

Detecting Reaction Intermediates in Liquids on the Millisecond Time Scale Using Desorption Electrospray Ionization

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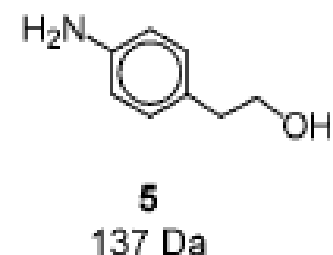
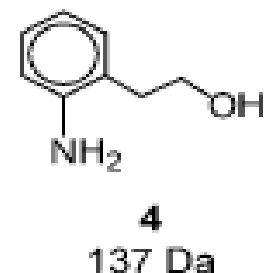
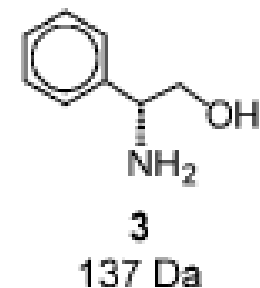
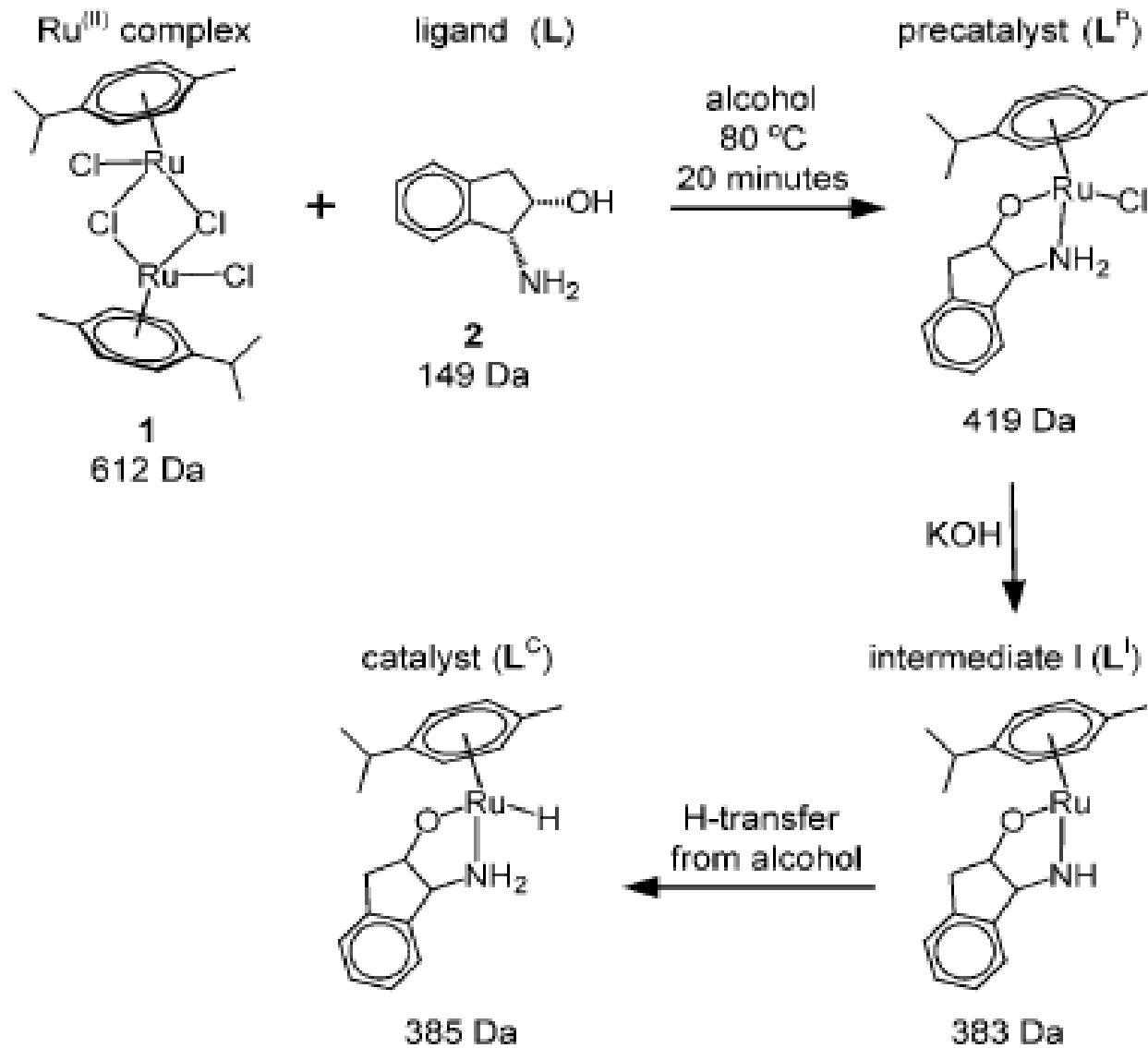
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INTRODUCTION

- Reactive reaction intermediates in solutions are very short-lived species
- Due to the development of atmospheric pressure ionization methods (ESI) it is possible to detect the reactive intermediates
- DESI is an ambient and high throughput MS technique where we can perform reaction using reagent in the spray solution and detect the intermediates in the millisecond time scale
- Transfer hydrogenation using Ru organometallic catalysts in the presence of a hydrogen donor is a simple, efficient, nonhazardous, and highly enantioselective approach for the reduction of multiple bonds
- One approach to synthesizing Ru(II) asymmetric transfer hydrogenation catalysts is to react $[\{\text{RuCl}_2(\text{p-cymene})\}_2]$ with amino alcohol ligands such as (1R, 2S)-cis-1-amino-2-indanol

EXPERIMENTAL



EXPERIMENTAL CONDITIONS

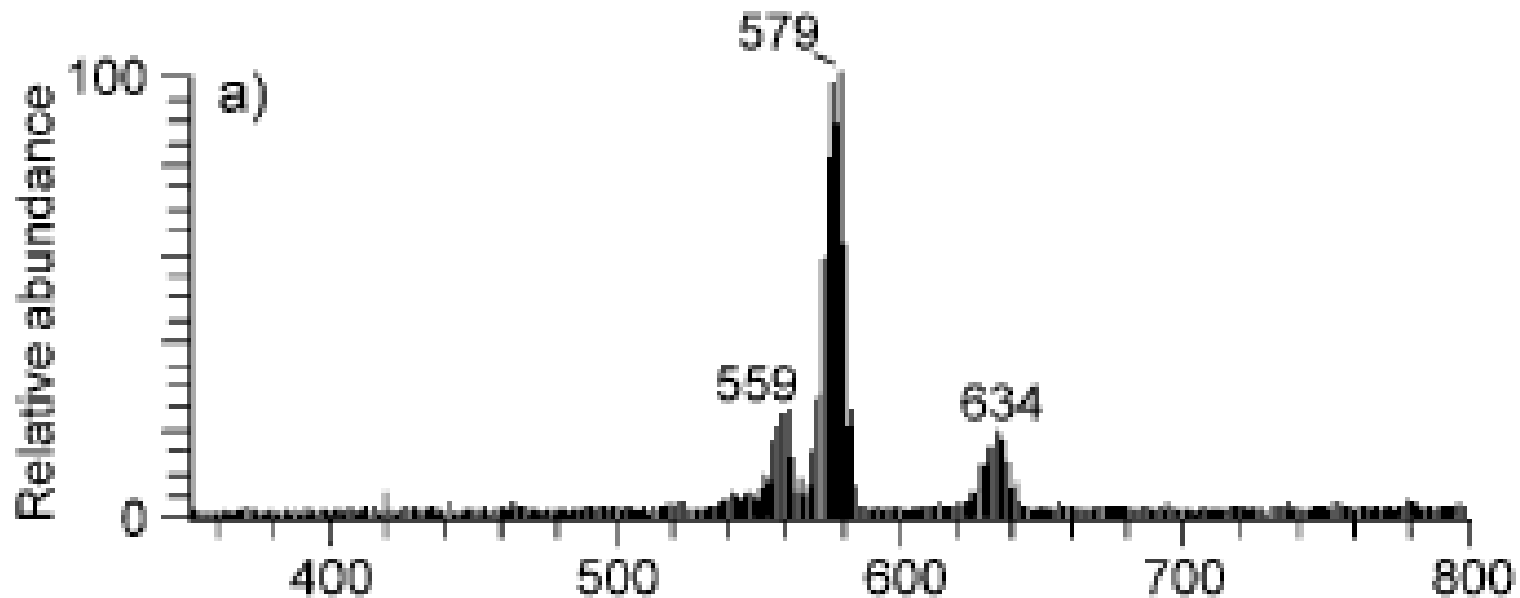
5 mL of 5×10^{-3} M solution in CH_2Cl_2 deposited on paper

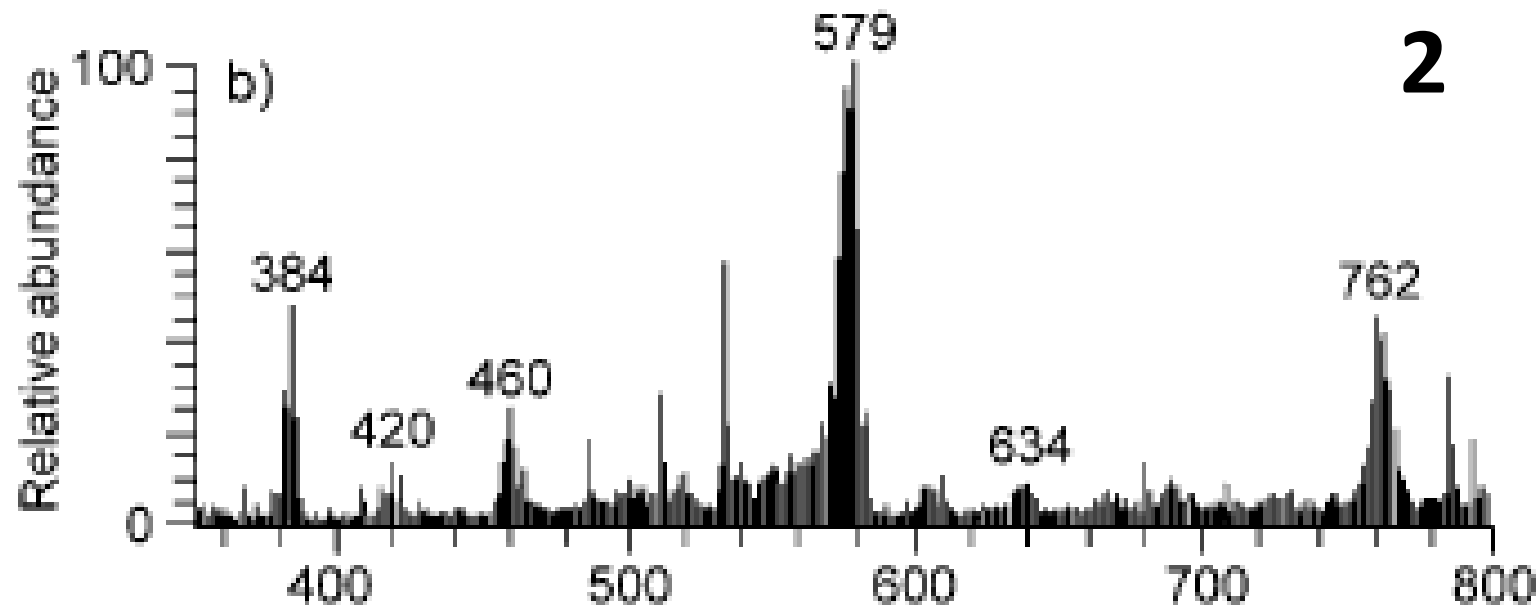
Reagent spray solution: Methanol

Liquid flow rate: $10 \mu\text{Lmin}^{-1}$

Nitrogen flow rate: 0.6 Lmin^{-1}

Spray voltage: 5 kV





Concentration of the amino alcohol 10^{-4} M in CH_3OH

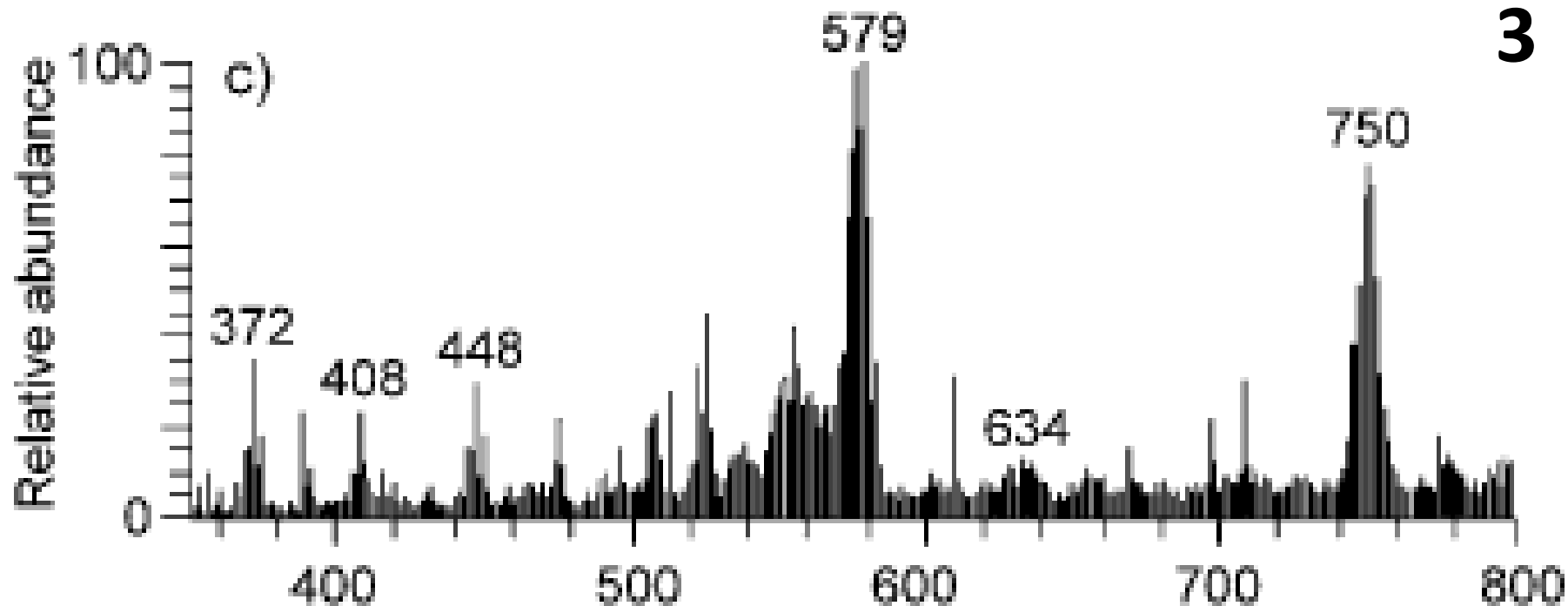
m/z 420: protonated 2^{P}

m/z 384: protonated 2^{I} and 2^{C}

(Supported by ESI-MS and X-ray crystallographic structures)

m/z 762: protonated form of the coordination species of 2 with 1
(Intermediate II, 2^{II})

m/z 460: reaction intermediate III, 2^{III}



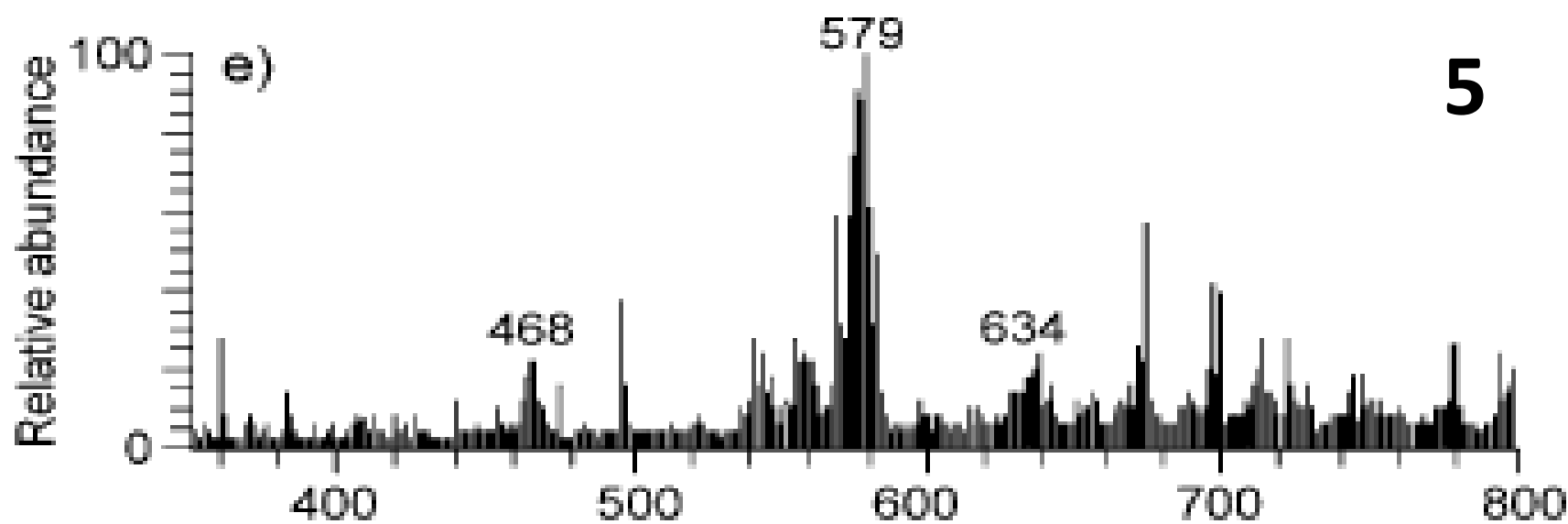
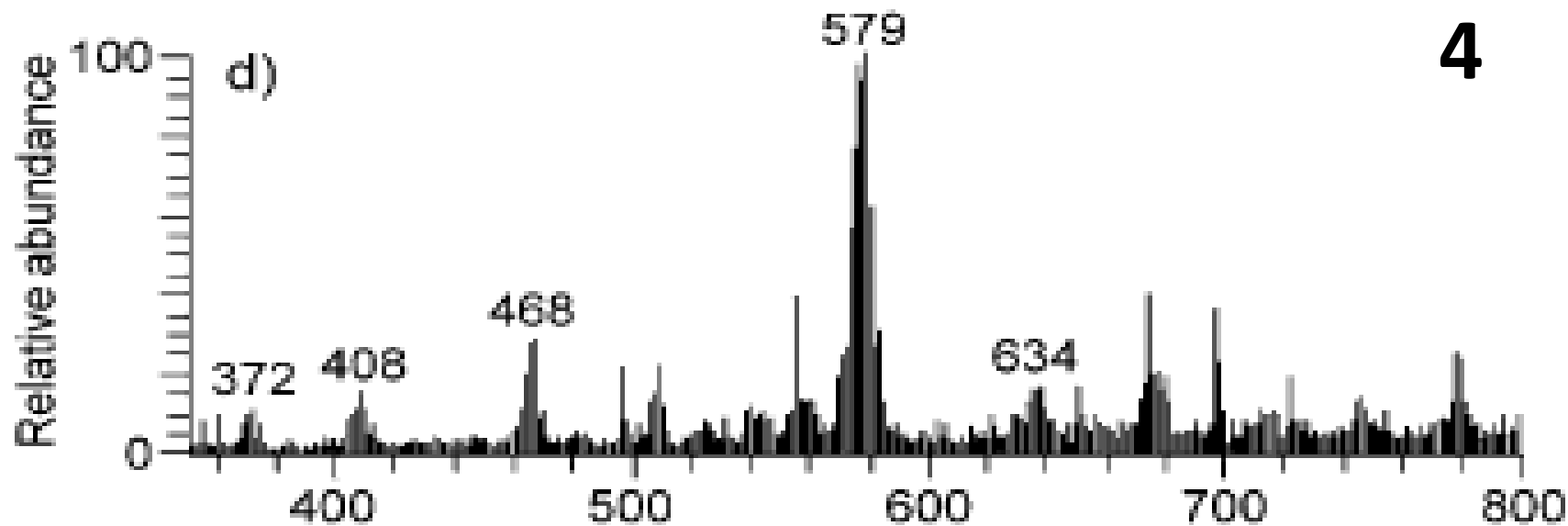
Concentration of the amino alcohol 10^{-4} M in CH_3OH

m/z 408: protonated 3^{P}

m/z 372: protonated 3^{I} and 3^{C}

m/z 750: protonated form of the coordination species of 3 with 1
(Intermediate II, 3^{II})

m/z 448: reaction intermediate III, 3^{III}



m/z 750 is absent in both the cases

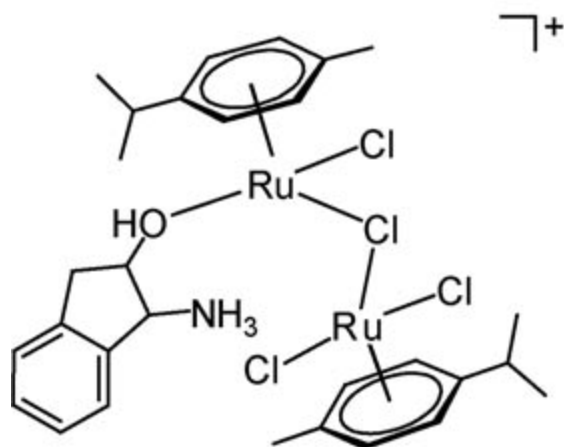
- Two new intermediates have been detected for amino alcohol 2 and 3
- For amino alcohol 4 and 5 (distance between OH and NH₂ groups are larger) no such intermediates have been detected
- Reaction of β-amino alcohols are kinetically or thermodynamically favored over the others
- The peak at m/z 408 and m/z 372 (fig. 1d) indicate that 4 also reacts with 1 (Because of C-C bond rotation intermediate 4^{II} is formed which facilitates the reaction, but does not happen for 5)
- The sum of the signal areas for m/z 372 and m/z 408 for 3 ($120 \pm 6 \times 10^7$) and 4 ($16 \pm 2 \times 10^7$) suggests that in the same time period, 3 produces 7.6 ± 1.0 times more of these species than 4
- A similar comparison for 2 ($114 \pm 18 \times 10^7$) and 3 illustrates that they produce similar amounts of L^P and [L^I+L^C]
- The intensity of L^P and [L^I+L^C] relative to m/z 579 is generally lower for 4 (5 ± 3 % and 9 ± 2 %) compared with 2 (6 ± 2 % and 17 ± 5 %) and 3 (9 ± 1 % and 13 ± 2 %). These lower abundances demonstrate that the reaction is more favoured when the NH₂ and OH groups of L are located on adjacent carbon atoms

OBSERVATION WITH ESI-MS

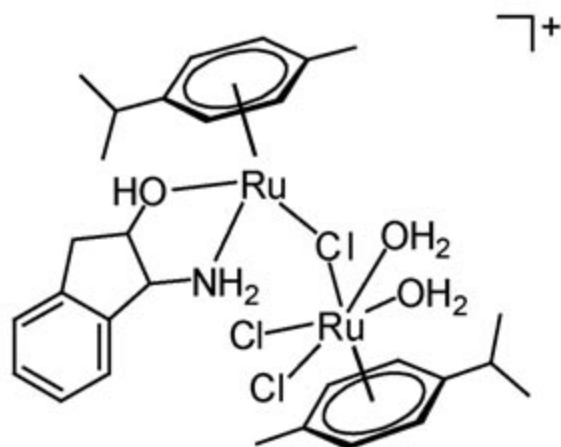
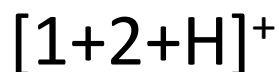
- With ESI-MS only the L^P , L^I , and L^C have been detected
- For 2 and 3 [L^I+L^C] is the most abundant distribution (absolute abundance 2×10^7 for both ligands and all the other signals have relative intensities lower than approximately 15%)
- For 4 and 5, species formed from the reaction of 1 with CH_3OH are the most abundant (absolute intensities 2×10^8 for all cases, all other signals have relative intensities lower than approximately 15%)

PROPOSED STRUCTURE OF INTERMEDIATE

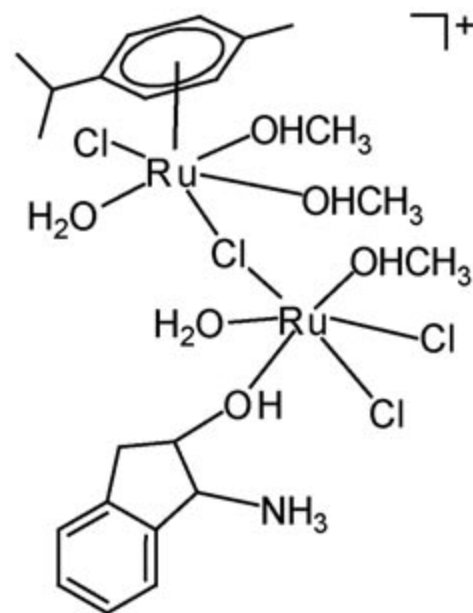
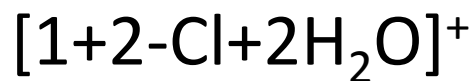
a)



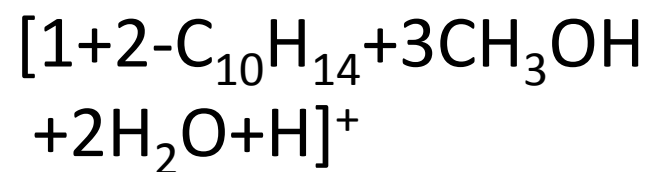
762 Da



762 Da

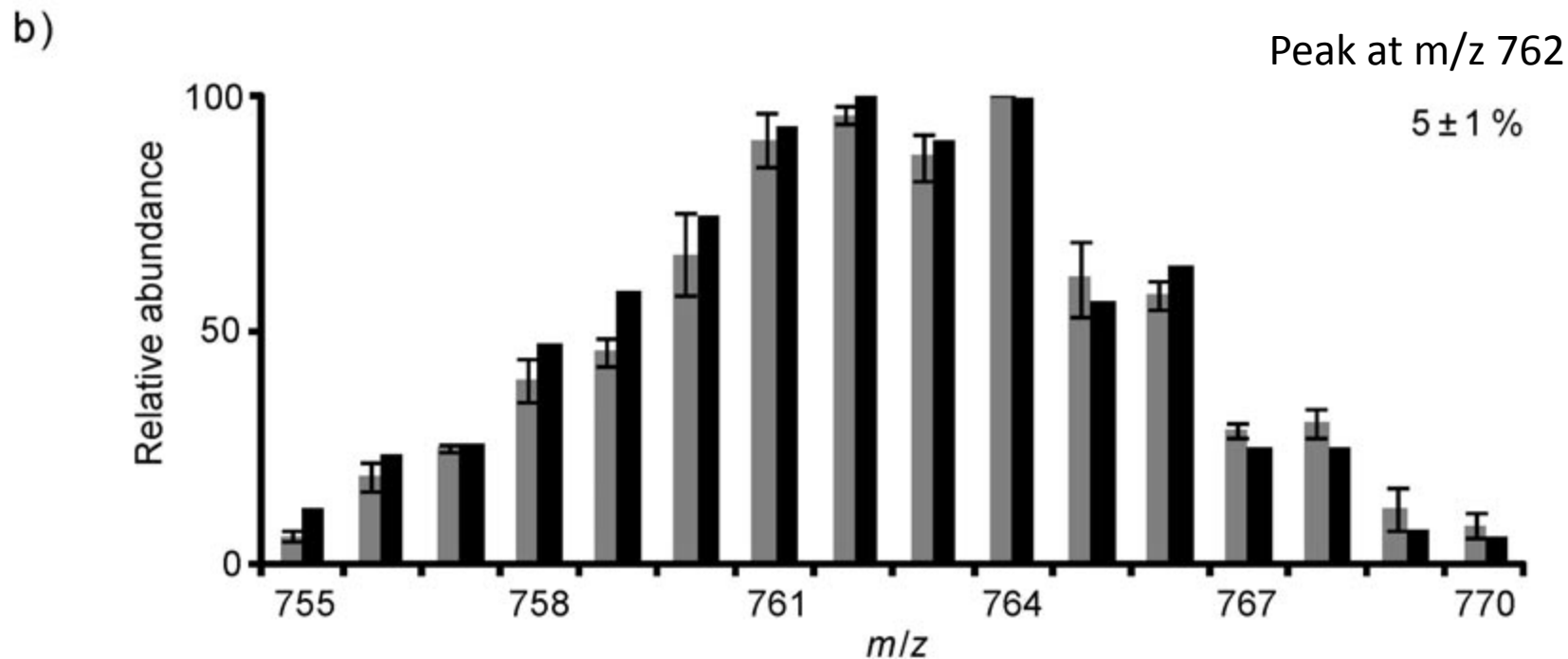


760 Da



All the structures satisfies 18 valence electrons for Ru if for last two structure one or both the *p*-cymenes adopt η^2 -coordination geometry

COMPARISON OF THE ISOTOPIC DISTRIBUTION

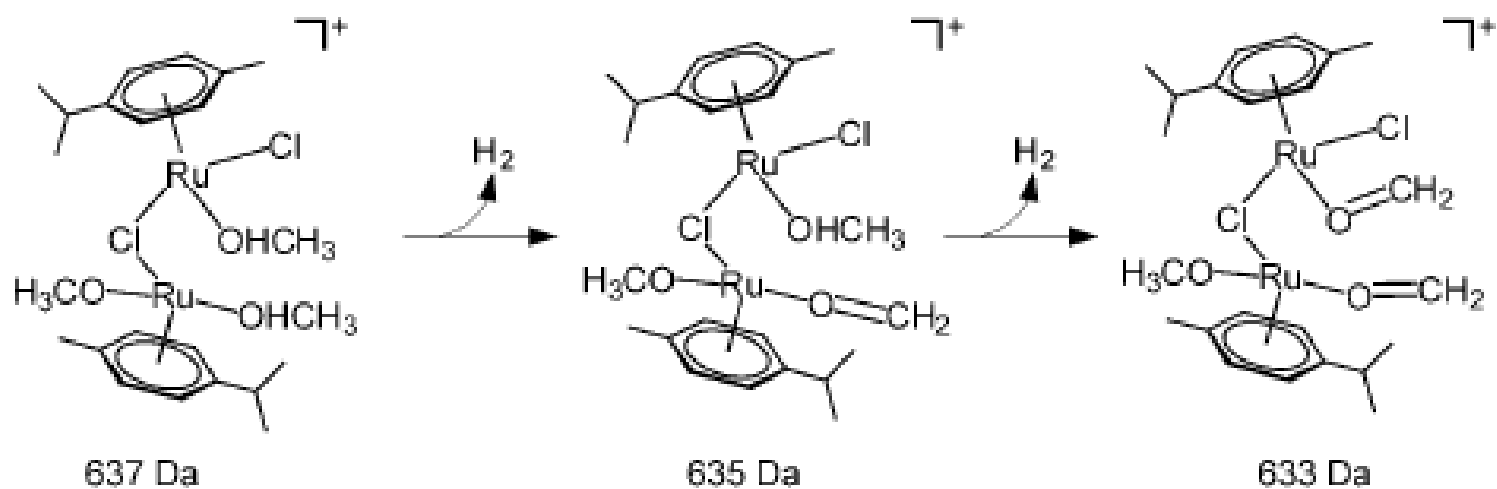
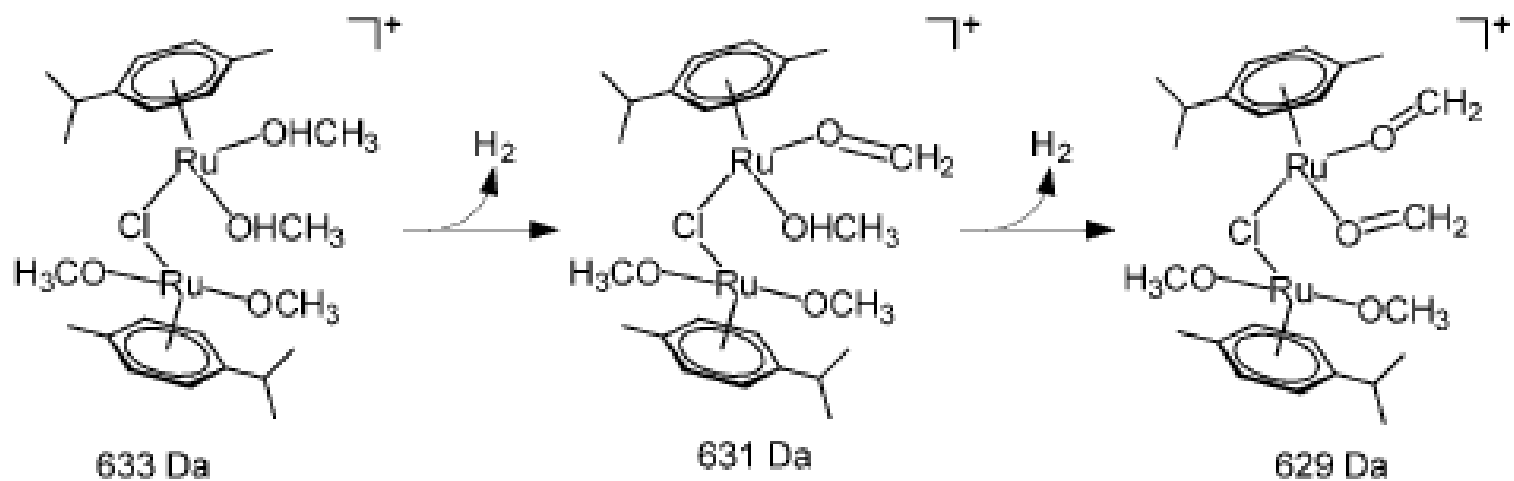


Experimental (grey)
Calculated (black)

The 3 species are present in 2:5:1 ratio

OTHER STRUCTURES

At m/z 634



REACTION OF 1 WITH METHANOL

m/z 634

$[1-3\text{Cl}+4\text{CH}_3\text{OH}-2\text{H}]^+$ (m/z 633) and $[1-2\text{Cl}+3\text{CH}_3\text{OH}-\text{H}]^+$ (m/z 637)

$[\text{m/z } 633-x\text{H}_2]^+$ and $[\text{m/z } 637-y\text{H}_2]^+$,

x and y are the number of H_2 eliminations

Isotopic deviation 5 ± 1 % (calculated ratio of 2:2:5:3 for x=0, x=2, y=0, and y=2, respectively)

m/z 579

$[1-\text{Cl}]^+$, $[1-\text{Cl}+2\text{H}_2\text{O}-\text{HCl}]^+$ and $[1-\text{Cl}-\text{C}_{10}\text{H}_{14}+3\text{CH}_3\text{OH}+2\text{H}_2\text{O}]^+$

Isotopic deviation 4 ± 0 % (calculated ratio of 5:2:1)

m/z 559

$[1-\text{Cl}+\text{H}_2\text{O}-\text{HCl}]^+$

Isotopic deviation 6 ± 2 %

TANDEM MS ANALYSIS

m/z 762 produces m/z 576, m/z 289 and m/z 303 in MS²

(m/z 289 and m/z 303 involve the coordination of H₂O and CH₃OH with [RuCl(p-cymene)], respectively)

m/z 576 produces m/z 468, m/z 503 and m/z 540 in MS³

m/z 540 produces m/z 503 and m/z 468 in MS⁴

m/z 503 produces m/z 468 in MS⁵

m/z 468 is also observed in MS spectra for 4 and 5 but not for 2 and 3 which suggests that reaction of 1 with β-amino alcohols is the preferred pathway

The MS³ spectra of m/z 634 (MS² of m/z 634 yields m/z 576) and the MS² spectra of m/z 579 for the reactions of 1 with 2 (or with 3) and CH₃OH are similar, and this observation further supports the proposed structure of 2^{II}. In addition to these observations, dissociation of 2^{III} and 2^P both yield the signal at m/z 384, which supports the conclusion that these species are relevant to the reaction pathway

CONCLUSION

Gas phase reaction intermediate vs.
solution phase reaction intermediate

Reactive DESI is possible

Imaging using reactive DESI

THANK YOU