CHEMPHYSCHEM

Supporting Information

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For the article

"The Gas Phase Chemistry of *cis*-Diammineplatin(II) Complexes: A Joint Experimental and Theoretical Study"

by

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1. Additional Experimental Information

a) Used Chemicals

Substance / Purity:	Company:	Based in:
Cisplatin (>99,99 %)	Lancaster Synthesis	Mühlheim, Germany
Methanol (>99.8 %)	J.T.Baker	Griesheim, Germany
Acetonitrile (>99.9 %)	J.T.Baker	Griesheim, Germany
2-Propanol (>99.7 %)	J.T.Baker	Griesheim, Germany
Ethanol (>99.9 %)	J.T.Baker	Griesheim, Germany
2-methyl-2-propanol (>99.5 %)	Merck KGaA	Darmstadt, Germany
Methanol-D3 (>99.8 %)	Merck KGaA	Darmstadt, Germany

b) Sample Preparation

b1) General Procedure

A 1.67 mmol L^{-1} (0.5 mg mL^{-1}) solution of Cisplatin was prepared in pure water. 10 µL of this solution were diluted with 90 µL of the particular solvent (solvent = water, methanol, ethanol, 2-propanol, 2-methyl-2-propanol, *c*(Cisplatin) = 167 µmol L^{-1} or 0.05). The second dilution step was performed within ten minutes before measurement to prevent complete solvolysis.

b2) Deuteration Experiments

For the formation of $[Pt(NH_3)_2(CD_3OH)Cl]^+$, Cisplatin was dissolved in a 1:2 water:methanol-D3 mixture and stirred for 10 min resulting with an initial concentration of Cisplatin of 167 mmol L^{-1}.

c) Instrumentation and Method

A hybrid ESI-FTICR mass spectrometer (Finnigan LTQ FTMS, Thermo Electron Co., Bremen, Germany), was used throughout all experiments. The linear ion trap (lIT) and the ion cyclotron resonance (ICR) cell were calibrated by the standard calibration procedure using caffeine, MRFA, and Ultramark 1620 as external calibrants. High resolution measurements performed in this study allow a mass accuracy of about 2 ppm (definition see formula (1)) and a resolution of about 100,000 at *m/z* 400 (transient acquisition of ca. 1 s). Due to peak intensity, some low abundant ions are detected in ion trap – only mode. The masses presented here are the most abundant ions of the particular simulated isotopic distribution, in this mass range consisting of ^{195}Pt, ^{1}H, ^{12}C, ^{14}N, ^{16}O and ^{35}Cl, respectively. Instrument parameters were optimized for caffeine and used unmodified for all samples. Flow rate (5 µL min^{-1}), spray voltage (4.3 kV) and sheath gas flow rate (15 arbitrary units,

dry N_2) were held constant. Due to solvent volatility, the entrance capillary temperature was adjusted (standard: 200°C, water and t-butanol as a solvent: 240°C, 2-propanol: 160°C). Fragmentation energy applied for MS^n (CID) was optimized to a gain of parent ion intensity of about 20 % relative intensity in the resulting fragment spectrum (referring to 1st abundant isotope, ^{194}Pt).
Both, calibration of the instrument and simulation of the respective ions refer to the masses presented in literature.[I] For the measurements and simulations, XCalibur 1.4.1 software (Thermo Electron Co.) was used.

d) Calculation of Mass Accuracy

Formula (1) was used to obtain the mass accuracy of the relative ions.

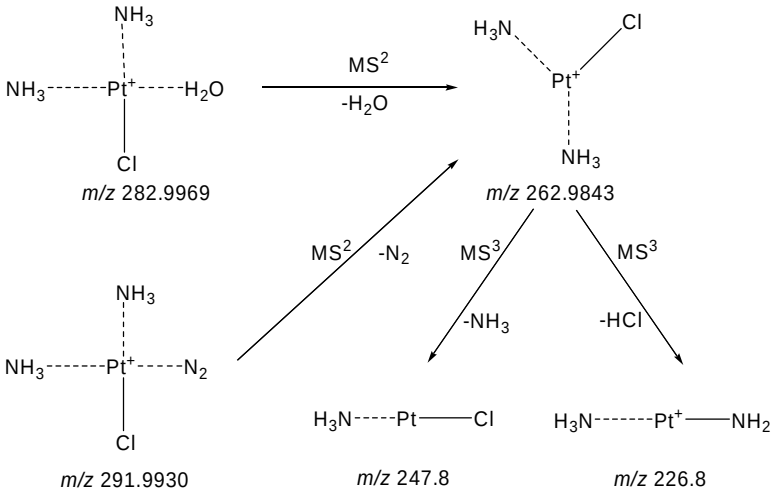
$$[ppm] = 10^6 \cdot \frac{|m/z_{calc} - m/z_{obs}|}{m/z_{obs}} \qquad (1)$$

with m/z_{obs} = observed *m/z and* m/z_{calc} = simulated *m/z;* for the simulations XCalibur 1.4 SR1 was used.

2. Supplementary Data:

2a) Complete Fragmentation Schemes for Fragmentations Mentioned

A: Fragmentation of $[Pt(NH_3)_2Cl(H_2O)]^+$ and $[Pt(NH_3)_2Cl(N_2)]^+$



B: Fragmentation of $[Pt(NH_3)_2Cl(CH_3CN)]^+$

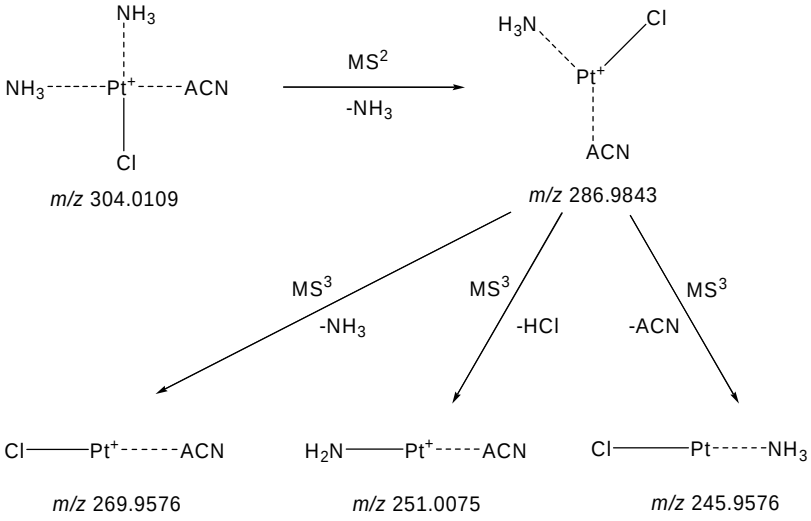
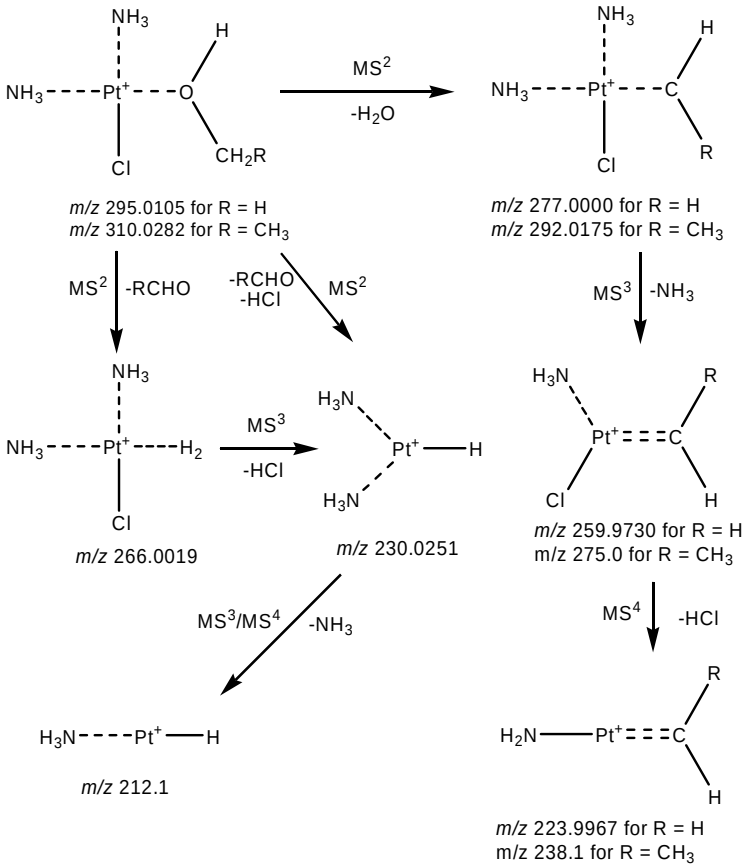


Figure S1: Fragmentation scheme for
A: $[Pt(NH_3)_2(H_2O)]^+$ (as shown by Cui et al.[II]), and $[Pt(NH_3)_2(N_2)Cl]^+$, MS^n
B: $[Pt(NH_3)_2Cl+ACN]^+$ (Genesis and fragmentation first mentioned by Ehrsson et al.[IV])

A: Fragmentation of $[Pt(NH_3)_2Cl(ROH)]^+$ (R = H, CH_3)



B: Fragmentation of $[Pt(NH_3)_2Cl((CH3)_3COH)]^+$

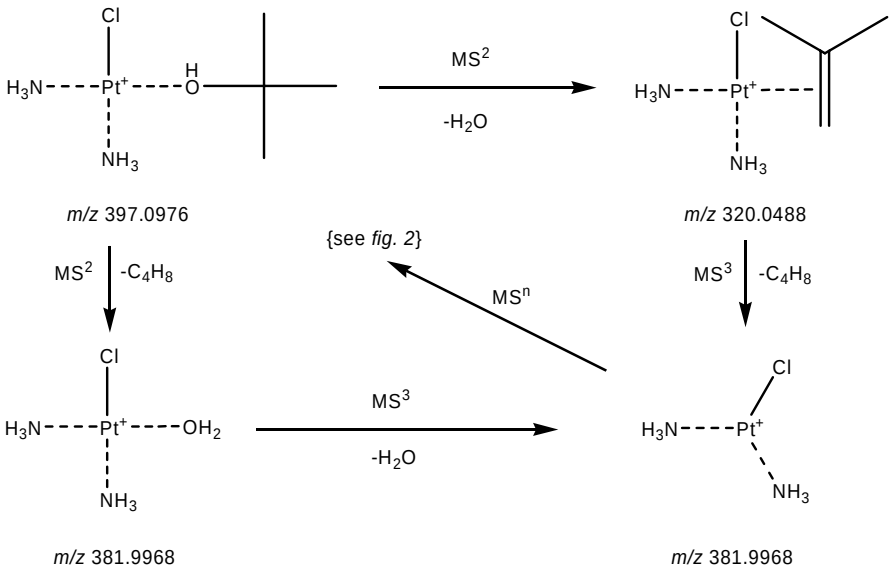


Figure S2:
A: Fragmentation scheme for $[Pt(NH_3)_2(RCH_2OH)Cl]^+$, MS^n, R = H*, CH_3
B: $[Pt(NH_3)_2((CH_3)_3COH)Cl]^+$, MS^n
*note: detected but not assigned by Cui et al.[III]

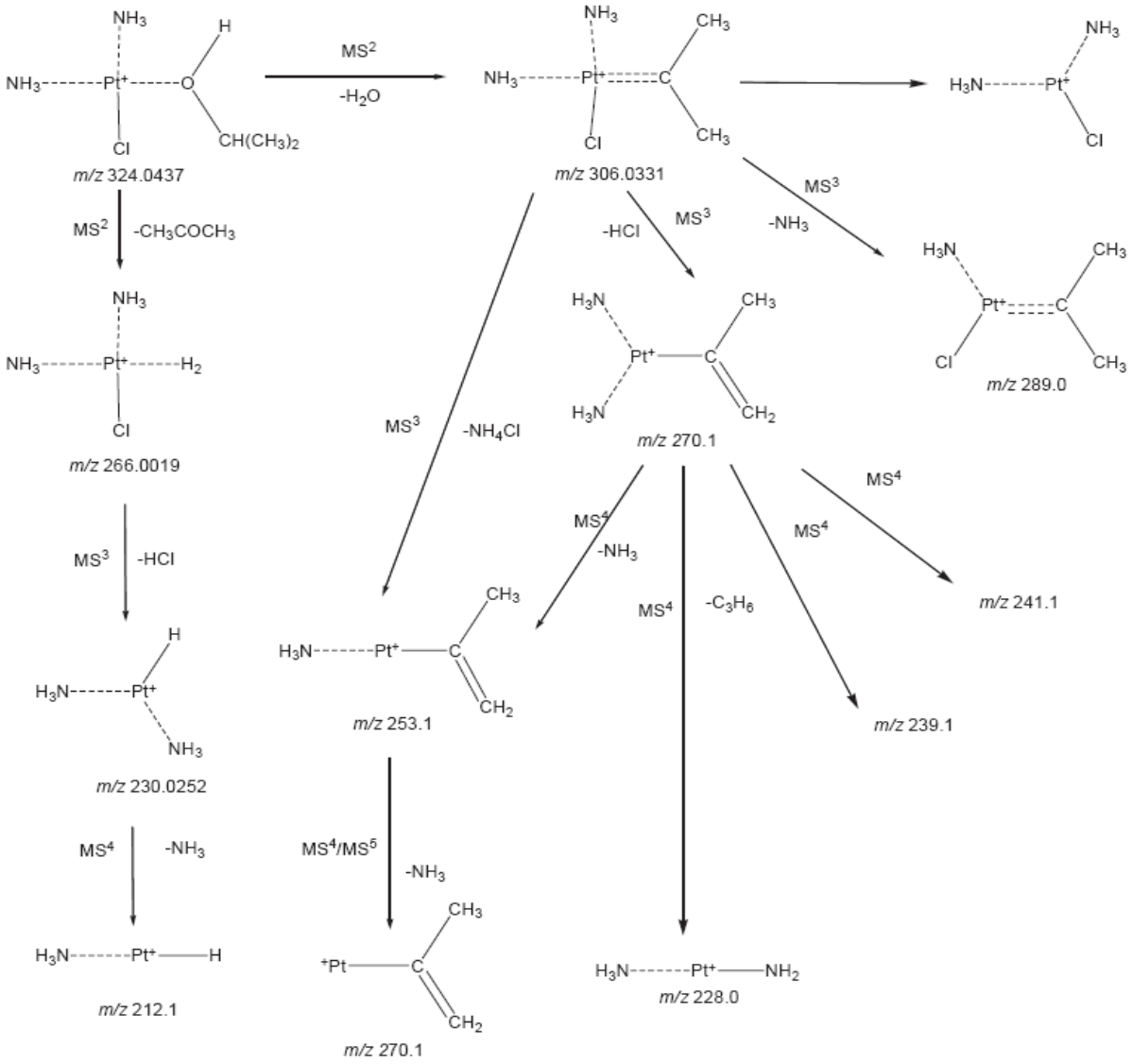


Figure S3: Fragmentation scheme for $[Pt(NH_3)_2((CH_3)_2CHOH)Cl]^+$, MS^n

2b) Additional information: Complexity of the initial mass spectra

2b1) Further Ions/Fragmentations:

$[Pt(NH_3)_2Cl_2+Cat]^+$ with Cat = Na^+, NH_4^+ also have been found. Fragmentation is analogue to $[Pt(NH_3)_2Cl_2+NH_4]^+$ shown in [Cui2003].

2b2) Additional: Higher Solvated Ions:

5-coordinated Pt^{II}-center: addition of the relative nucleophilic solvent, leading to $[(Pt(NH_3)_2Cl+$*solvent1*$)+$*solvent2*$]^+$ with *solvent1*=H_2O or relative additional solvent and *solvent2*=relative additional solvent
Fragmentation: fifth ligand is lost in MS^2 at very low activation energy (100%), daughter ion then follows the presented fragmentation pathways

2c) Original Mass Spectra and Simulations

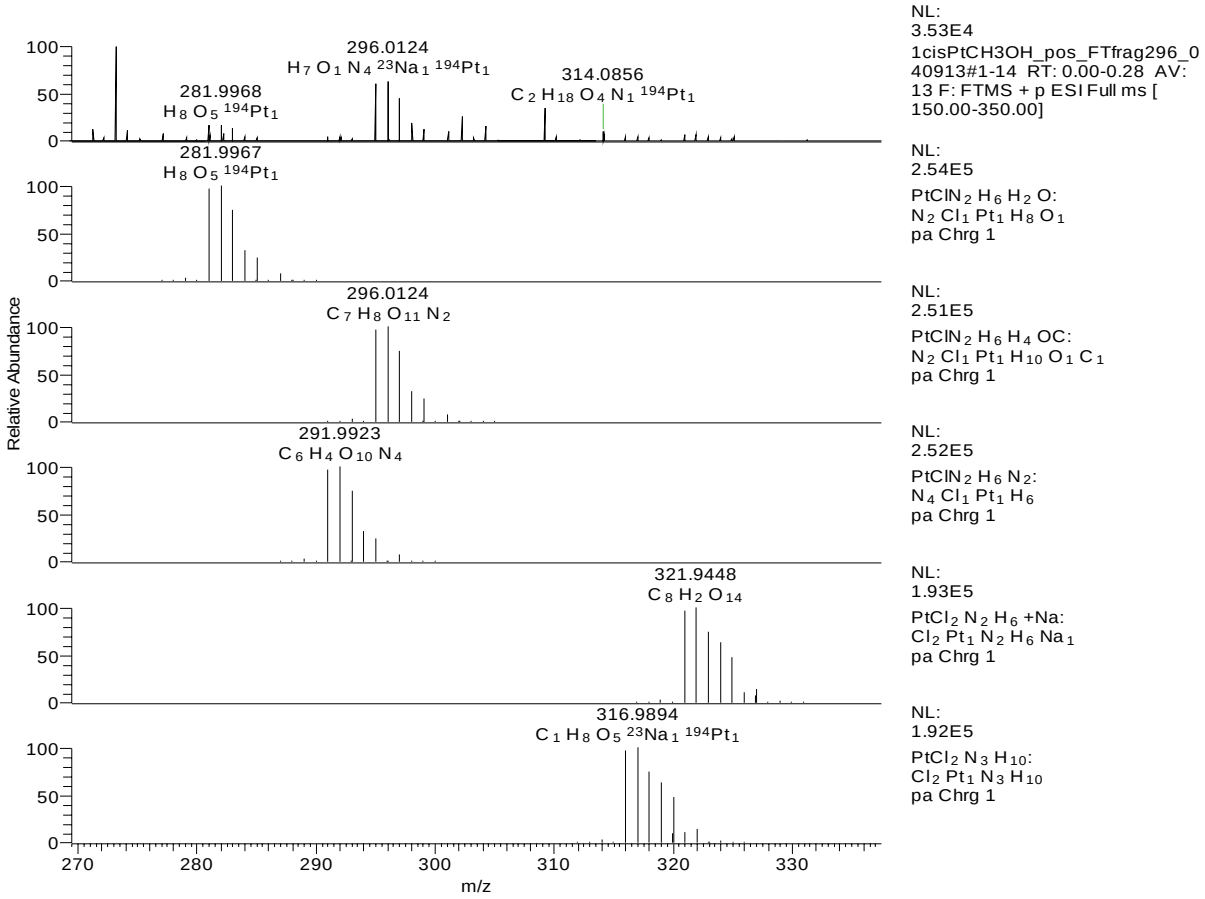


Figure S4: Full scan spectrum of Cisplatin, dissolved in water/MeOH (top) and simulations

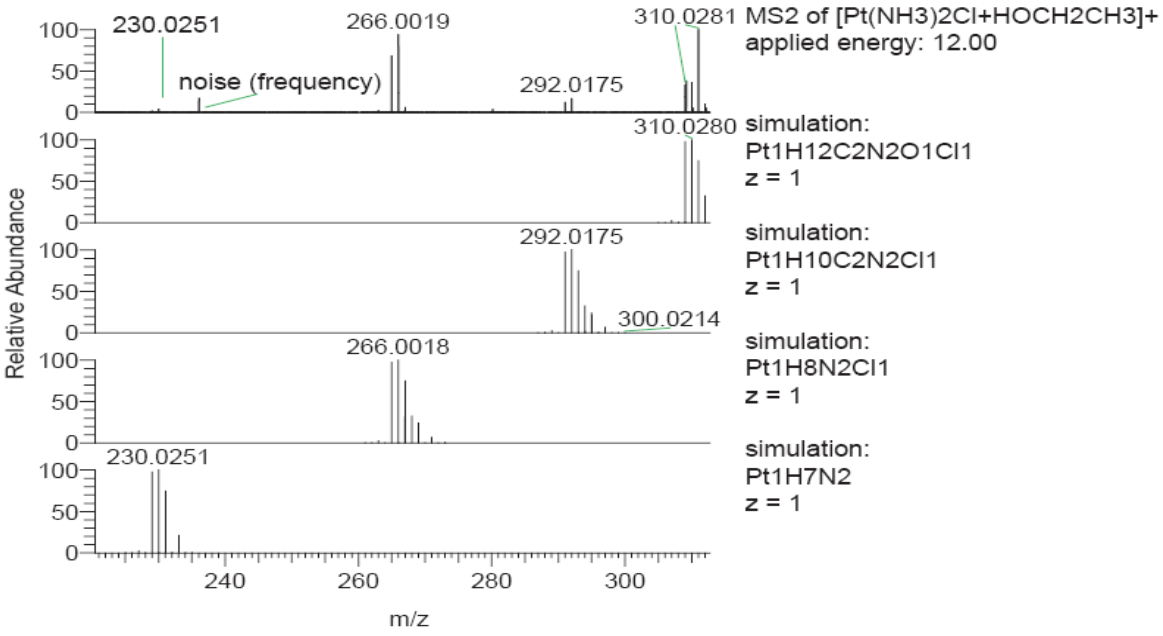


Figure S5: MS^2 of $[Pt(NH_3)_2(CH_3CH_2OH)Cl]^+$, spectrum (top) and simulation

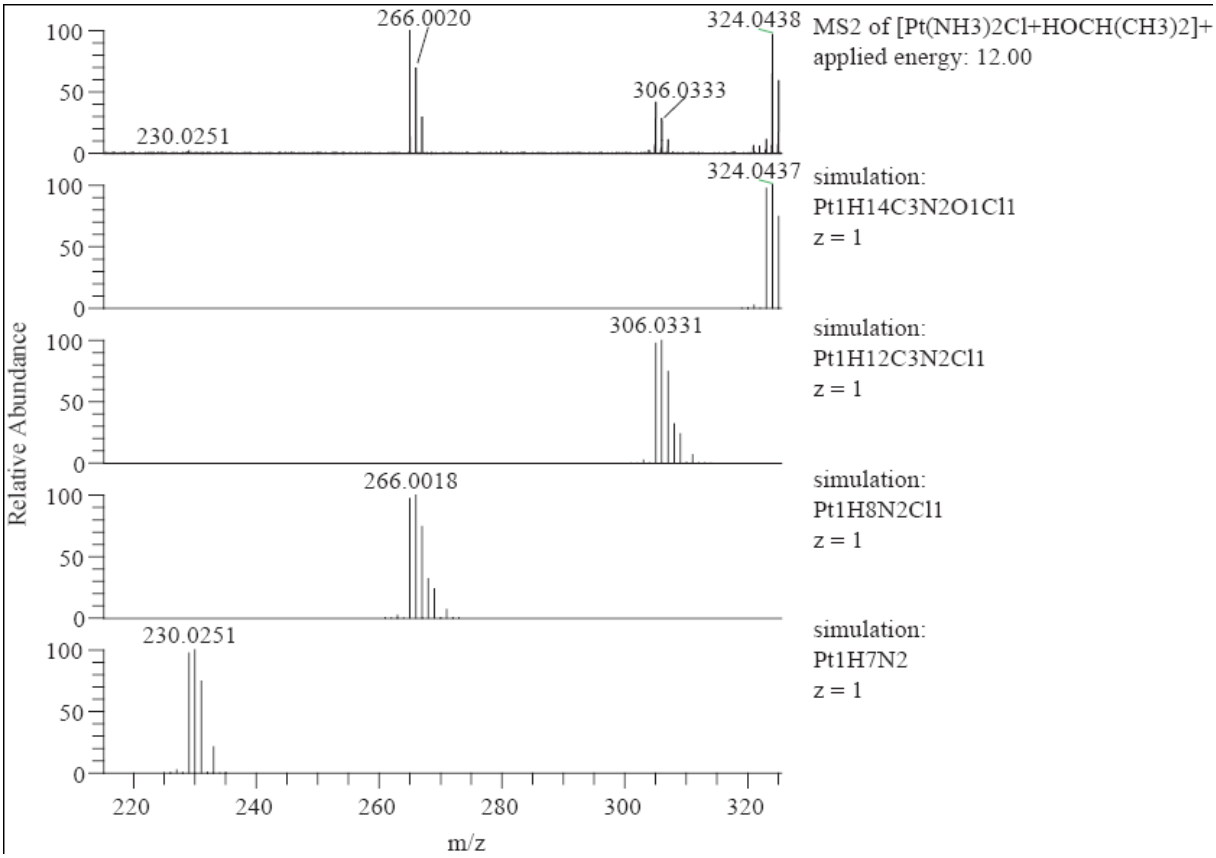


Figure S6: MS^2 of $[Pt(NH_3)_2((CH_3)_2CHOH)Cl]^+$, spectrum (top) and simulation

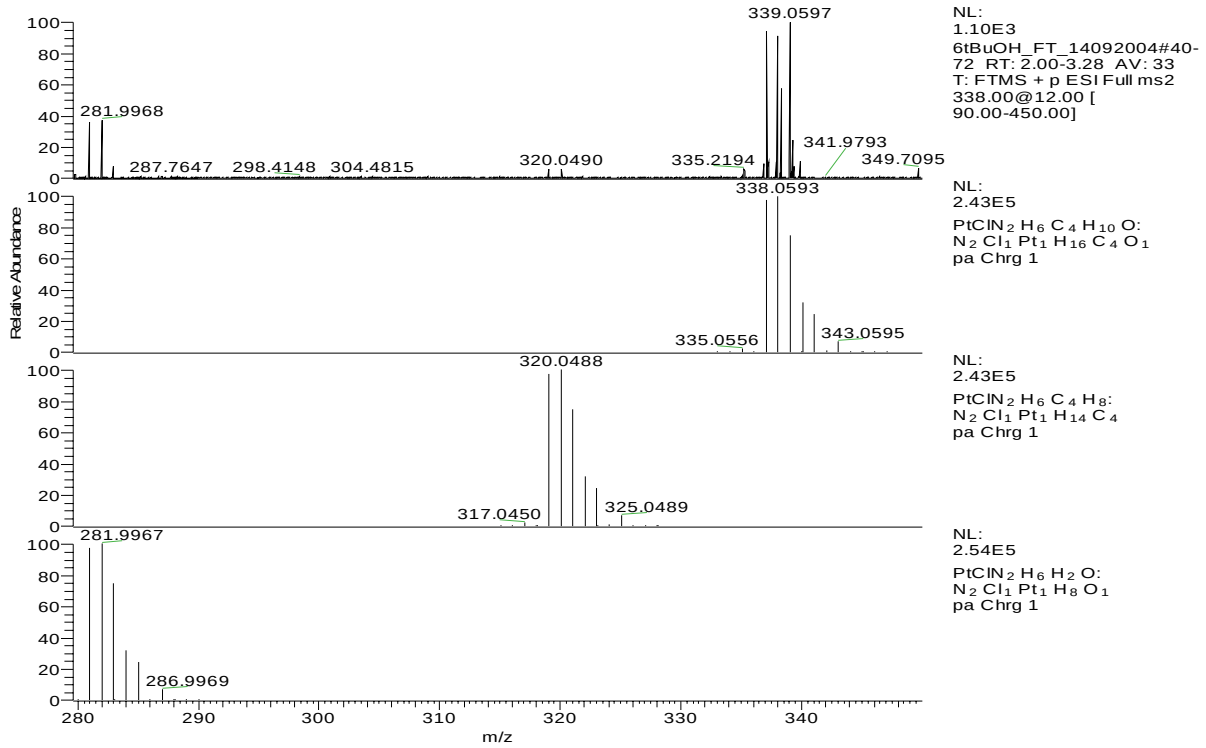


Figure S7: MS^2 of $[Pt(NH_3)_2((CH_3)_3COH)Cl]^+$, spectrum (top) and simulation

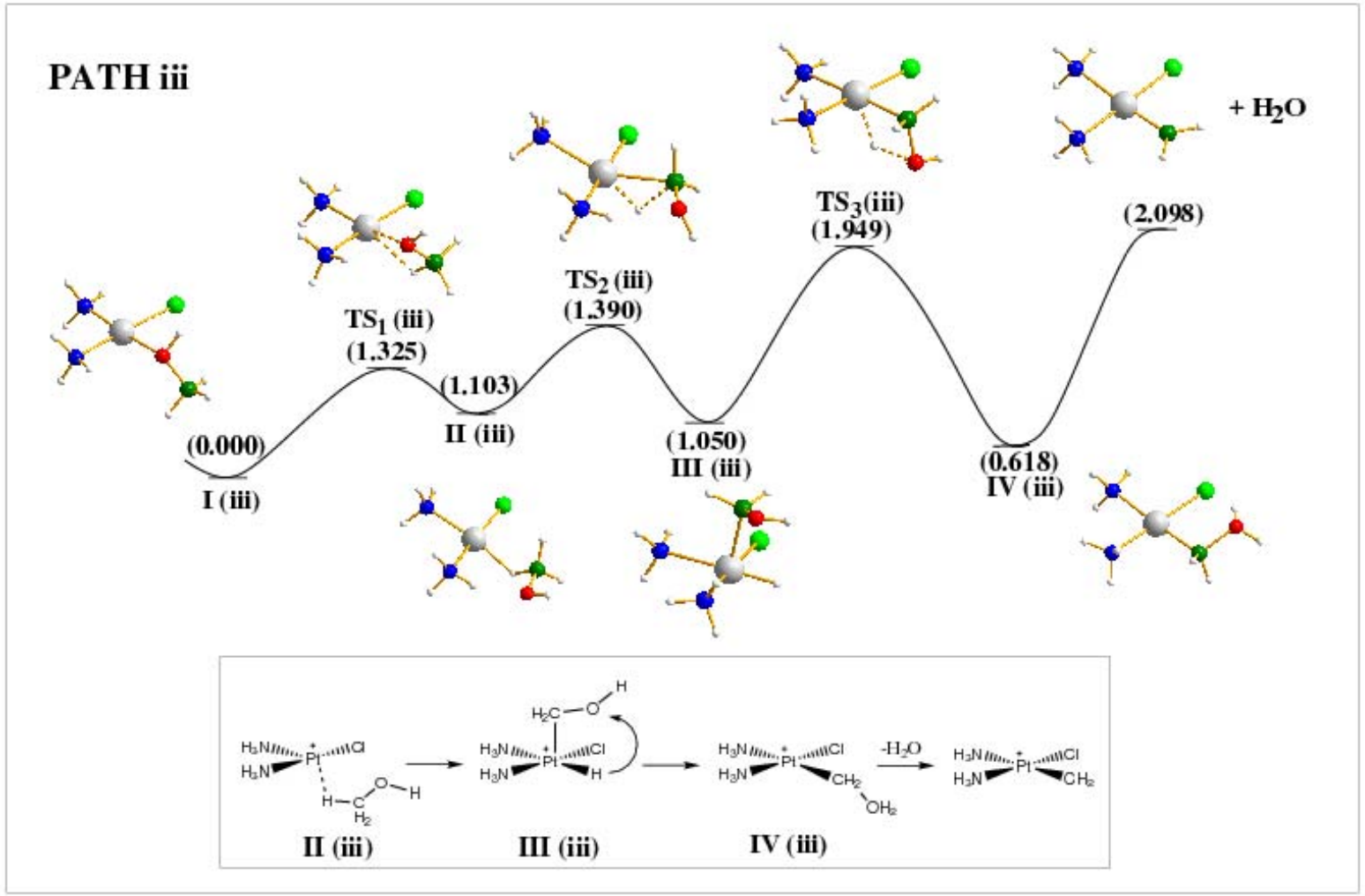


Figure S8: The upper part shows the reaction profile along a water fragmentation pathway (path iii) on the example of $[Pt(NH_3)_2(CH_3OH)Cl]^+$. First, the α-CH is activated (III(iii)) and then H-atom transfer from the platinum center (IV(ii)) to the OH group (IV(iii)) occurs followed by H_2O release. Notice that in contrast to path I in the paper the H-atom is directly transferred to the alcohol group which is energetically less convenient by 0.187eV. In the lower part the scheme illustrates the mechanism. All energies are given in eV with respect to the energy of the initial Cisplatin-methanol complex I(iii).

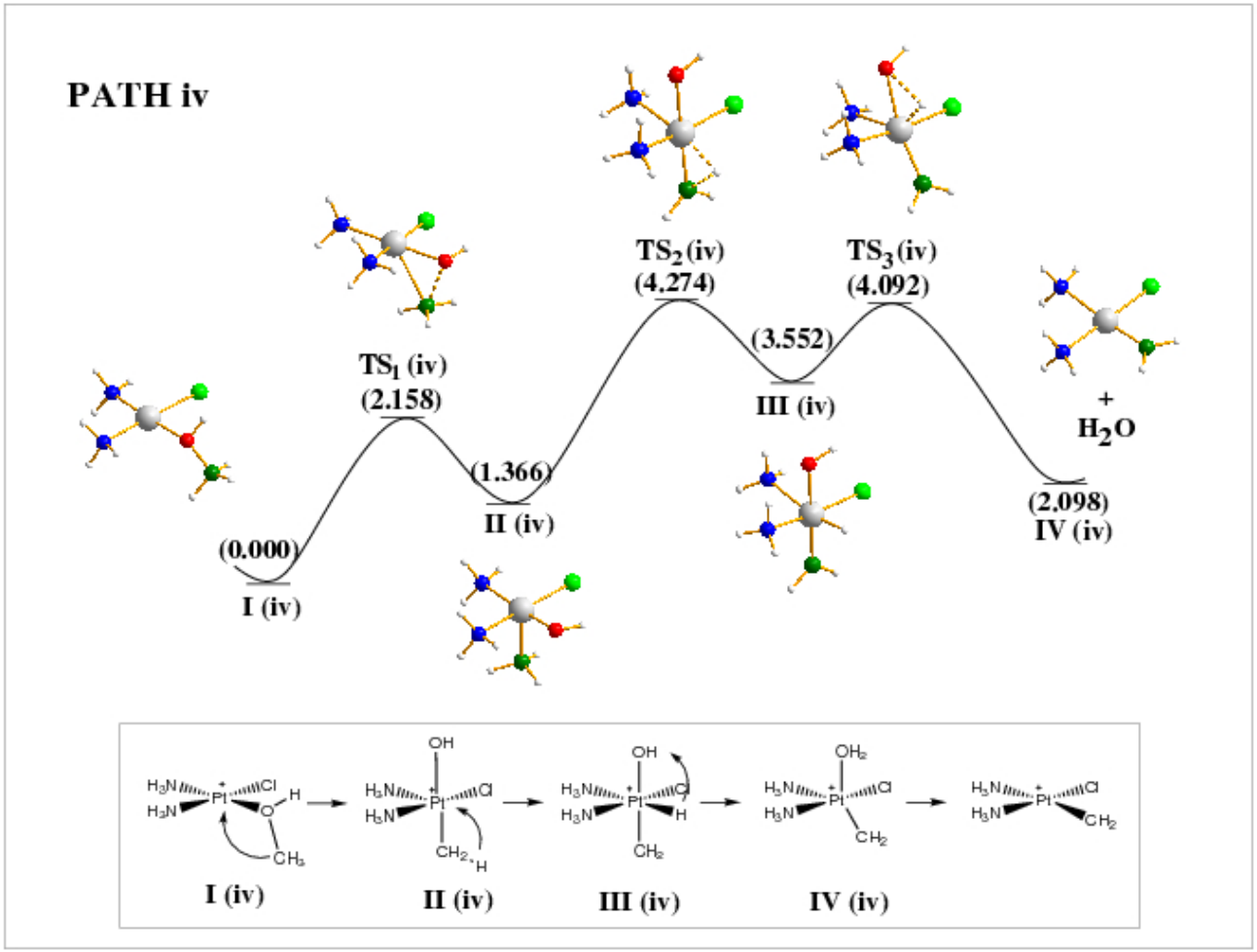


Figure S9: The upper part shows the reaction profile along a water fragmentation pathway (path iv) on the example of $[Pt(NH_3)_2(CH_3OH)Cl]^+$. First, the CO bond is activated (II(iv)) and then H-atom transfer from the methyl group to the platinum center (III(iv)) occurs. The six-coordinated platinum complex III(iv) is energetically very unfavorable due to the fact that the hydroxyl group and the carbene ligand are trans with respect to each other. In a next step, the H-atom bound to platinum is transferred to the OH-group followed by H_2O release. Notice that along this pathway the activation step requires similar energy than for the alcohol dissociation. In the lower part the scheme illustrates the mechanism. All energies are given in eV with respect to the energy of the initial Cisplatin-methanol complex I(iv).

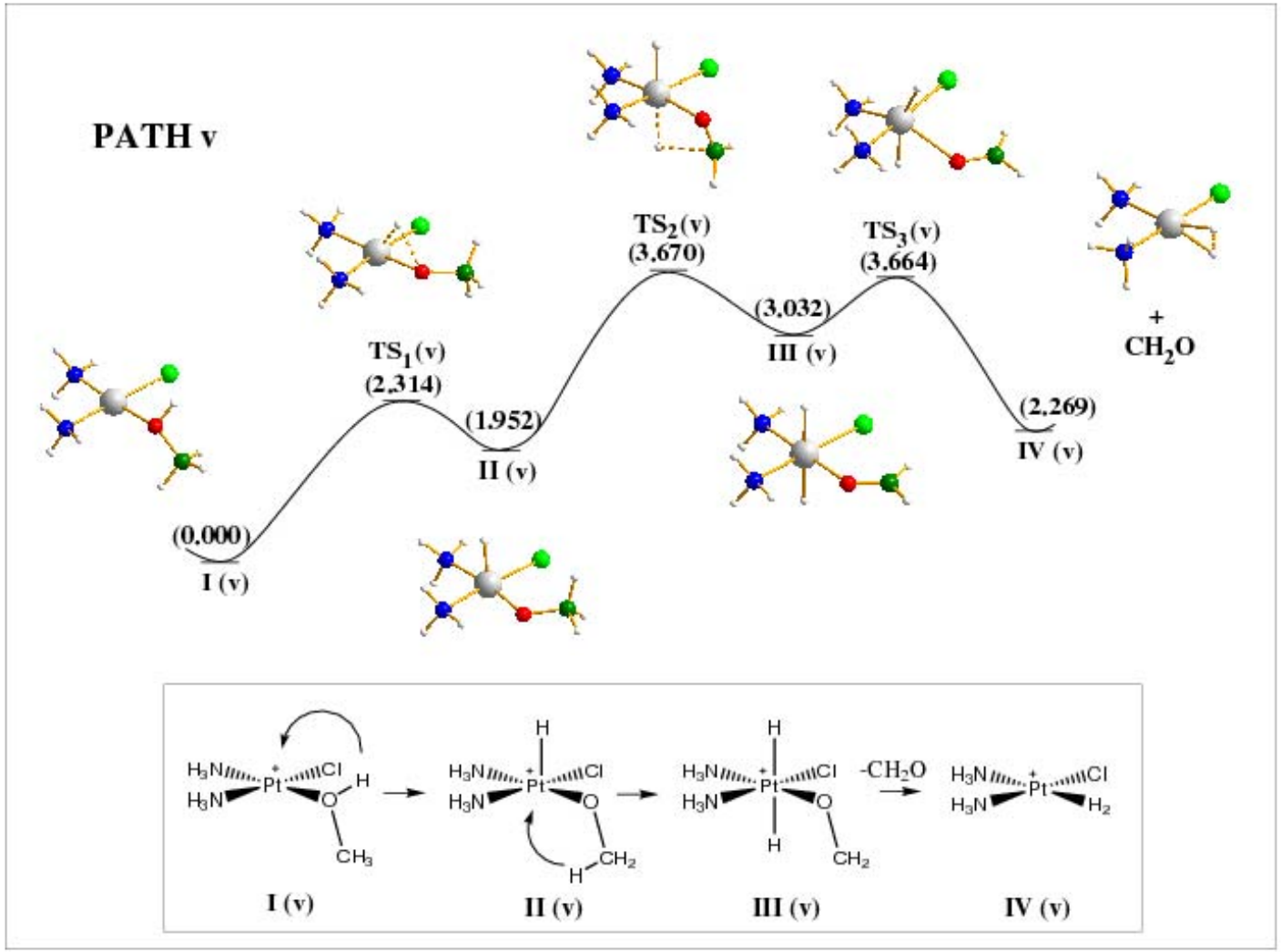


Figure S10: The upper part shows the reaction profile along a formaldehyde fragmentation pathway (path v) on the example of $[Pt(NH_3)_2(CH_3OH)Cl]^+$. First, the O-H bond is activated (II(v)) and then H-atom transfer occurs from the methyl group to the platinum center (III(v)). The coordinated formaldehyde CH_2O is released forming the dihydrogen complex IV(v) as the product species. Notice that along this pathway the activation step requires similar energy than for the alcohol dissociation. In the lower part the scheme illustrates the mechanism. All energies are given in eV with respect to the energy of the initial Cisplatin-methanol complex I(v).

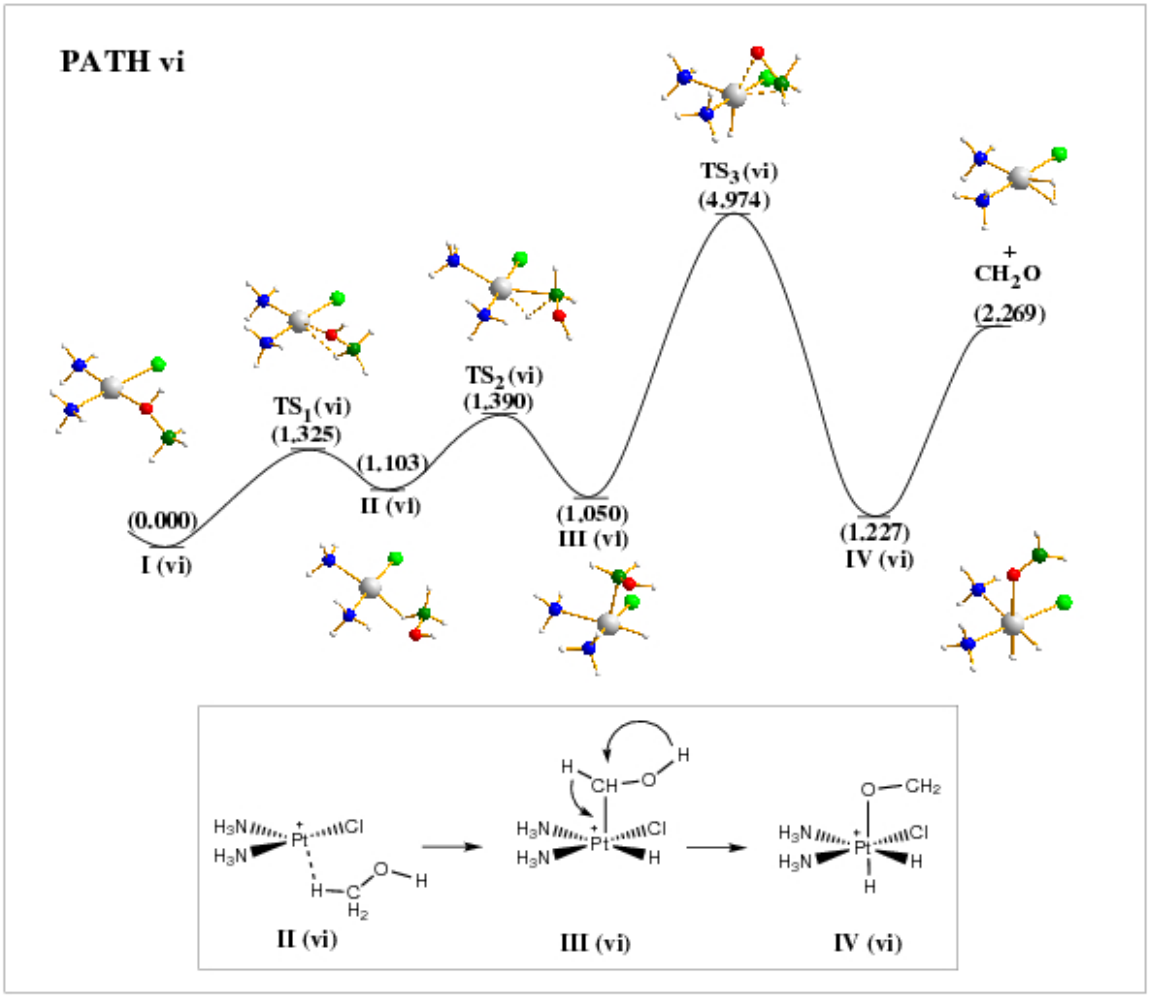


Figure S11: The upper part shows the reaction profile along a formaldehyde fragmentation pathway (path vi) on the example of $[Pt(NH_3)_2(CH_3OH)Cl]^+$. First, in analogy to the most convenient pathway path i, the fragmentation is initiated by insertion of Pt into the α-CH bond (III(vi)). Then, simultaneously H-atom transfer from the OH group to the methyl group and hydrogen shift of the H-atom from the methyl group to Pt (IV(vi)) occur. The coordinated formaldehyde CH_2O is released forming the dihydrogen complex IV(vi) as the product species. The activation step (insertion into the a-CH bond, is similar like in the proposed mechanism for formaldehyde production (path ii) but in contrast the barrier for the second step is significantly higher making the fragmentation along this pathway unfavorable. All energies are given in eV with respect to the energy of the initial Cisplatin-methanol complex I(vi).

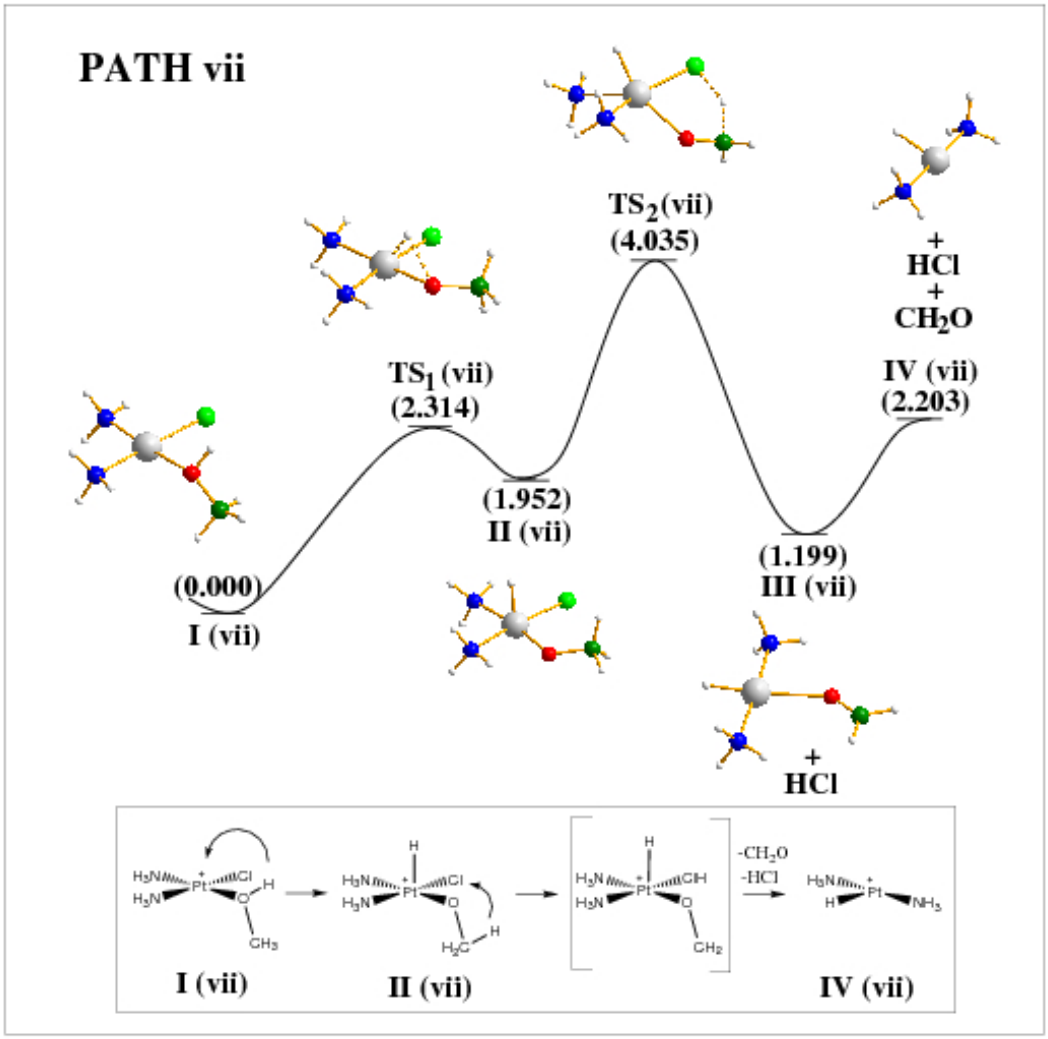


Figure S12: The upper part shows the reaction profile along a pathway for the simultaneous fragmentation of HCl and formaldehyde CH_2O (path vii) on the example of $[Pt(NH_3)_2(CH_3OH)Cl]^+$. The fragmentation is initiated by insertion of Pt into the OH bond (II(vii)). Then, a H-atom is transferred from the methyl group to chlorine leading to fragmentation of HCl (III(vii)). Subsequent cleavage of the CH_2O molecule leads to the product ion $[Pt(NH_3)_2H]^+$ with the geometry shown in the figure. All energies are given in eV with respect to the energy of the initial Cisplatin-methanol complex I(vii).

Literature cited:

[I] G. Audi, A. H. Wapstra, *Nucl. Phys. A* **1995**, *595*, 409.
[II] M. Cui, Z. Mester, *Rapid Commun. Mass Spectrom.* **2003**, *17*, 1517.
[III] M. Cui, L. Ding, Z. Mester, *Anal. Chem.* **2003**, *75*, 5847.
[IV] H. C. Ehrsson, I. B. Wallin, A. S. Andersson, P. E. Edlund, *Anal. Chem.* **1995**, *67*, 3606.