

Új kábítószerek szerkezetazonosítása, speciális vizsgálatok, referenciaanyagok

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Mi minősül „új anyagnak”?

Számunkra új az az anyag, amely hazánkban korábban még nem fordult elő lefoglalásokban, nem azonosítottuk.

Analitikai adatok:

- nemzetközi adatbázisokban megtalálható 😊
- nem található az adatbázisokban ☹️

Új az „új”?

Példa katinonok megjelenésére

1930-as évek (USA): az **amfetaminok** depresszió ellen ható, fogyást elősegítő, légúti megbetegedések ellen bevezetett készítmények hatóanyagai



"...if the individual is depressed..."

... If the individual is depressed or anhedonic... you can change his attitude... by physical means just as surely as you can change his digestion by distressing thought... In other therapeutics are just as physical therapeutics as good advice and analysis and must be used together with these latter agents of cure."

Myerson, A.—*Anhedonia*—*Am. J. Psychiatry*, July, 1922.

When this was written—in 1922—the only stimulant drugs employed in the treatment of simple depression were of limited effectiveness.

SMITH, KLINE & FRENCH LABORATORIES, PHILADELPHIA, PA.

XIII

Only in the last decade has there been available—in Benzedrine Sulfate—a therapeutic weapon capable of alleviating depression, overcoming "chronic fatigue" and breaking the vicious circle of anhedonia.

BENZEDRINE SULFATE TABLETS
(amfetamin-sulfát)



IN MILD PSYCHOGENIC DEPRESSIVE STATES...

this
IN MINUTES!
...WITH

RAPHETAMINE PHOSPHATE
Brand of Amphetamine Phosphate

CHEERFULNESS
MENTAL ALERTNESS
OPTIMISM

• Smooth, fast acting RAPHETAMINE Phosphate acts in restoring mental alertness, cheerfulness and active states... and in the management of obesity.

With contraindications chiefly limited to hypertension, cardiac defects, or hypersensitivity to this may be postponed.

Newly accepted parenteral RAPHETAMINE Phosphate can successfully be used in treating barbiturate addiction because of its immediate action.

Clinical supply of both dosage forms available on request. Write: Wm. R. J. Strassenburgh Co., Rochester 14, N. Y.

parenteral: RAPHETAMINE Phosphate, parenteral containing 25 mg. monobasic racemic amphetamine phosphate per cc. available in 10 cc. multidose vials.

Tablet: RAPHETAMINE Phosphate tablets containing 5 mg. amphetamine phosphate per tablet available in bottles of 100, 500 and 1000.

Strassenburgh
ROCHESTER 14, N. Y.

Példa katinonok megjelenésére

1960-as évek (USA): függőség nagy számban volt felismerhető, hosszútávú mellékhatások megjelenése, a helyzet válságossá vált, kísérletek indultak hasonló hatású, kevésbé addiktív és káros mellékhatásoktól mentes szerek kidolgozására.

ANDREAS J ROTTENDORF CHEMISCHE FABRIK

1967

Appetite-suppressing and weight reducing composition

1969

THERAPEUTICALLY ACTIVE SECONDARY AND TERTIARY 1-HALOGENPHENYL-2-AMINO-ALKANONES

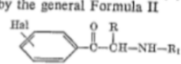
United States Patent Office 3,313,687
Patented Apr. 11, 1967

1
3,313,687
APPETITE-SUPPRESSING AND WEIGHT REDUCING COMPOSITION

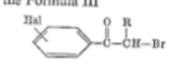
Harm Siemer, Warendorf, Westphalia, Germany, assignor to Andreas J. Rottendorf Chemische Fabrik, Emmerloh, Westphalia, Germany
No Drawing. Filed Sept. 17, 1962, Ser. No. 224,603
Claims priority, application Germany, Sept. 18, 1961, R 31,127; May 16, 1962, R 32,737; May 19, 1962, R 32,756
5 Claims. (Cl. 167-55)

The present invention relates to novel therapeutically effective compounds, and a process of preparing the same. The compounds of this invention are secondary and tertiary 1-halogen-phenyl-2-amino-alkanones (1) which are very useful agents having appetite suppressing properties.

2
bromophenyl-2-ethylamino-propanone (1) and which are represented by the general Formula II



5 can be prepared in good yields by reacting α -Bromo-alkanones (1) of the Formula III



10 where in R has the meaning as above, with primary amines of the formula H_2N-R_1 , e.g., methylamine, ethylamine, butylamine or isobutylamine, the reaction taking place at elevated temperatures, preferably in the range of 60-80° C. in the presence of a solvent.

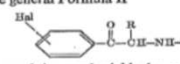
United States Patent Office 3,465,039
Patented Sept. 2, 1969

1
3,465,039
THERAPEUTICALLY ACTIVE SECONDARY AND TERTIARY 1-HALOGENPHENYL-2-AMINO-ALKANONES (I)

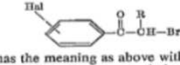
Harm Siemer, Warendorf, Westphalia, Germany, assignor to Andreas J. Rottendorf Chemische Fabrik, Emmerloh, Germany
No Drawing. Original application Sept. 17, 1962, Ser. No. 224,603, now Patent No. 3,313,687, dated Apr. 11, 1967. Divided and this application Feb. 16, 1967, Ser. No. 664,574
Int. Cl. C07c 97/10; A61k 25/00
U.S. Cl. 260-570.5
12 Claims

2
In view of the just mentioned low side effects, these compounds are very useful drugs in the treatment of obesity and particularly in pre-existing hypertension. Moreover, no abuse is to be expected because of the comparatively low central stimulation, such abuse being due to the stimulating and euphoric effect of known anorexigenic agents.

The secondary 1-halogenphenyl-2-alkylamino-alkanones (1) according to the invention in which in Formula I the symbol $X=NH-R_1$, wherein R_1 is an alkyl radical with straight or branched chain having 1 to 5 C-atoms e.g., 1-o-chlorophenyl-2-ethylamino-propanone (1), 1-o-chlorophenyl-2-propylamino-propanone (1) or 1-o-bromophenyl-2-ethylamino-propanone (1) and which are represented by the general Formula II

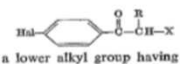


15 can be prepared in good yields by reacting α -bromo-alkanone (1) of the Formula III



20 where in R has the meaning as above with primary amines of the formula H_2N-R_1 , e.g., methylamine, ethylamine, butylamine or isobutylamine, the reaction taking place at elevated temperatures, preferably in the range of 60-80° C., in the presence of a solvent, e.g., in aqueous-alcoholic solution. It is desirable to use the amine in excess. The solution resulting from the reaction is neu-

ABSTRACT OF THE DISCLOSURE
1-p-halogenphenyl-2-amino-alkanones-(1) of the formula:

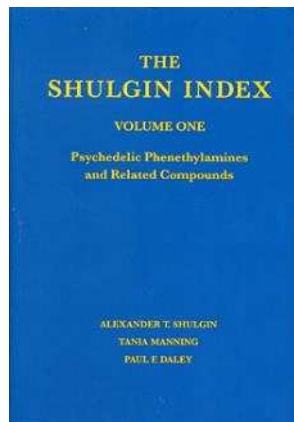
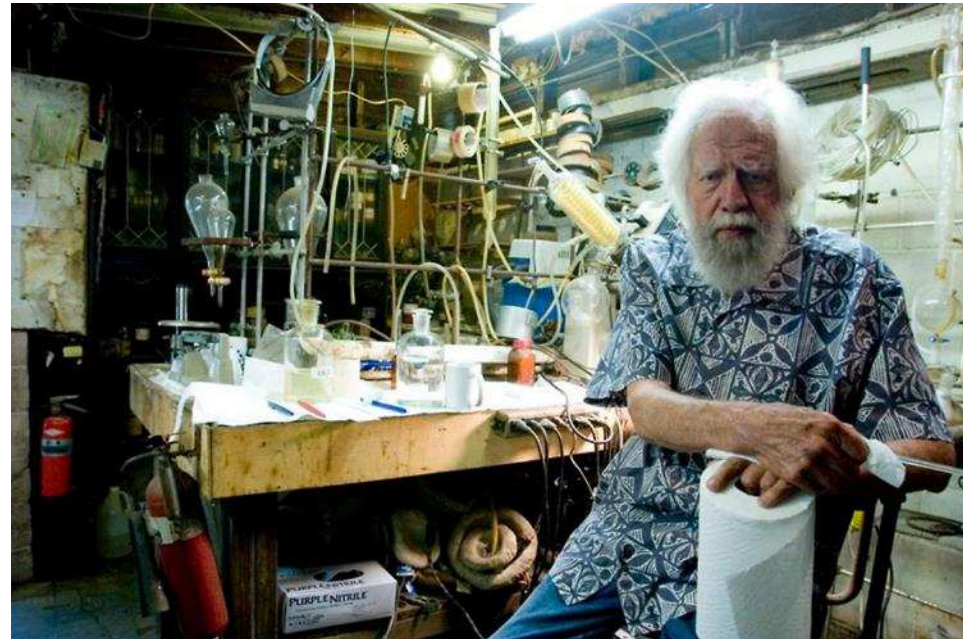
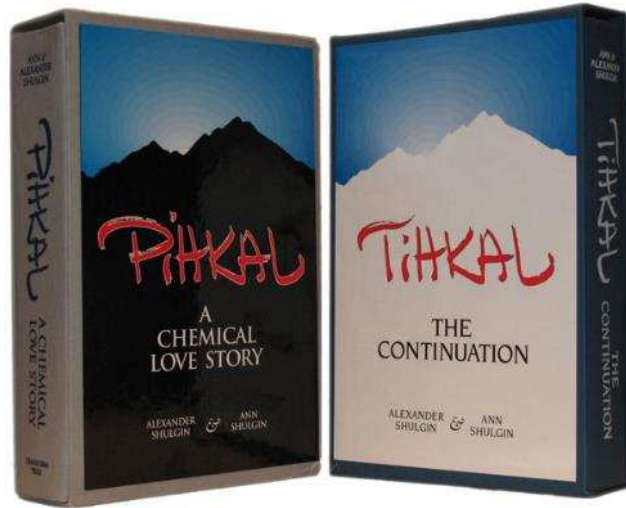


wherein R is a lower alkyl group having 1 to 3 carbon atoms, X is monoalkylamino or dialkylamino in which each of the alkyl moieties has 1 to 5 carbon atoms, and Hal is chlorine or bromine; also, acid addition salts of these compounds.

This application is a division of copending application, Ser. No. 224,603, filed Sept. 17, 1962, now matured into U.S. Patent No. 3,313,687.

1971: ENSZ pszichotróp egyezmény - az amfetamin és egyes származékai is listára kerültek

Triptaminok és fenetilaminok



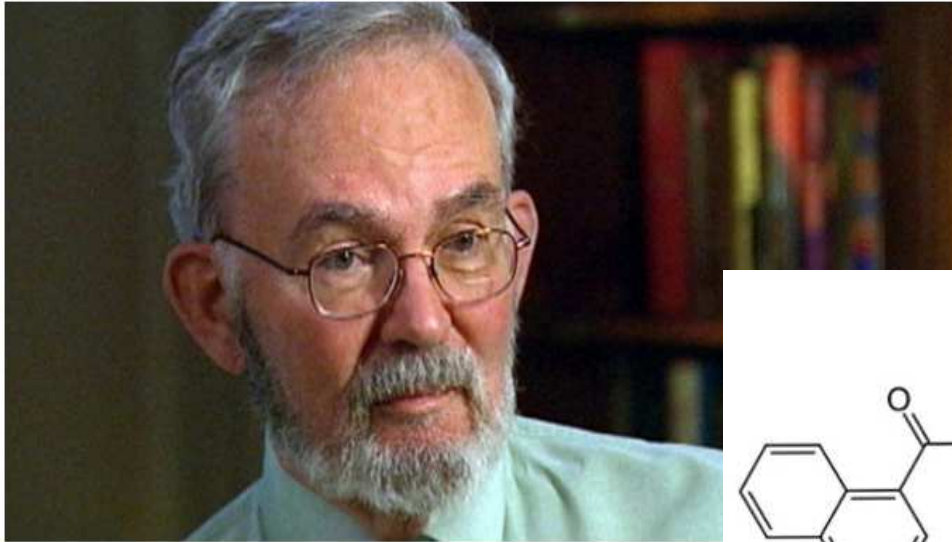
Alexander Theodore
"Sasha" Shulgin (June 17,
1925 – June 2, 2014) was an
American medicinal chemist



- önkísérletek, adagok

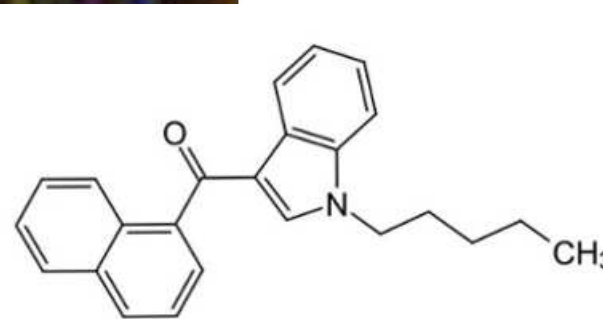
Kannabinoidok

John William Huffman , Clemson University

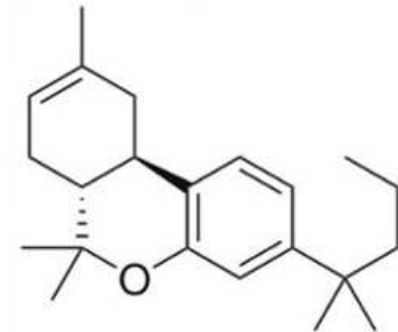


John W. Huffman and his team created more than 450 synthetic chemicals that mimic m

Journal of Pharmacology & Experimental Therapeutics (1998, 285, 995)."



JWH-018

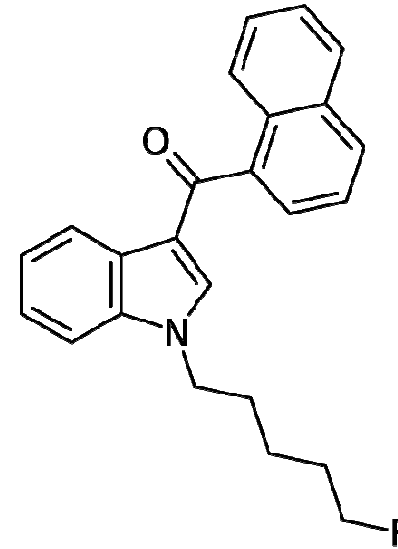


JWH-133

Some of the JWH compounds are far more potent than natural marijuana

Kannabinoidok

Alexandros Makriyannis Northeastern University



AM-2201

- [AM-087](#) — an [analgesic](#) CB₁ agonist derived from Δ^8 THC substituted with a side chain on the 3-position, it has a [K_i](#) of 0.43nM making it roughly 100x as potent as THC.
- (...)
- (...)
- cannabinoid receptors with some selectivity for CB₂.
- [AM-2201](#) — a potent agonist at both CB₁ and CB₂ with moderate selectivity for CB₁, with a K_i of 1.0nM at CB₁ and 2.6nM at CB₂.
- [AM-2212](#) — a potent agonist at both CB₁ and CB₂ with dodecal selectivity for CB₁, with a K_i of 1.4nM at CB₁ and 18.9nM at CB₂.^[5]

Mire számíthatunk?

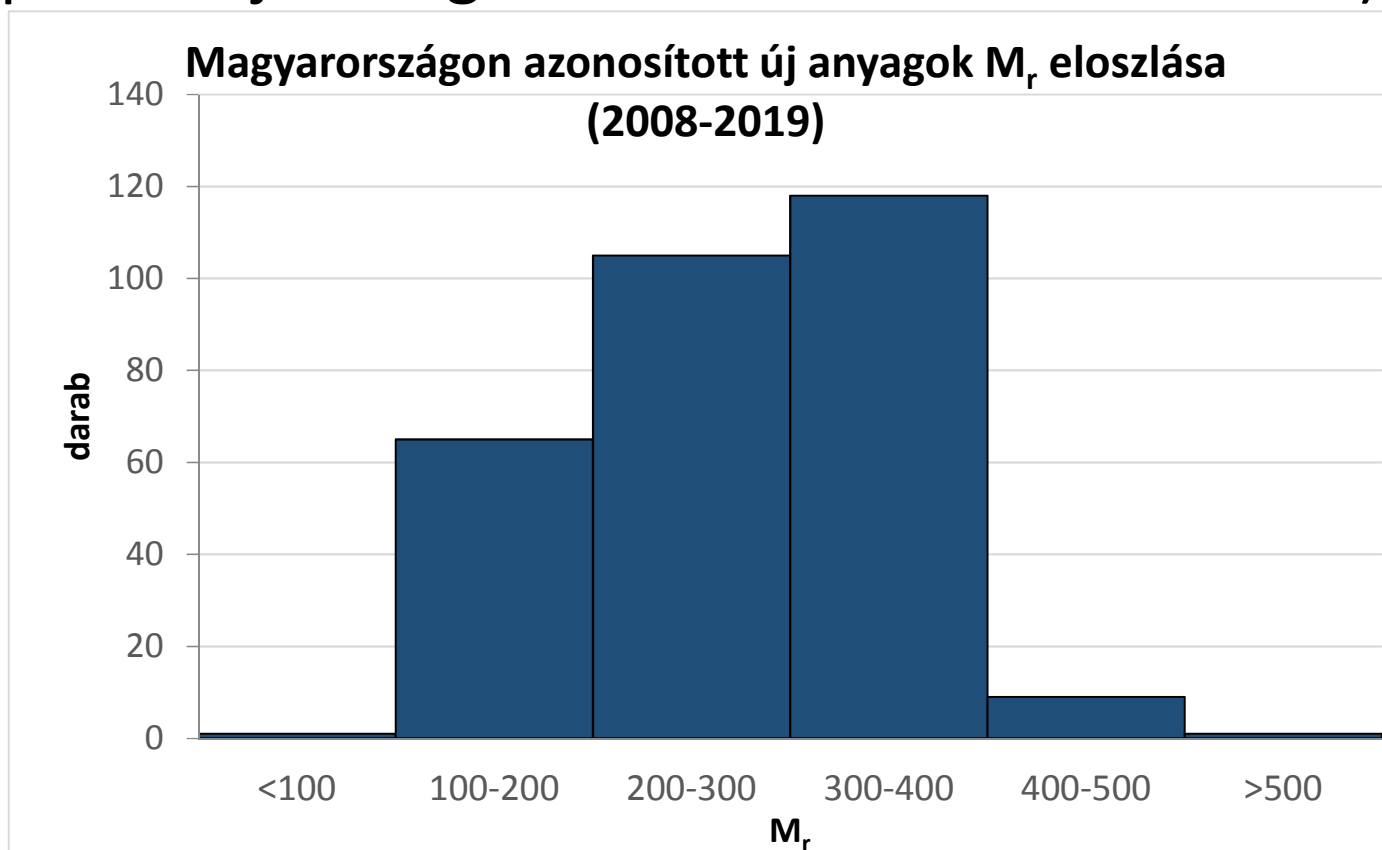
Milyen anyagban találhatunk új hatóanyagot?

- Por
- Tabletta
- Növényi anyagra abszorbeált/impregnált hatóanyag
- Bélyeg / papír
- Tárgyak felületén jelenlévő anyagmaradvány

Mire számíthatunk?

Milyen molekulára bukkanhatunk?

- Szerves kismolekulák (erre vagyunk berendezkedve, így pl. fehérje mérgeket nem tudunk azonosítani)

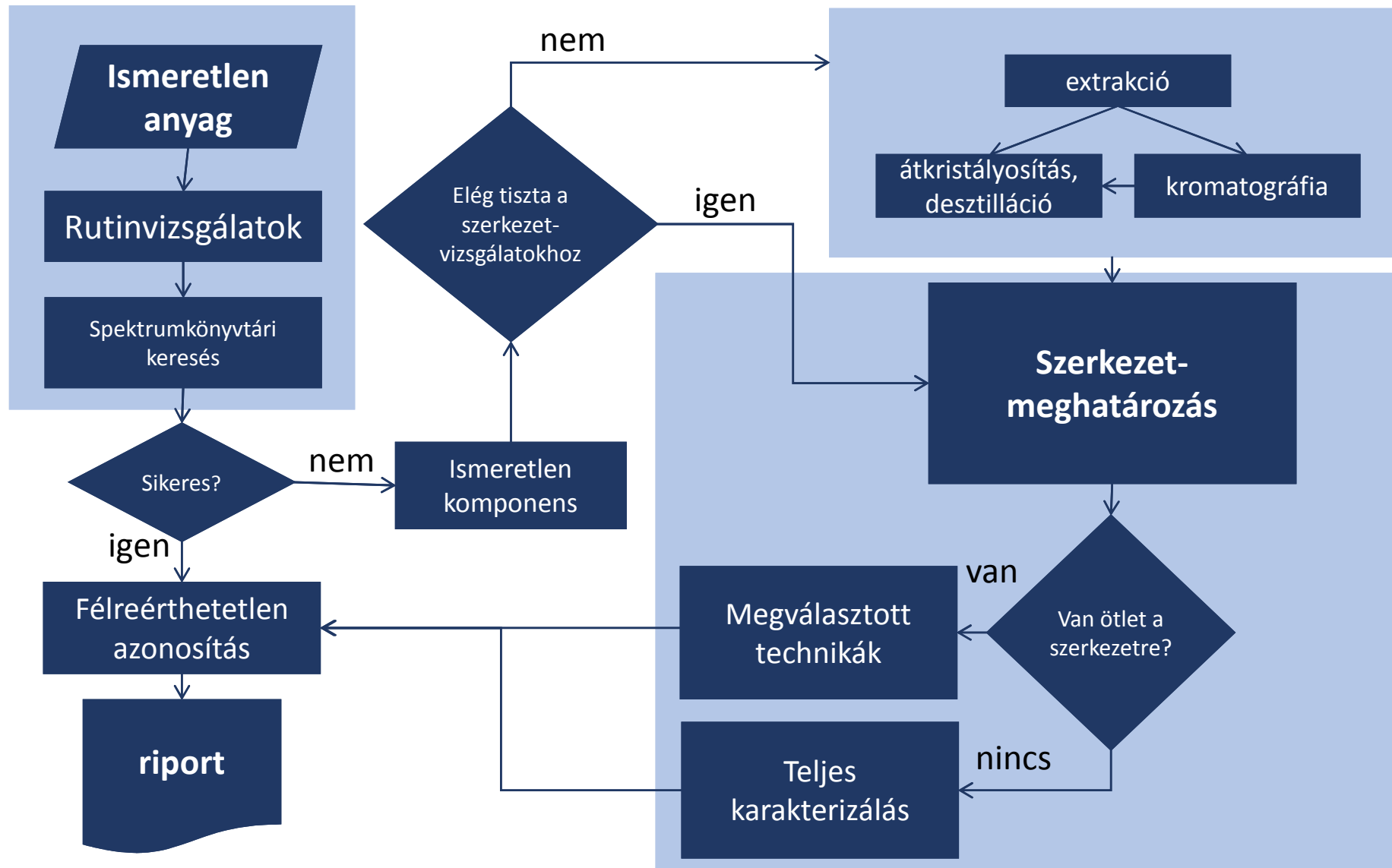


Ezt kaptuk:



- Felismerés: túl vagyunk a rutin analitikán, nincs egyezés a könyvtárakban lévő spektrumokkal, új anyaggal állunk szemben.

Stratégia (út a szakvéleményig)



Ismeretlen anyag kinyerése

homogenizálás

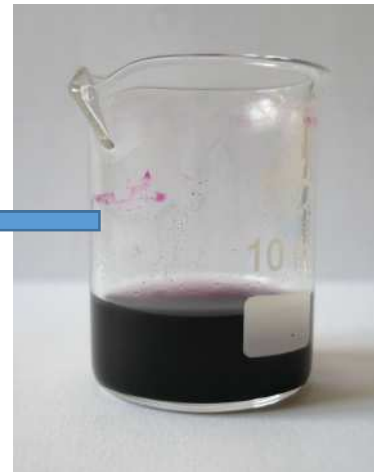
extrakció



kromatográfia

mintaelőkészítés az analízisre

átkristályosítás



Szerkezet-
vizsgálat

Mennyire részletes
szerkezetvizsgálatra van szükség?

Izomerek

Konstitúciós izomerek

- Láncizomerek
- Regio-izomerek (ipso, orto, meta, para)
- Funkciós izomerek
- Tautomerek (enol-oxo) nem jellemző*

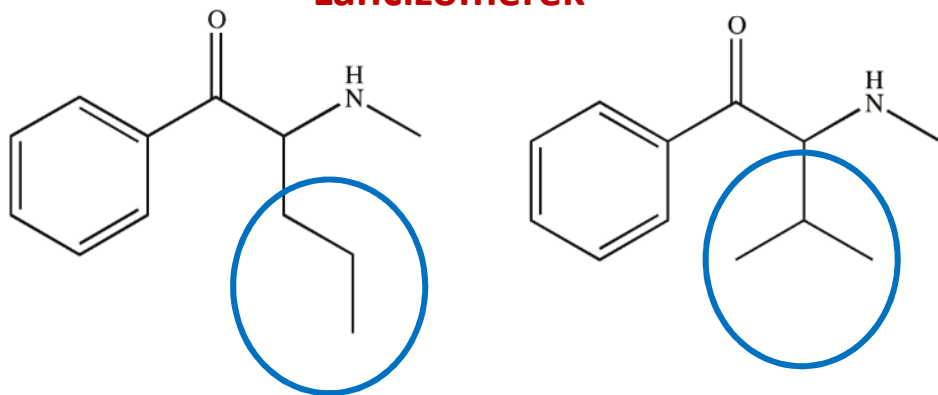
Térizomerek

- Geometriai izoméria (cisz-transz)
- Optikai izoméria (diasztereomerek, centrális enantiomerek)

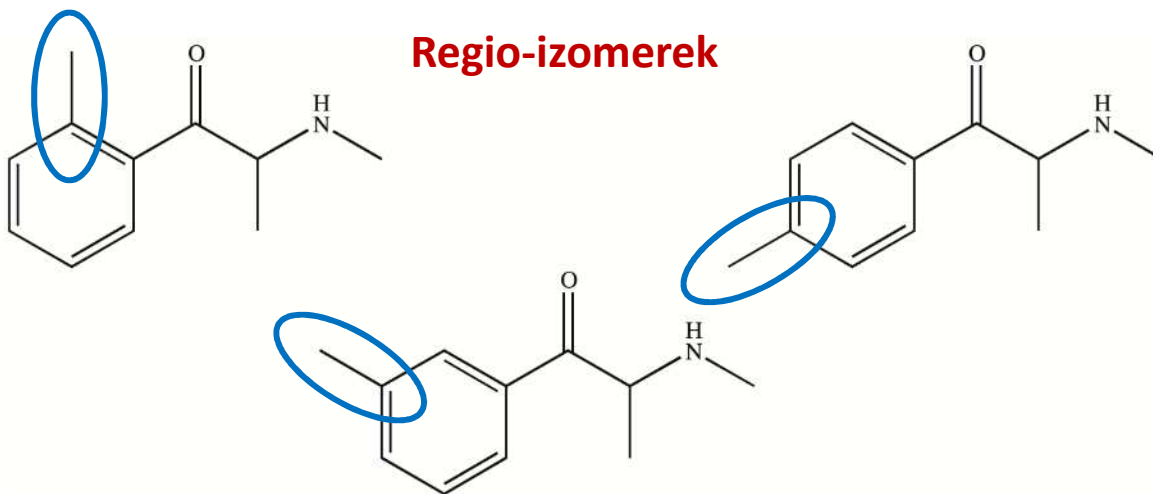
A jogban jelenlévő szerkezetleírások (egyes vegyületek kémiai/IUPAC neve, generikus leírás) határozzák meg azt milyen mélységig kell a szerkezetet bizonyítani. Azonban az analitikus számára sokszor jelent előnyt bizonyos izomériák lehetőségének felismerése adott rendszerben

pl. enol-oxo tautoméria, diasztereomerek elválása kromatográfiás körülmények között

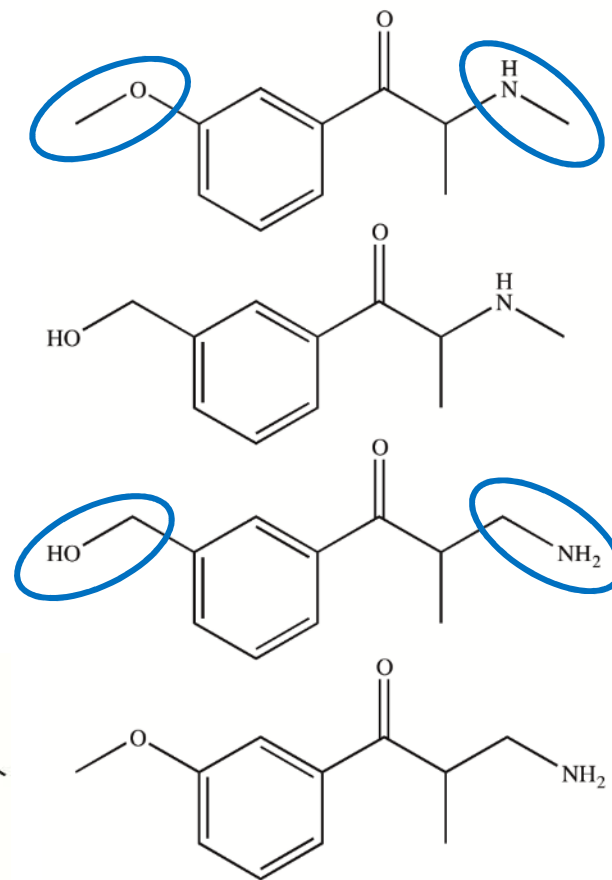
Láncizomerek



Regio-izomerek

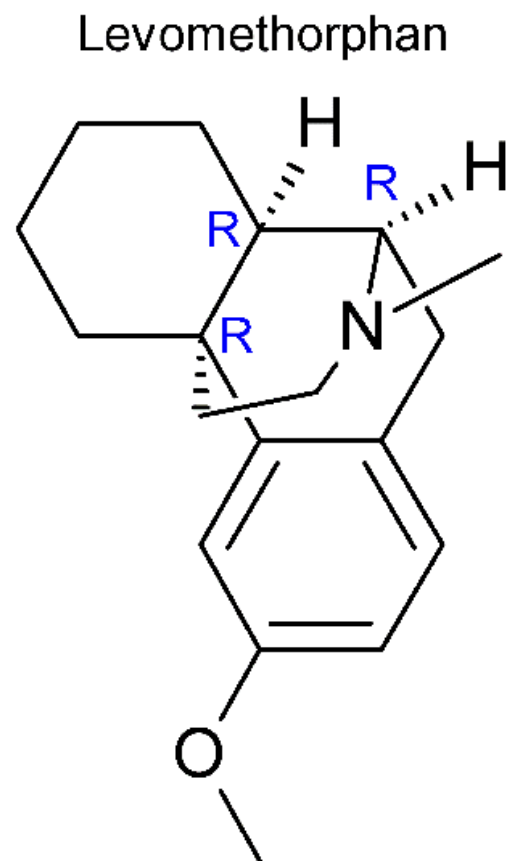


Funkciós izomerek

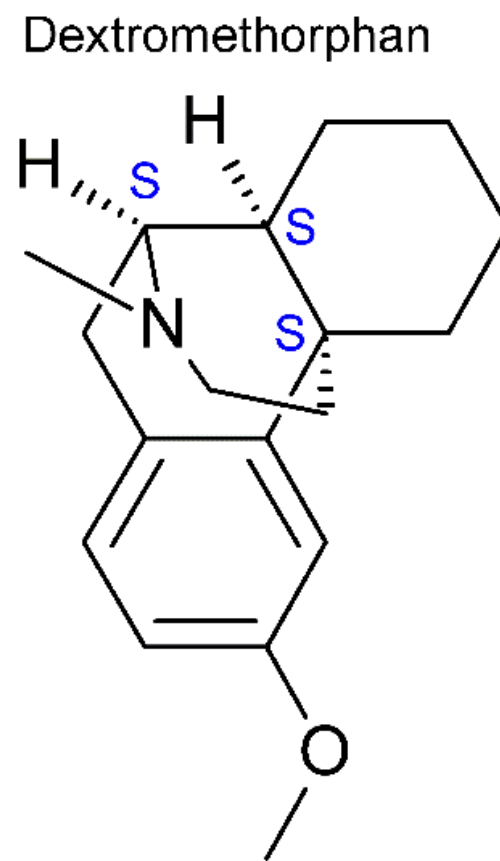


Enantiomerek

A jog nem tesz különbséget, de egyetlen kivétel van:



kábítószer



nincs szabályozás alatt

Tömegspektrometria (MS) (destruktív módszer)



Pontos molekulatömeg
Fragmentáció

HPLC-qTOF

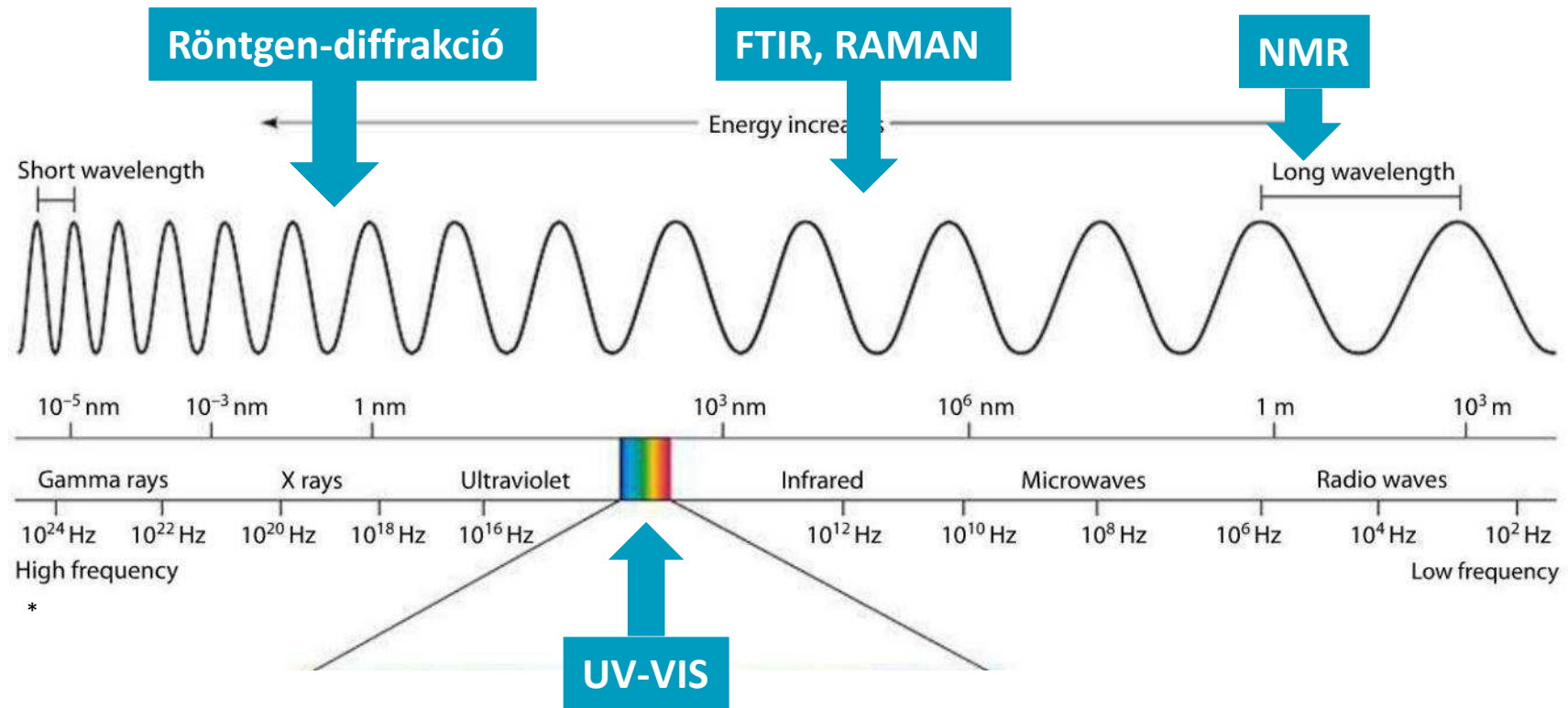


Fragmentáció

LC-MS



Nem destruktív módszerek



*<https://classconnection.s3.amazonaws.com/255/flashcards/4013255/jpg/electromagneticspectrum-141B490BAC872789434.jpg>

Nuclear Magnetic Resonance (NMR) mágneses magrezonancia spektroszkópia



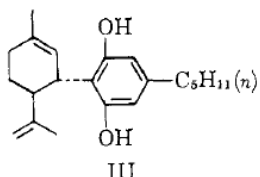
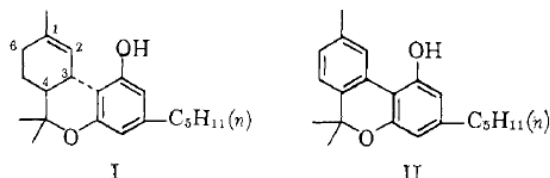
Delta-9-THC szerkezetmeghatározása

Isolation, Structure, and Partial Synthesis of an Active Constituent of Hashish¹

Sir:

Hashish (marihuana), the psychotomimetically active resin of the female flowering tops of *Cannabis sativa* L. is one of the most widely used illicit narcotic drugs. A number of groups have reported the isolation of active constituents.² Most of these substances are not fully characterized, and comparisons with or between them are difficult.

We now wish to report the isolation of an active constituent of hashish to which we assign structure I (Δ^1 -3,4-*trans*-tetrahydrocannabinol).³ This is the first active component whose constitution is fully elucidated.⁴



Chromatography of a hexane extract of hashish on Florisil yielded an active fraction, which on repeated chromatography on alumina could be separated into the inactive cannabinol (II)^{2a} and the tetrahydrocannabinol (I). Further purification of the latter was achieved by the preparation of the crystalline⁵ 3,5-dinitrophenylurethane of I [m.p. 115–116°, $[\alpha]_{\text{CHCl}_3}^{\text{D}}$ -14(°); *Anal.* (C₂₈H₃₃O₇N₃). Found: C, 64.17; H, 6.54],

Az első kereskedelmi forgalomban kapható NMR készülék



TABLE I^a
N.M.R. SPECTRUM OF TETRAHYDROCANNABINOL (I)

Group	Chemical shift, p.p.m.		
-CH ₃	0.88 (t) (3)		
-CH ₃ (olefinic and α to O)	1.08 (s)	1.38 (s)	1.65 (s)
	(9)		
C-3H	3.14 (br,d; $J = 10$ c.p.s.)		
C-2H	6.35 (br,s) (1)		
H (aromatic)	6.00 (d; $J = 2$ c.p.s.) (1)		
	6.18 (d; $J = 2$ c.p.s.) (1)		
-OH ^b	(1) ^b		

^a Determined on a Varian A-60 spectrometer in CCl₄; values are given in p.p.m. relative to (CH₃)₄Si as internal standard; letters in parentheses denote singlet (s), doublet (d), triplet (t), broad (br), coupling constant (J); numbers in parentheses denote number of protons determined by integration of areas.

^b Peak disappears on addition of D₂O.

NMR - szerkezetfejtés

^1H NMR spektrum

Kémiai eltolódás szerkezetfüggése:

Magok hibridállapota

- 0,0 – 1,5 ppm $\text{sp}^3 \text{C} - ^1\text{H}$, $\text{sp}^3 \text{C}$ szomszéd maggal
- 1,5 – 2,5 ppm $\text{sp}^3 \text{C} - ^1\text{H}$, $\text{sp}^2 \text{C}$ szomszéddal
- 2,5 – 4,5 ppm $\text{sp}^3 \text{C} - ^1\text{H}$, heteroatom szomszéddal
- 4,5 – 6,5 ppm $\text{sp}^2 \text{C} - ^1\text{H}$
- 6,5 – 8,0 ppm aromás $\text{C} - ^1\text{H}$

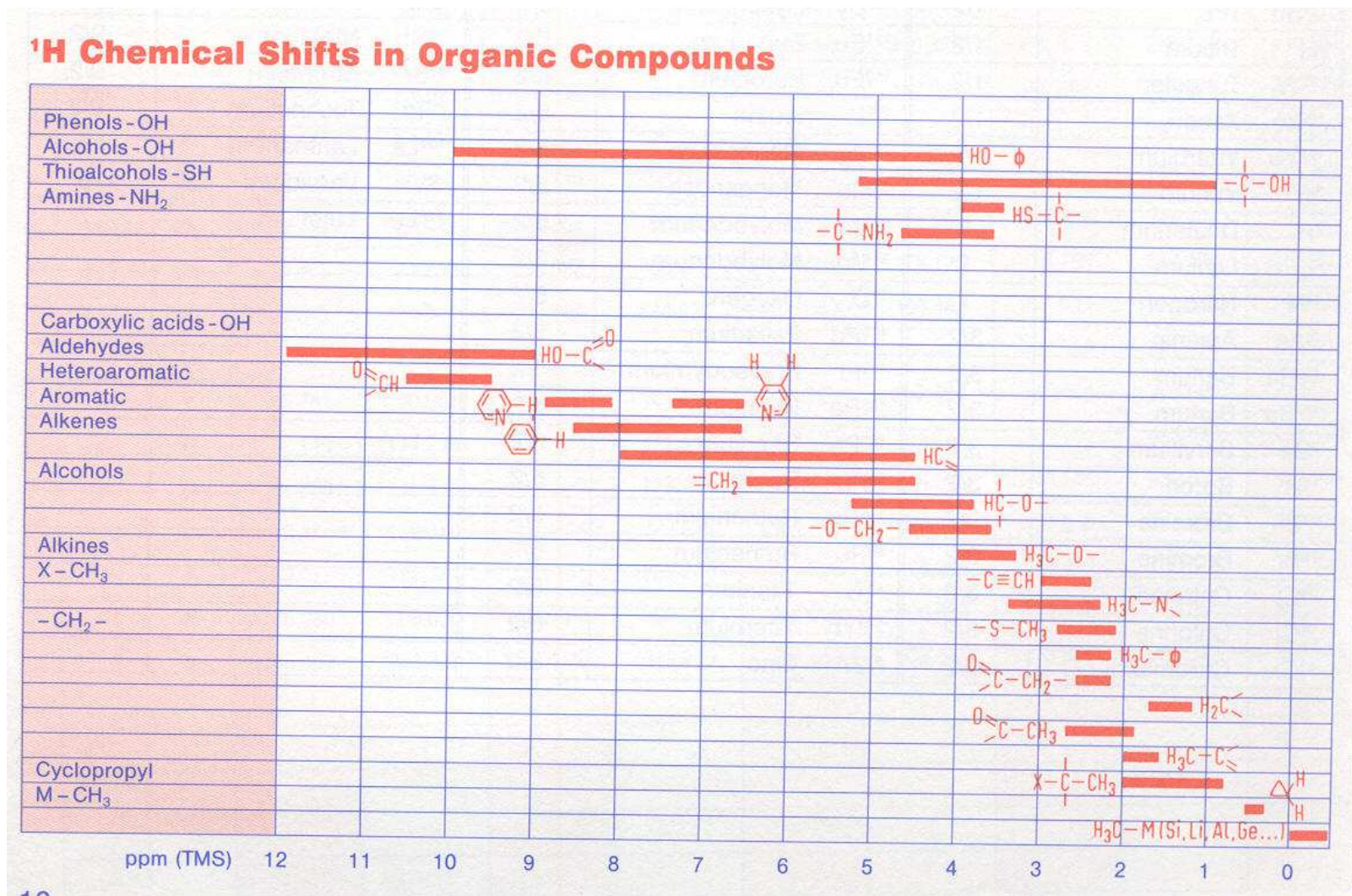
Szomszédos magok elektronegativitása

Pl. halogének elektronszívó hatásuk miatt csökkentik a mag körüli e- sűrűséget -> növelik a kémiai eltolódást

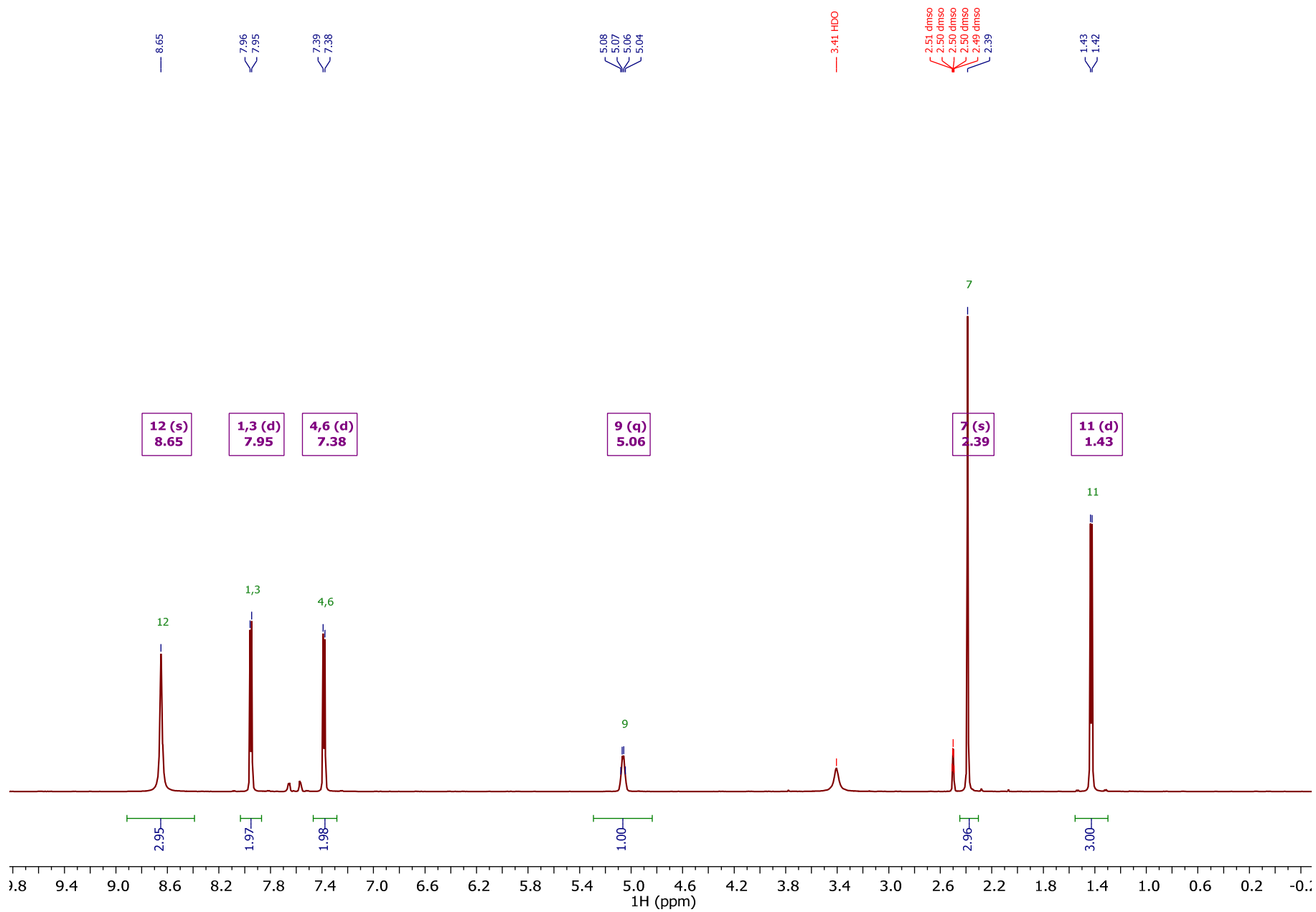
Elektronsűrűséget befolyásoló összes tényező (pl. mátrix hatás)

Jelfelhasadás szabály: $k=2NI+1$ *N:szomszédos csatolt magok száma; l: spin*
l=1/2 spin és egymás közötti ekvivalencia esetén $k=N+1$

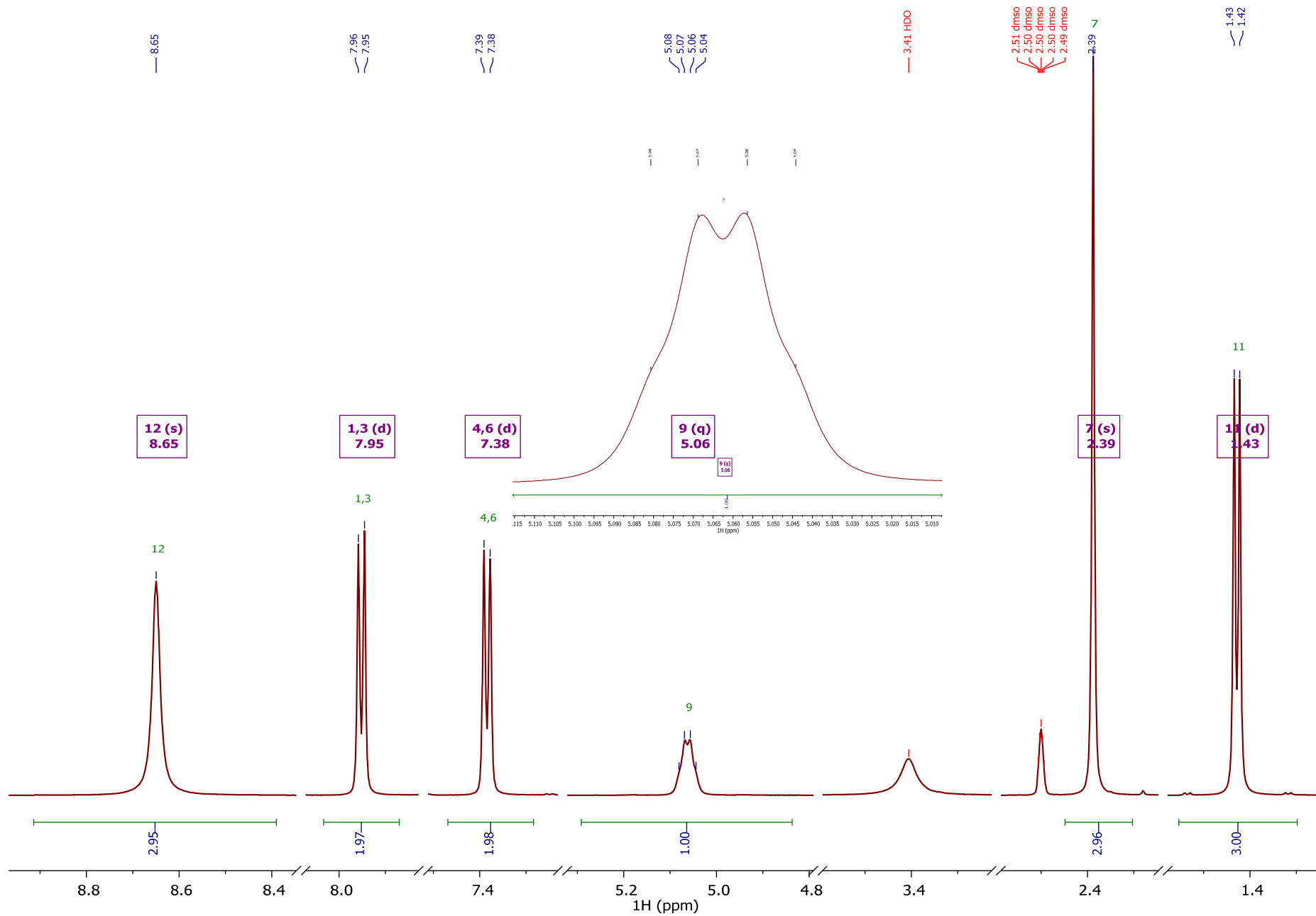
^1H -NMR Kémiai eltolódás diagram



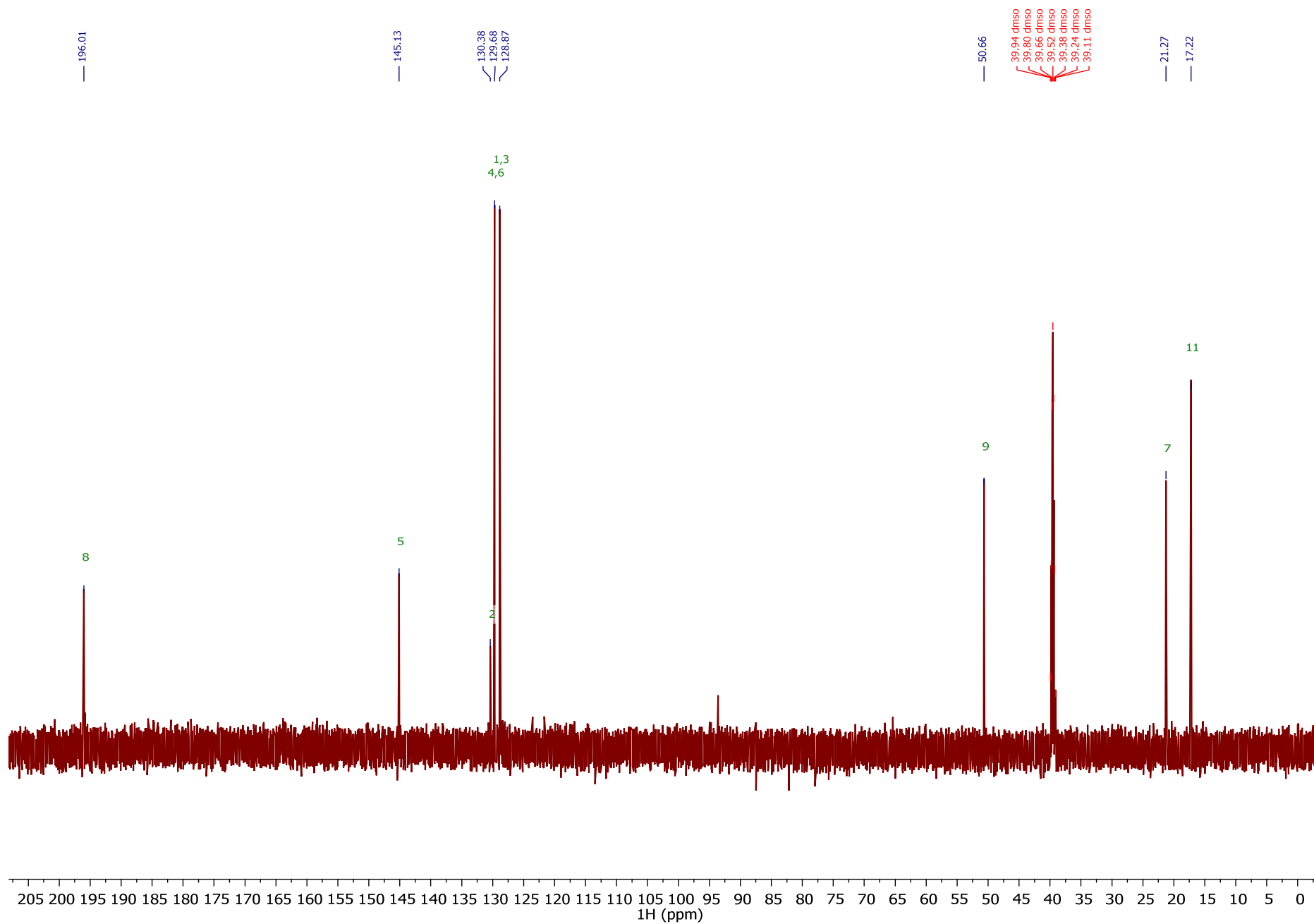
Példa C₁₀H₁₃NO



Példa C₁₀H₁₃NO

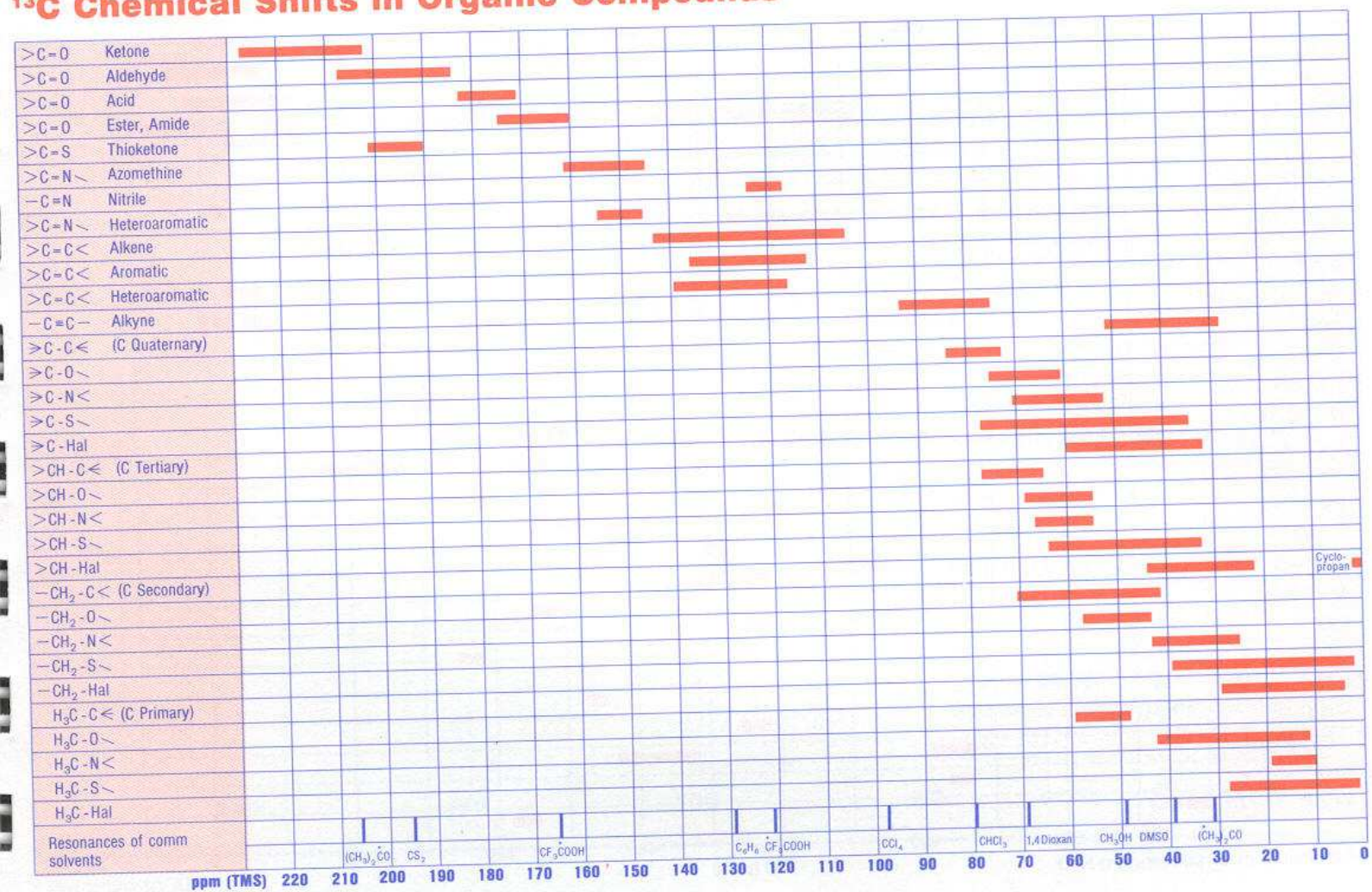


Példa C₁₀H₁₃NO

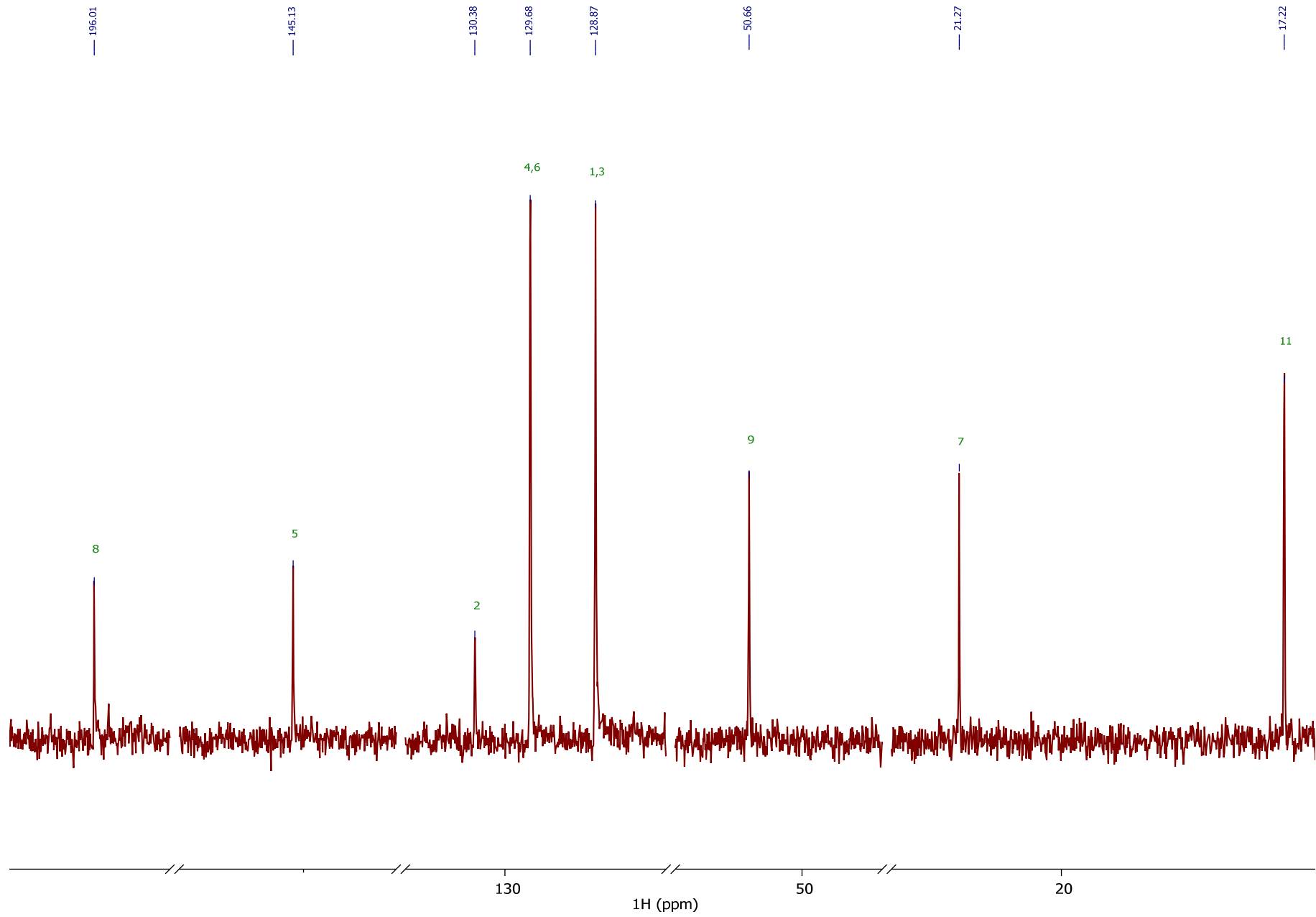


^{13}C -NMR kémiai eltolódás diagram

^{13}C Chemical Shifts in Organic Compounds *



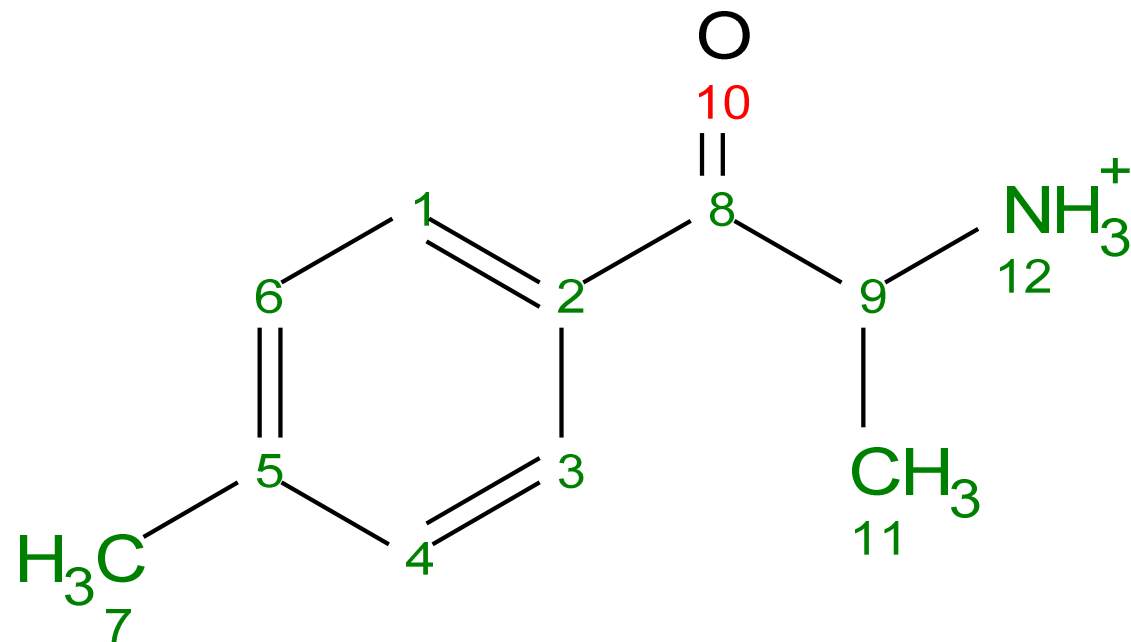
Példa C₁₀H₁₃NO



Példa C₁₀H₁₃NO

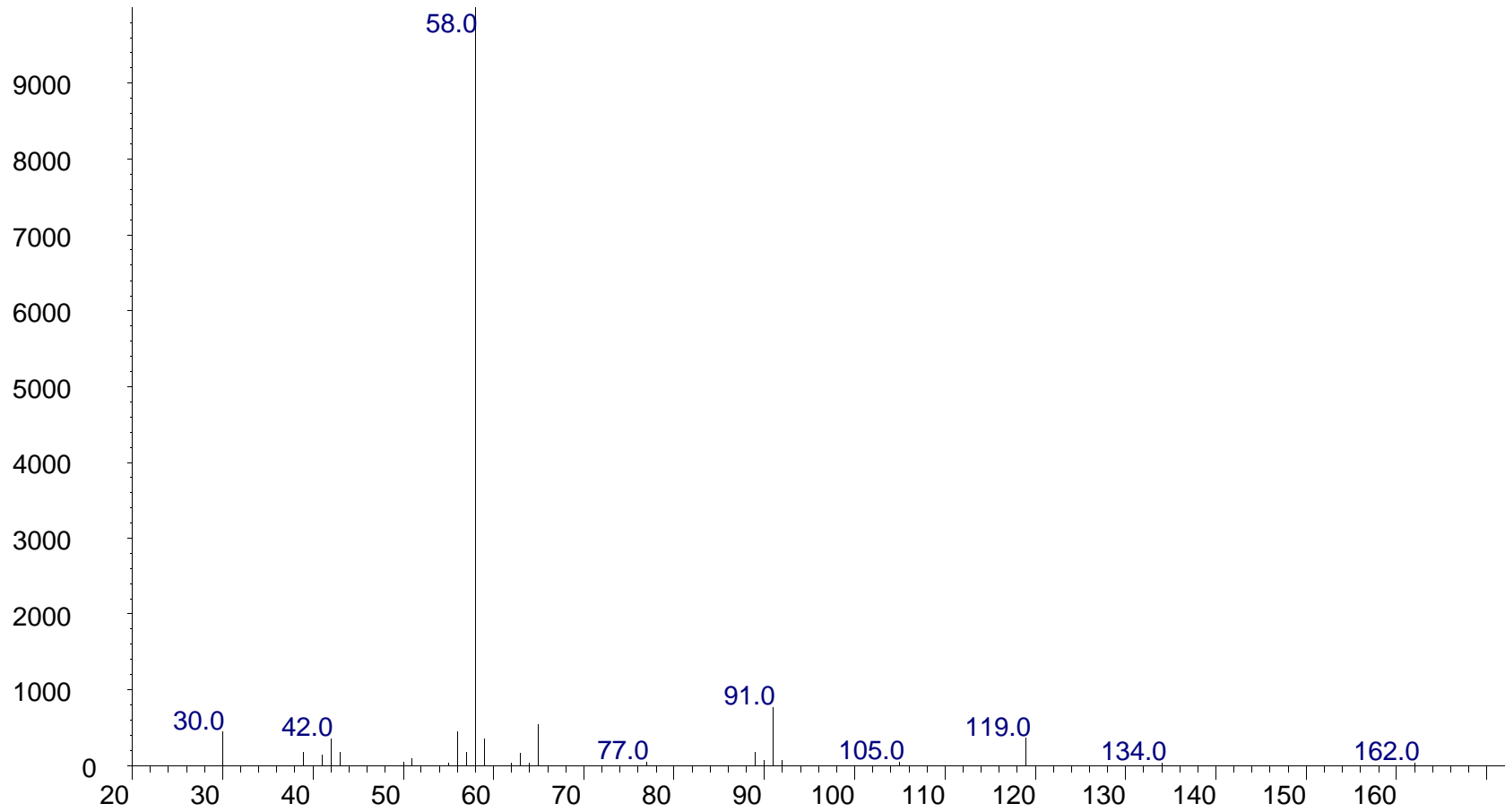
normefedron

2-amino-1-(4-methylphenyl)propan-1-one



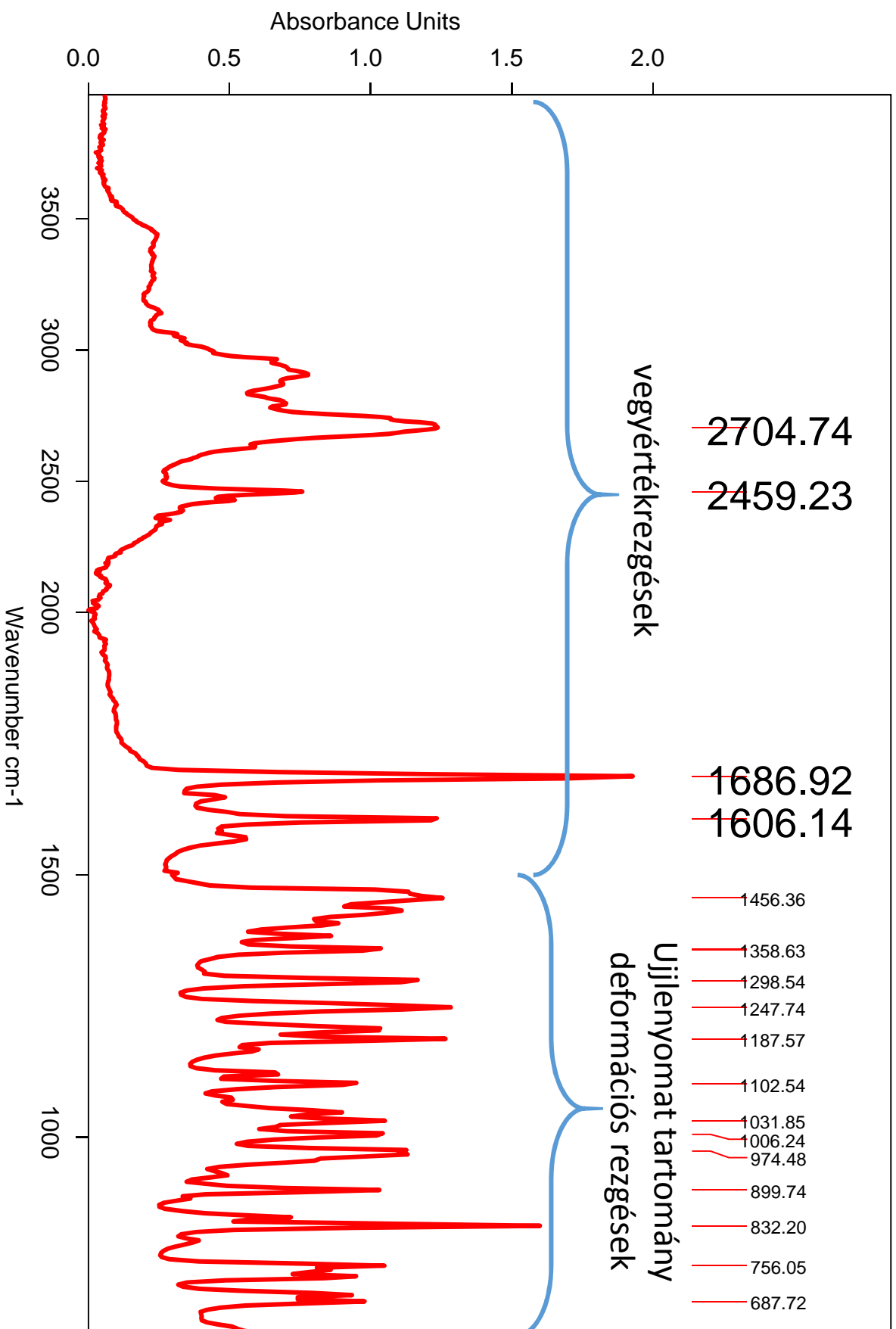
Példa C₁₁H₁₅NO

Abundance



m/z-->

Példa C₁₁H₁₅NO



REFERENCIAANYAGOK

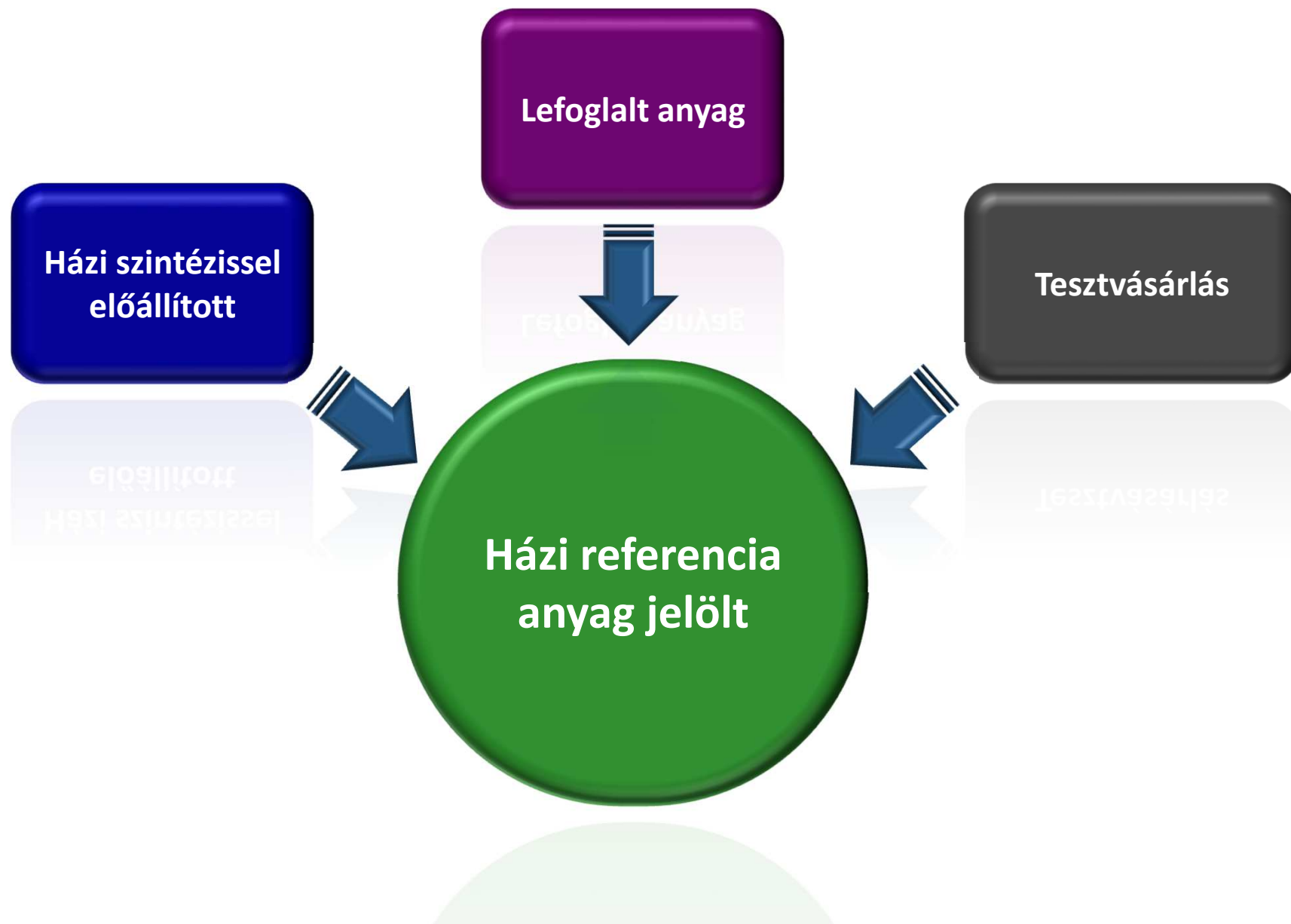
Probléma:

- **Nem elérhető** kereskedelmi forgalomban a szükséges referencia anyag
- Nem várhatunk, 60+30 nap alatt ki kell adni a szakvéleményt (*új pszichoaktív anyagnak minősülő új anyagról be kell bizonyítani, hogy jogi határ alatti vagy fölötti mennyiségről van e szó*)
- A megfelelő minősítéssel rendelkező referencia anyagok **drágák**
- HPLC az igavonó a mennyiségi meghatározásokban, de szüksége van referencia anyagra

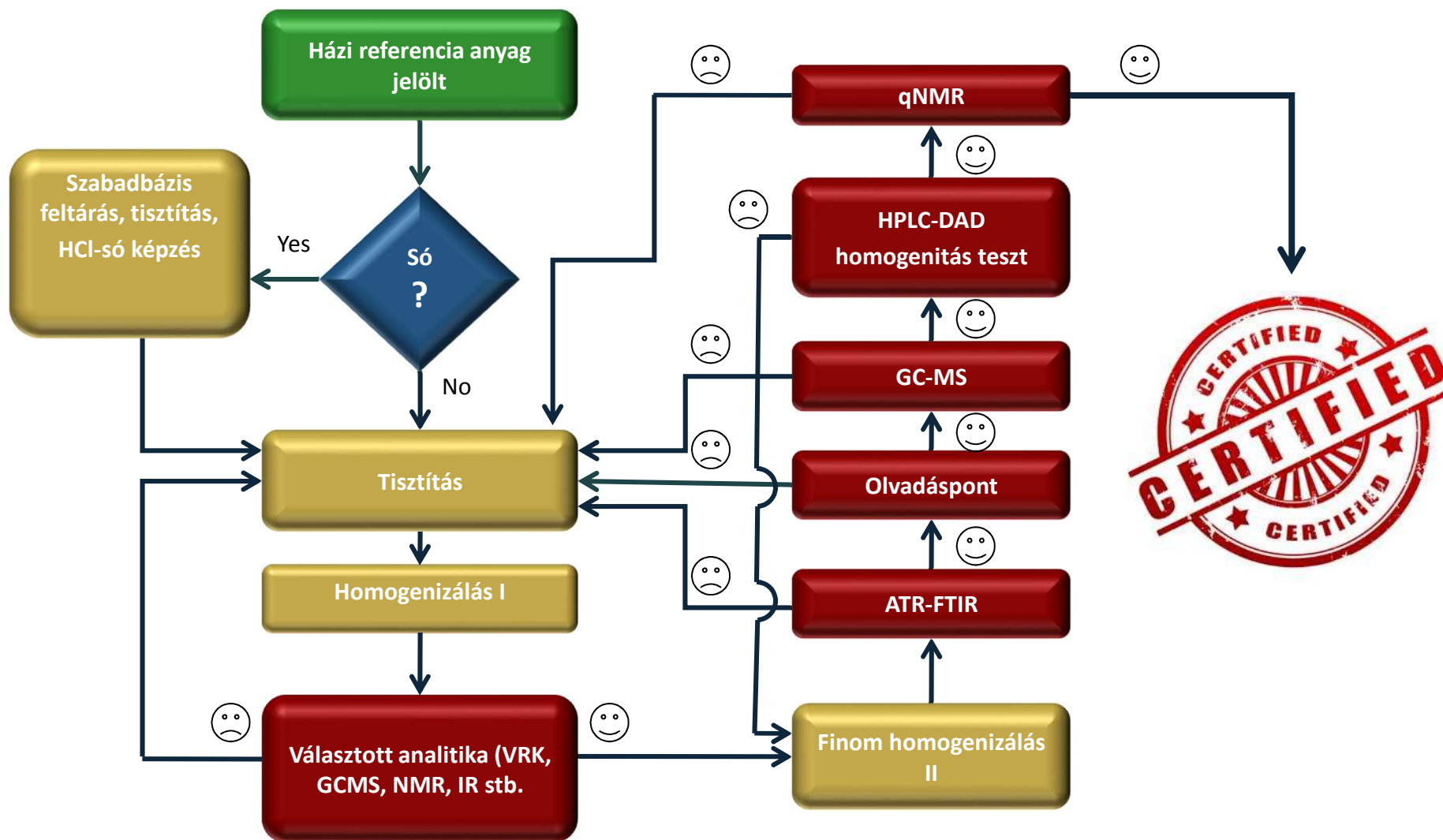
Megoldás:

- Referencia anyagok **házi szintézise**
- Kvantitatív NMR (**qNMR**) alkalmazása.
 - Előnye: mely nem igényel a mérendő anyaggal azonos kémiai szerkezetű referencia anyagot, elválasztástechnikát nem igényel
 - Hátránya: elválasztástechnika hiányában a bonyolultabb mátrixok a mérendő anyagon kívüli NMR aktív komponensei megghiúsíthatják a mérést. Ekkor csak a HPLC a megoldás.










Referenciaanyagok



Házi standard minősítése

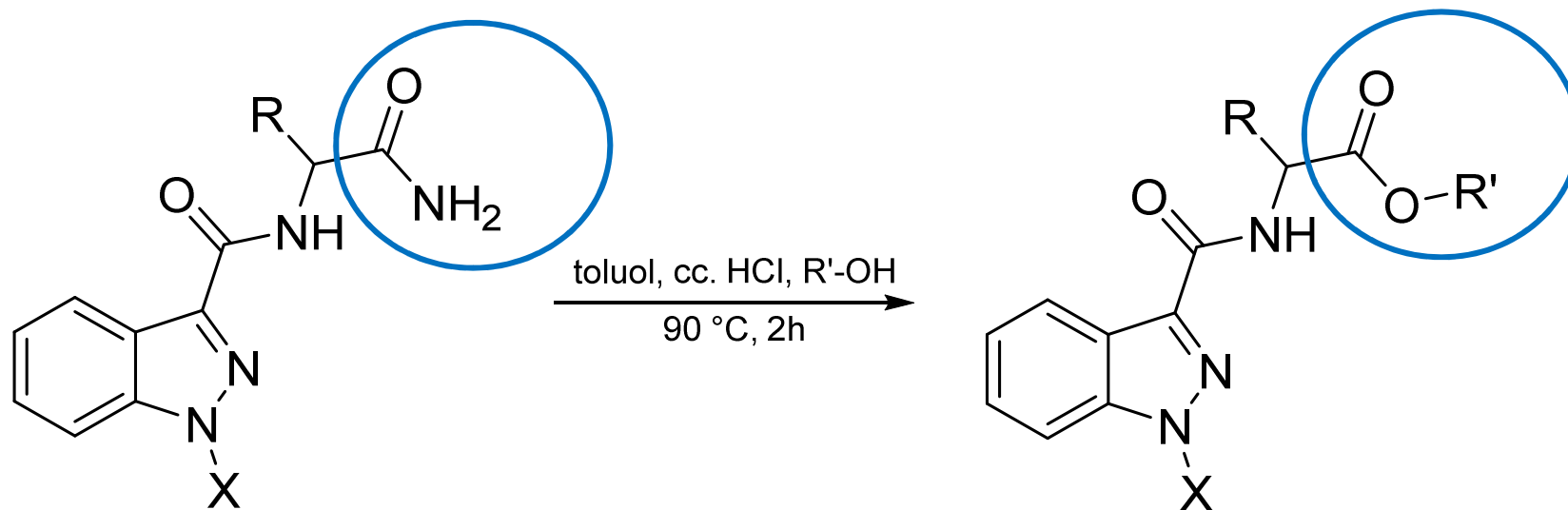


Házi standard minősítése

Technika	Szerkezet információ	Tisztaság	Szennyező
NMR			Egyes szénhidrátok, oldószermaradványok, melléktermékek, rokonszennyező (izomer, homolog stb), kiindulási anyag egyéb szerves szennyezők
ATR-FTIR			Szénhidrátok, oldószermaradványok, kristályoldószeres, melléktermékek, rokonszennyező (izomer, homolog stb), kiindulási anyag egyéb szerves szennyezők, szervetlen és szerves sók, regio-izomerek
Olvadáspont	-		Sejthető, hogy van vagy nincs szennyező, kristályos-amorf szerkezet
GC-MS			Melléktermékek, rokonszennyezők, kiindulási anyag
HPLC-DAD			Melléktermék, rokonmolekulák, egyes szénhidrátok

Házi standard szintézis

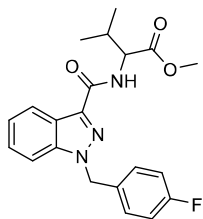
- Házi standard szintézisének elve: minél olcsóbb, minél gyorsabb szintézisút kidolgozása/megválasztása.



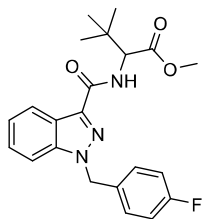
Kiindulási anyag	metilészter	etilészter	izopropilészter
AB-FUBINACA	MMB-FUBINACA	EMB-FUBINACA	iPMB-FUBINACA
ADB-FUBINACA	MDMB-FUBINACA	EDMB-FUBINACA	iPDMB-FUBINACA
AB-CHMINACA	MMB-CHMINACA	EMB-CHMINACA	iPMB-CHMINACA
5F-APP-PINACA	5F-MPP-PINACA	5F-EPP-PINACA	5F-iPPP-PINACA

Házi standard szintézis

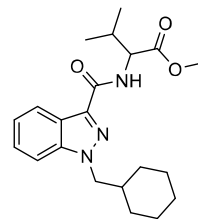
- Egyszerű észterezésel 12 referencia anyagot jött létre



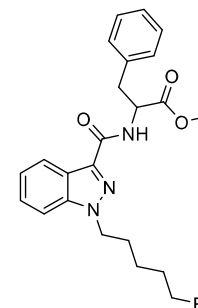
MMB-FUBINACA
 $M = 383 \text{ g/mol}$



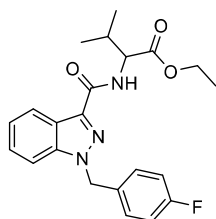
MDMA-FUBINACA
 $M = 397 \text{ g/mol}$



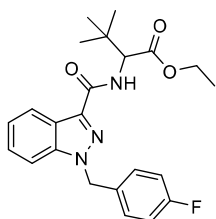
MMB-CHMINACA
 $M = 371 \text{ g/mol}$



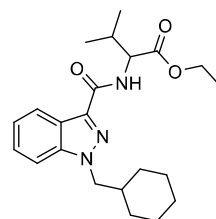
5F-MPP-PINACA
 $M = 411 \text{ g/mol}$



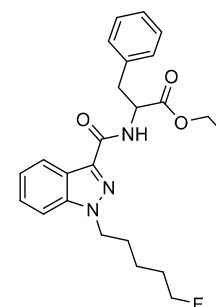
EMB-FUBINACA
 $M = 397 \text{ g/mol}$



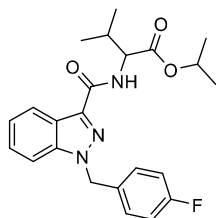
EDMB-FUBINACA
 $M = 411 \text{ g/mol}$



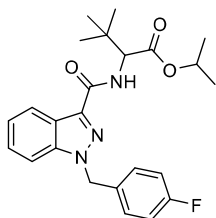
EMB-CHMINACA
 $M = 385 \text{ g/mol}$



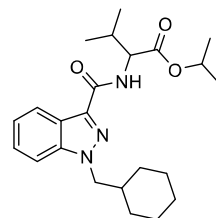
5F-EPP-PINACA
 $M = 425 \text{ g/mol}$



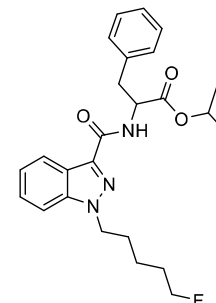
iPMB-FUBINACA
 $M = 411 \text{ g/mol}$



iPDMB-FUBINACA
 $M = 425 \text{ g/mol}$



iPMB-CHMINACA
 $M = 399 \text{ g/mol}$



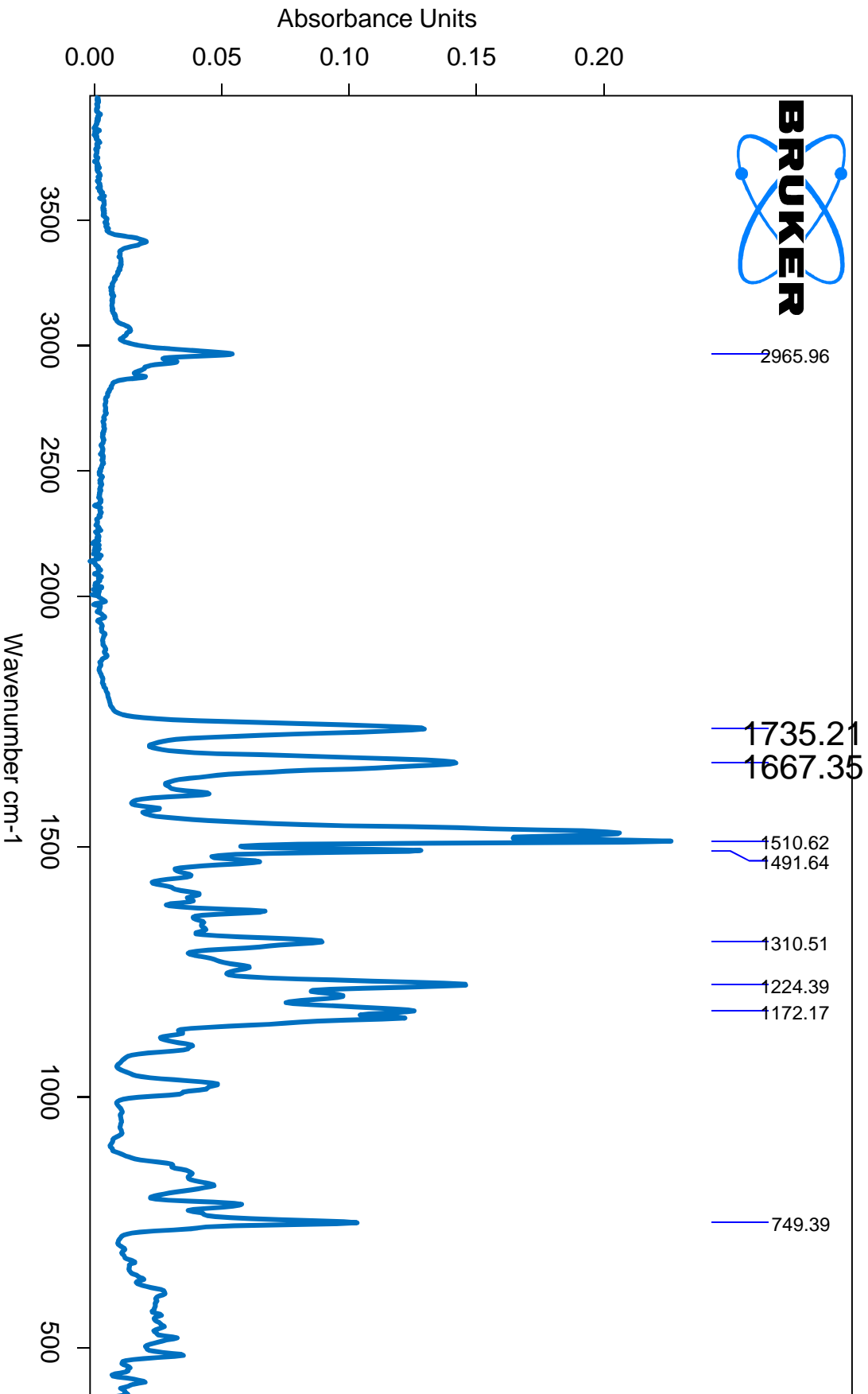
5F-iPPP-PINACA
 $M = 439 \text{ g/mol}$

Szintetizált házi standard minősítése

- ATR-FTIR
- olvadáspont
- GCMS
- HPLC-DAD homogenitásvizsgálat (UV spektrum)
- NMR szerkezetazonosítás, kvantitatív NMR (qNMR)

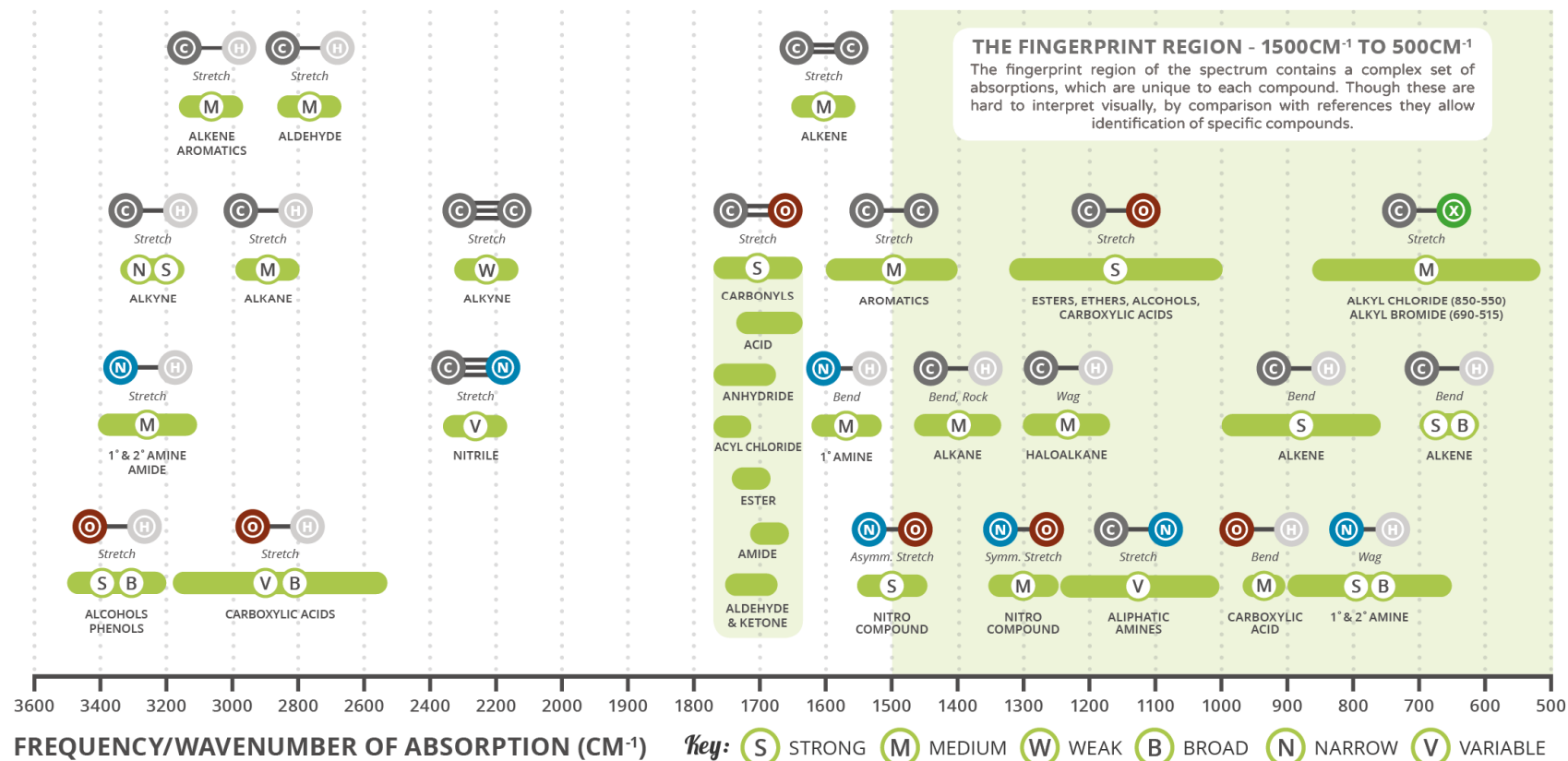
ATR-FTIR

Péida: EMB-FUBINACA



ANALYTICAL CHEMISTRY - INFRARED SPECTROSCOPY

Commonly referred to as IR spectroscopy, this technique allows chemists to identify characteristic groups of atoms (functional groups) present in molecules.

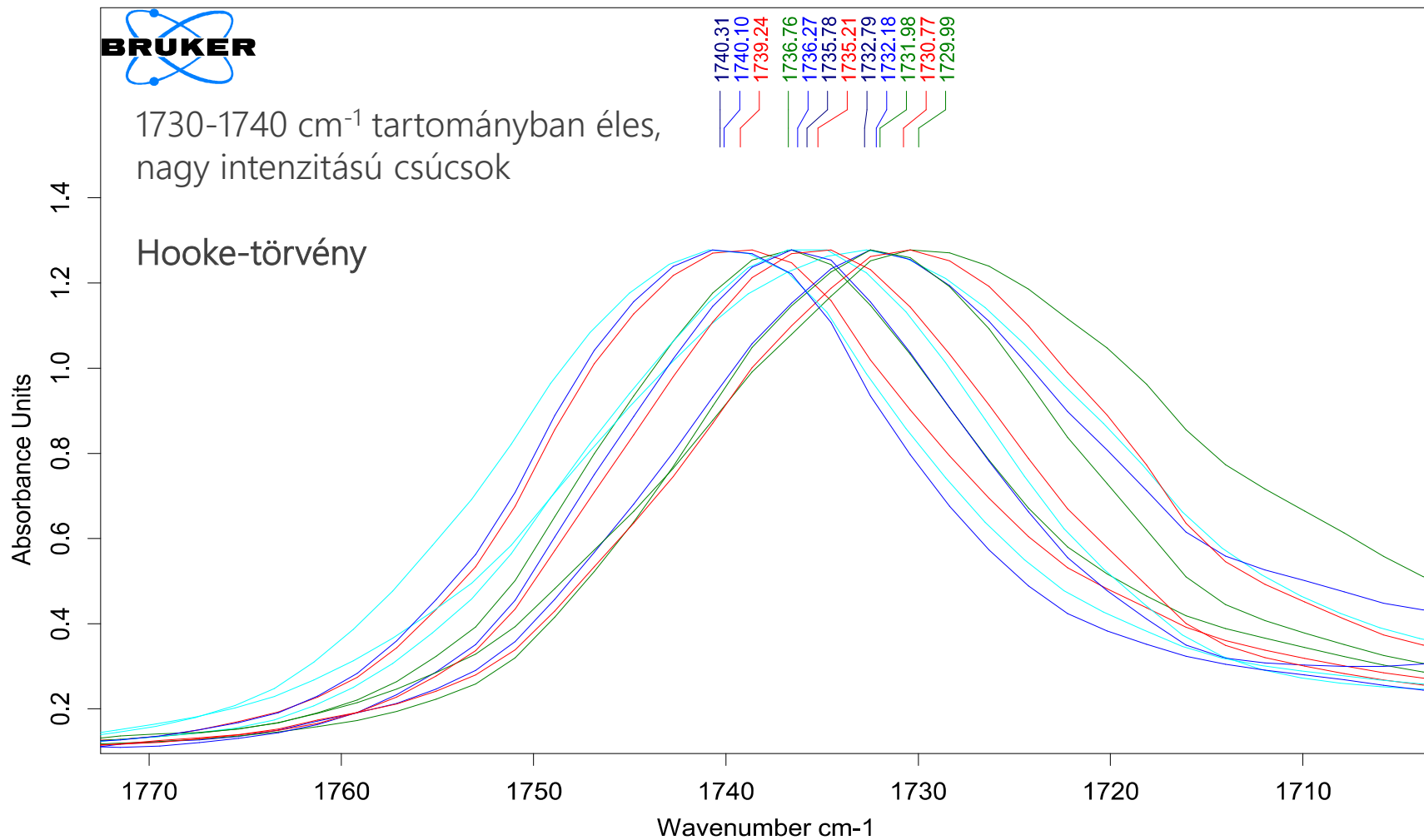


Infrared frequencies make up a portion of the electromagnetic spectrum. If a range of infrared frequencies are shone through an organic compound, some of the frequencies are absorbed by the chemical bonds within the compound. Different chemical bonds absorb different frequencies of infrared radiation. There are a number of characteristic absorptions which allow functional groups (the parts of a compound which give it its particular reactivity) to be identified. This graphic shows a number of these absorptions.



A 12 vegyület észtercsoport karbonil részének ($\nu_{C=O}$) jelei az IR spektrumokban

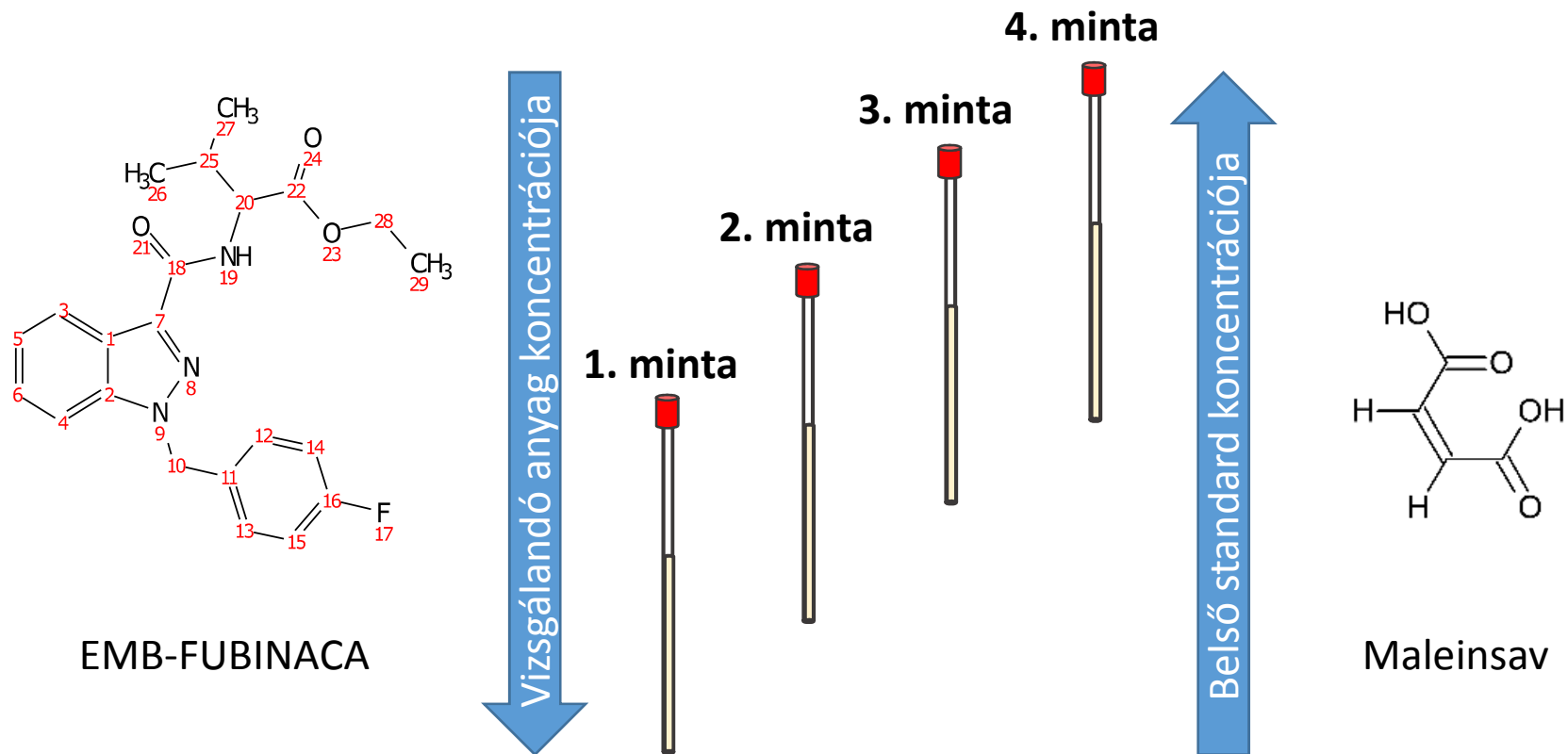
izopropilészter <- etilészter <- metilészter



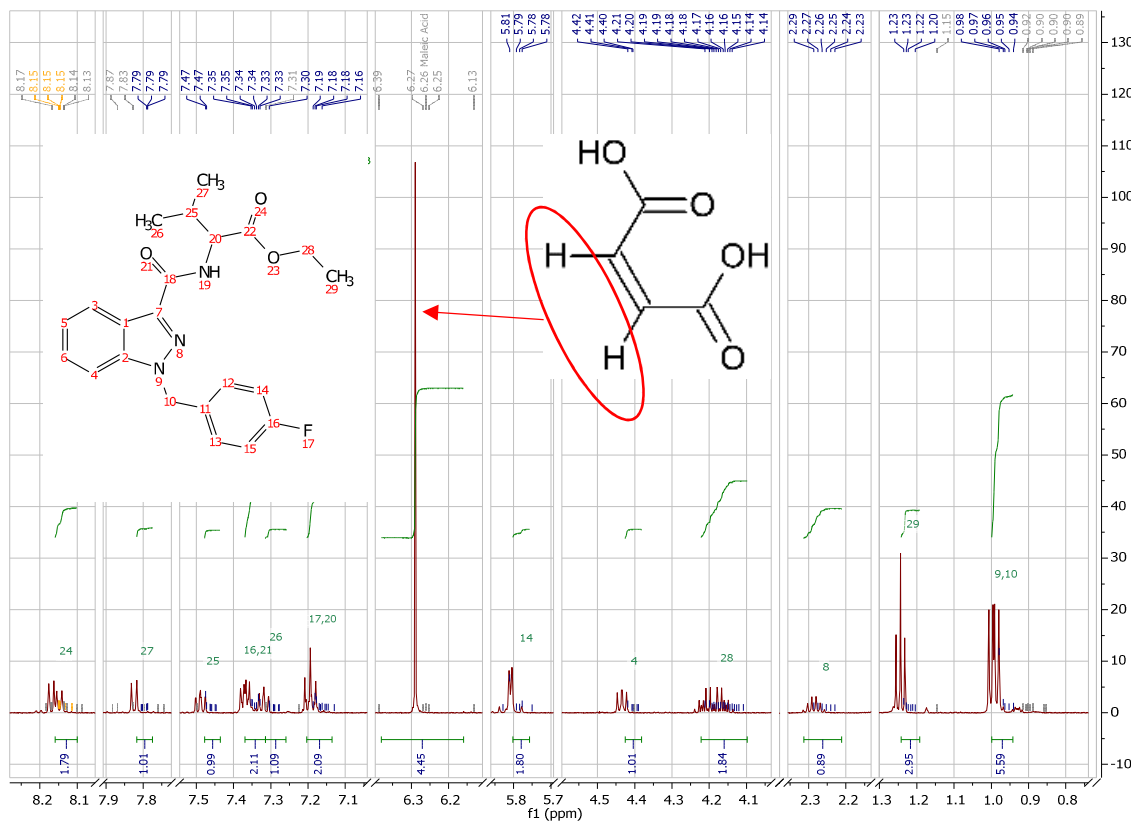
qNMR - belső standard módszer - gyakorlata

Oldatkészítés (négy párhuzamos oldat):

Vizsgálandó anyag és a tőle eltérő kémiai szerkezetű, megfelelő minősítéssel rendelkező referencia anyag bemérése és oldása deuterizált oldószerben (pl. dimetilszulfoxid-d6).



EMB-FUBINCACA mennyiségi referencia anyagga minősítése



$$P_x = \frac{I_x}{I_{std}} \frac{N_{std}}{N_x} \frac{M_x}{M_{std}} \frac{m_{std}}{m_x} P_{std}$$

P – az adott protoncsoporthoz tartozó tisztaság/koncentráció

I – integrál értéke

N – a csúcshoz tartozó ekvivalens protonok száma

M – moláris tömeg

m – a bemért anyag tömege

x – ismeretlen anyag

std – standard

Protoncsoport azonosító	I	II	III	IV	V	VI	VII	VIII	IX	X	XI	XII	XIII	XIV	
Protoncsoporthoz tartozó protonok	26+27	29	25	DMSO	28	20	10	BST	14+15	13	6+12	5	19	3+4	
Bemérés	1.	97,76	103,26	93,58	-	96,45	105,82	94,28	-	109,54	114,35	110,48	103,69	105,49	93,98
	2.	97,60	100,37	94,86	-	96,35	105,81	94,38	-	109,34	113,90	110,75	103,85	105,78	93,67
	3.	97,77	99,54	95,31	-	96,68	105,82	94,53	-	109,08	113,80	110,69	104,10	105,46	94,10
	4.	97,71	99,98	95,89	-	97,07	106,02	94,47	-	109,06	113,84	110,67	104,50	105,74	94,10

EMB-FUBINACA tartalom:

95,92 ± 1,44%

Időfüggő 3D kémiai szerkezet

Kémiai környezet

Dinamika
Kémiai cserefolyamatok

Relatív konfiguráció

Elektronsűrűség

Hőmérsékletfüggés

Atomtávolságok

Árnyékolás

Jelkiszélesedés
-kettőződés

Dipoláris keresztrelaxáció

Szilárd fázis

Kémiai eltolódás

Relaxáció sebessége

NMR képkötés MRI

2D NMR

Csatolás

Lauterbur, Mansfield

Oldat fázis

Kapcsolódási sorrend

Bloch egyenletek

^1H ^{15}N ^{19}F

Jelek mintázata

$J(\text{H,H})$

homonukleáris skaláris csatolási állandó

1D

^{13}C ^{31}P

2D Kismolekula

$^1J(\text{H,X})$ és $^nJ(\text{H,X})$

Jeener, Ernst

Egykötéses és távolható

heteronukleáris skaláris csatolási állandó

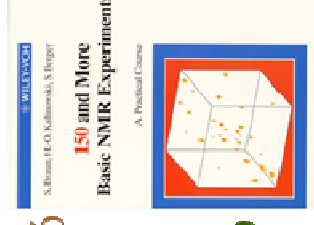
nD

Wüthrich

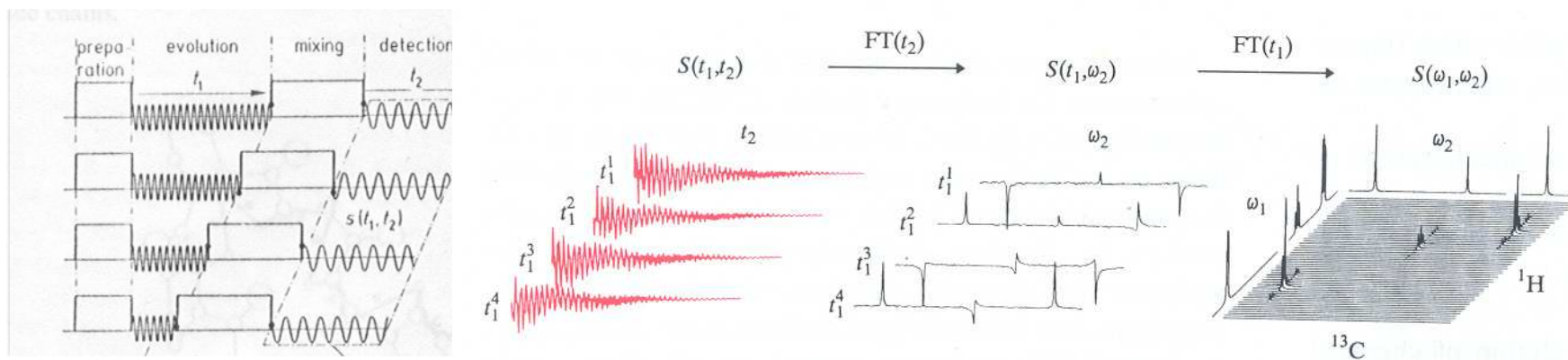
Karplus összefüggés

Biopolimer

Torziós szögek



2D-NMR elve



R. R. Ernst: *Angew. Chem.*, **31**, 805-823 (1992)

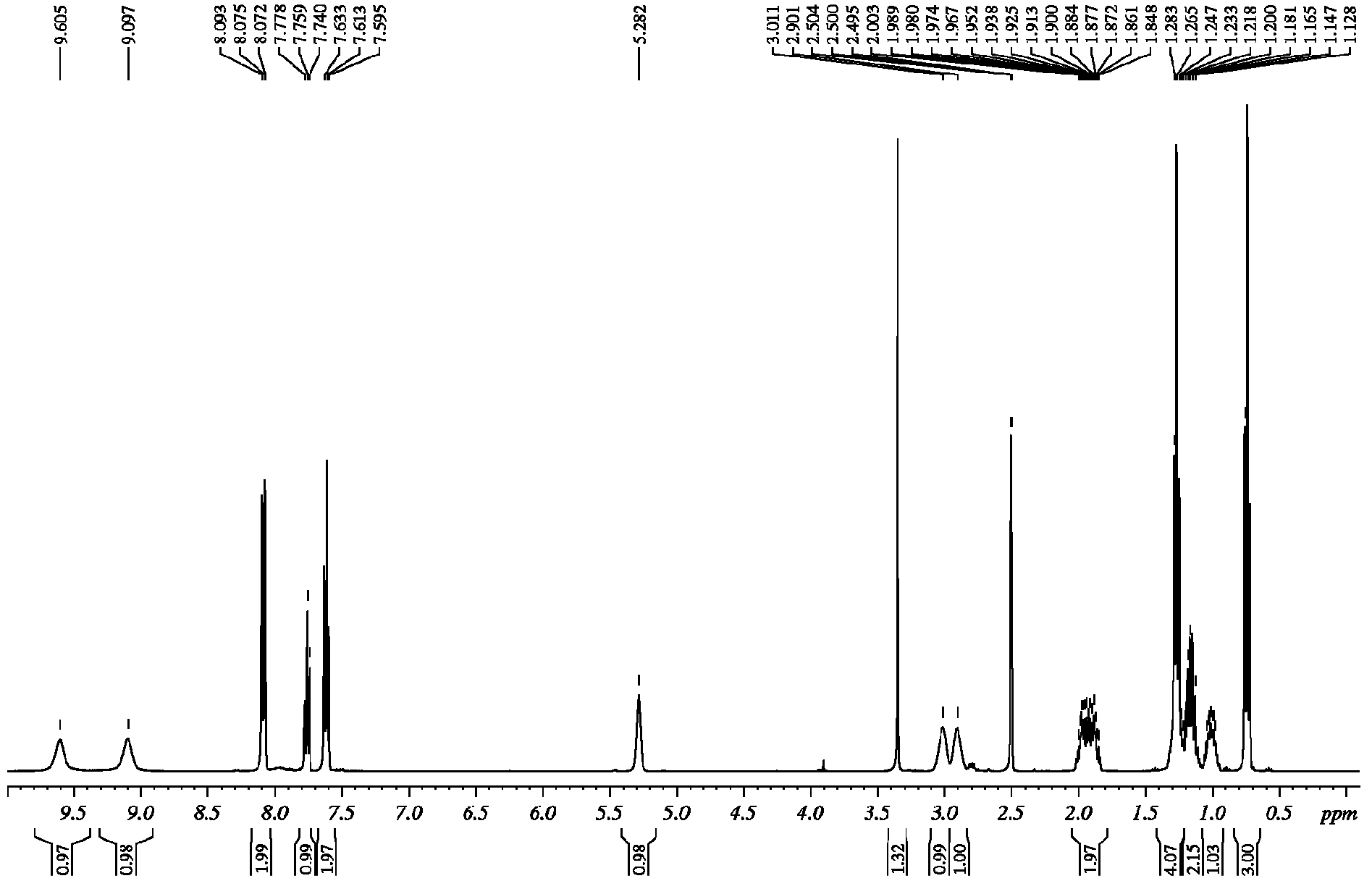
H. Kessler, M. Gehrke, C. Griesinger: *Angew. Chem.*, **27**, 490-536 (1988)

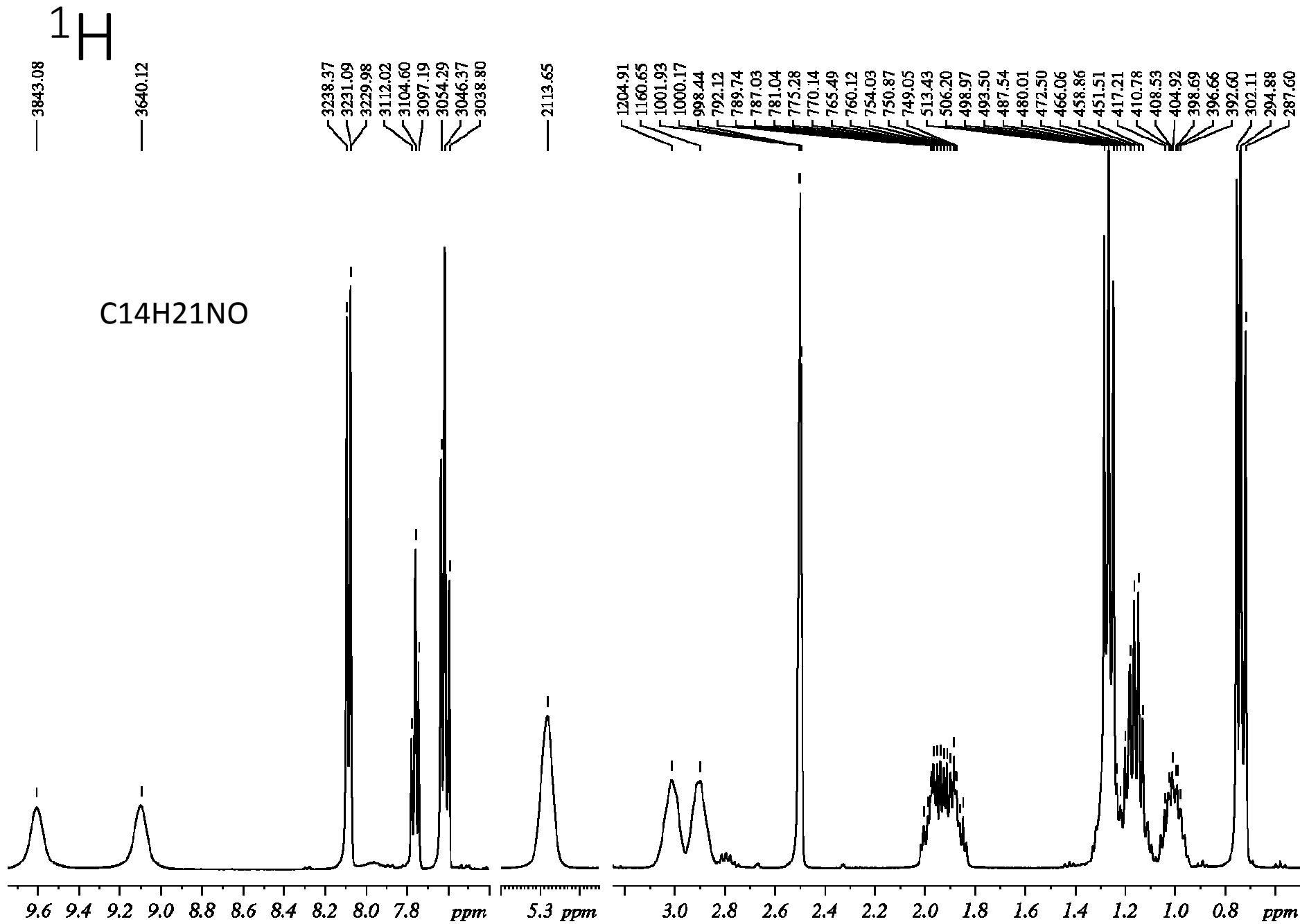
Az NSZKK NMR műszere



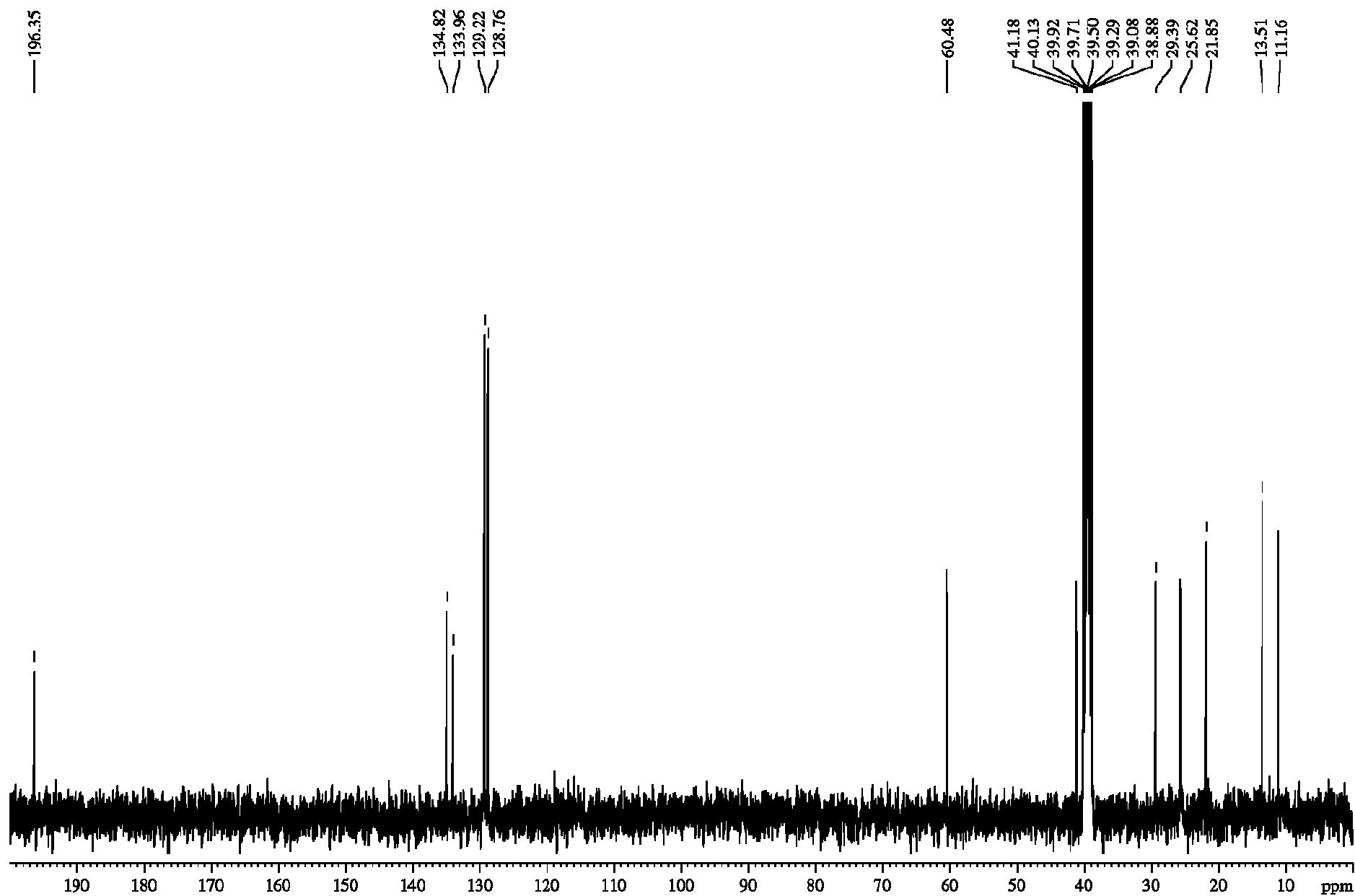
Etil-hexedron NMR vizsgálata

1
H





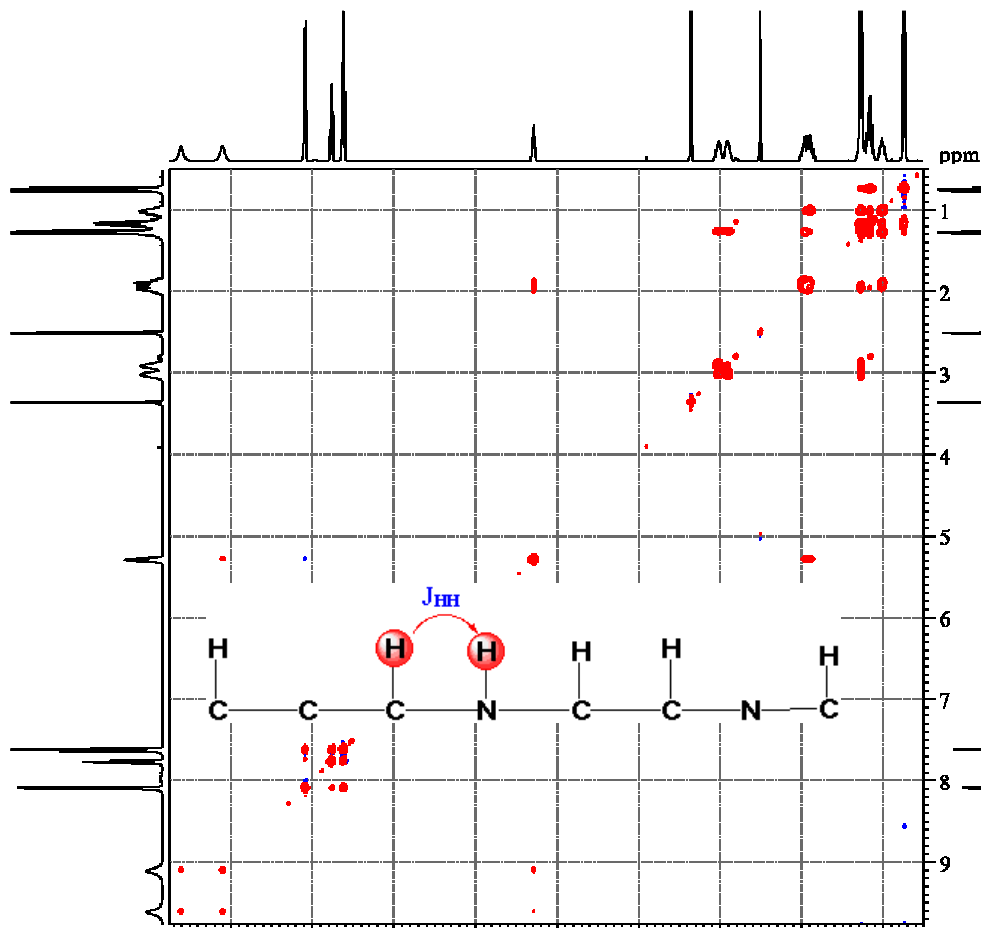
^{13}C



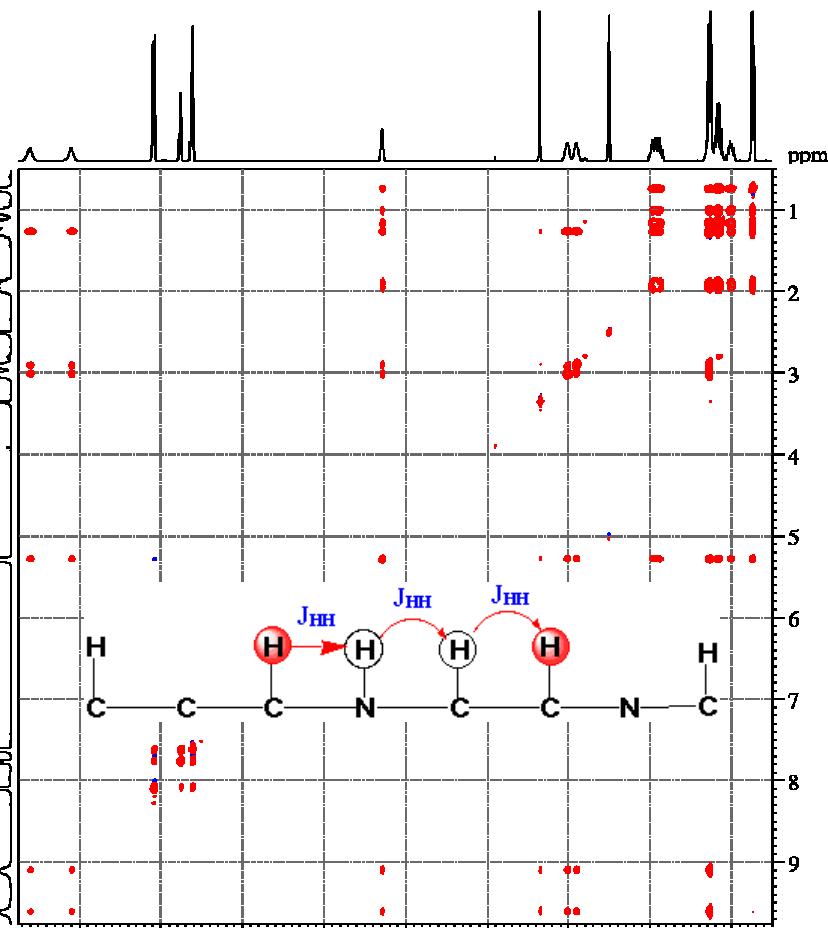
Homonukleáris technikák

zqs-clip-COSY
(COrrrelation
SpectroscopY)

zqs-TOCSY
(TOtal Correlation
SpectroscopY)

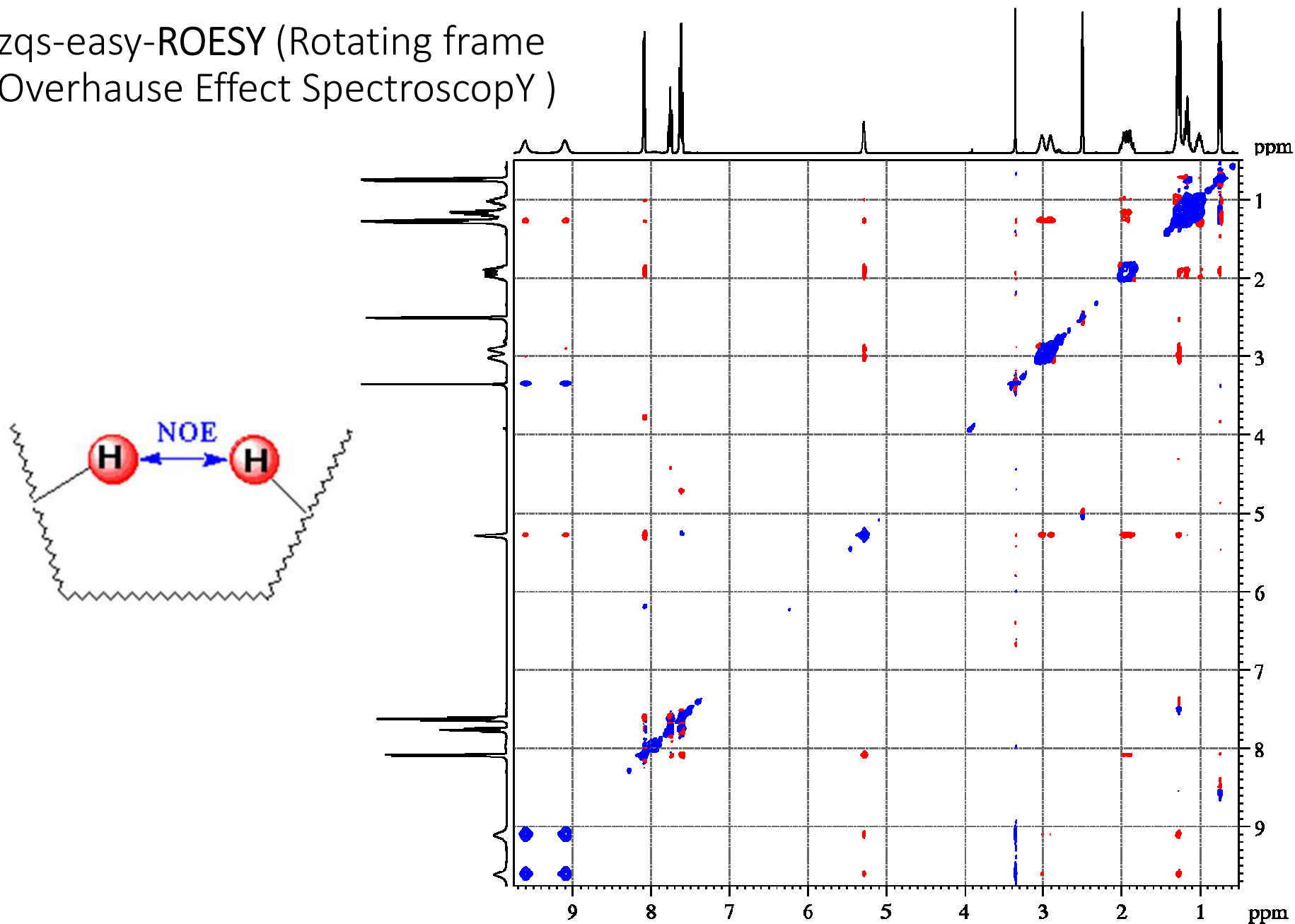


M. R. M. Koos, G. Kummerloew, L. Katschnee, C. M. Thiele, B. Luy: *Angew. Chem. Int. Ed.*, **55**, 7655-7659 (2016)



M. J. Tripleton, J. Keeler: *Angew. Chem. Int. Ed.*, **42**, 3938-3941 (2003)

zqs-easy-ROESY (Rotating frame Overhauser Effect Spectroscopy)

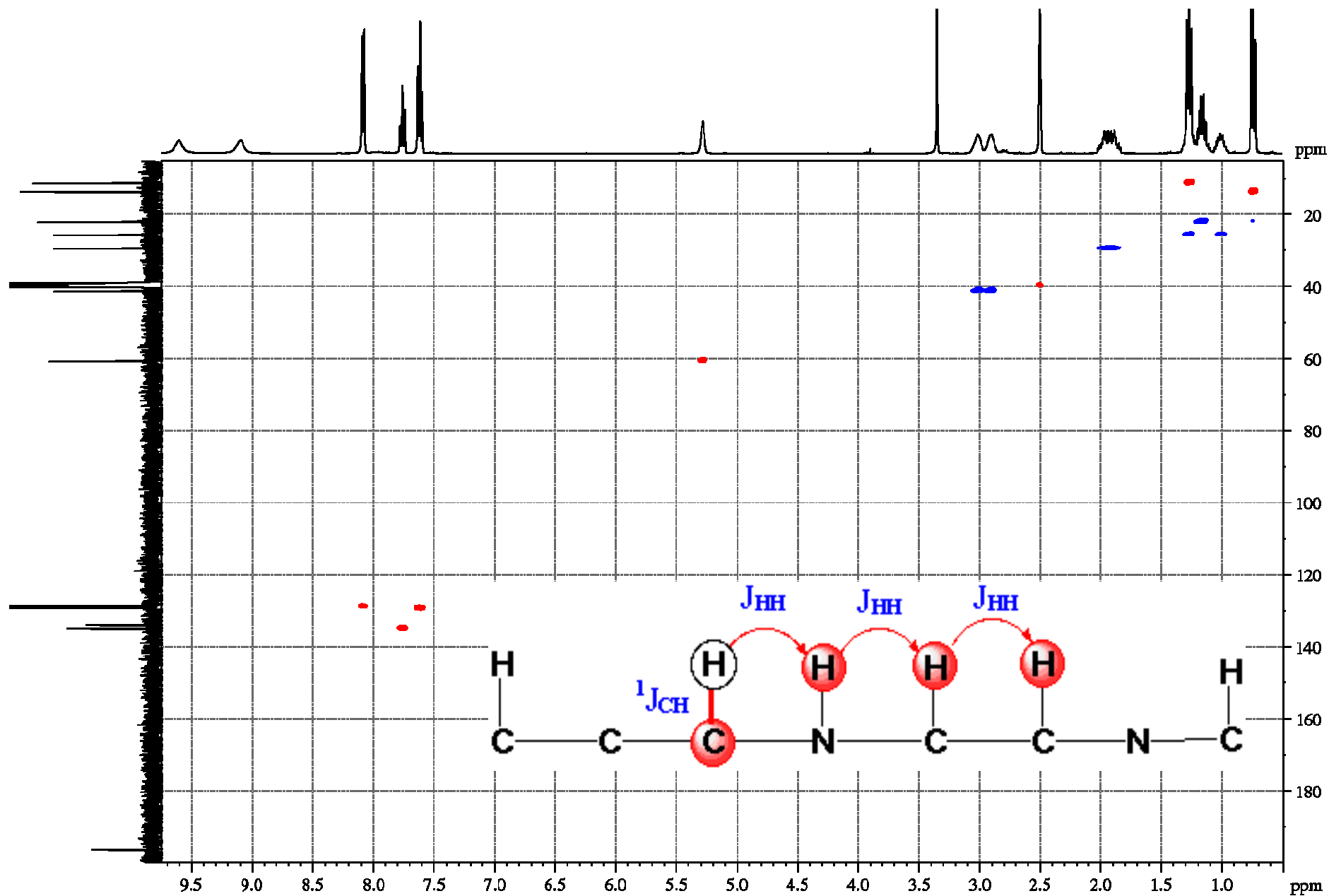


S. Boros, Gy. Batta:

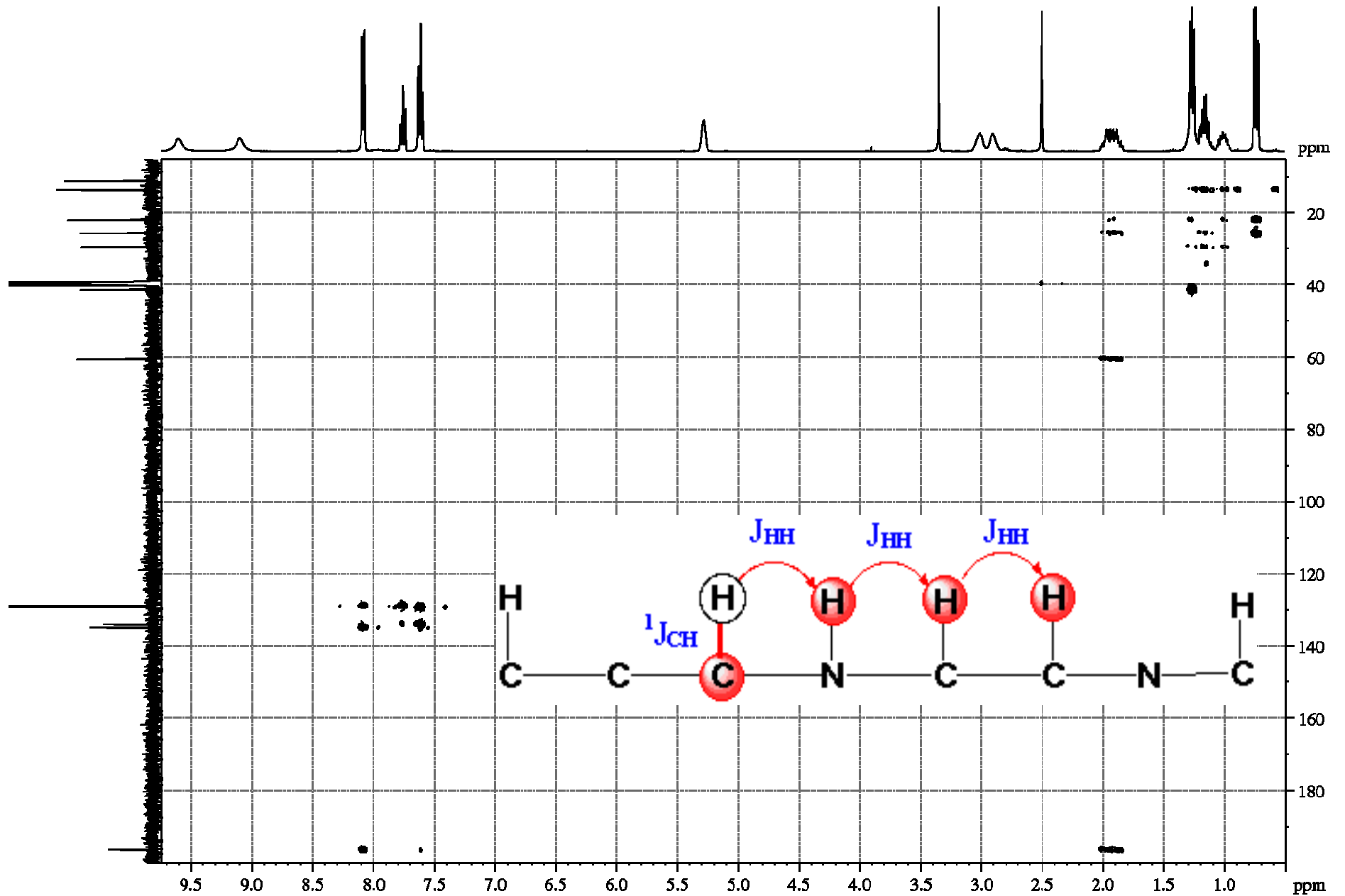
Offset-compensated and zero-quantum suppressed ROESY provides accurate ^1H - ^1H distances in small to medium-sized molecules

Magn. Reson. Chem., **54**, 947-952 (2016) DOI: 10.1002/mrc.4474

ed-HSQC (Heteronuclear Single Quantum Coherence)

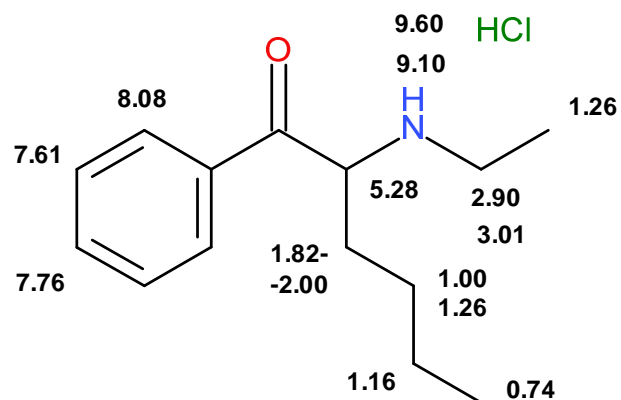


HMBC (Heteronuclear Multiple-Bond Correlation)

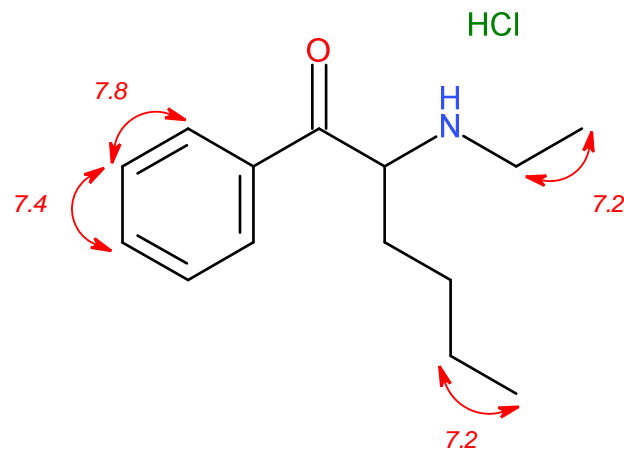


Etil-hexedron *HCl

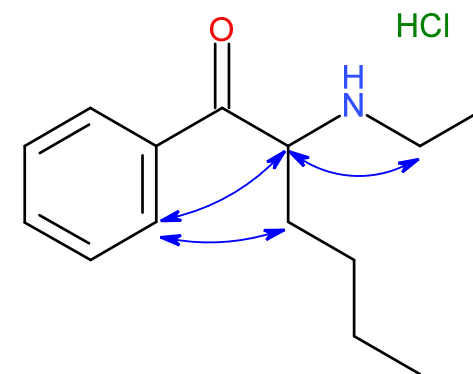
¹H-NMR chemical shifts δ [ppm]



$J(H,H)$ couplinc constants [Hz]

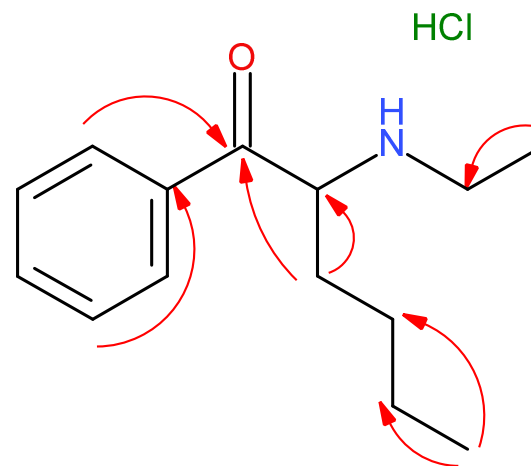
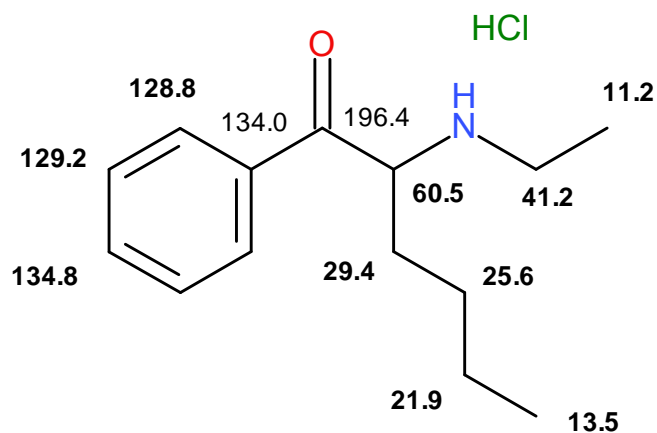


Characteristic steric proximities detected by zqs-easy-ROESY



Characteristic heteronucleur long-range coupling detected by HMBC method H → C

¹³C-NMR chemical shifts δ [ppm]

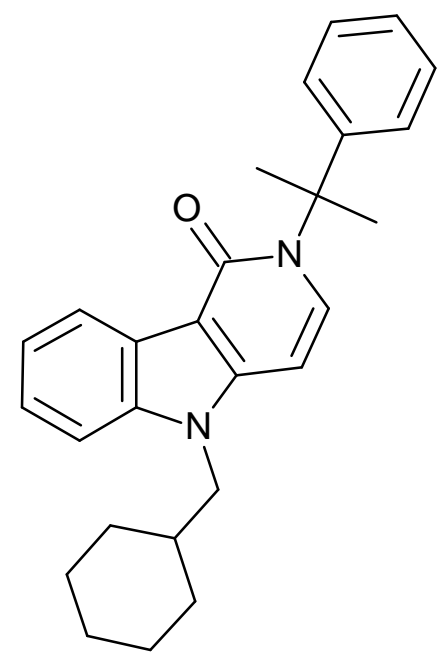
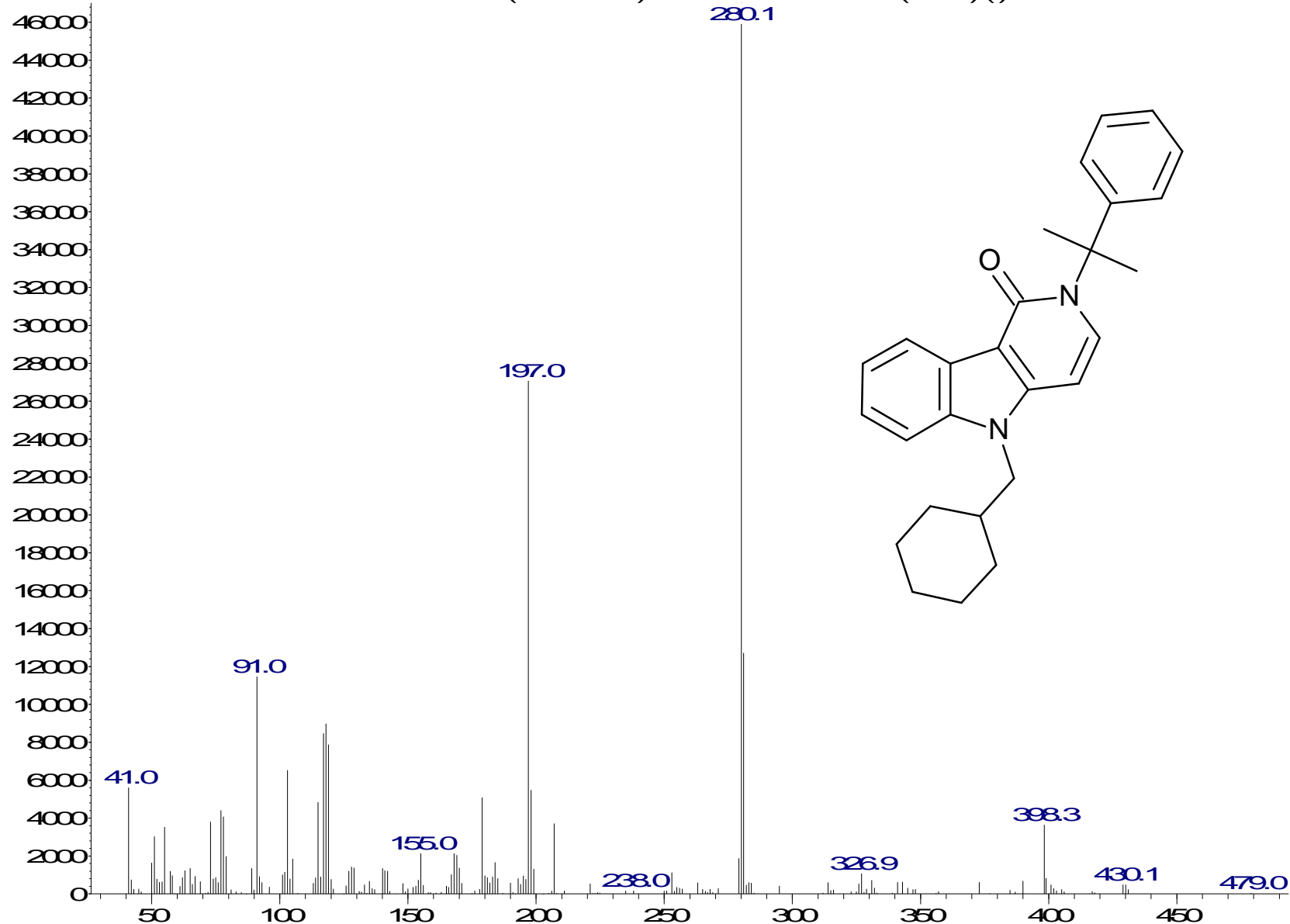


Formula Weight: 219,32264 (Base)
 Exact Mass: 219,162314302
 Molecular Formula: C₁₄H₂₁NO

CUMYL-CH-MEGACLONE

Abundance

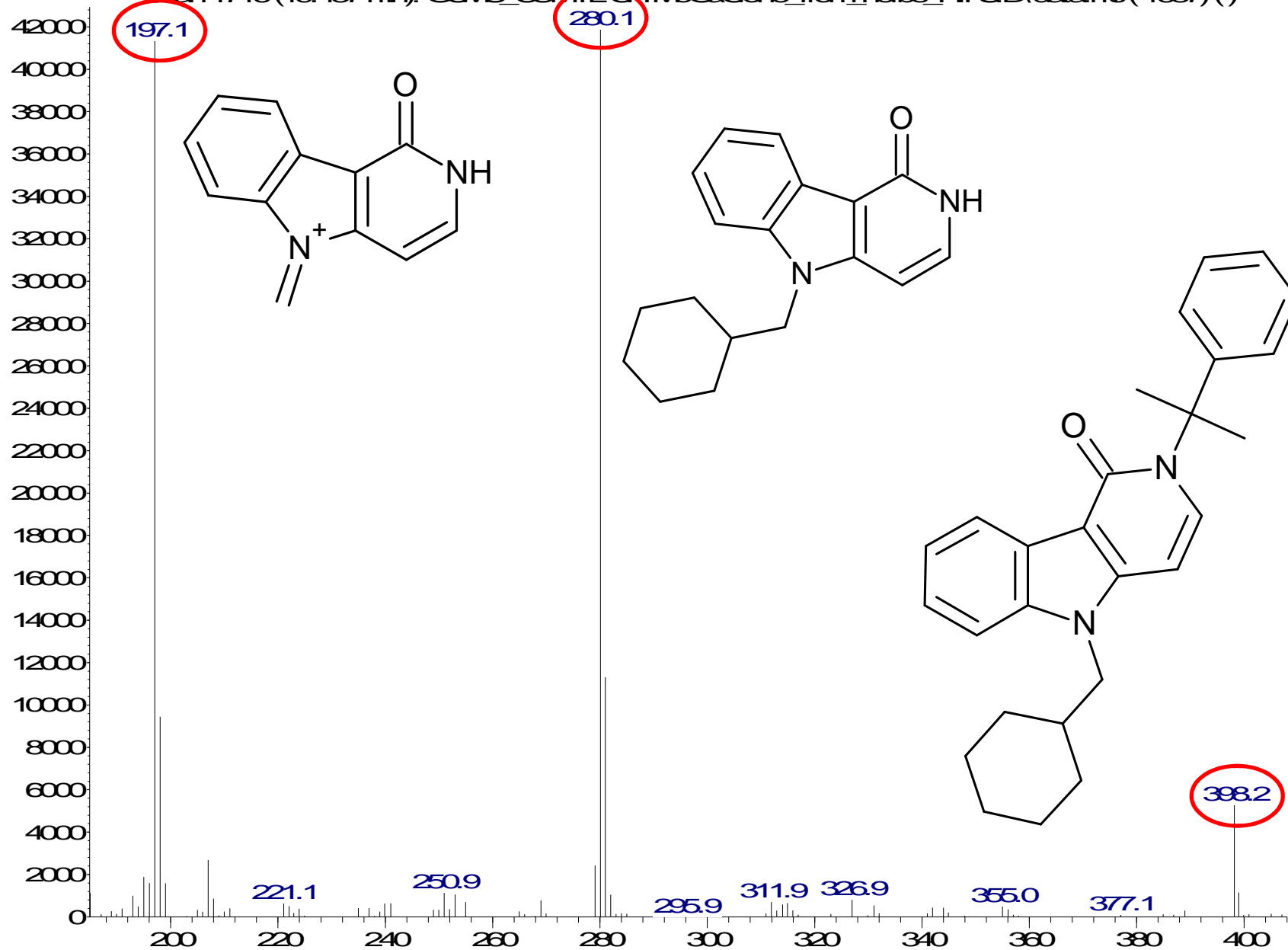
Scan 1718 (19.458 min): 38583-11.D\data.ms (-1702) (-)



m/z->

Abundance

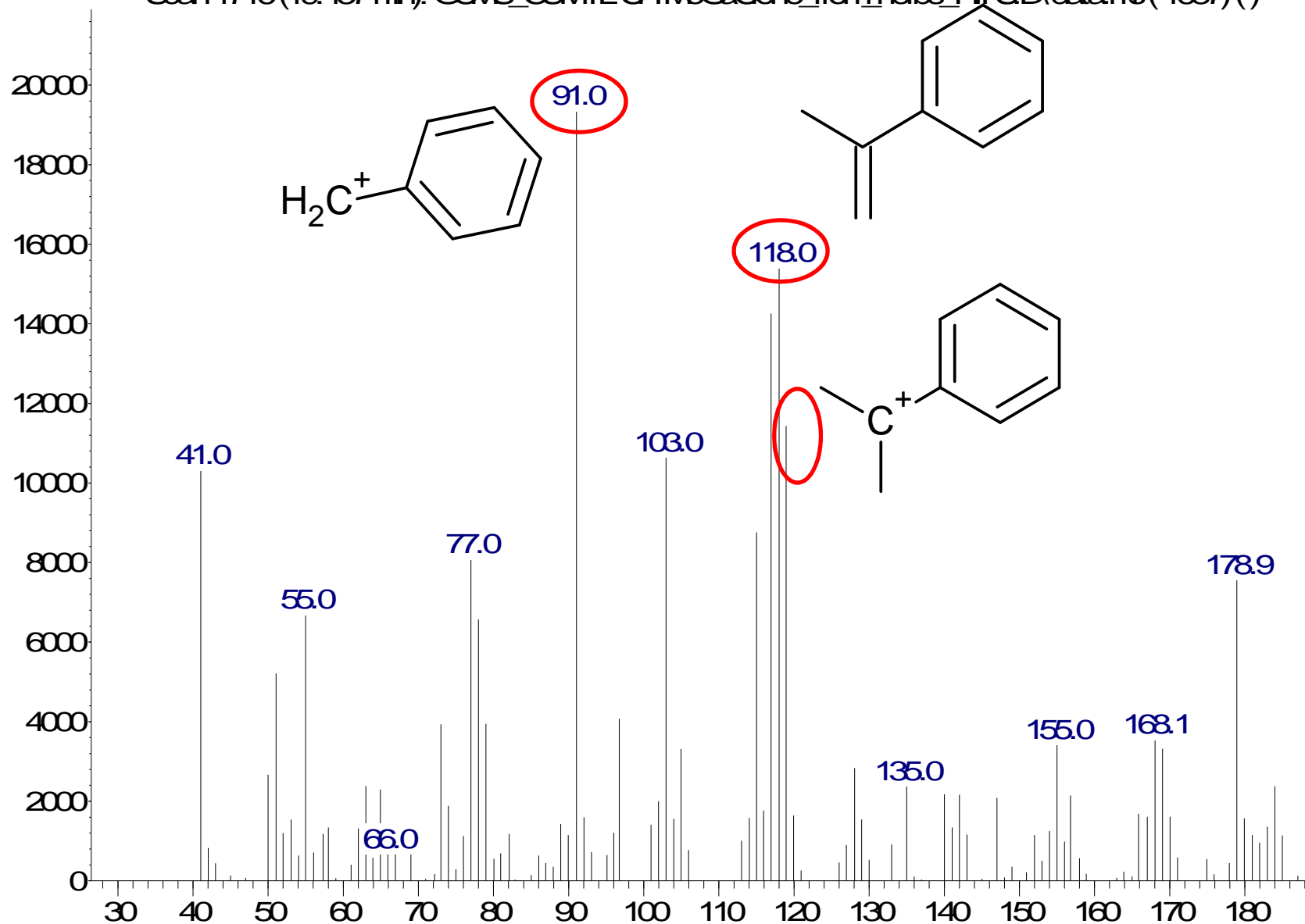
Scan 1716 (19.437 min): GCMS_CUMMILCHMeGaClone_from_herbs_HFSD\data.ms (-1687) (-)



m/z->

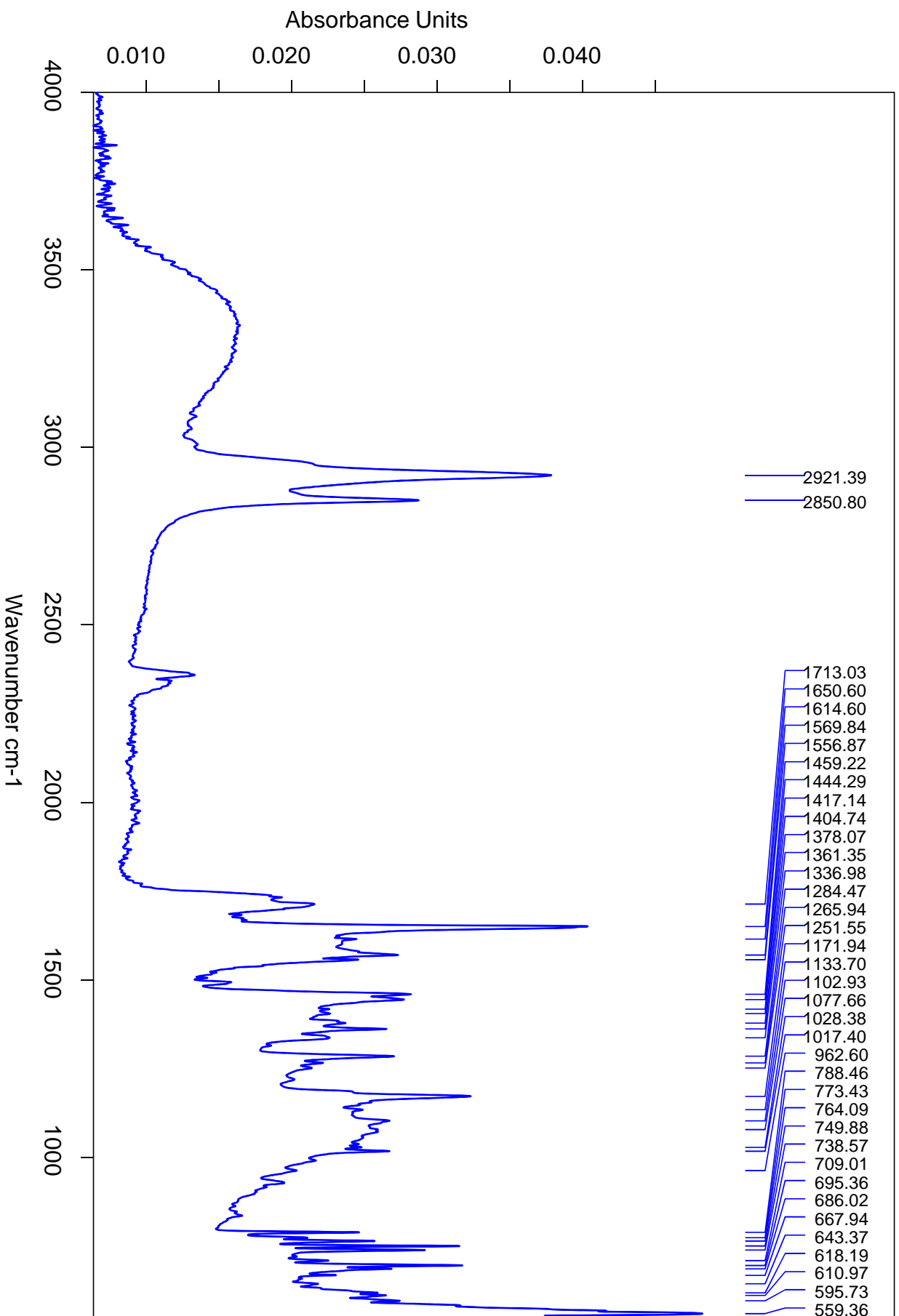
Abundance

Scan 1716 (19.437 min): GCMS_CUMYL-CHMeGaClone_from_herbs_HFSD\data.ms (-1687) (-)

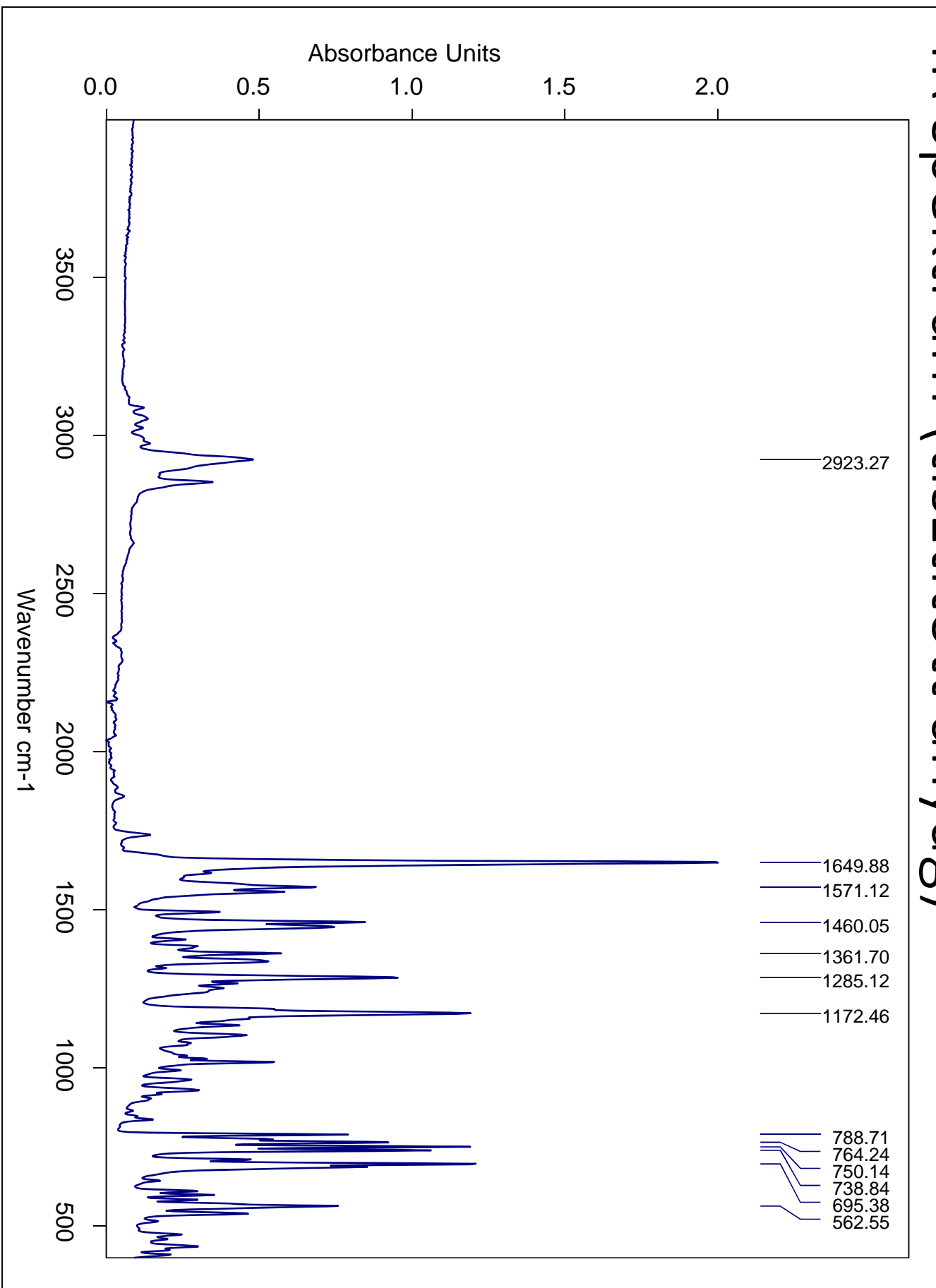


m/z->

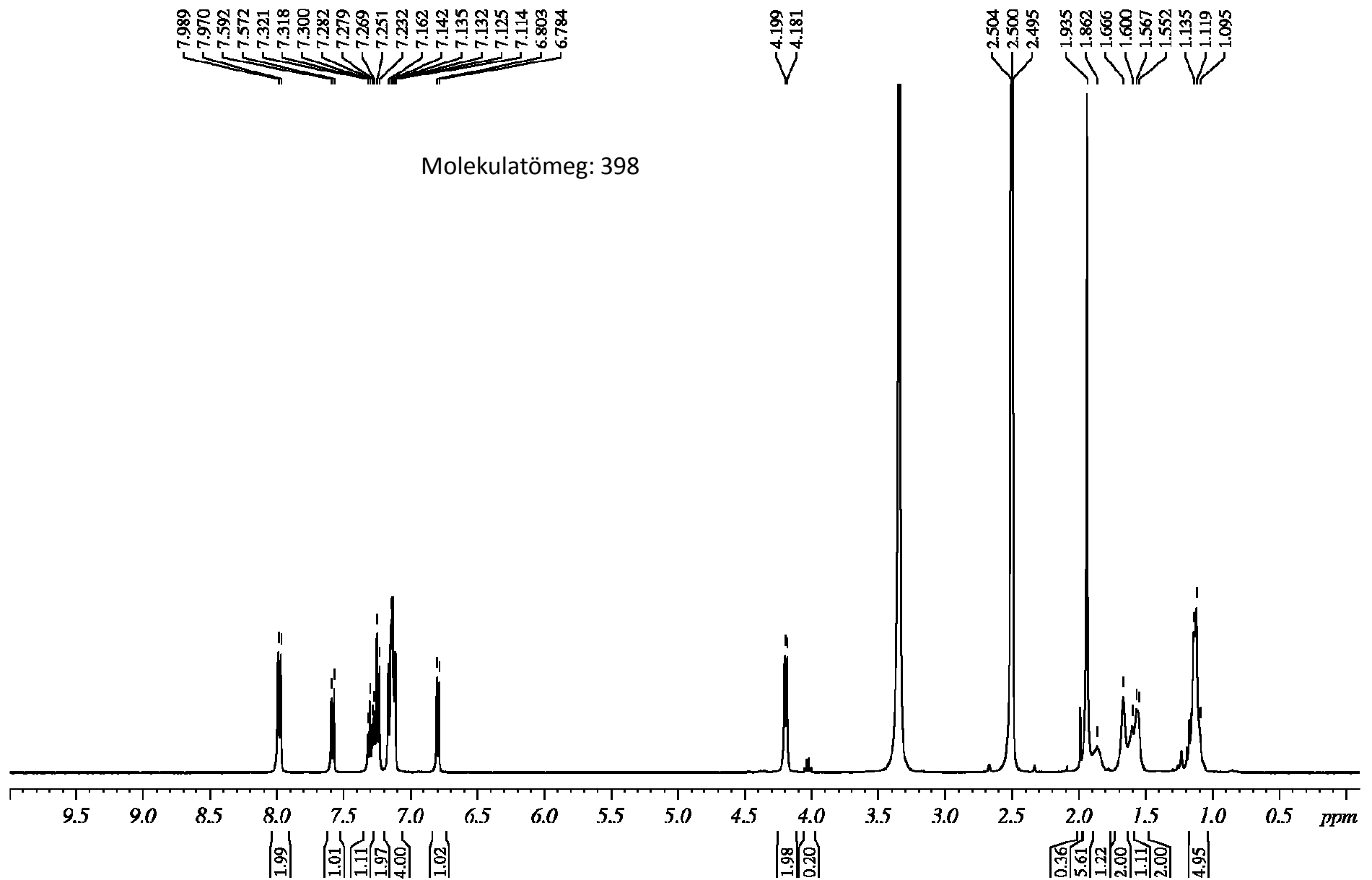
IR spektrum (növényről leoldott anyag)



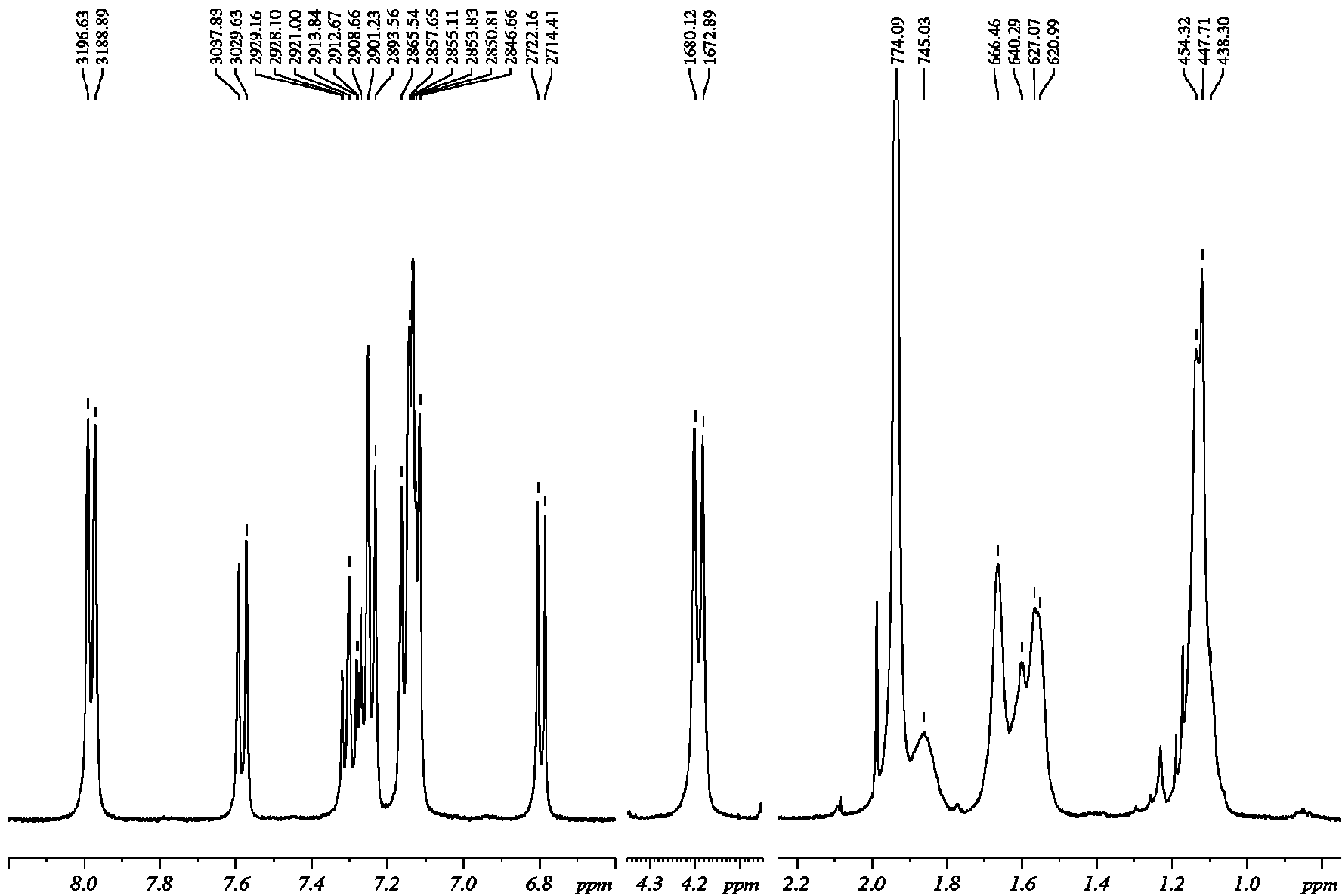
IR spektrum (tisztított anyag)



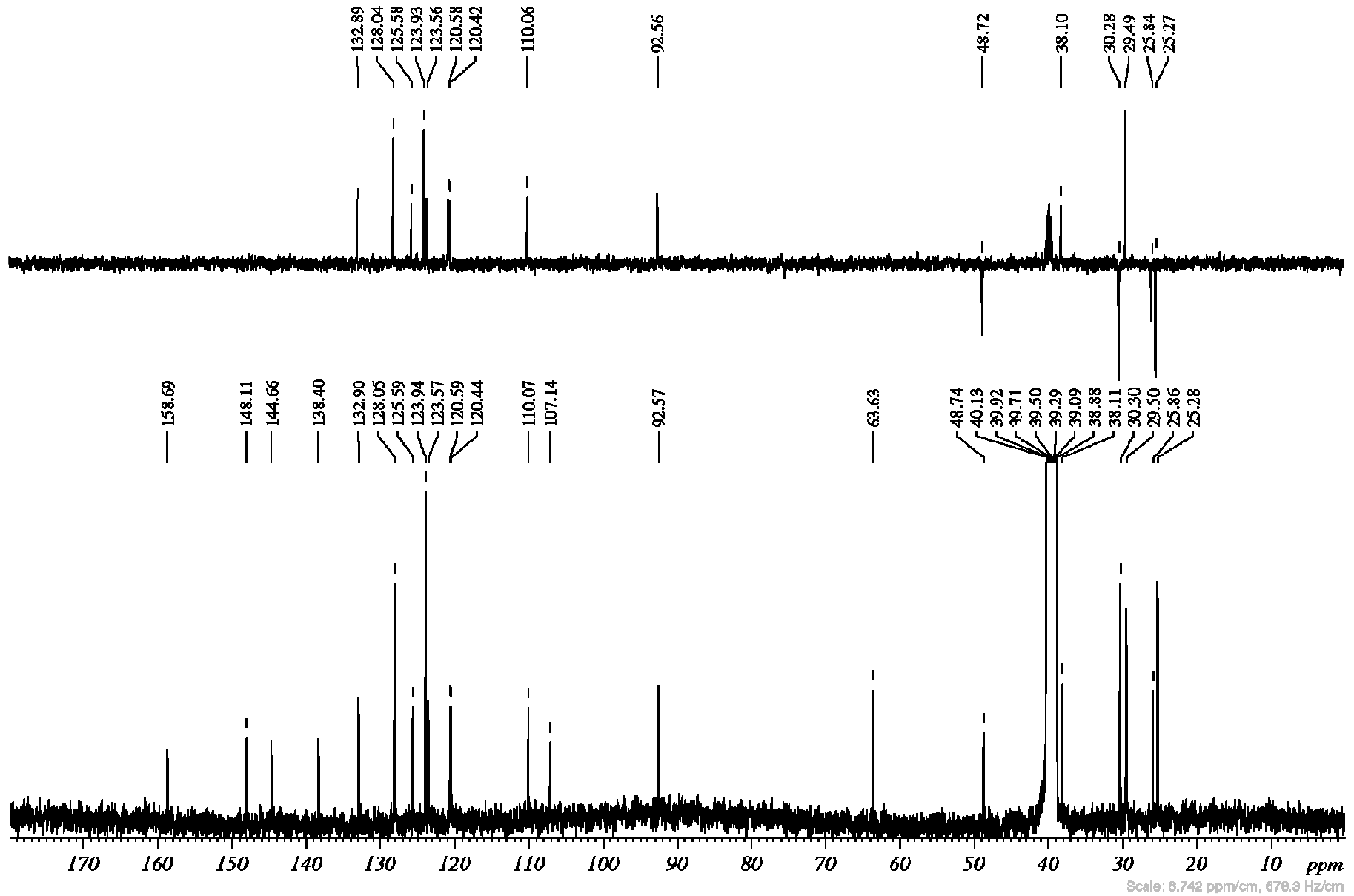
^1H -NMR spektrum



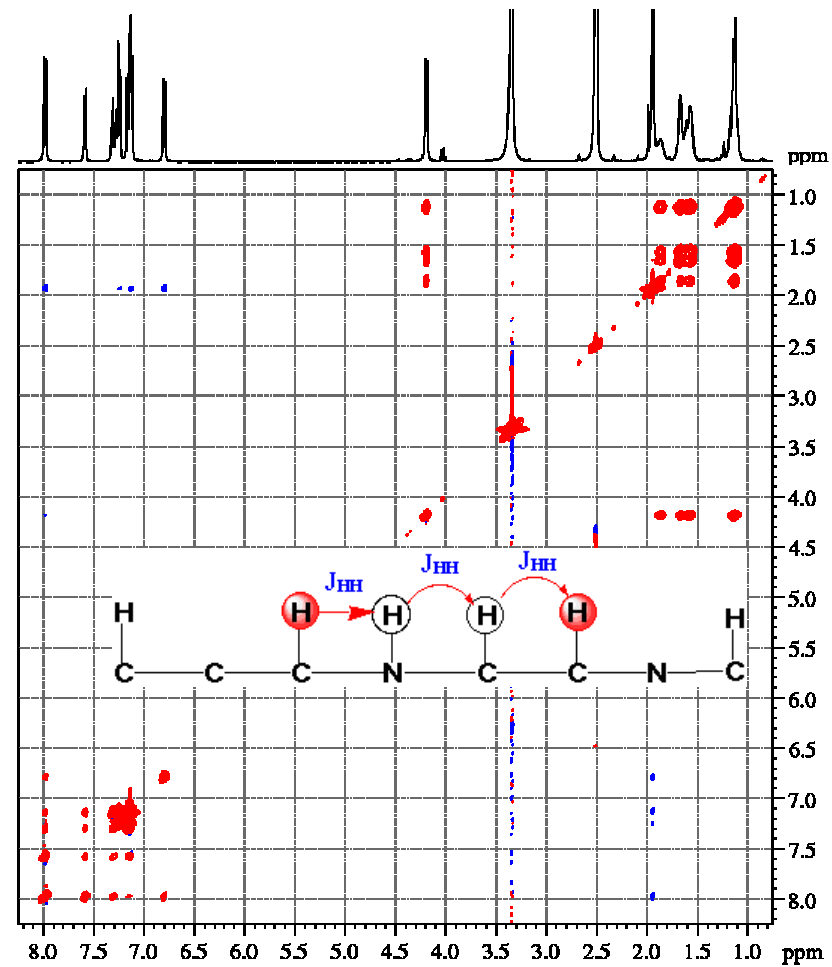
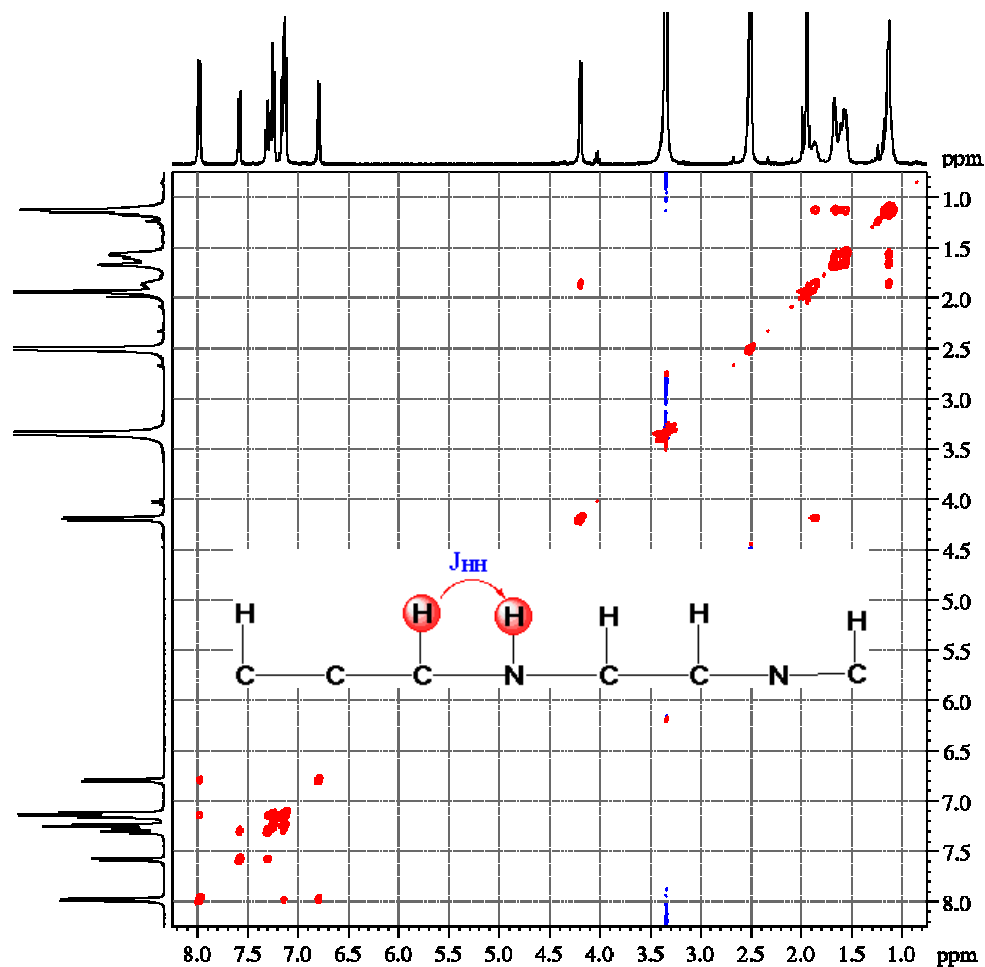
^1H -NMR spektrum, részletek



^{13}C -NMR és DEPT-135 spektrum

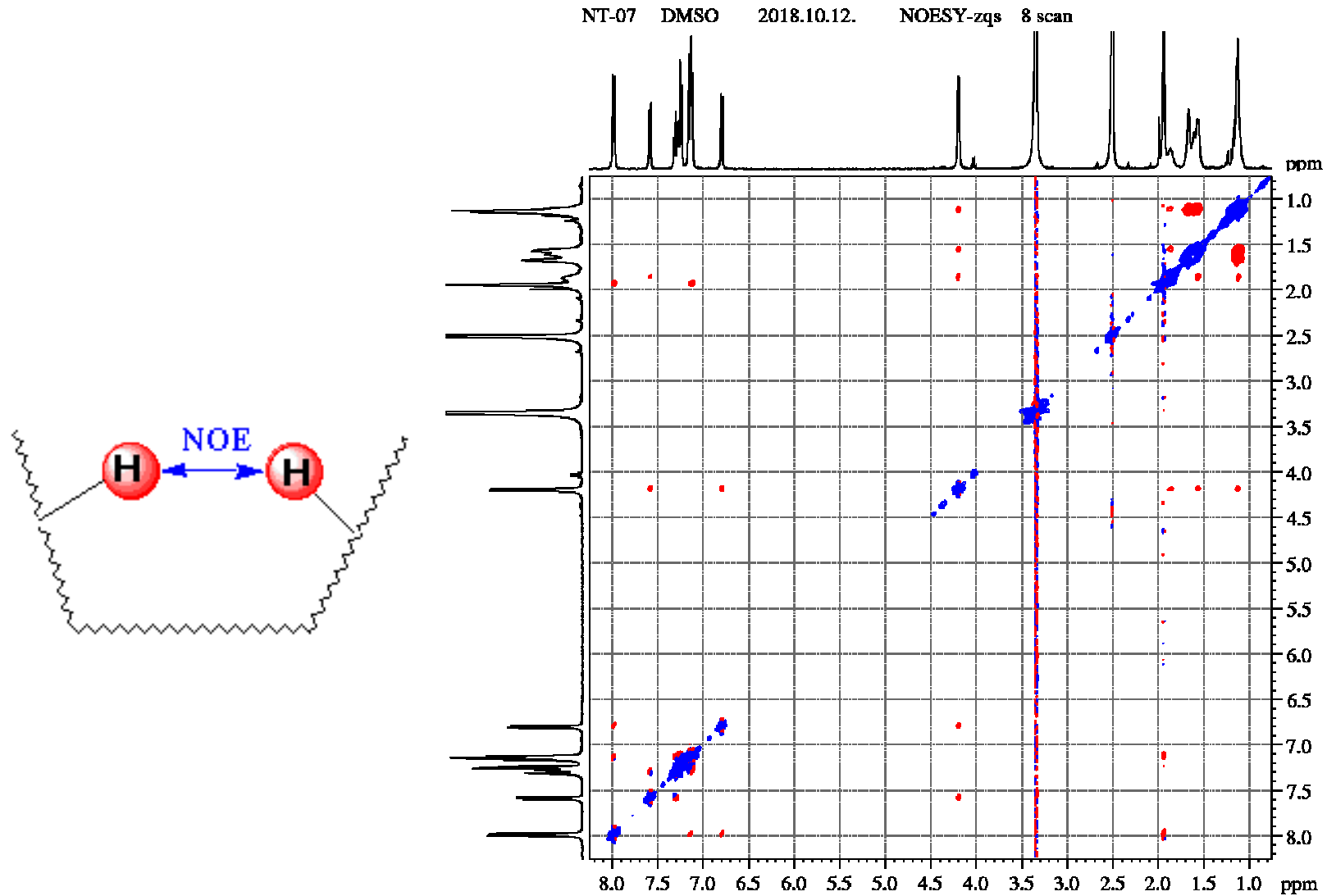


Zqs-clip-COSY és zqs-TOCSY spektrum

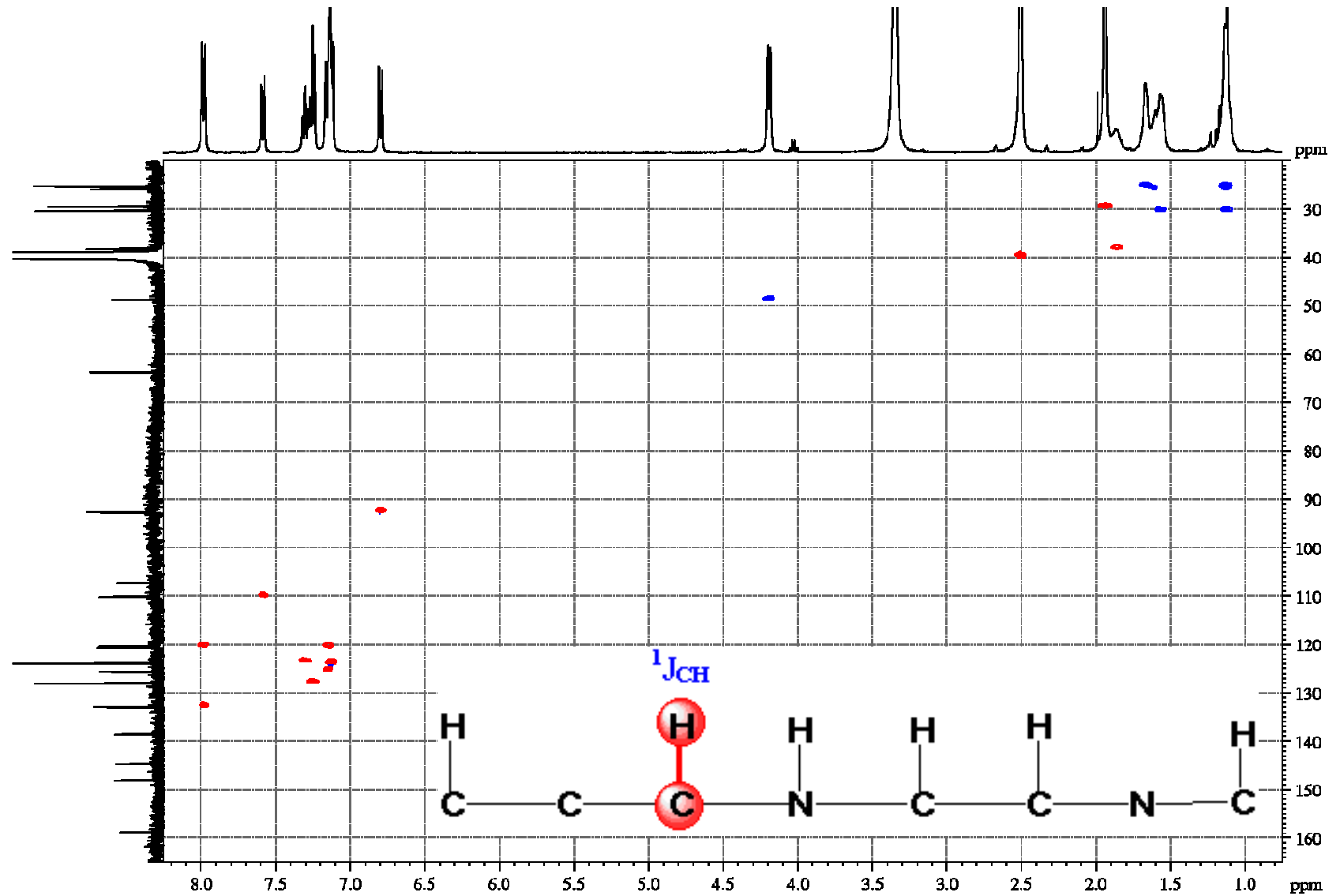


M. R. M. Koos, G. Kummerloewe, L. Kaltschnee, C. M. Thiele, B. Luy:
CLIP-COSY: A Clean In-Phase Experiment for the Rapid Acquisition of COSY-type
Correlations
Angew. Chem. Int. Ed., **55**, 7655-7659 (2016)

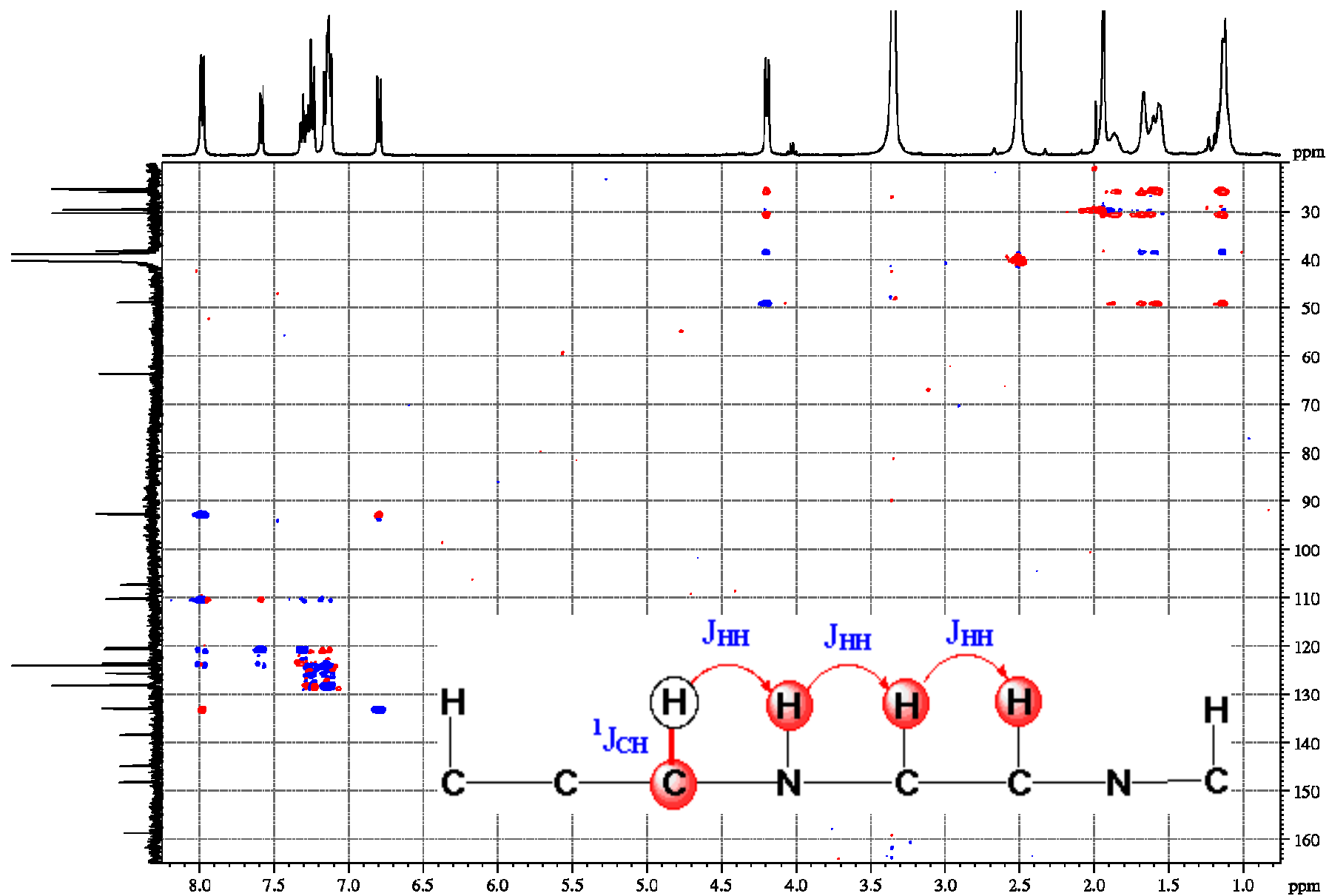
Zqs-NOESY spektrum



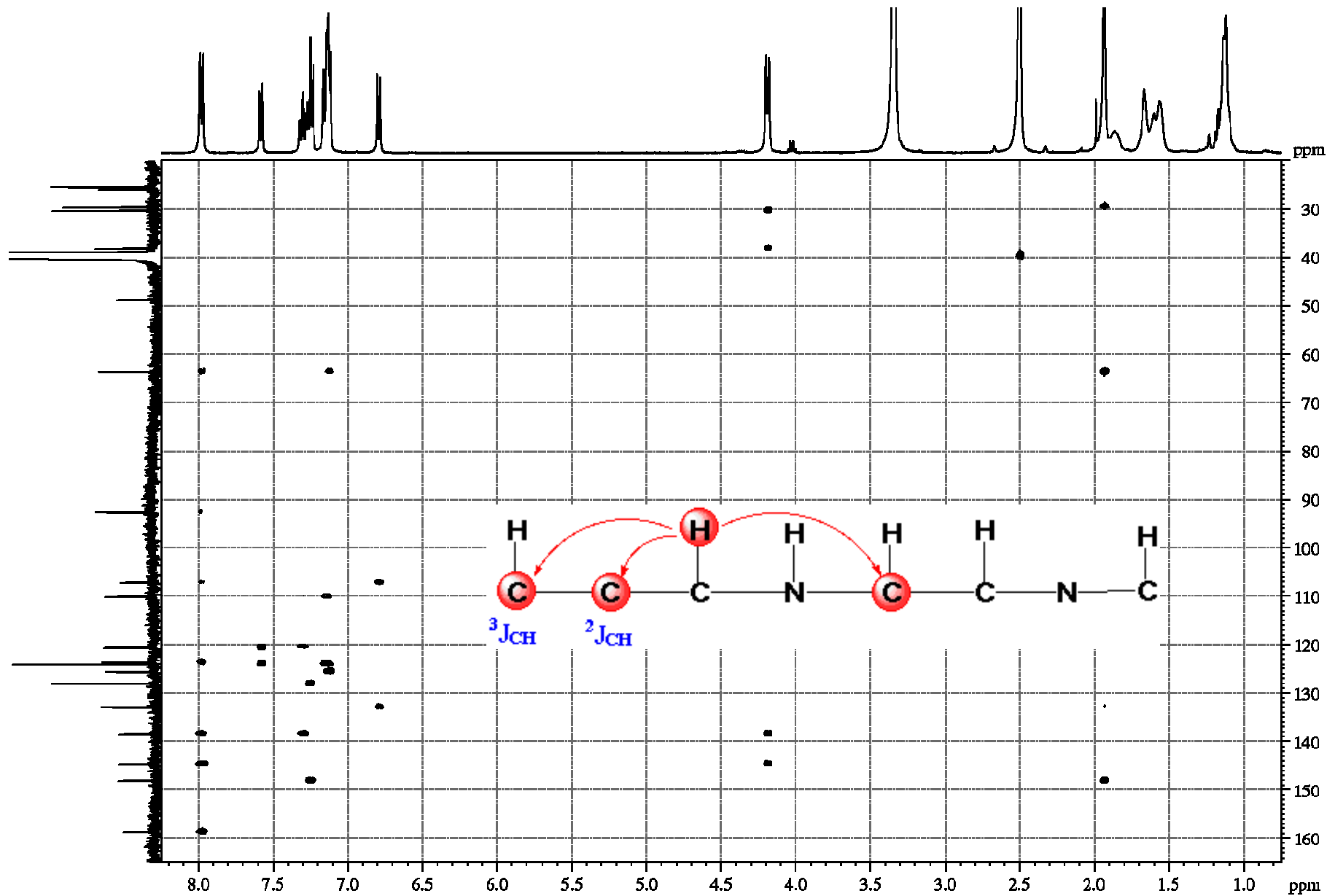
Multiplicitásszerkesztett HSQC spektrum



Ed-HSQC-TOCSY spektrum

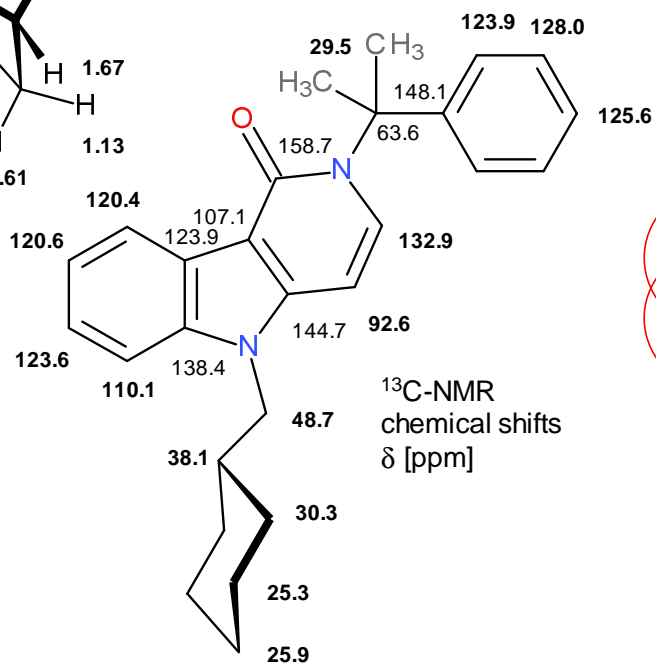
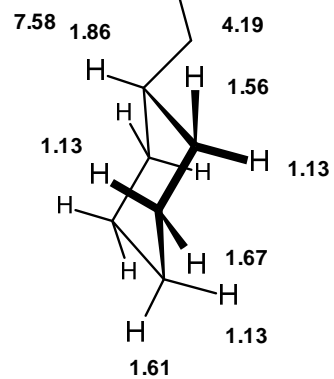
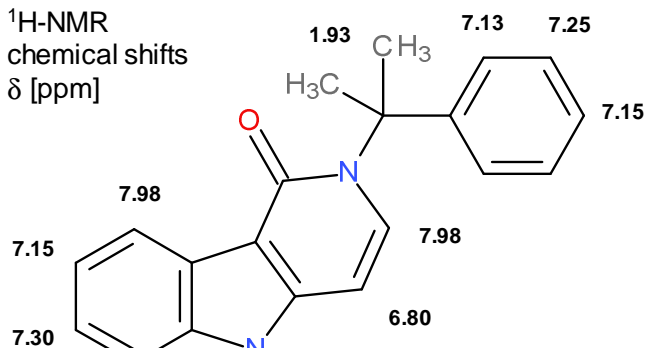


HMBC spektrum



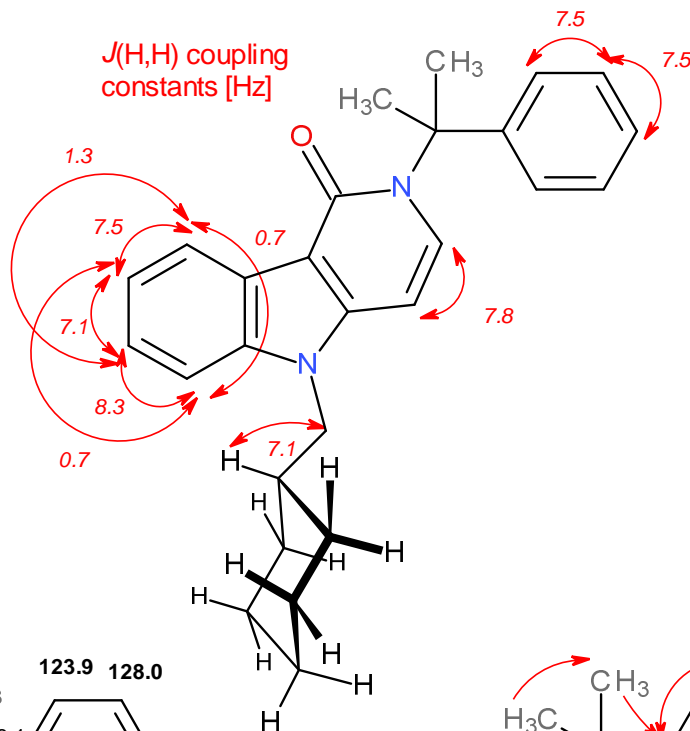
NT-07 in DMSO-d₆ solution

¹H-NMR
chemical shifts
δ [ppm]

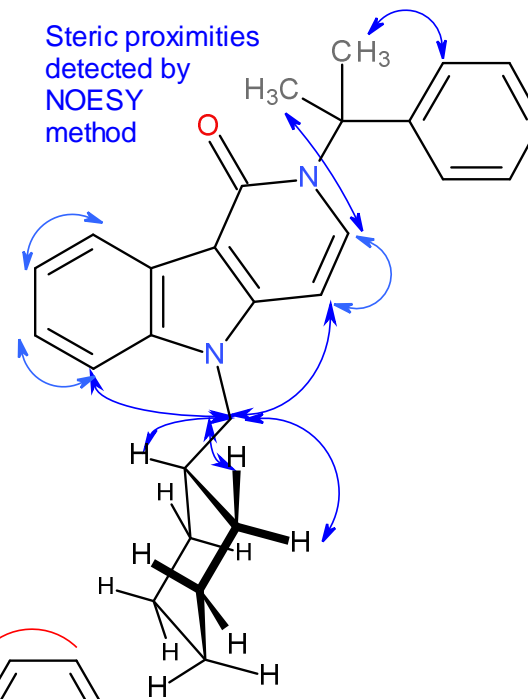


¹³C-NMR
chemical shifts
δ [ppm]

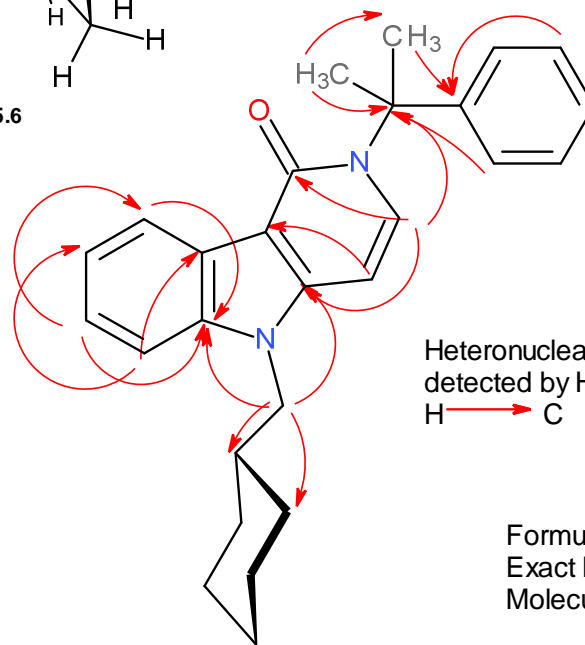
J(H,H) coupling
constants [Hz]



Steric proximities
detected by
NOESY
method



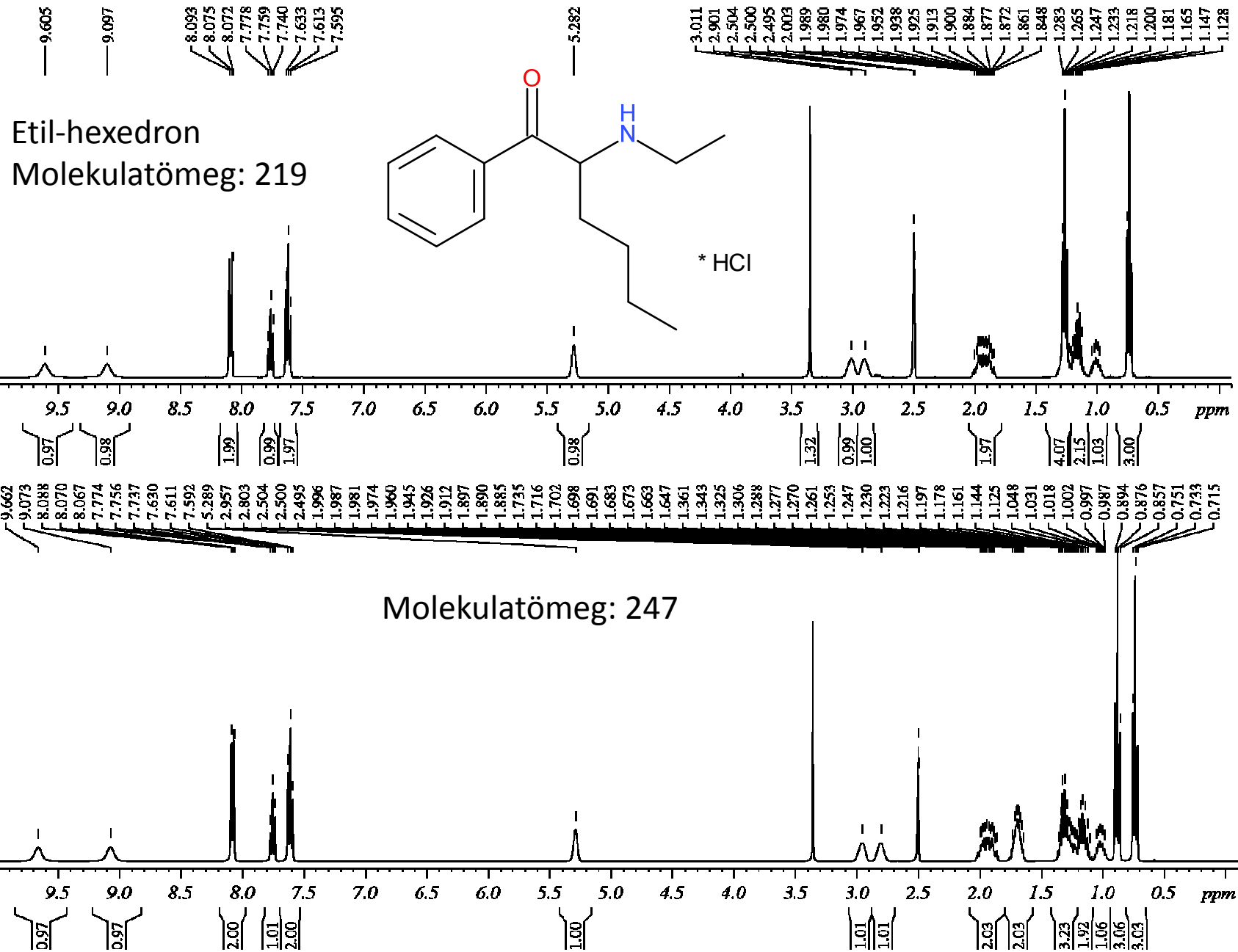
Heteronuclear long-range coupling
detected by HMBC method
H → C



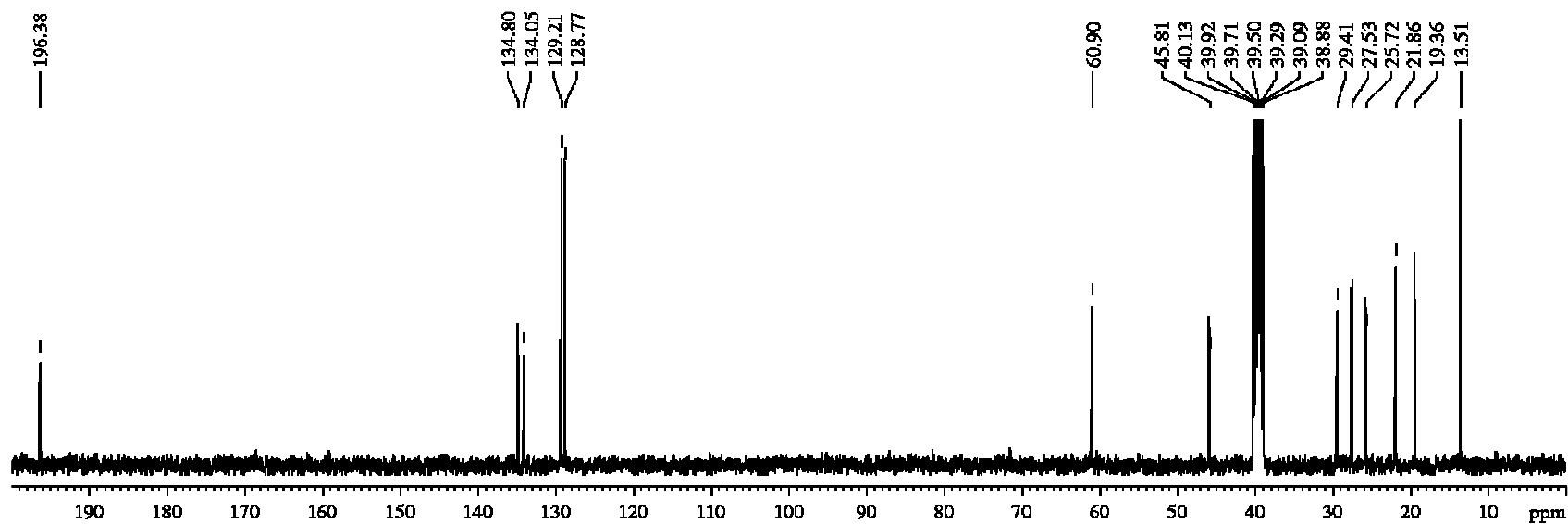
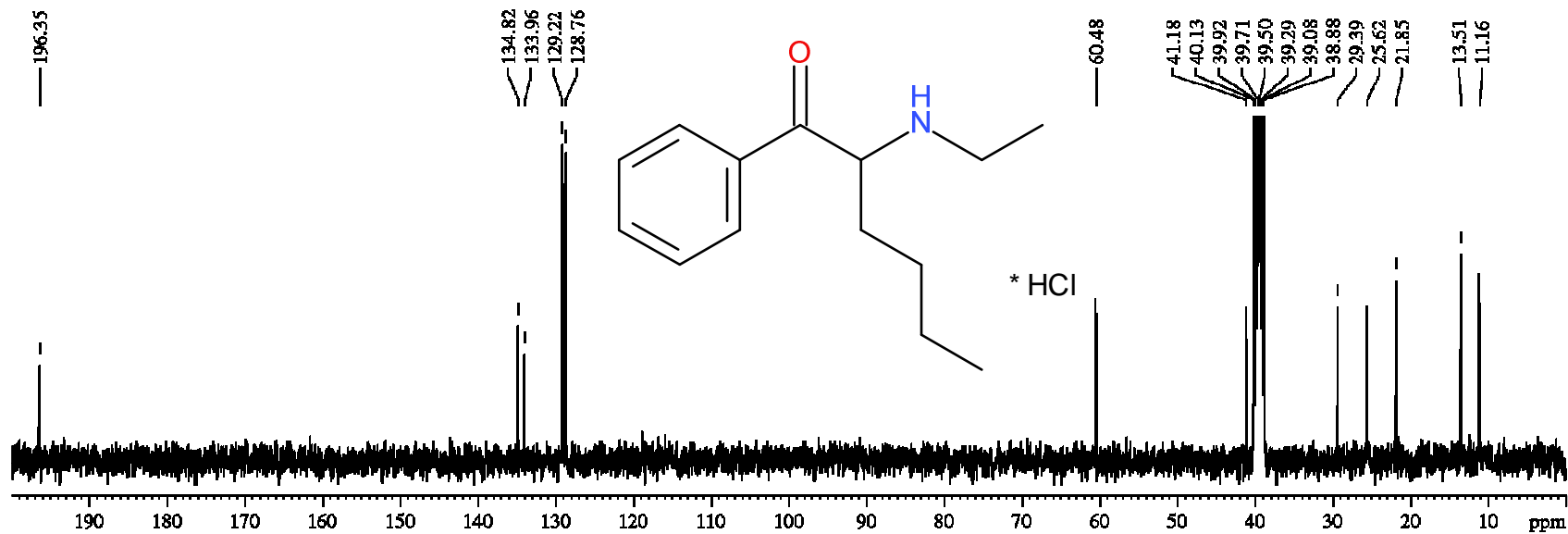
Formula Weight: 398,5399
Exact Mass: 398,2358136
Molecular Formula: C₂₇H₃₀N₂O

Ismeretlen anyag szerkezetvizsgálata

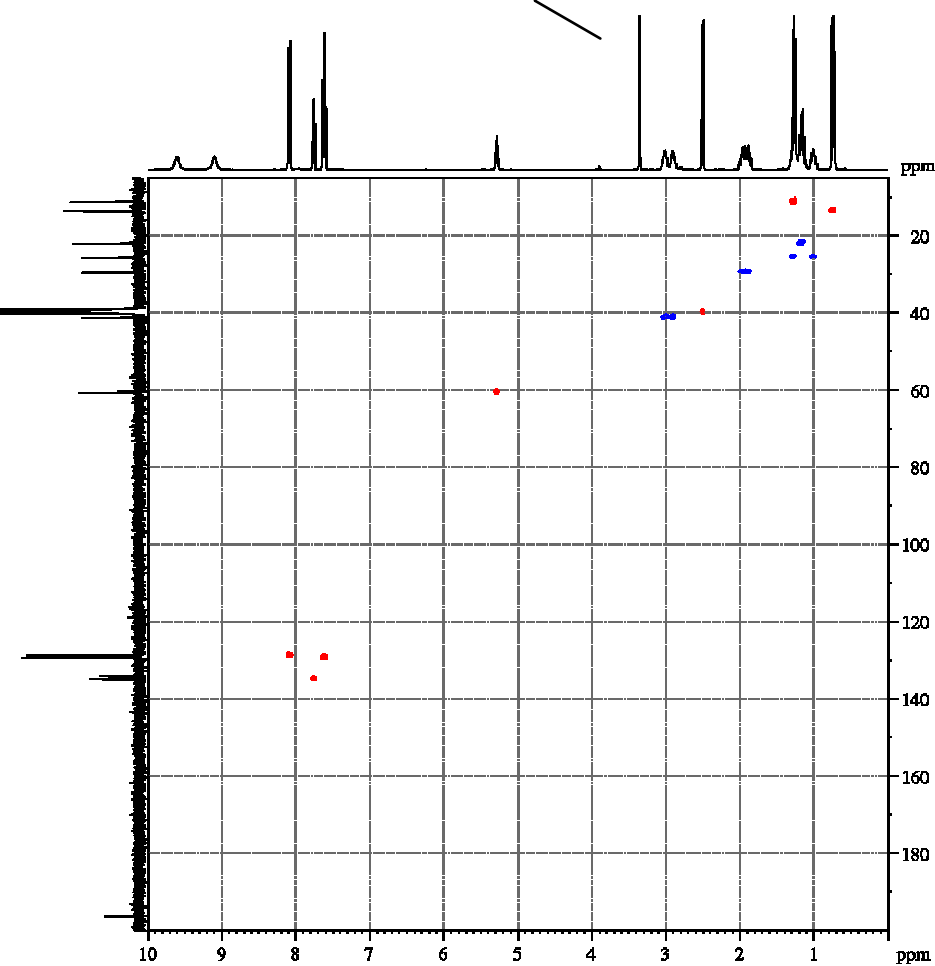
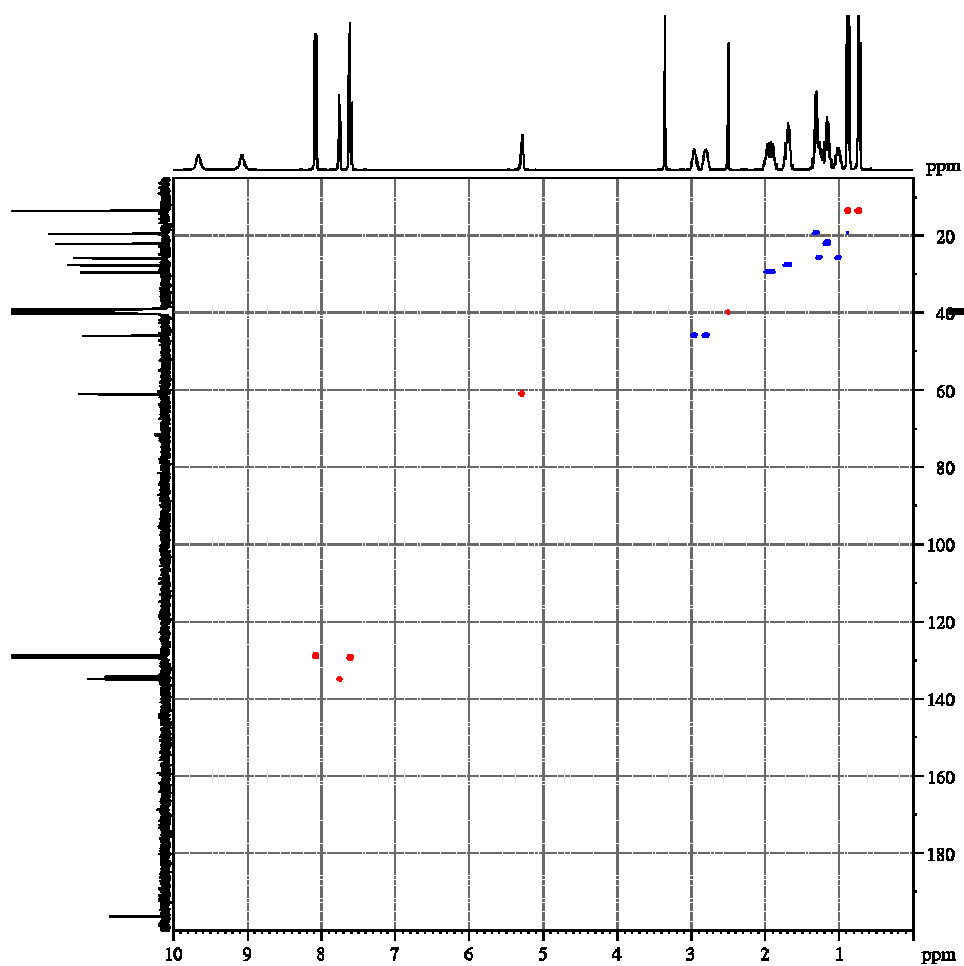
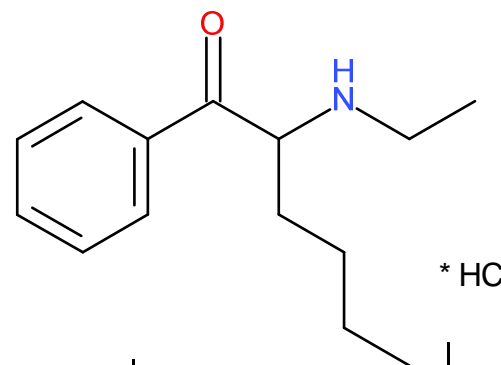
$^1\text{H-NMR}$ spektrum



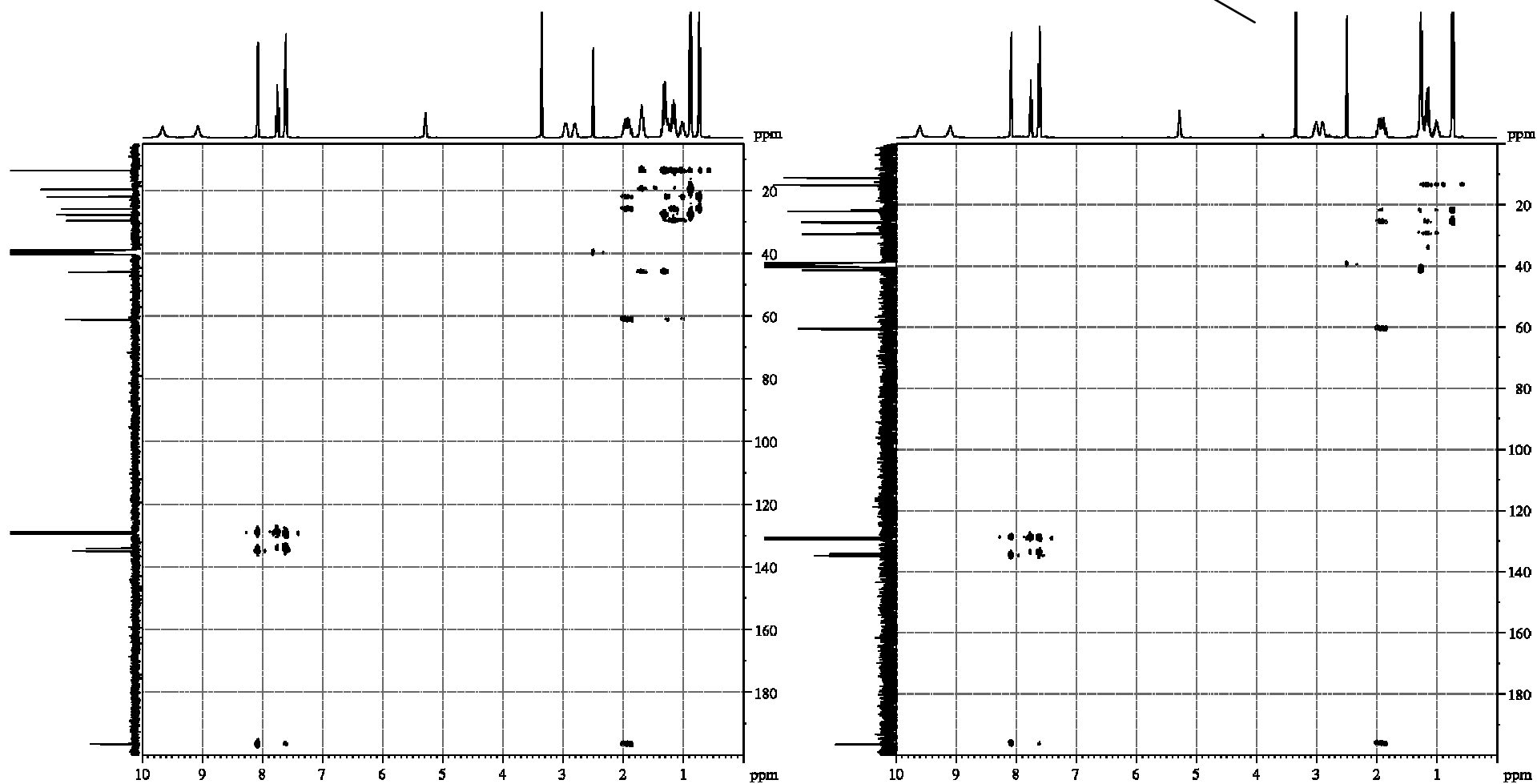
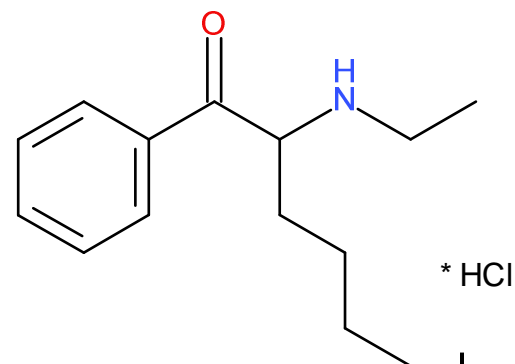
^{13}C -NMR spektrum



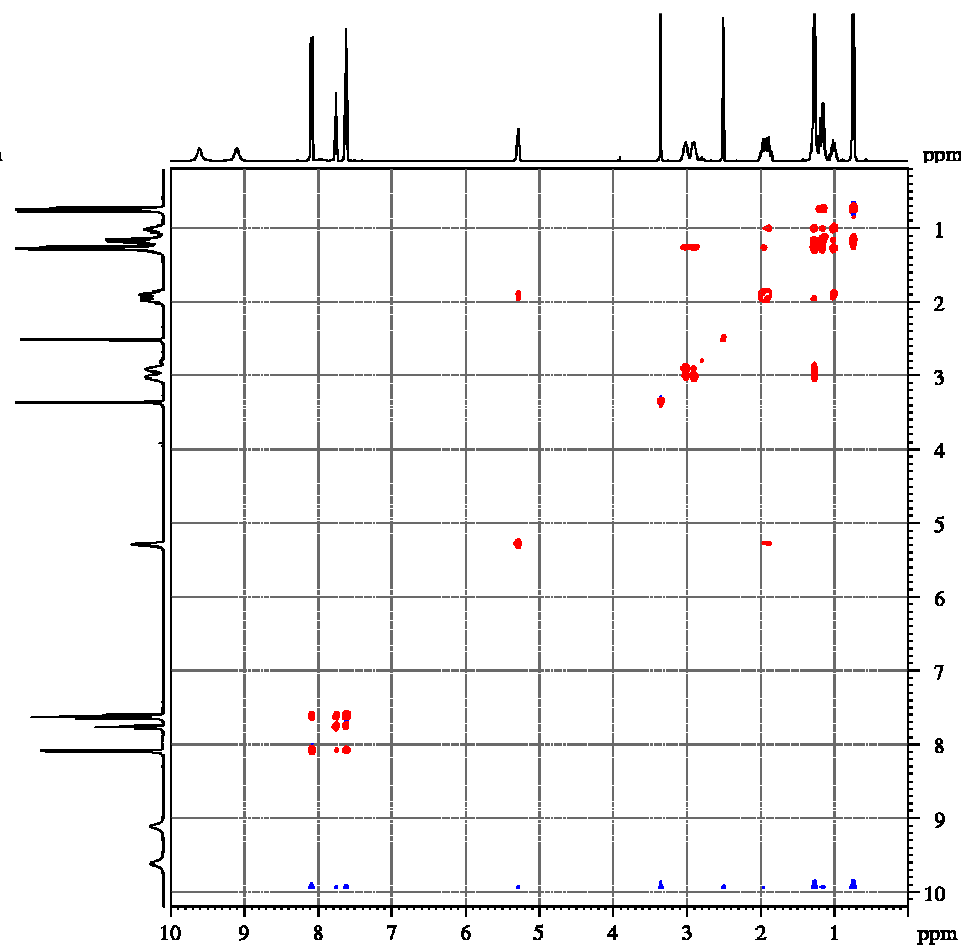
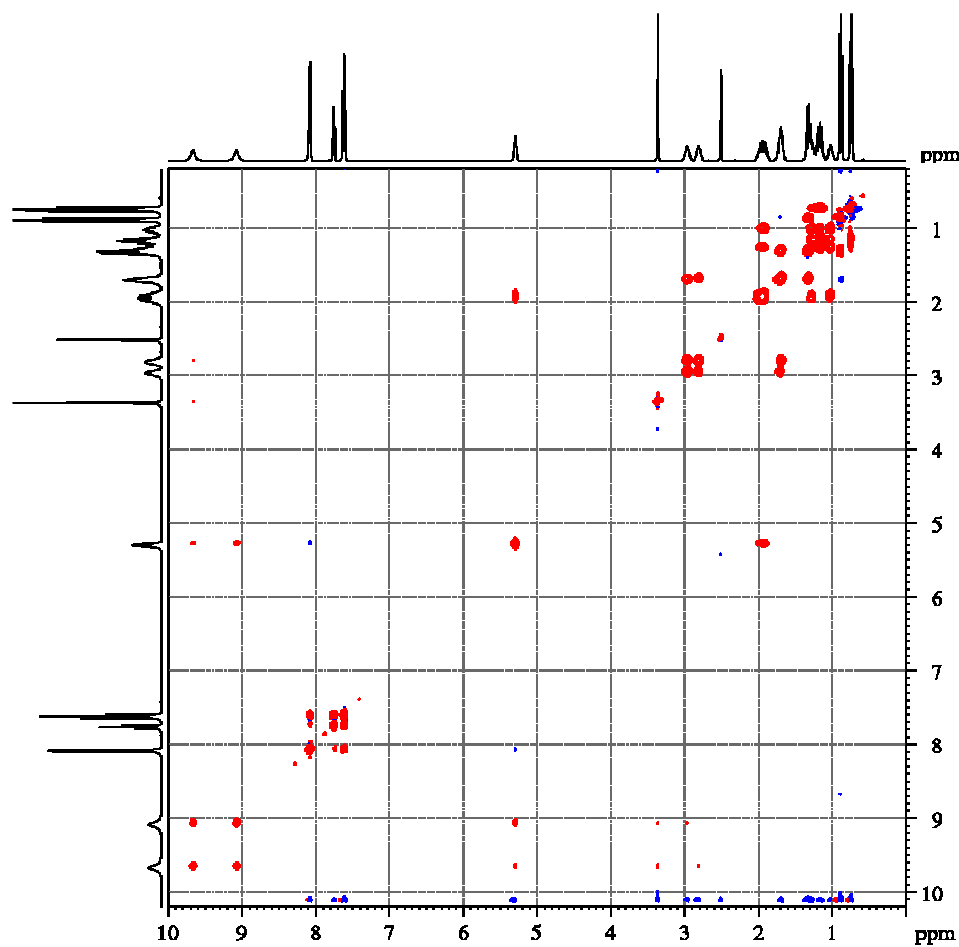
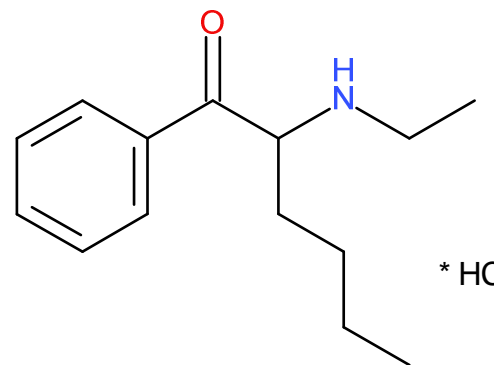
Ed-HSQC spektrum



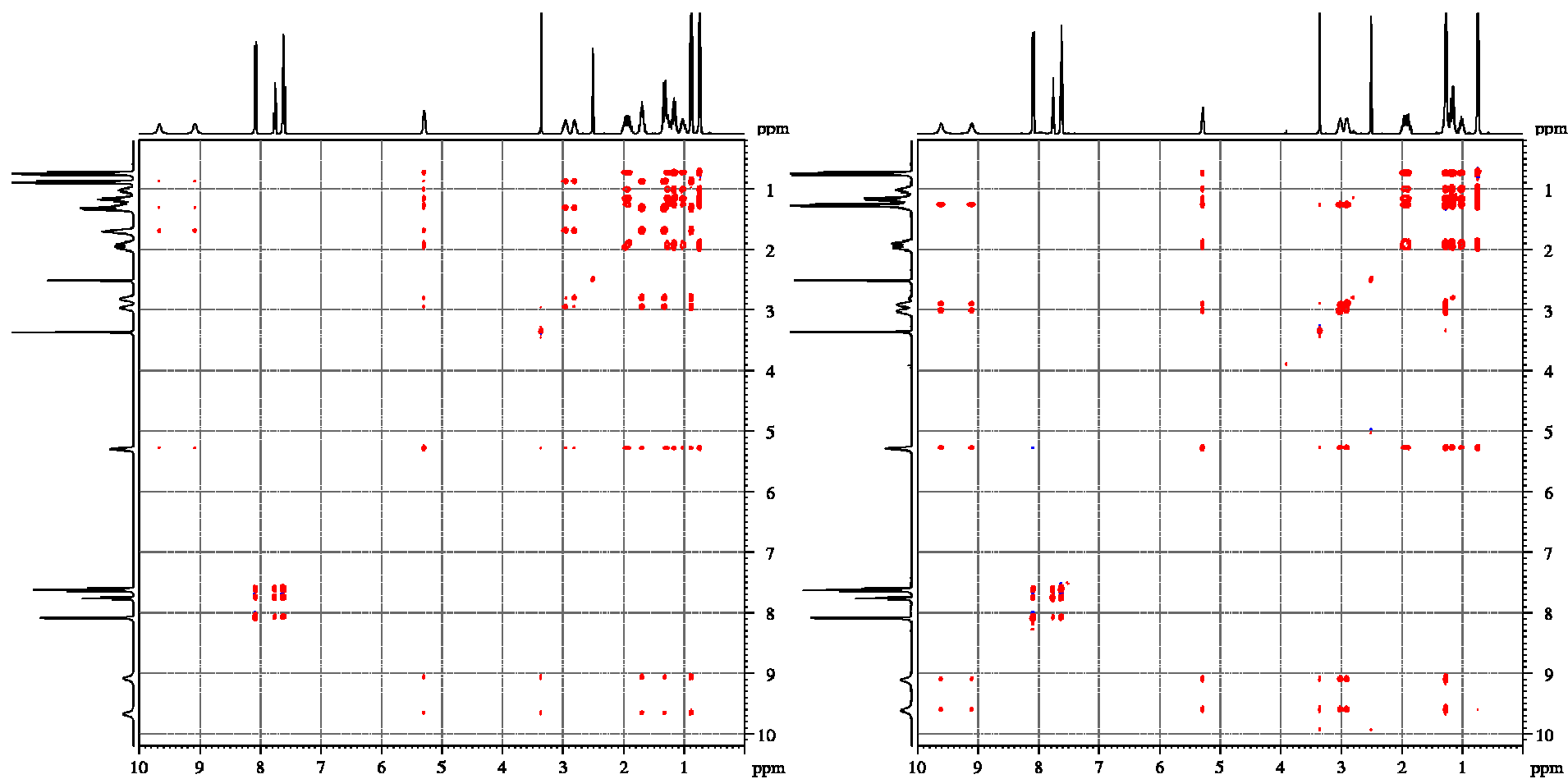
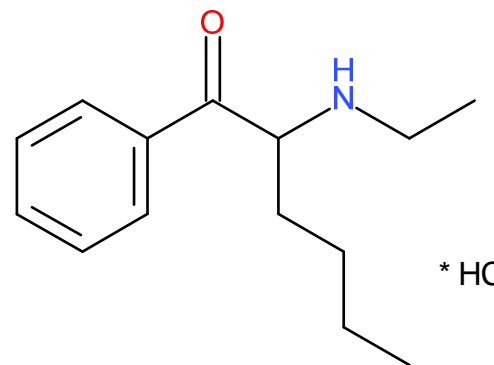
HMBC spektrum



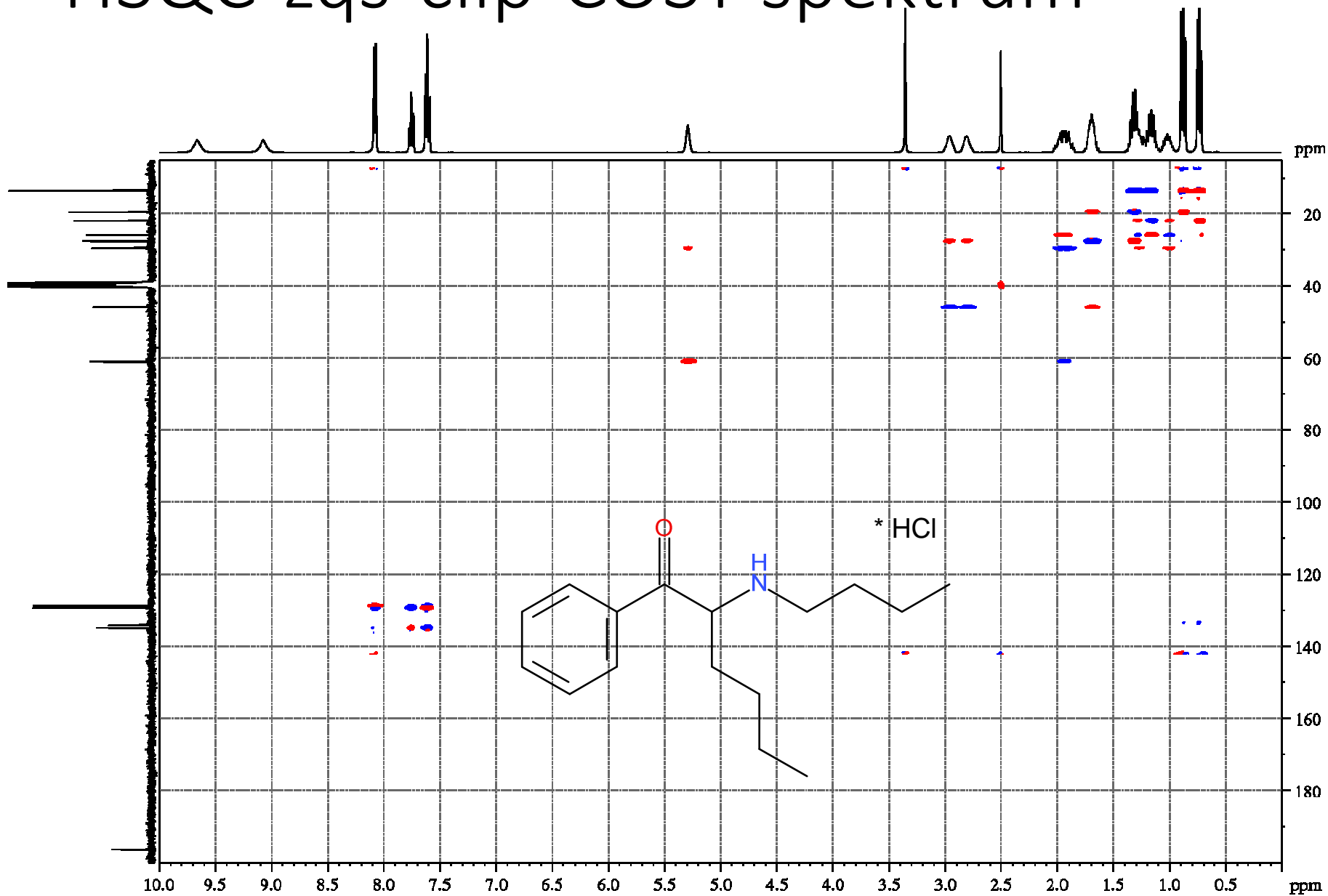
zqs-clip-COSY spektrum



zqs-TOCSY spektrum



HSQC-zqs-clip-COSY spektrum



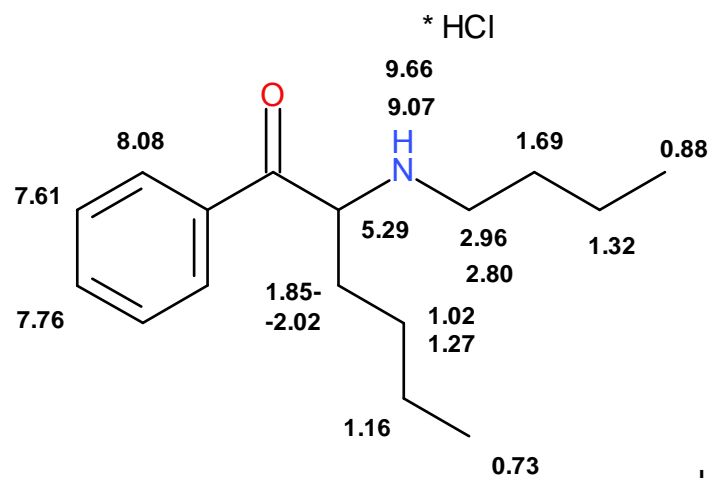
T. Gyöngyösi, I. Tímári, J. Haller, M. R. M. Koos, B. Luy, K. E. Kövér:

Boosting the NMR assignment of carbohydrates with clean in-phase correlation experiments

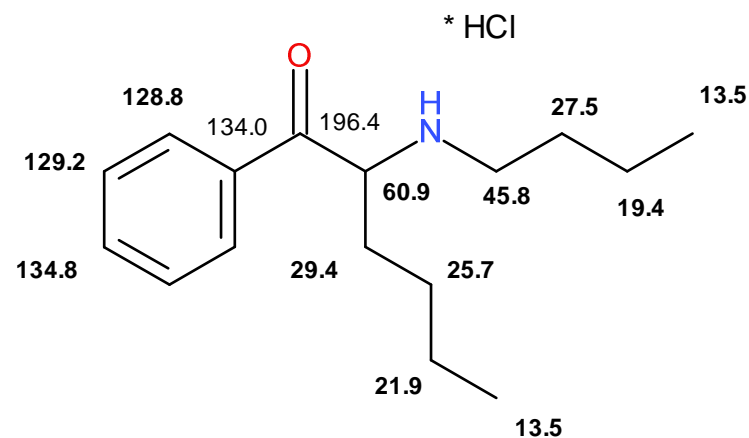
Chem. Plus Chem., **83**, 53-60 (2018)

A szerkezet megoldása: butil-hexedron

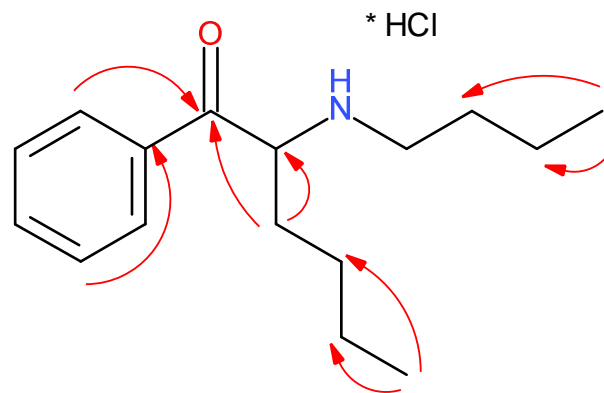
$^1\text{H-NMR}$ kémiai eltolódások δ [ppm]



$^{13}\text{C-NMR}$ kémiai eltolódások δ [ppm]



HMBC méréssel talált jellemző heteronukleáris távolható csatolások
H \rightarrow C



Köszönjük a figyelmet!

