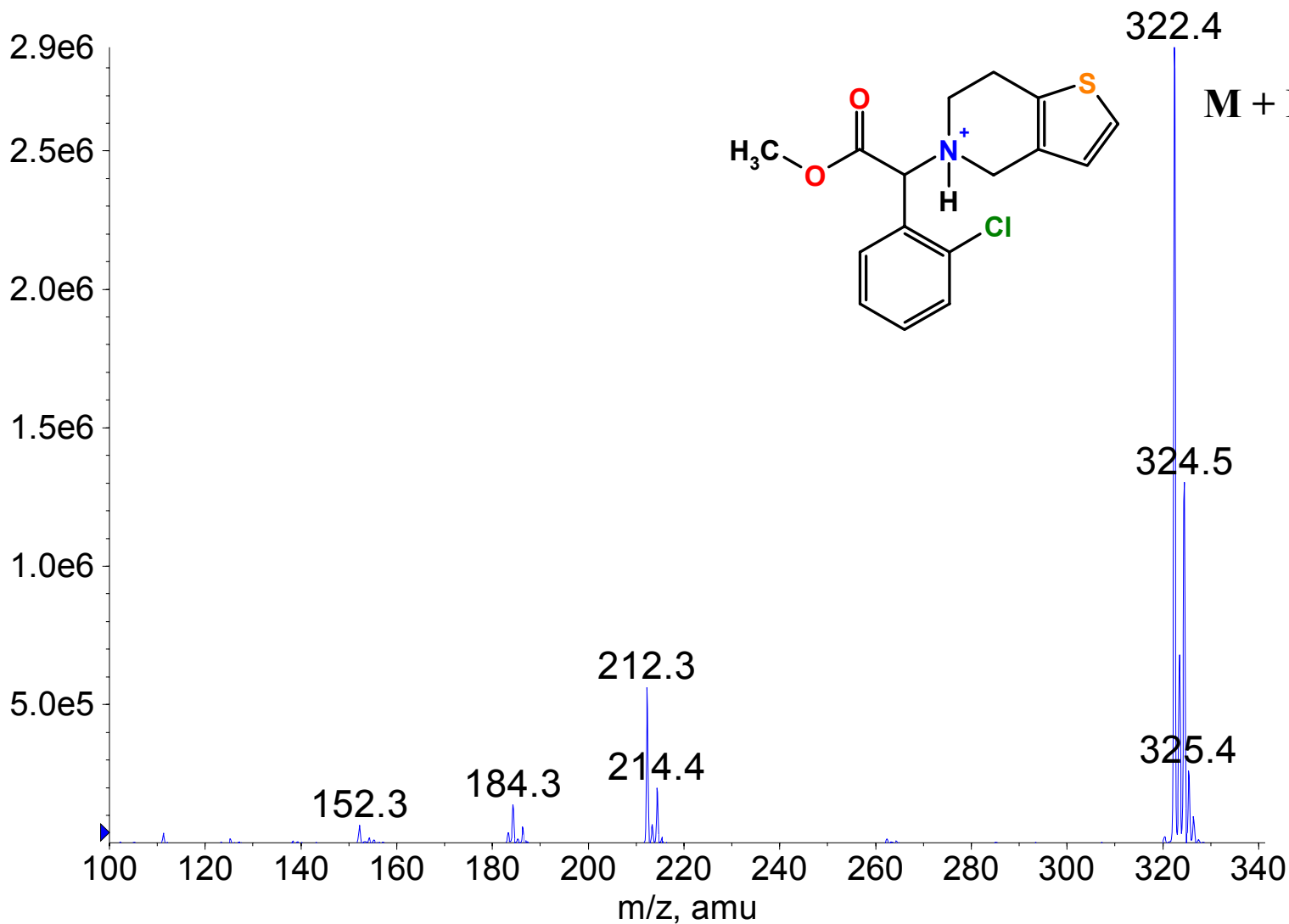
Fragmentacja Clopidogrelu i identyfikacja jego zanieczyszczeń



Widmo ESI(+) Clopidogrelu

■ +Q1: 2.172 to 2.406 min from Sample 3 (9/1 ACN H2O AcOH 0.6 ml/min 270 nm) of 050301....

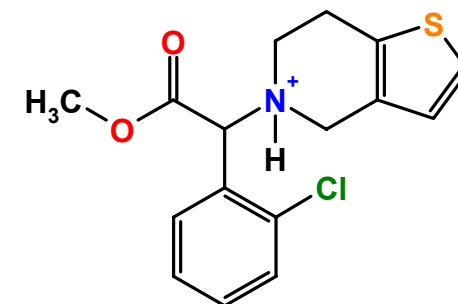
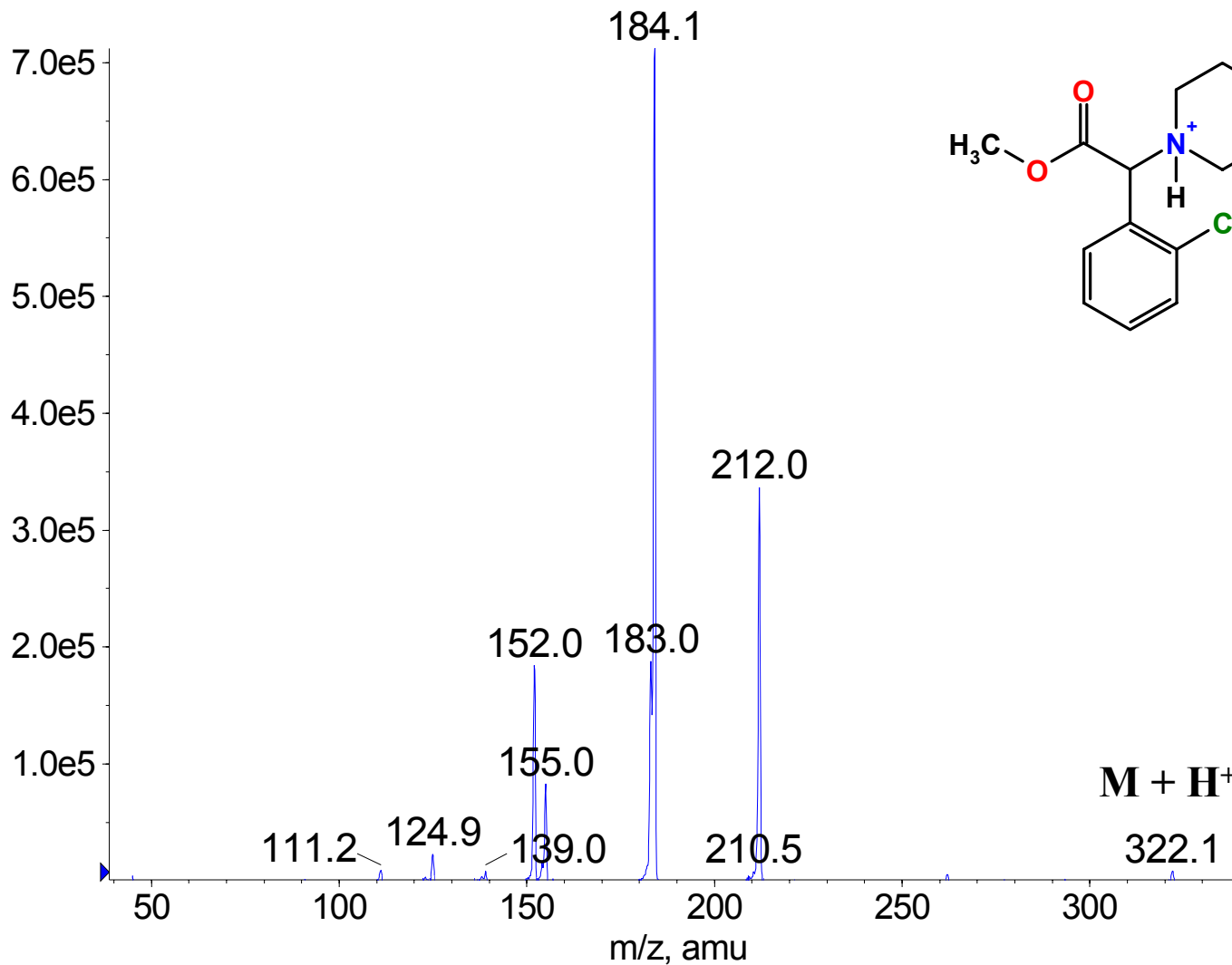
Max. 2.9e6 cps.



Fragmentacja Clopidogrelu

■ +MS2 (322.40) CE (30): Period 3, Exp 2, 2.345 to 2.596 min from Sample 4 (frag 9/1 ACN H2...)

Max. 7.1e5 cps.



Fragmentacja Clopidogrelu – dane literaturowe

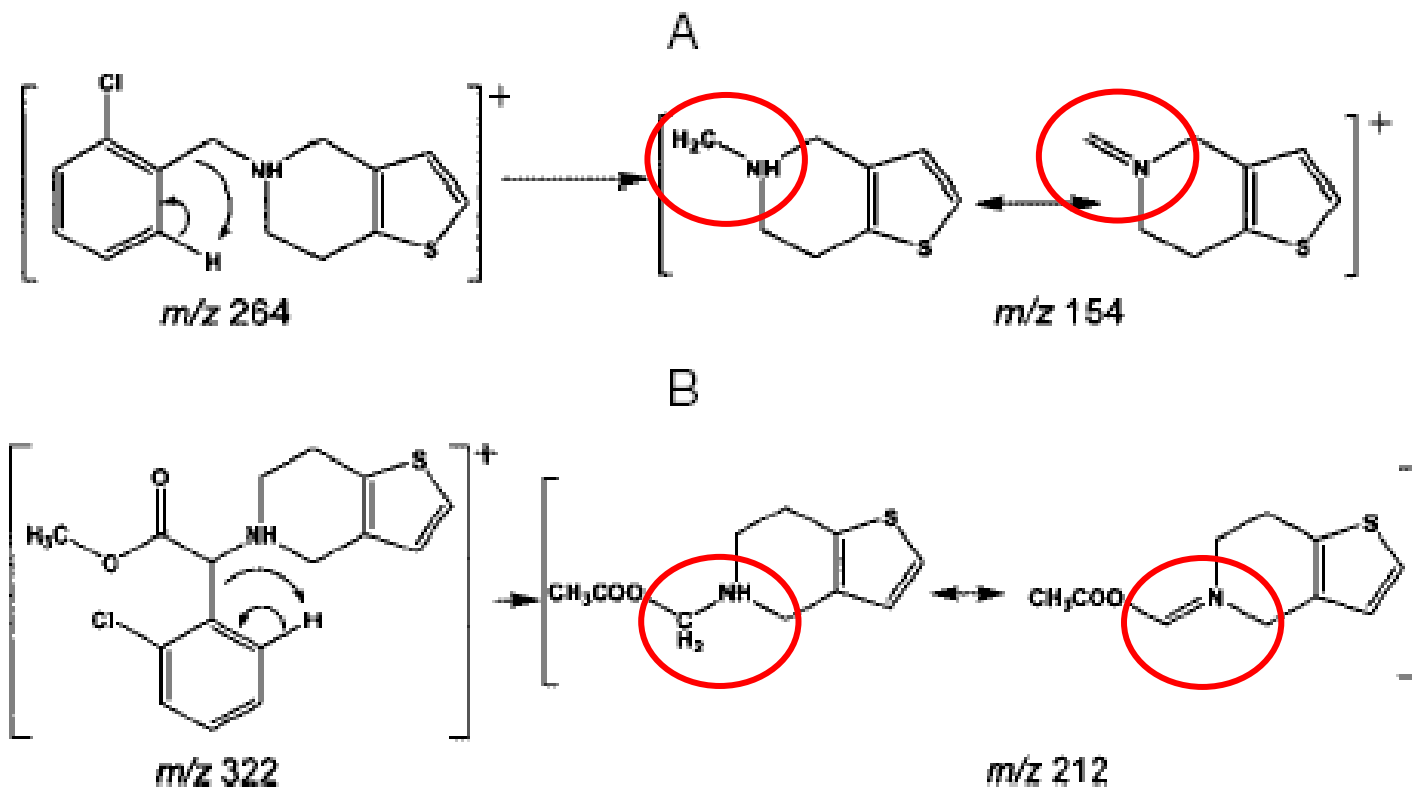
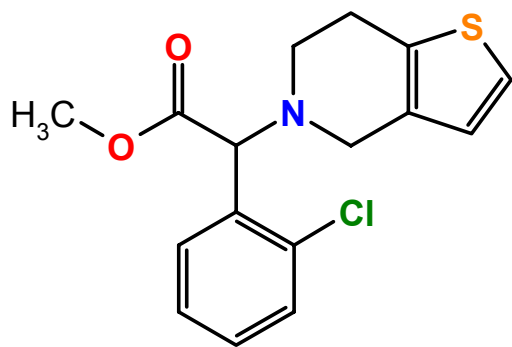


Figure 3. Proposed fragmentation pathways for (A) ticlopidine and (B) clopidogrel.

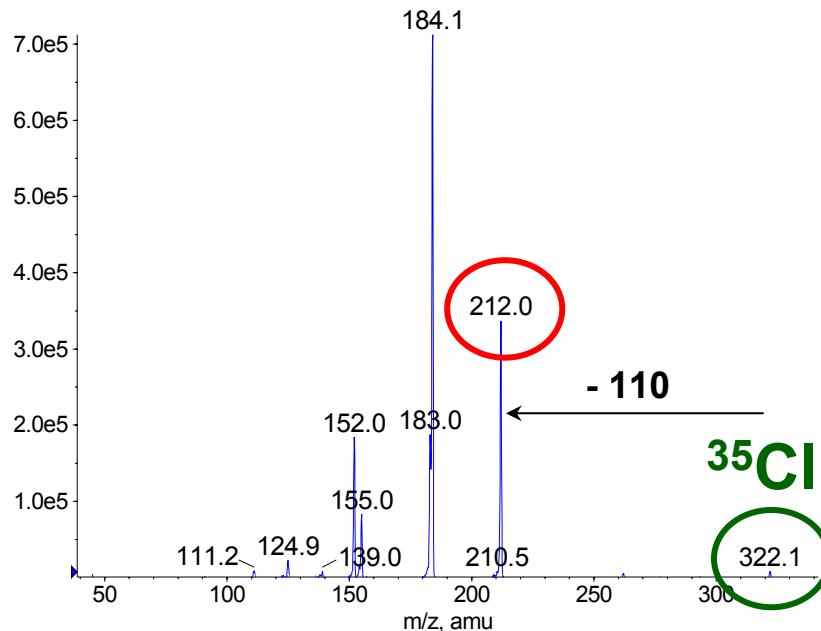
N. C. do Carmo Borges, G. D. Mendes, A. Borges, S. E. de Oliveira, R. E. Barrientos-Astigarraga and G. De Nucci, *J. Mass Spectrom.*, 2004; **39**, 1562-1569

Fragmentacja Clopidogrelu – fragmentacja jonów zawierających izotop ^{35}Cl i ^{37}Cl



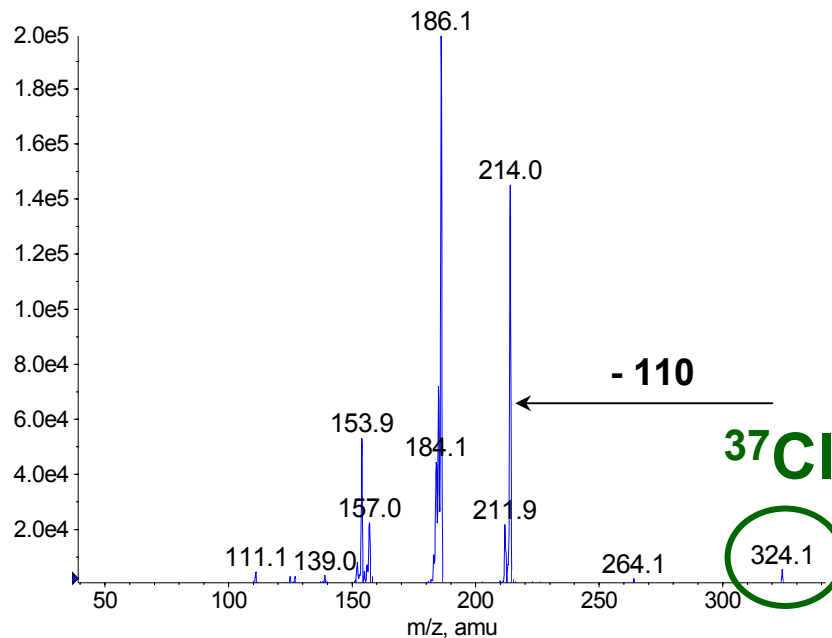
+MS2 (322.40) CE (30): Period 3, Exp 2, 2.345 to 2.596 min from Sample 4 (frag 9/1 ACN H2...)

Max. 7.1e5 cps.

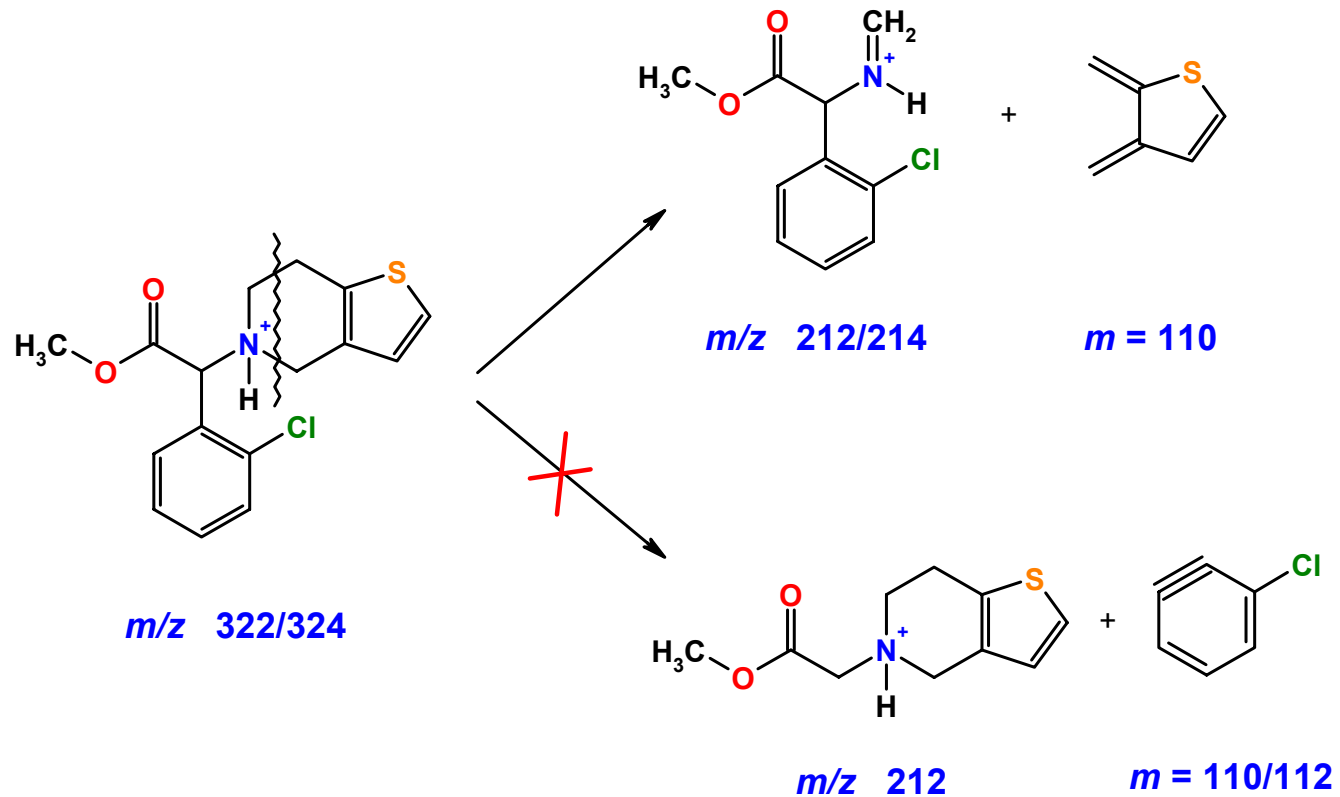


+MS2 (324.40) CE (30): Period 3, Exp 3, 2.362 to 2.613 min from Sample 4 (frag 9/1 ACN H2...)

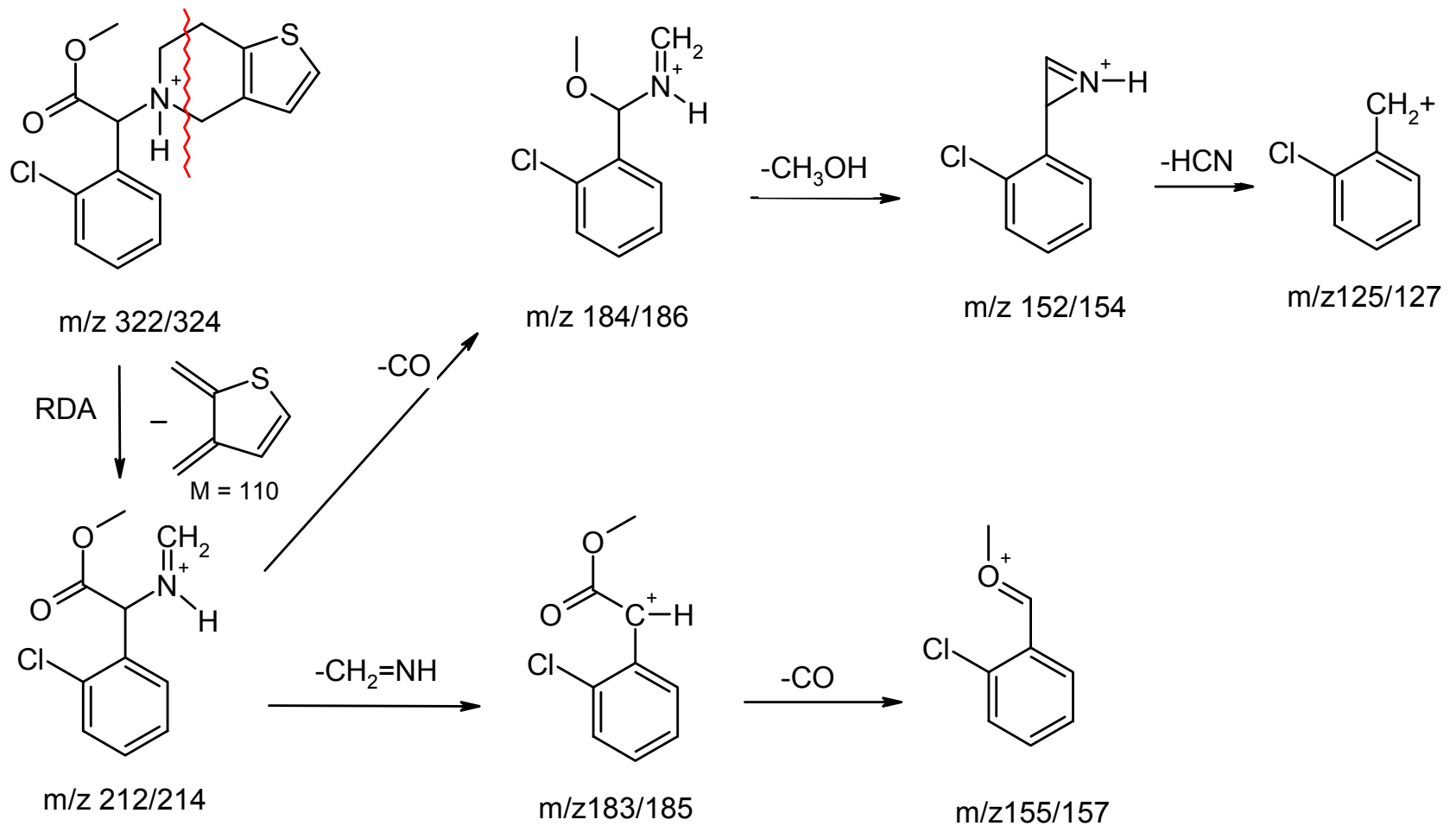
Max. 2.0e5 cps.



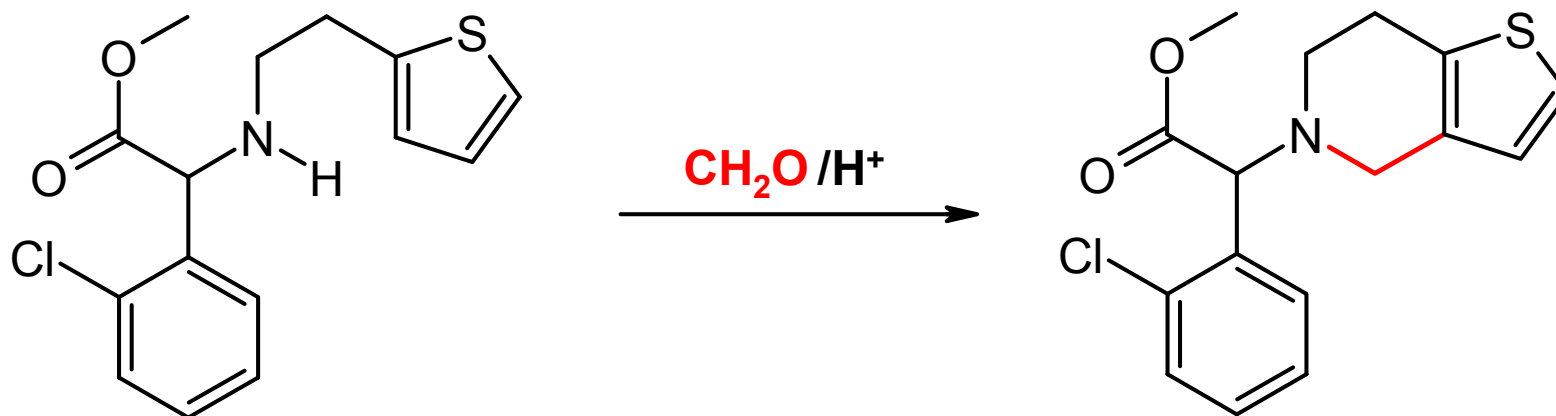
Fragmentacja Clopidogrelu – rzeczywisty przebieg



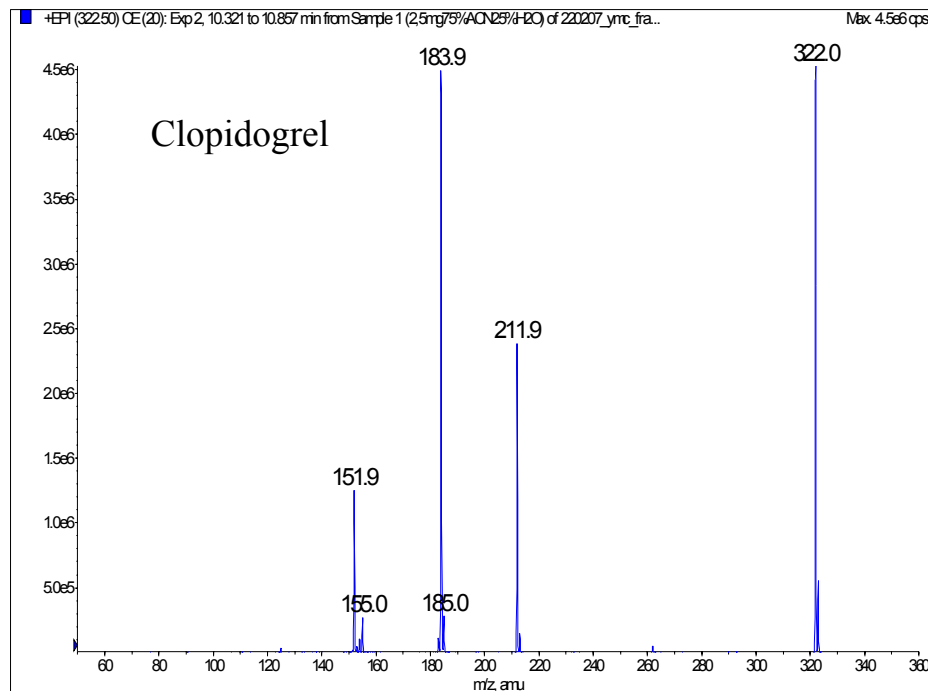
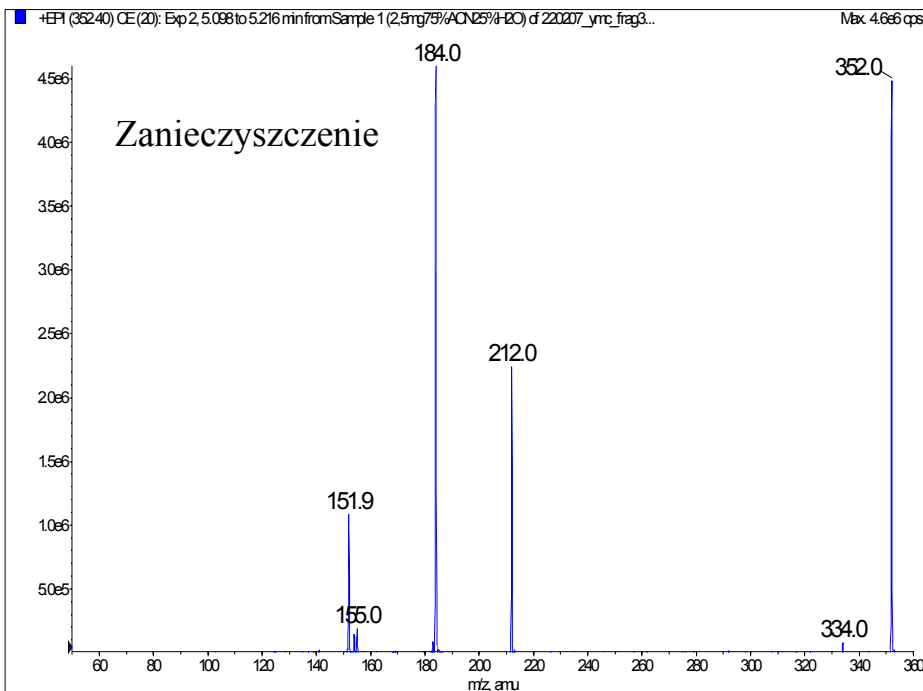
Schemat fragmentacji Clopidogrelu



Synteza Clopidogrelu (ostatni etap)



Zanieczyszczenie Clopidogrelu o masie 351/353 Da

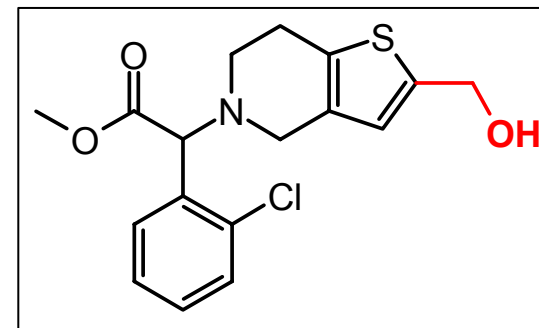


Różnica masy: +30 Da (np. CH_2O).

Drogi fragmentacji: identyczne jak w Clopidogrelu – powstają te same jony fragmentacyjne.

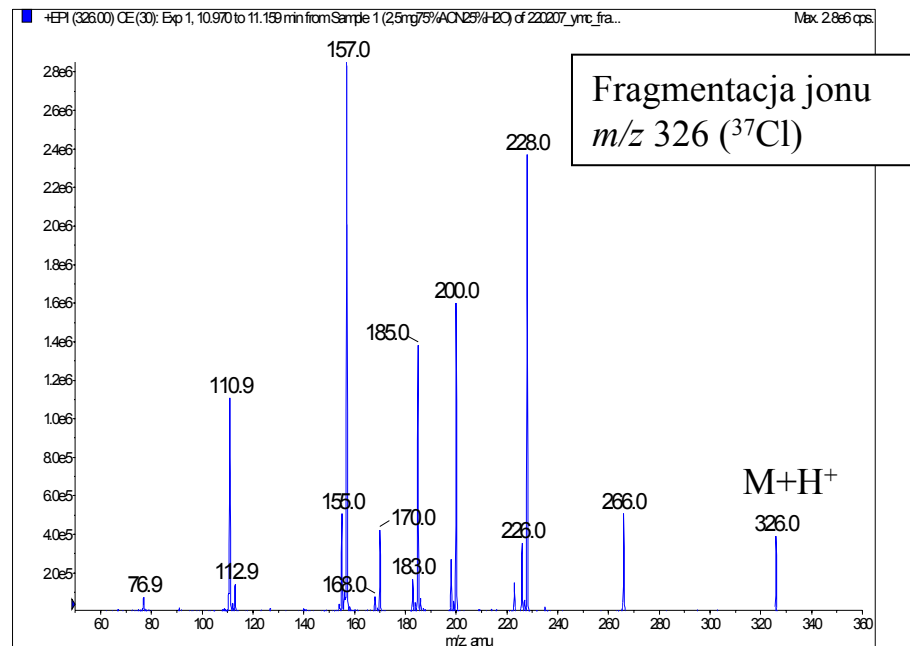
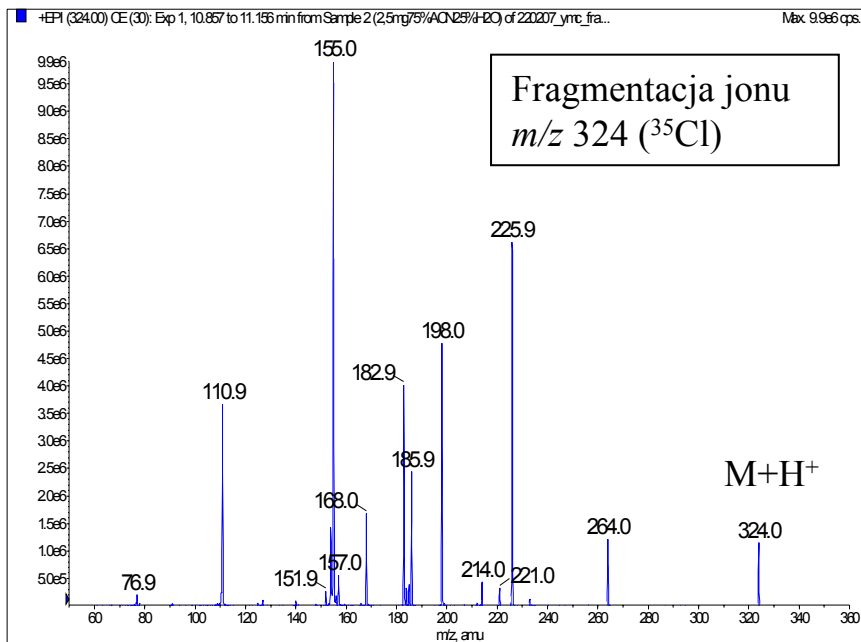
Wnioski: badany związek ma grupę o masie 31 Da w pierścieniu tiofenowym

Prawdopodobna struktura:



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Zanieczyszczenie Clopidogrelu o masie 323/325 Da

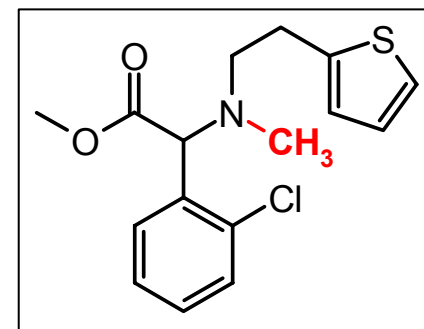


Różnica masy: +2 Da (2H).

Drogi fragmentacji: istotne różnice w porównaniu z Clopidogrelem, ale niektóre jony wspólne (183/185, 155/157).

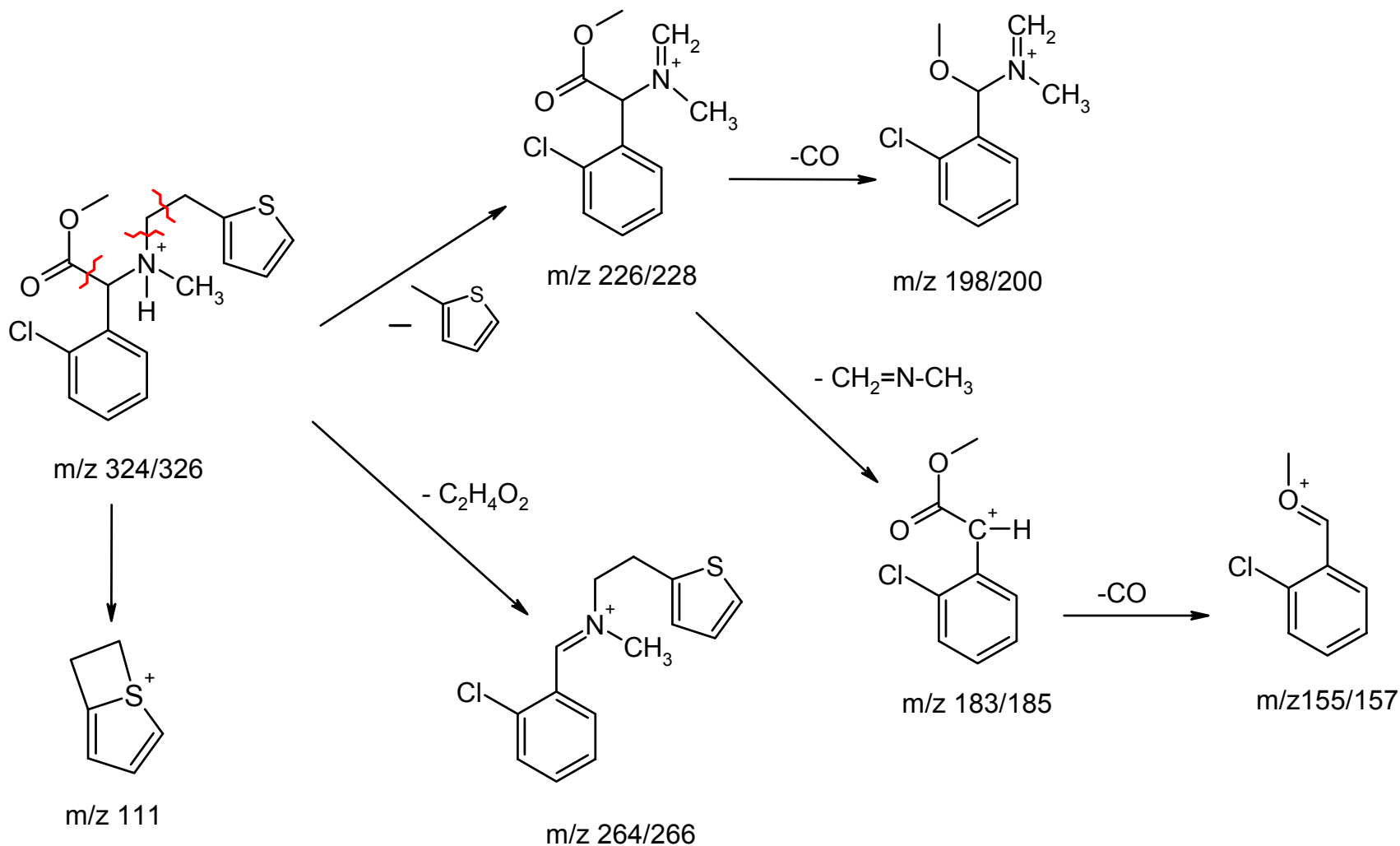
Wnioski: brak fragmentacji typu RDA świadczy o nieobecności pierścienia 6-członowego z atomem azotu.

Prawdopodobna struktura:



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Proponowane drogi fragmentacji zanieczyszczenia o masie 323/325



Literatura polskojęzyczna z dziedziny spektrometrii mas

