EU FT-ICR MS

SC3- Roma, 25-27 June 2019

Applications of Ion Chemistry in FT-ICR MS

SAPIENZA
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Types of Ion-Molecule Reactions

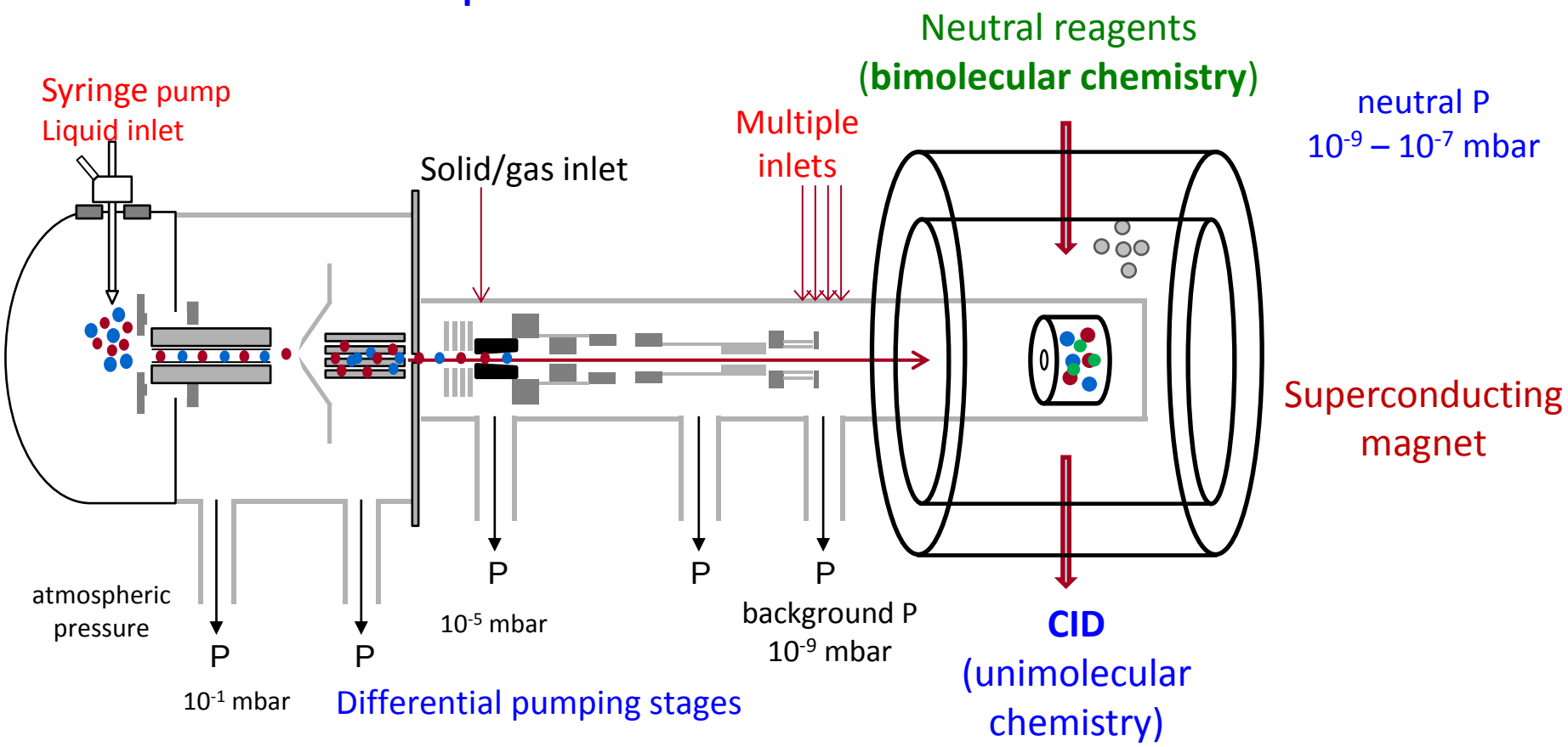
- Electron-Transfer
- Proton transfer
- H-atom/ O-atom transfer
- R^+ transfer
- H/D exchange
- Nucleophilic displacement
- Radiative association

environment; atmosphere; health (diagnosis/monitoring)

A large set of IMR concerns selective reactions of neutral reagents with analyte ions performed in a FT-ICR cell to:

- identify
  - . functional groups in organic compounds
  - . functional groups in biomolecules
- differentiate
  - . (stereo)isomers
  - . charge state
- determine
  - . enantiomeric excess
  - . kinetic, thermodynamic parameters

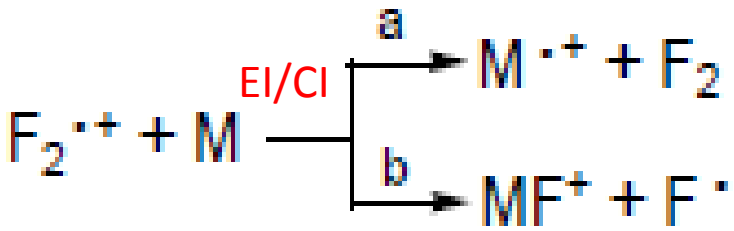
FT-ICR mass spectrometer



J. Am. Chem. Soc. **1997,** *119,* 9499−9503

Positive Ion Chemistry of Elemental Fluorine

Romano Cipollini, Maria Elisa Crestoni, and Simonetta Fornarini*



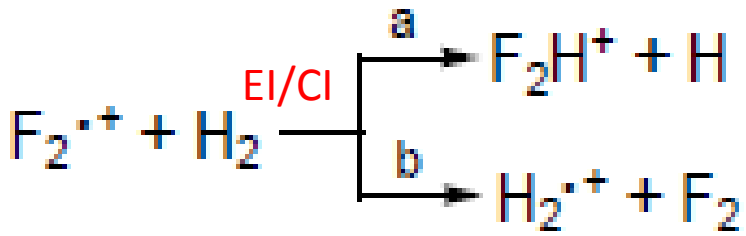
$F_2^{\cdot+} + M \rightarrow M^{\cdot+} + F_2$ (a)

$F_2^{\cdot+} + M \rightarrow MF^{+} + F^{\cdot}$ (b)

M =Xe, O_2, NO, H_2O, CO_2

M = Ar, CO, N_2

$F_2^{+\cdot}$ is a source of electrophilic F !



$F_2^{\cdot+} + H_2 \rightarrow F_2H^{+} + H$ (a)

$F_2^{\cdot+} + H_2 \rightarrow H_2^{\cdot+} + F_2$ (b)

$PA(F_2) = 79 \pm 5$ kcal mol^{-1}

Compendium of the Reactions of H_3O^+ With Selected Ketones of Relevance to Breath Analysis Using Proton Transfer Reaction Mass Spectrometry

frontiers in Chemistry

ORIGINAL RESEARCH
published: 13 June 2019
doi: 10.3389/fchem.2019.00401

Michaela Malásková[1†], David Olivenza-León[2†], Felix Piel[3,4†], Paweł Mochalski[1,5], Philipp Sulzer[3], Simone Jürschik[3], Chris A. Mayhew[1,2] and Tilmann D. Märk[3,4]*

soft chemical ionization, such as proton transfer reactions MS:

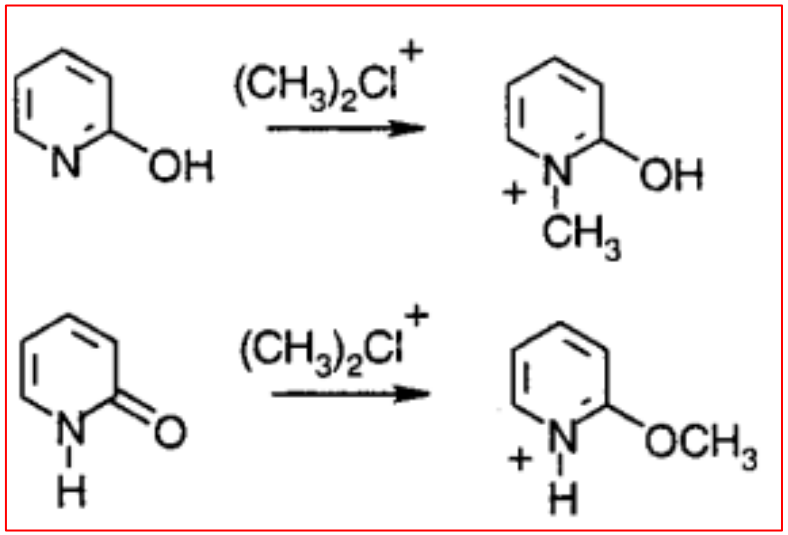
$$H_3O^+ (H_2O)_n \ (n = 0, 1) \ + \ M \longrightarrow MH^+ \longrightarrow \text{fragments}$$

M = 2-butanone, 2-pentanone, 3-pentanone, 3-heptanone, 4-heptanone, 3-octanone, 2-nonanone, 3-nonanone, cyclohexanone

Detecting ketones in the breath may be used for the diagnosys of diabetic ketosis

The protonation may be partly dissociative; from the branching it is possible to distinguish different isomers without the need of pre-separation.

Identification of functional groups in organic compounds



O'Hair, Eur. J. Mass Spectrom. 1995

identification via CID of independently synthetized products

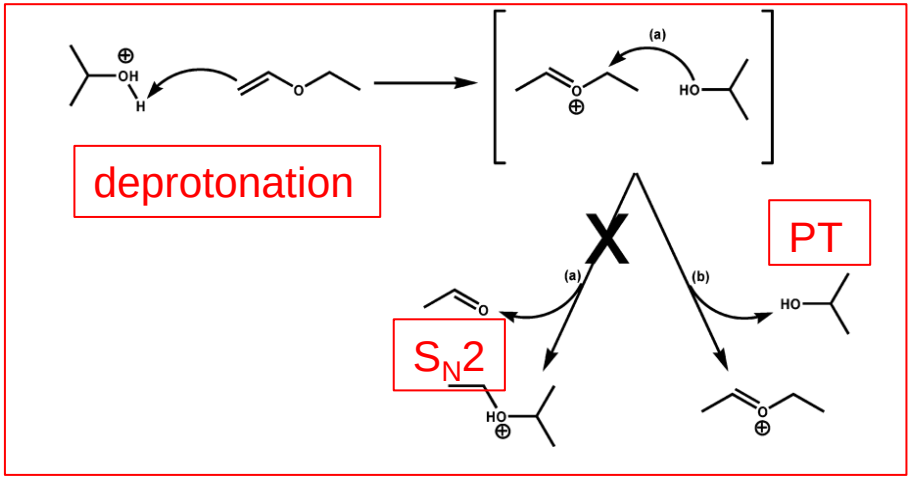
Identification of functional groups in organic compounds

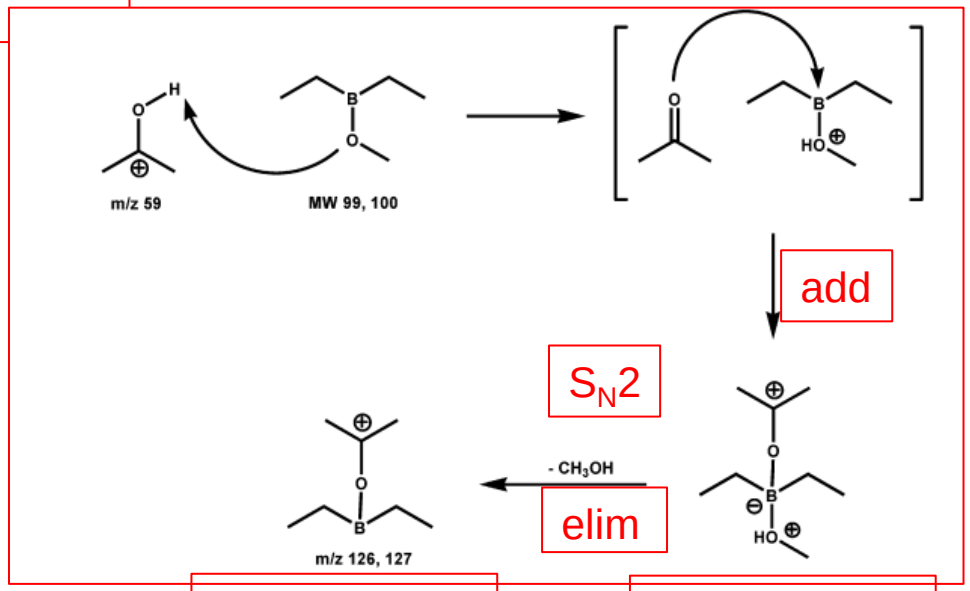
Anal. Chem. **2004,** *76,* 964−976

Ion−Molecule Reactions for Mass Spectrometric Identification of Functional Groups in Protonated Oxygen-Containing Monofunctional Compounds

Michael A. Watkins,[†] Jason M. Price,[†,‡] Brian E. Winger,[§] and Hilkka I. Kenttämaa*,[†]

1) ethyl vinyl ether
2) diethylmethoxyborane





diethylmethoxyborane reacts with protonated monofunctional oxygen-containing analytes (**alcohols, ketones, aldehydes, esters, ethers, carboxylic acids, amides**) by deprotonation followed by substitution of methanol: provides structure elucidation for unknown mixture components

Identification of functional groups in organic compounds

J. Am. Soc. Mass Spectrom. (2012) 23:12-22
DOI: 10.1007/s13361-011-0249-y

RESEARCH ARTICLE

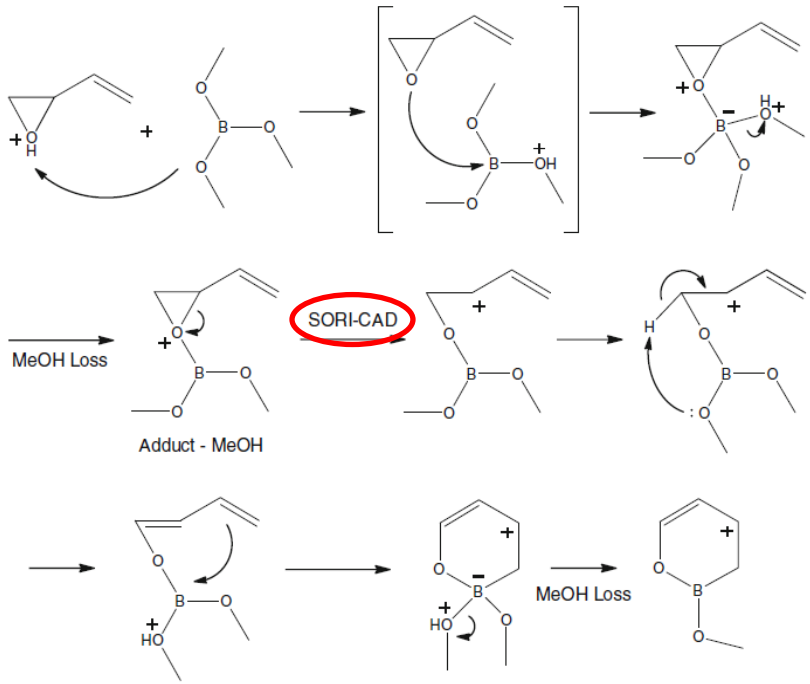
Identification of Epoxide Functionalities in Protonated Monofunctional Analytes by Using Ion/Molecule Reactions and Collision-Activated Dissociation in Different Ion Trap Tandem Mass Spectrometers

Ryan J. Eismin, Mingkun Fu, Sonoeun Yem, Fanny Widjaja, Hilkka I. Kenttämaa
Department of Chemistry, Purdue University, 560 Oval Drive, West Lafayette, IN 47907, USA

IMR involves **proton transfer** from the protonated analyte to TMB, followed by **addition** of the analyte to TMB and **elimination** of methanol

TMB is able to depronate O functionalities but not N groups

Vinyl and phenyl epoxides can be differentiated from other O-containing analytes, based on the **loss of a second methanol molecule** upon CID of the addition/methanol elimination product.



Mechanism for elimination of two methanol molecules upon reaction of protonated butadiene monoxide with TMB

Identification of functional groups in organic compounds

Anal. Chem. **2005,** *77,* 5311–5316

Compound Screening for the Presence of the Primary *N*-Oxide Functionality via Ion–Molecule Reactions in a Mass Spectrometer

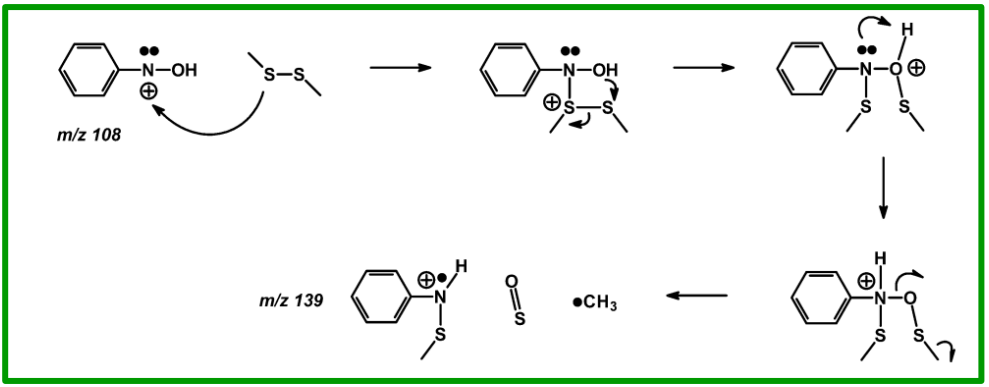
Michael A. Watkins,† Danielle V. WeWora,† Sen Li,† Brian E. Winger,‡ and Hilkka I. Kenttämaa*,†

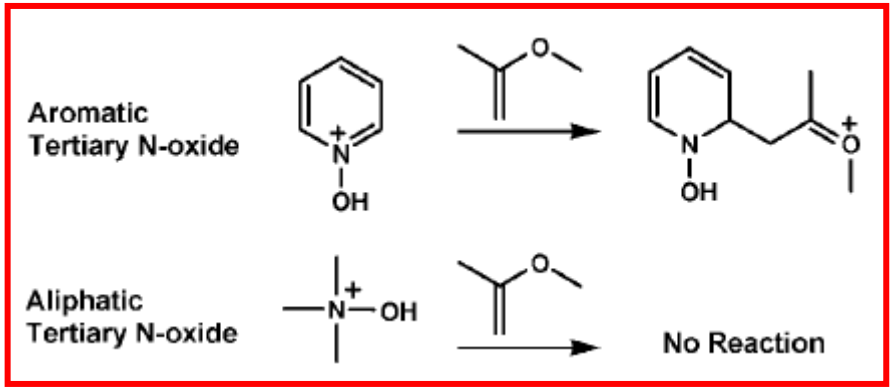
JOC *Article*

J. Org. Chem. **2008**, *73*, 4888–4894

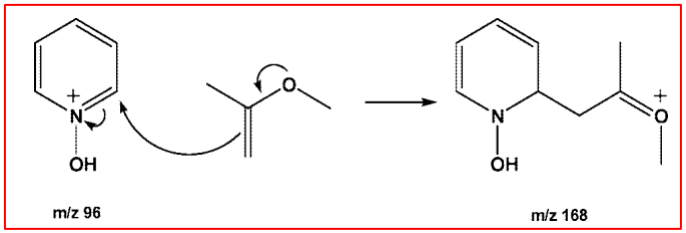
Identification of the Aromatic Tertiary *N*-Oxide Functionality in Protonated Analytes via Ion/Molecule Reactions in Mass Spectrometers

Penggao Duan,† Todd A. Gillespie,‡ Brian E. Winger, and Hilkka I. Kenttämaa*,†





protonated primary N-oxides selectively react with $(CH_3S)_2$ forming a product with 31 Da higher mass.



protonated aromatic tertiary N-oxides selectively add 2-methoxy-propene

H. I. Kenttamaa, *Anal. Chem.* 2005; *J. Org. Chem.* 2008

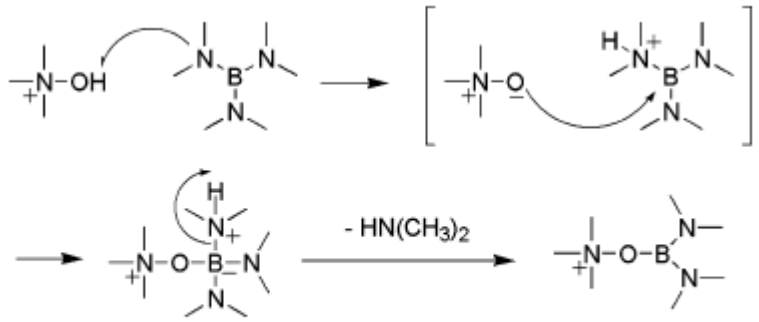
Identification of functional groups in organic compounds

JOC *Article*

J. Org. Chem. **2009**, *74*, 1114–1123

Identification of Aliphatic and Aromatic Tertiary N-Oxide Functionalities in Protonated Analytes via Ion/Molecule and Dissociation Reactions in an FT-ICR Mass Spectrometer

Penggao Duan,† Mingkun Fu,† Todd A. Gillespie,‡ Brian E. Winger,‡ and Hilkka I. Kenttämaa*,†



Scheme 1. Mechanism proposed for the reaction between protonated N-oxide containing analyte and neutral TDMAB.

aliphatic and aromatic tertiary N-oxides react with tri(dimethylamino)borane yielding add-elim products identified via SORI-CID

Journal of Pharmaceutical and Biomedical Analysis 51 (2010) 805–811

Contents lists available at ScienceDirect

Journal of Pharmaceutical and Biomedical Analysis

journal homepage: www.elsevier.com/locate/jpba

Liquid chromatography/tandem mass spectrometry utilizing ion-molecule reactions and collision-activated dissociation for the identification of N-oxide drug metabolites

Steven C. Habicht, Penggao Duan[1], Nelson R. Vinueza, Mingkun Fu, Hilkka I. Kenttämaa*

Department of Chemistry, Purdue University, West Lafayette, IN 47907, USA

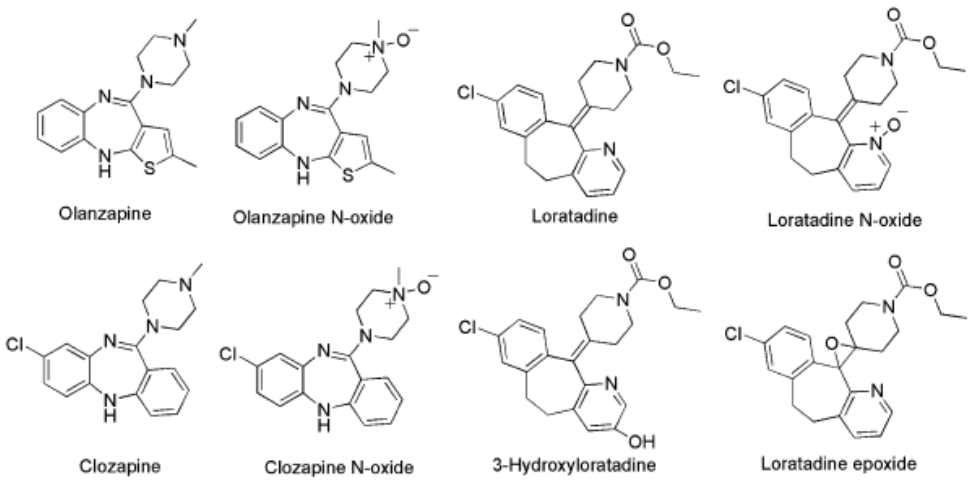
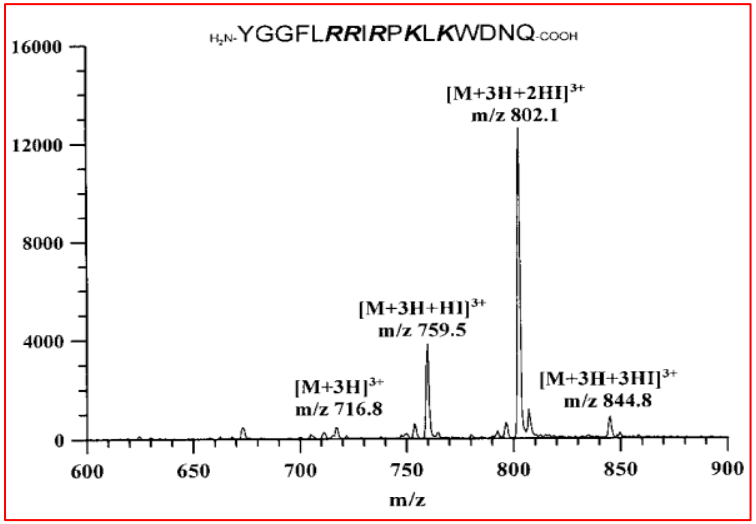


Fig. 1. Drugs and derivatives used to demonstrate the feasibility of the method.

application in the pharmaceutical setting

Identification of functional groups in biomolecules

S. A. McLuckey, *Anal. Chem.* 1997



the adducts possess as many HI units as the total number of basic aas (arginine, lysine) and the N-terminus

Research Article

Rapid Communications in Mass Spectrometry

Received: 25 January 2014 Revised: 27 February 2014 Accepted: 27 February 2014 Published online in Wiley Online Library

Rapid Commun. Mass Spectrom. **2014**, *28*, 1107–1116
(wileyonlinelibrary.com) DOI: 10.1002/rcm.6884

Probing the exposure of the phosphate group in modified amino acids and peptides by ion-molecule reactions with triethoxyborane in Fourier transform ion cyclotron resonance mass spectrometry

Francesco Lanucara[1,2*], Simonetta Fornarini[3], Claire E. Eyers[2] and Maria Elisa Crestoni[3]

$[\text{Peptide-O-P(O)(OH)}_2\text{+nH}]^{n+} + \text{B(OR)}_3 \rightarrow [\text{Peptide-O-PO(OH)OB(OR)}_2\text{+nH}]^{n+} + \text{ROH}$

Scheme 1. Addition-elimination reaction of phosphorylated amino acids and peptides with alkoxyboranes $B(OR)_3$.

set of phosphorylated peptides comprising phosphorylated serine and threonine, bearing a C-terminus lysine or arginine residue and holding naturally occurring sequences

Potential to measure the effect of local environment, the exposure and accessibility of a phosphate moiety on the surface of a biomolecule and to distinguish positional phosphorylated peptide isomers

The efficiency of such reactions allows to explore the accessibility of phosphate groups in biomolecules

S. A. McLuckey et al., *Anal. Chem.* 1997;
Lanucara et al., *Rapid Commun. Mass Spectrom.* 2014

Identification of functional groups in biomolecules

J Biol Inorg Chem (2007) 12:22–35
DOI 10.1007/s00775-006-0159-9

ORIGINAL PAPER

Heme-peptide/protein ions and phosphorous ligands: search for site-specific addition reactions

Maria Elisa Crestoni · Simonetta Fornarini

insight in the coordination environment of the prosthetic group in systems of increasing complexity

- **Fe(III)-heme$^+$**
- **MP11**
- **cyt c**
- **myoglobin**

+ $OP(OMe)_3$ (GB: 206 kcal/mol)
+ $P(OMe)_3$ (GB: 215.3 kcal/mol)

Effect of axial ligand: free and ligated heme-type ions

Identification of functional groups in biomolecules

J Biol Inorg Chem (2007) 12:22–35
DOI 10.1007/s00775-006-0159-9

ORIGINAL PAPER

Heme-peptide/protein ions and phosphorous ligands: search for site-specific addition reactions

Maria Elisa Crestoni · Simonetta Fornarini

+ $OP(OMe)_3$ (GB: 206 kcal/mol) «-ate»
+ $P(OMe)_3$ (GB: 215.3 kcal/mol) «-ite»

- $Fe(III)\text{-heme}^+ + OP(OMe)_3 \longrightarrow$ mono-adduct
- $Fe(III)\text{-heme}^+ + P(OMe)_3 \longrightarrow$ bis-adduct

back-acceptor ability of -ite

- $[MP11+H]^{2+} + OP(OMe)_3 \not\longrightarrow$ no- reaction
- $[MP11+2H]^{3+} + OP(OMe)_3 \longrightarrow$ tris-adduct

folded conformation
elongated conformation

- $[MP11+H]^{2+} + P(OMe)_3 \longrightarrow$ mono-adduct
- $[MP11+2H]^{3+} + P(OMe)_3 \longrightarrow$ mono-adduct

Is the heme iron the site of attack of –ite in $[MP11+H]^{2+}$?

Identification of functional groups in biomolecules

J Biol Inorg Chem (2007) 12:22–35
DOI 10.1007/s00775-006-0159-9

ORIGINAL PAPER

Heme-peptide/protein ions and phosphorous ligands: search for site-specific addition reactions

Maria Elisa Crestoni · Simonetta Fornarini

- **cyt c**
- **myoglobin**

+ $OP(OMe)_3$ (GB: 206 kcal/mol)
+ $P(OMe)_3$ (GB: 215.3 kcal/mol)

the addition of phosphite is always limited to just one molecule, irrespective of charge state, in contrast with a charge-dependent number of added phosphate ligands

- **$OP(OMe)_3$ is engaged in H bonding to protonated sites**
- **$P(OMe)_3$ is sampling the protein prosthetic group**

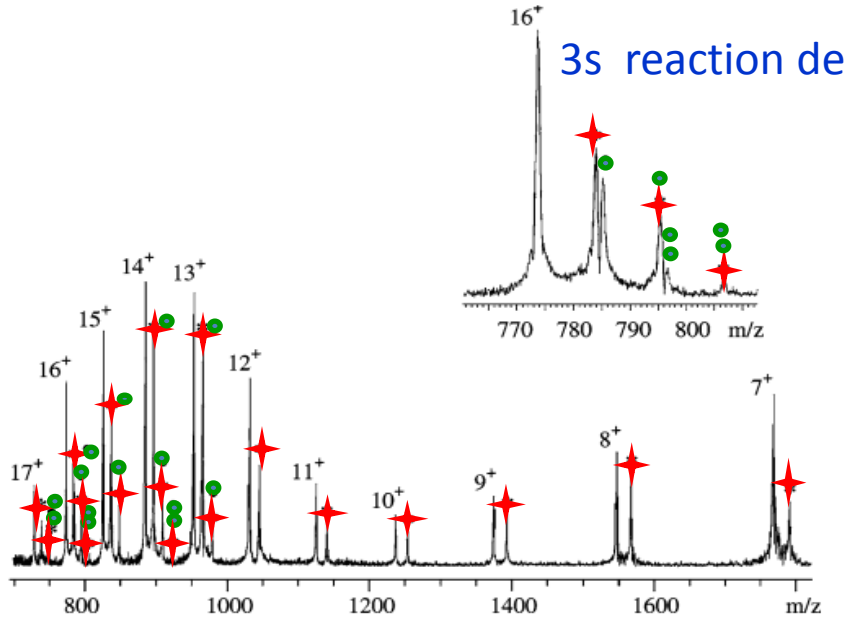


Fig. 9 FT-ICR mass spectrum of cyt *c* allowed to react with a 70:30 mixture of triethylphosphite, $P(OEt)_3$, and triethylphosphate, $OP(OEt)_3$, at 2.4×10^{-8} mbar for 3 s. *Numbers* denote the charge states of cyt *c* ions. Each charge state forms adducts with a single $P(OEt)_3$ molecule (represented by a *star*). The high charge states add up to four $OP(OEt)_3$ molecules; each $OP(OMe)_3$ molecule is represented by a *circle*

Identification of functional groups in biomolecules

Anal. Chem. 2008, *80*, 303–311

Ozone-Induced Dissociation: Elucidation of Double Bond Position within Mass-Selected Lipid Ions

OzID

Michael C. Thomas, Todd W. Mitchell, David G. Harman, Jane M. Deeley, Jessica R. Nealon, and Stephen J. Blanksby*

crude lipids extracts $\xrightarrow{ESI_{neg}}$ $[M-H]^-$ $\xrightarrow{CID}$ lipid class, total Cs, DBs

phospholipids

isomers indistinguishable

@ m/z 281, the 18:1 = 9Z-18: (oleic acid) ???

ESI_{pos}

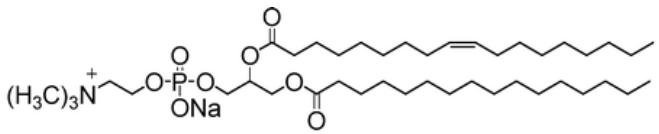
$[M+Na]^+$

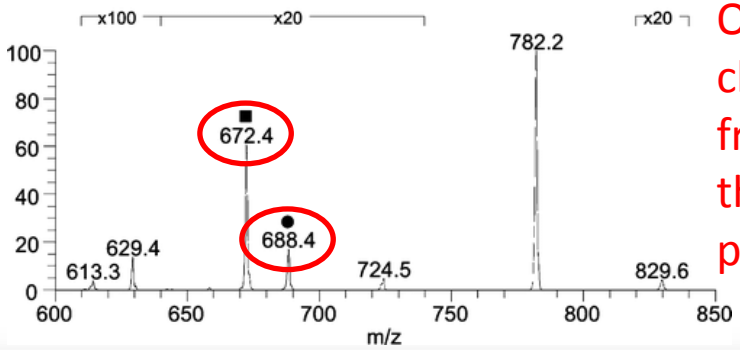
isolation

$[phosphatidylcholine+Na]^+$

O_3, 10 s

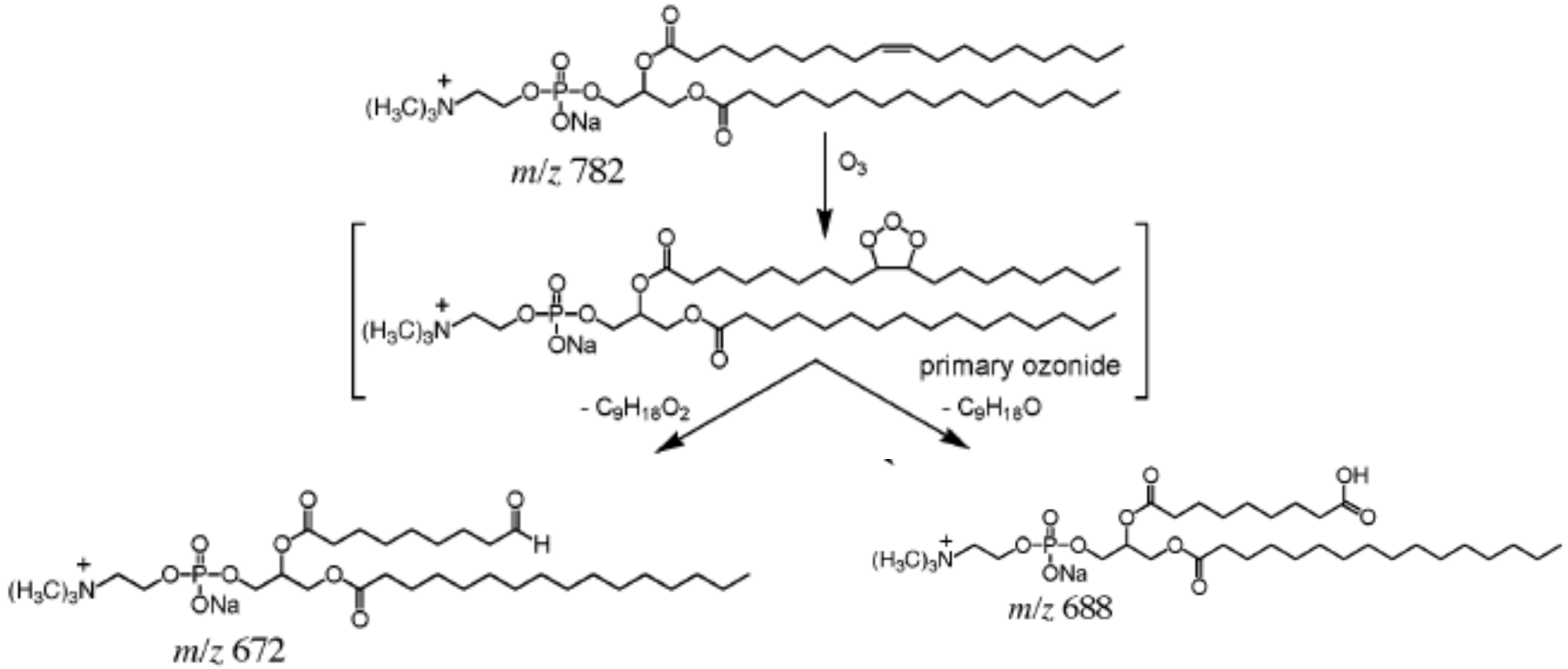
But other regioisomers are also present in nature !





Ozonolysis provides two chemically induced fragment ions for each DB that can identify DB position

S. J. Blanksby, *Anal. Chem.* 2008



2-(9-oxononanoyl)-
1-palmitoyl-sn-glycero-3-phosphocholine

OzID allow Double Bond position to be assigned for several precursor ions:
$[M+H]^+$, $[M+Li]^+$, $[M+Na]^+$, $[M-H]^-$
obtained from sources including human lens, bovine kidneys, commercial olive oil

Differentiation of (stereo)isomers

ELSEVIER

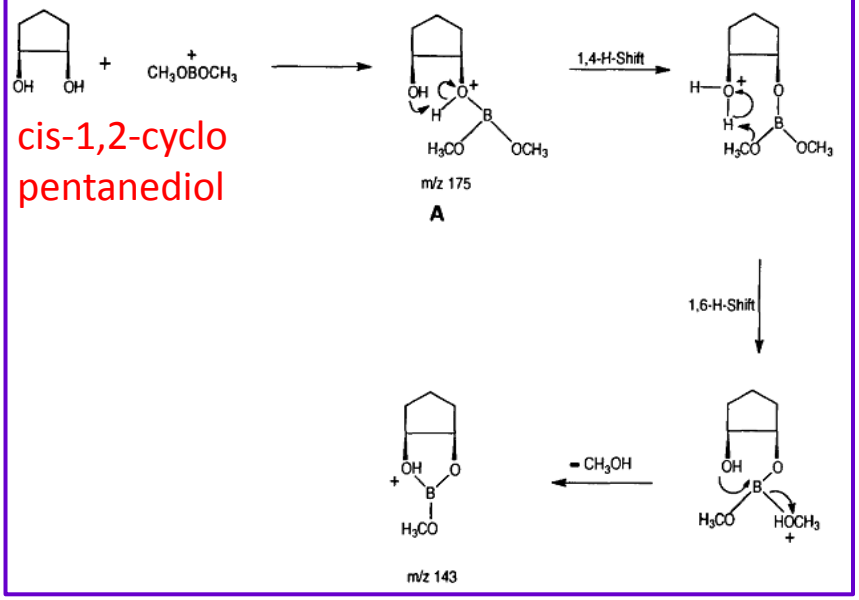
International Journal of Mass Spectrometry and Ion Processes 141 (1995) 229–240

International Journal of Mass Spectrometry and Ion Processes

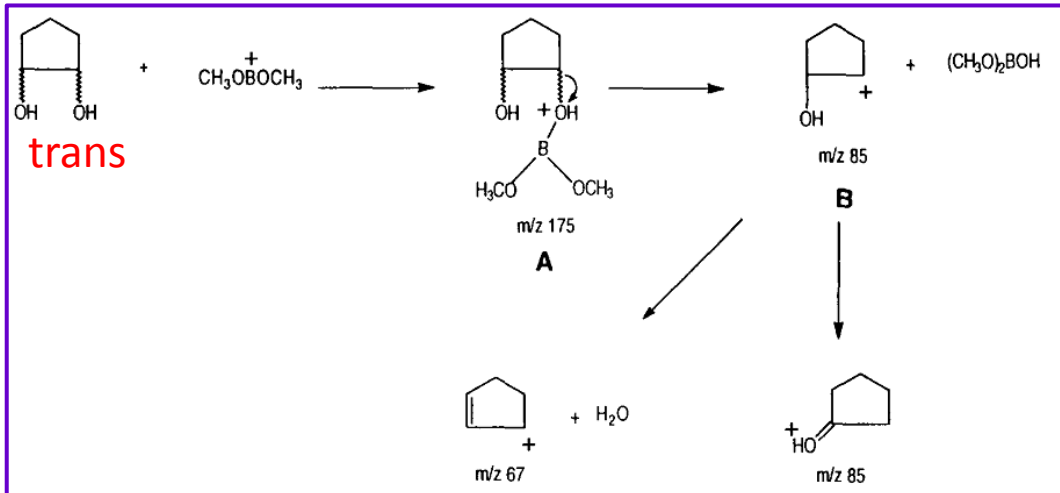
Differentiation of stereoisomeric diols by using $CH_3OB^+OCH_3$ in a small Fourier transform ion cyclotron resonance mass spectrometer

D.T. Leeck[a], T.D. Ranatunga[a], R.L. Smith[a], T. Partanen[b], P. Vainiotalo[b,*], H.I. Kenttämaa[a,*]

cis-1,2-cyclo pentanediol



trans



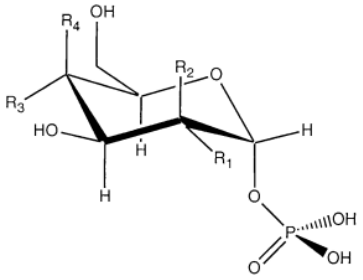
H. I. Kenttamaa, *Int. J. Mass Spectrom. Ion Proc.* 1995

Differentiation of (stereo)isomers

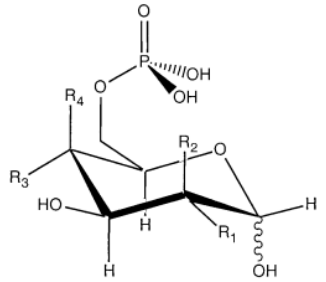
Investigation of Ion/Molecule Reactions as a Quantification Method for Phosphorylated Positional Isomers: An FT-ICR Approach

J Am Soc Mass Spectrom 2003, 14, 916–924

Hong Gao, Christopher J. Petzold, Michael D. Leavell, and Julie A. Leary



1-phosphorylated monosaccharide

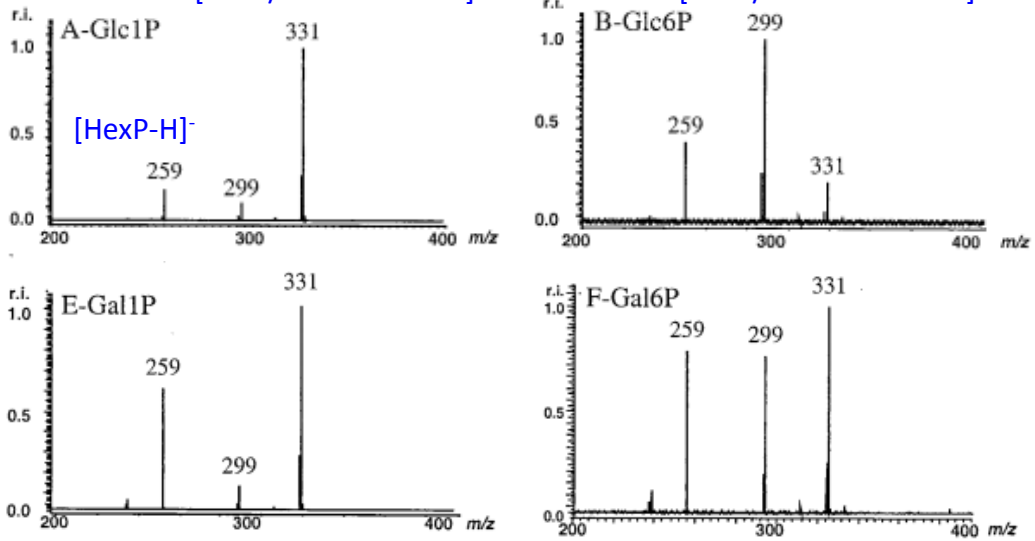


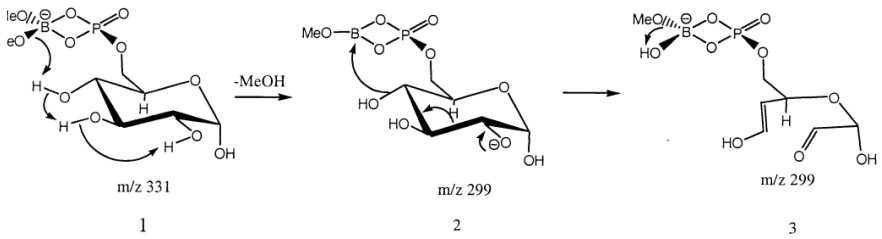
6-phosphorylated monosaccharide

Multicomponent quantification method + IMR with $B(OMe)_3$ in FT-ICR cell

[HexP/TMB-MeOH-H]$^-$

[HexP/TMB-2MeOH-H]$^-$





Product ion distribution differs significantly for isomers phoshorylated either in the 1- or 6-position

further confirmed by CID

accurate mixture composition

Differentiation of (stereo)isomers

A. Piatkivskyi *et al.*, *Eur. J. Mass Spectrom.* **20**, 177–183 (2014)
Received: 25 January 2014 ■ Accepted: 13 February 2014 ■ Publication: 25 February 2014

EJMS EUROPEAN JOURNAL OF MASS SPECTROMETRY

Utilisation of gas-phase ion–molecule reactions for differentiation between phospho- and sulfocarbohydrates

Andrii Piatkivskyi,[a] Yuriy Pyatkivskyy,[b,*] Matt Hurt[c] and Victor Ryzhov[a]

X :
Trimethylborate (TMB)
Triethylborate (TEB)
Diethylmethoxyborane (DEMB)
Diisopropoxymethylborane (DIBMP)

$-OSO_3^- + X \not\rightarrow A$

$-OPO_3H^- + X \rightarrow B$

B: $[M-H+TMB-MeOH]^-$ + $[M-H+TMB-2MeOH]^-$

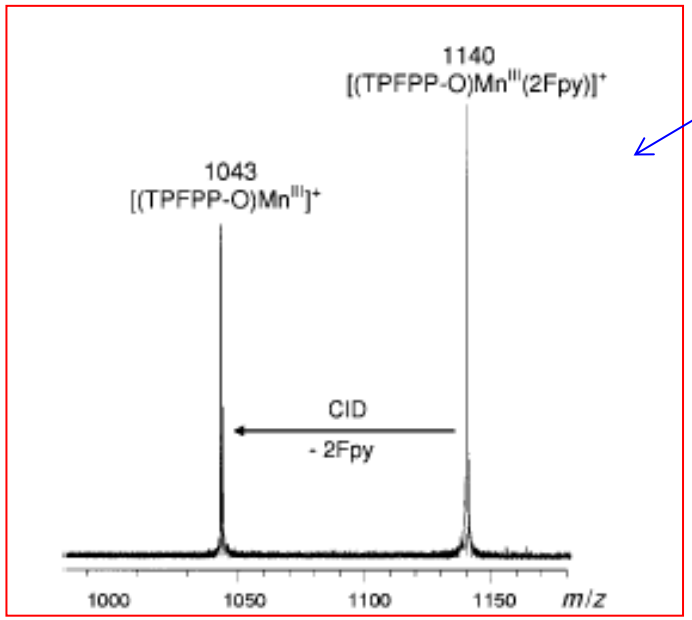
Differentiation of (stereo)isomers

Gas-phase titration

$[(TPFPP)Mn^{V}O]^{+}$ + β-pinene ⟶ $[(TPFPP)Mn^{III}]^{+}$ % > 60%

$[(TPFPP\text{-}O)Mn^{III}]^{+}$ + β-pinene ⤫

$[(TPFPP\text{-}O)Mn^{III}]^{+}$ + 2Fpy ⟶ $[(TPFPPO)Mn^{III}(2Fpy)]^{+}$



CID

Table 1. Kinetic data for the reaction of $[(TPFPP)Mn^{V}O]^{+}$ (**1**) with selected olefins in the gas-phase.[a]

Olefin (IE)[b]	k_{exp}[c,d]	Φ[e]
propene (9.73)	0.0020	0.021
3,3-dimethyl-1-butene (9.45)	0.041	0.43
(*E*)-2-butene (9.10)	0.072	0.78
(*Z*)-2-butene (9.11)	0.75	8.1
allylbenzene (7.8–8.7)	0.070	0.76
styrene (8.46)	0.63	6.8
cyclohexene (8.95)	0.75	7.7
1,4-cyclohexadiene (8.8)	0.69	7.8
1-propene, 2-methoxy (8.64)[f]	1.7	16
1,3,5-cycloheptatriene (8.30)	1.9	21
(+)-camphene (≤8.86)	2.6	28
indene (8.14)[g]	1.2	12
(1*S*)-(−)-α-pinene (8.07)	9.0	100
β-pinene (n.a.)	9.3	100
(*R*)-(+)-limonene (8.3)	9.2	100

The ion population reacts to completion only in the presence of both neutrals

M. E. Crestoni, et al. *Chem. Eur. J. 2009*

Differentiation of (stereo)isomers

H/D exchange reactions

for counting the active Hs and probe the structure of biomolecules

the ions can be trapped for extended periods of time in the presence of a background pressure of the exchange reagent

to observe H/D exchange, the energy released by complex formation must be sufficient to overcome the barrier to internal PT

$$\text{(Reaction 1)} \quad D_0 + CH_3OD \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} D_1 + CH_3OH$$

$$\text{(Reaction 2)} \quad D_1 + CH_3OD \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} D_2 + CH_3OH$$

$$\text{(Reaction 3)} \quad D_2 + CH_3OD \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} D_3 + CH_3OH$$

$$\text{(Reaction 4)} \quad D_3 + CH_3OD \underset{k_{-4}}{\overset{k_4}{\rightleftharpoons}} D_4 + CH_3OH$$

one approach to analyze the kinetics is the «independent site treatment», where the rate constants are determined iteratively

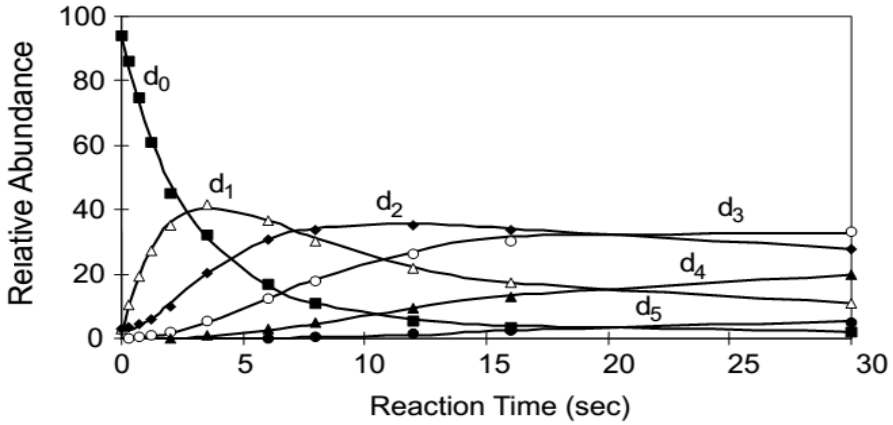


Figure 7. Time plot of the deuterium exchange products of ATP^- reacting with CD_3OD (4.2×10^{-8} mbar)

Table 1. Relative apparent rate constants[a] for the protonated and sodiated adenine nucleotides with reagent gases

Parent ion	m/z	Rea
$AMPH^+$	348	CD
$ADPH^+$	428	
$ATPH^+$	508	

One advantage:

- H/D exchange probes several sites in a molecule (proton transfer involves a single site)

C. B. Lebrilla et al., *MSR* 1997

M. E. Crestoni, S. Fornarini, *J. Mass Spectrom.* 2003

Differentiation of charge states

NO binding to Fe(II) and Fe(III)-hemes

Inorg. Chem. 2008, 47, 7792−7801
Inorganic Chemistry
Article

Unravelling the Intrinsic Features of NO Binding to Iron(II)- and Iron(III)-Hemes

Barbara Chiavarino,[†] Maria Elisa Crestoni,[†] Simonetta Fornarini,*[,†] and Carme Rovira*[,‡]

Table 1. Rate and equilibrium constants for NO binding to iron(II)/iron(III) porphyrin complexes and heme proteins[9]

Iron(II)/(III) porphyrin[(a)]	k_f / M^{-1} s^{-1}	k_r / s^{-1}	K / M^{-1}
Mb(II)	1.7×10^7	1.2×10^{-4}	1.4×10^{11}
Mb(III)	1.9×10^5	13.6	1.4×10^4
Hb(II)	2.5×10^7	4.6×10^{-5}	5.3×10^{11}
Hb(III)	4×10^3	1	4×10^3
Fe^{II}(TPPS)	1.8×10^9	≈ 0	$> 10^9$
Fe^{III}(TPPS)	7.2×10^5	6.8×10^2	1.1×10^3
Fe^{II}(TMPS)	1×10^9	–	–
Fe^{III}(TMPS)	3×10^6	7.3×10^2	4.1×10^3

[(a)] Mb: myoglobin; Hb: hemoglobin; TPPS: meso-tetra(4-sulfonatophenyl)porphyrinato dianion; TMPS: meso-tetra(sulfonatomesityl)porphyrinato dianion.

NO addition is governed by:
- Fe coordination number
- Fe oxidation state

Differentiation of charge states

tetracoordinated

$$[Fe^{II}\text{-hemeH}]^+ + NO \underset{k_r}{\overset{k_f}{\rightleftharpoons}} [Fe^{II}\text{-hemeH(NO)}]^+$$

$$[Fe^{III}\text{-heme}]^+ + NO \underset{k_r}{\overset{k_f}{\rightleftharpoons}} [Fe^{III}\text{-heme(NO)}]^+$$

pentacoordinated

Table 4. Kinetics and Equilibrium Data for NO Binding to $[Fe^{II}\text{-hemeH}]^+$ and $[Fe^{III}\text{-heme}]^+$ Ions in the Gas Phase

reagent ion	K_1 ($\times 10^{-11}$)[a]	k_f ($\times 10^{11}$)[b]	k_r ($\times 10^{3}$)[c]
$[Fe^{II}\text{-hemeH}]^+$	5.7	3.3	0.8
$[Fe^{III}\text{-heme}]^+$	5.3	2.2	0.9

[a] Equilibrium constant for the association of NO to the heme ions at 300 K, obtained from the $H^{II}CB/H^{III}CB$ values reported in Table 3 (K_1 = exp(HCB/RT)). Standard state 1 atm. [b] Forward rate constant for the association of NO to the heme ions, in units of cm^3 $molecule^{-1}$ s^{-1}, at 300 K. refs 8b and 10. [c] Reverse rate constant for the association of NO to the heme ions, in s^{-1}, at 300 K. This work.

$HCB^{II}_{(NO)} = HCB^{III}_{(NO)} = 67$ kJ mol $^{-1}$ at 300 K

both oxidation states show similar kinetic and thermodynamic behaviour

S. Fornarini et al. Inorg. Chem. 2008

Determination of enantiomeric excess

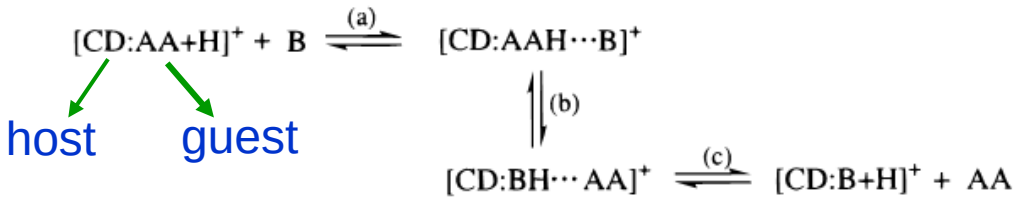
J. Am. Chem. Soc. **1998,** *120,* 7387−7388

Gas-Phase Chiral Differentiation of Amino Acid Guests in Cyclodextrin Hosts

Javier Ramirez, Fei He, and Carlito B. Lebrilla*

chiral differentiation of AAs is of immediate analytical importance

Scheme 1



- complexes of protonated β-cyclodextrin-amino acid (Ala; Val; Phe) react with n-propylamine by **exchanging the** AA **guest of cyclodextrin host** for alkylamine;
- the exchange rates are found to differ according to the chirality of the AA
- Valine is the most reactive and shows the greatest selectivity: k_L/k_D= 1.6 (Alanine); k_L/k_D= 3.1 (Valine); k_L/k_D= 0.8 (Phenylalanine).
- **the differences may be related to the way the AA is included into the host cavity.**

C. B. Lebrilla et al., J. Am. Chem. Soc. 1998;
M. Speranza et al. Chiral. 2009

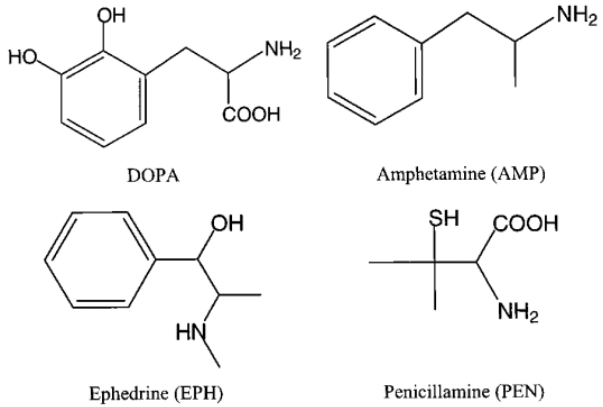
Determination of enantiomeric excess

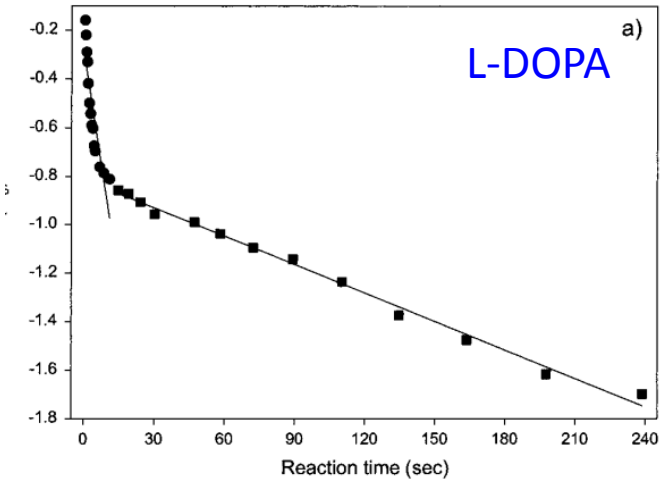
Anal. Chem. **2001,** *73,* 1684−1691

Enantiomeric Analysis of Pharmaceutical Compounds by Ion/Molecule Reactions

Gabriela Grigorean and Carlito B. Lebrilla*

A diastereoisomeric complex of an oligosaccharide host with a chiral analyte guest reacts with an alkylamine to produce a guest exchange





The presence of more than one reacting species, observed with DOPA and PEN, in the reaction with B=1,3-diamminopropane, suggests at least two reacting species, where the analyte interacts with the host by different arrangements.

Determination of kinetic parameters

- measurements of rate constants
- determination of reaction efficiency

Determination of thermodynamic parameters

Association Reactions

- solvation of an ion by weak electrostatic or hydrogen bonding;
- ion ligation involving bonds of intermediate strength;
- strong chemical bond formation

$$A^{\pm} + B \rightleftharpoons (AB)^{\pm *}$$

$$(AB)^{\pm *} \longrightarrow AB^{\pm} + h\nu \quad \text{----------} \rightarrow \text{FT-ICR}$$

$$(AB)^{\pm *} + M \longrightarrow AB^{\pm} + M \quad \text{----------} \rightarrow \text{Ion-trap}$$

at the low operating pressures of the FT-ICR cell: thermal equilibration of the adduct ion via IR radiative emission

The rate of radiative emission is expected to increase with increasing size of the ion

F.W. Mc Lafferty et al., *J. Am. Chem. Soc. 2001*

Determination of thermodynamic parameters

Binding of Gaseous Fe(III)-Heme Cation to Model Biological Molecules: Direct Association and Ligand Transfer Reactions

Fausto Angelelli, Barbara Chiavarino, Maria Elisa Crestoni, and Simonetta Fornarini

Department of Studies on Chemistry and Technology of Biologically Active Substances, University of Rome, "La Sapienza," Rome, Italy

Ligand association equilibrium

$$\text{Fe(III)-heme}^+ + \text{L} \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} \text{Fe(III)-heme(L)}^+$$

L= NO, amines, carbonyl compounds, ethers, nitriles, sulfides, phosphoryl compounds

$$HCB(L) = -\Delta G^\circ = -RT\ln K_{eq}$$

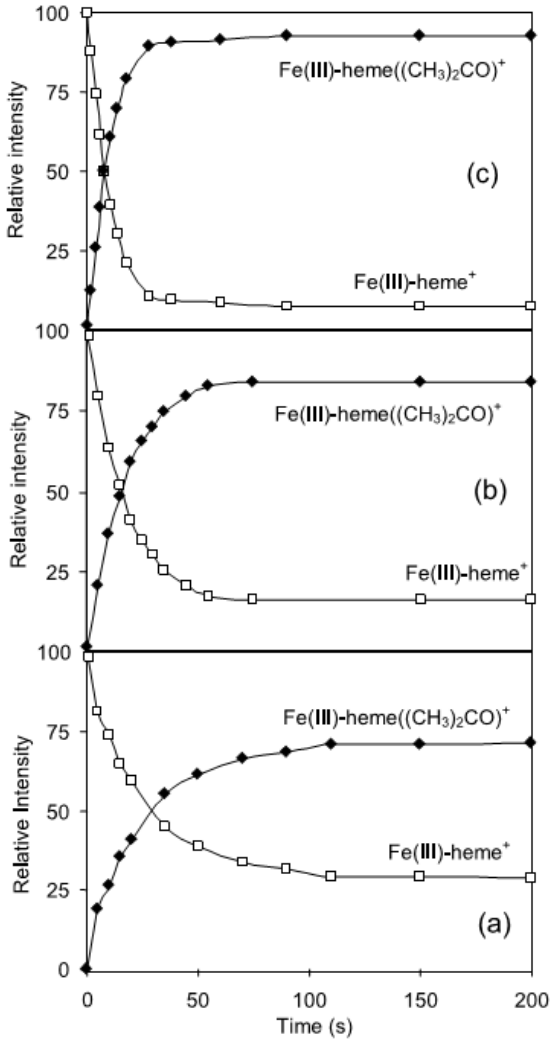


Figure 5. Time dependence of ion abundances for the Fe(III)-heme$^+$ ion reaction with acetone at 5.2×10^{-8} mbar (**a**), 8.7×10^{-8} mbar (**b**), 2.1×10^{-7} mbar (**c**).

Determination of thermodynamic parameters

$$Fe(III)\text{-}heme(L_1)^+ + L_2 \rightleftarrows Fe(III)\text{-}heme(L_2)^+ + L_1$$

Ligand transfer equilibria

$$HCB(L_1) - HCB(L_2) = -\Delta G^\circ = -RT\ln K_{eq}$$

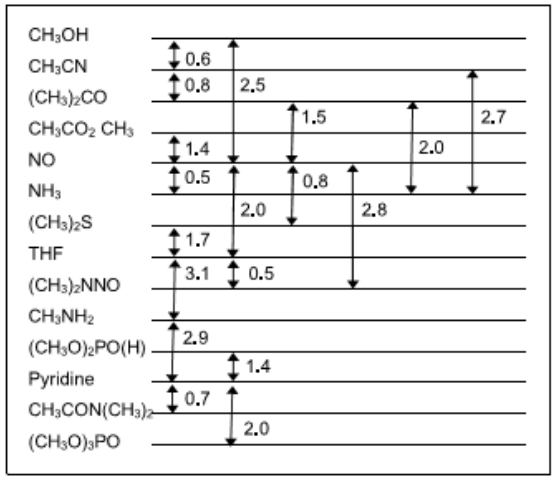


Figure 7. ΔG_5° (kcal mol^{-1}, 300 K) ladder for the Fe(III)-heme$^+$ transfer reactions between selected pairs of ligands. The values in the ladder correspond to HCB differences for each couple of ligands.

Table 6. Free energy changes for gas-phase ligand binding toward H^+ and Fe(III)-heme$^+$

L	GB[a]	HCB[b]
CH_3OH	173.2	13.1
CH_3CN	179.0	13.7
$(CH_3)_2CO$	186.9	14.6
CH_3CO_2 CH_3	189.0	14.8
NO	120.8	16.1
NH_3	195.7	16.6
$(CH_3)_2S$	191.5	
Tetrahydrofuran	189.9	
$(CH_3)_2N$-NO	203.0[c]	
CH_3NH_2	206.6	
$(CH_3O)_2PO(H)$	206.1	
Pyridine	214.7	
$CH_3CON(CH_3)_2$	209.6	
$(CH_3O)_3PO$	205.7	

A linear correlation between HCBs and ΔGBs of the ligands suggests that similar effects play a role when a lone pair donor binds to a proton or to Fe(III)heme$^+$

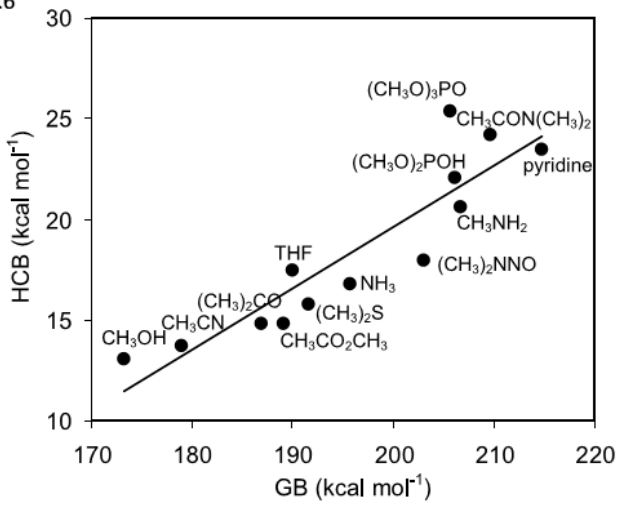


Figure 9. General correlation between Fe(III)-heme$^+$ cation basicities (HCB, equal to $-\Delta G_1^\circ$ for the ligand association reaction) and gas phase basicity toward the proton (GB) values.

Summary

IMRs for analytical applications,

structural studies,

fine mechanistic elucidation.

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