JUSTUS-LIEBIG-
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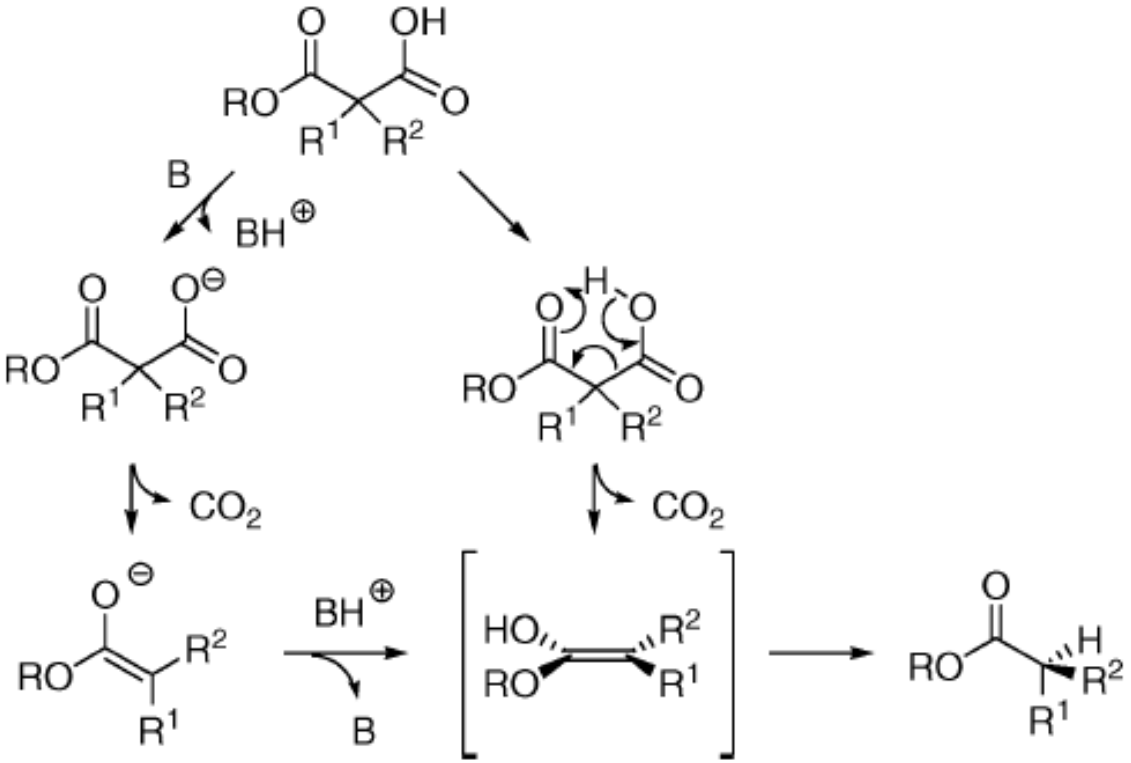
Institute of Organic Chemistry
Justus-Liebig University

Cis- and *Trans*-1,2-Ethenediol: Enols of Glycolaldehyde as Key High-Energy Prebiotic Molecules in Carbohydrate Cycle

Artur Mardyukov

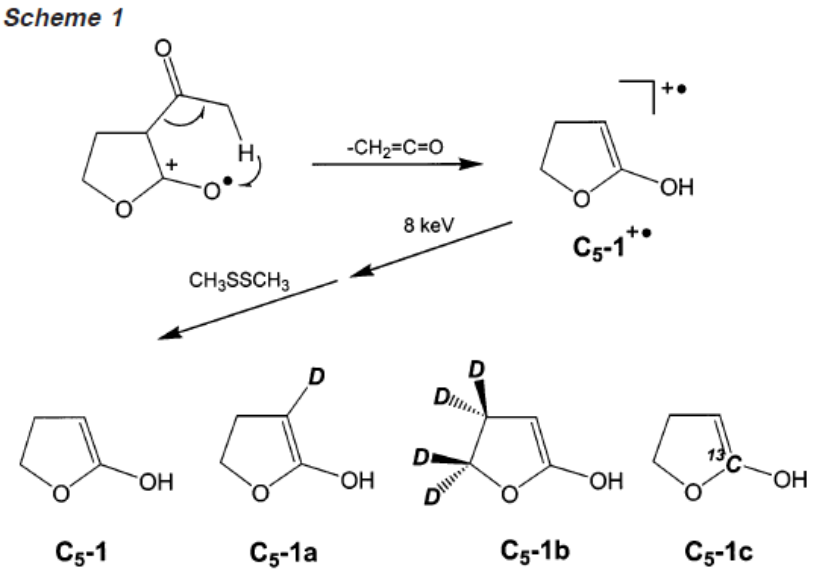
April 1, 2022

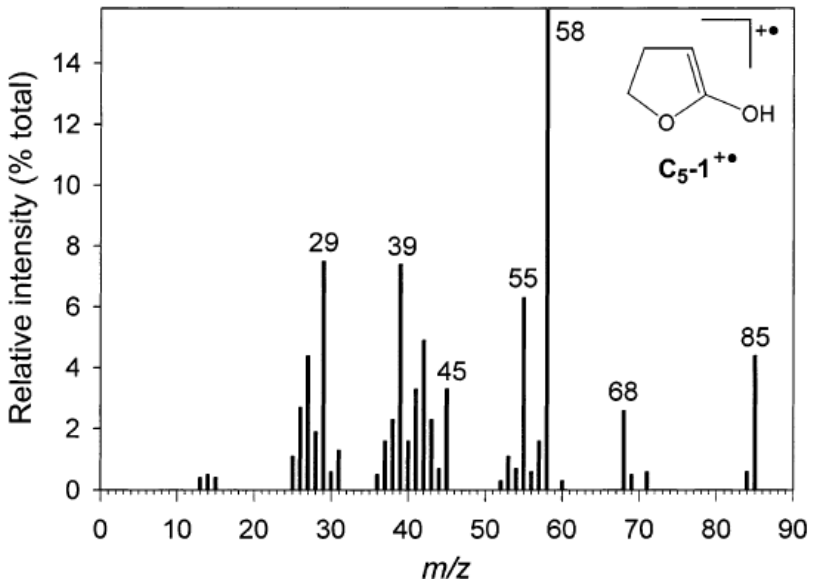
The enantioselective decarboxylative protonation (EDP) of malonic acid derivatives is a synthetic methodology by which the chirality of the product is generated during the enol/enolate protonation step.



Blanchet et al., *Eur. J. Org. Chem.* **2008**, 5493–5506.

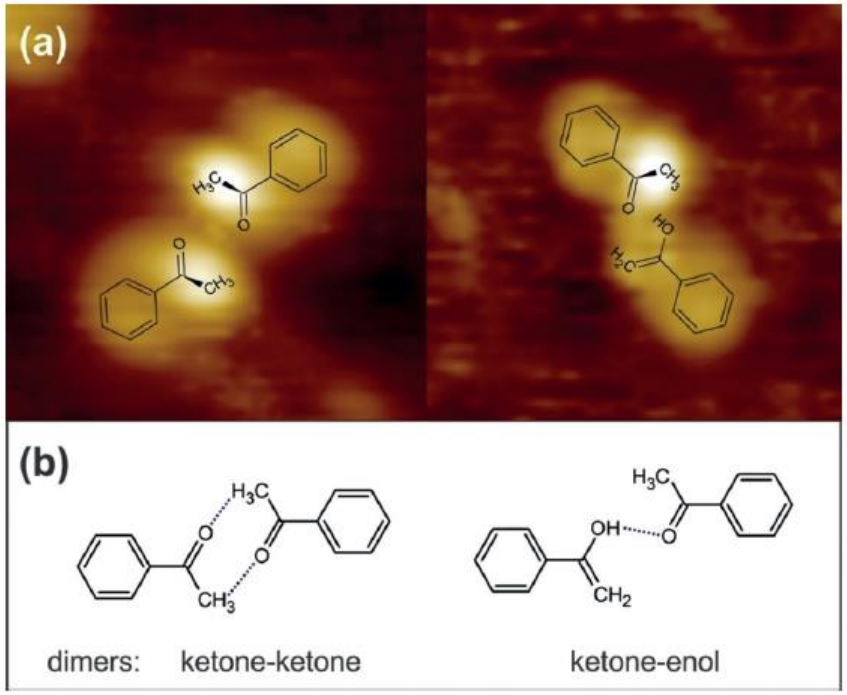
Lactone Enols are Stable in the Gas Phase but Highly Unstable in Solution

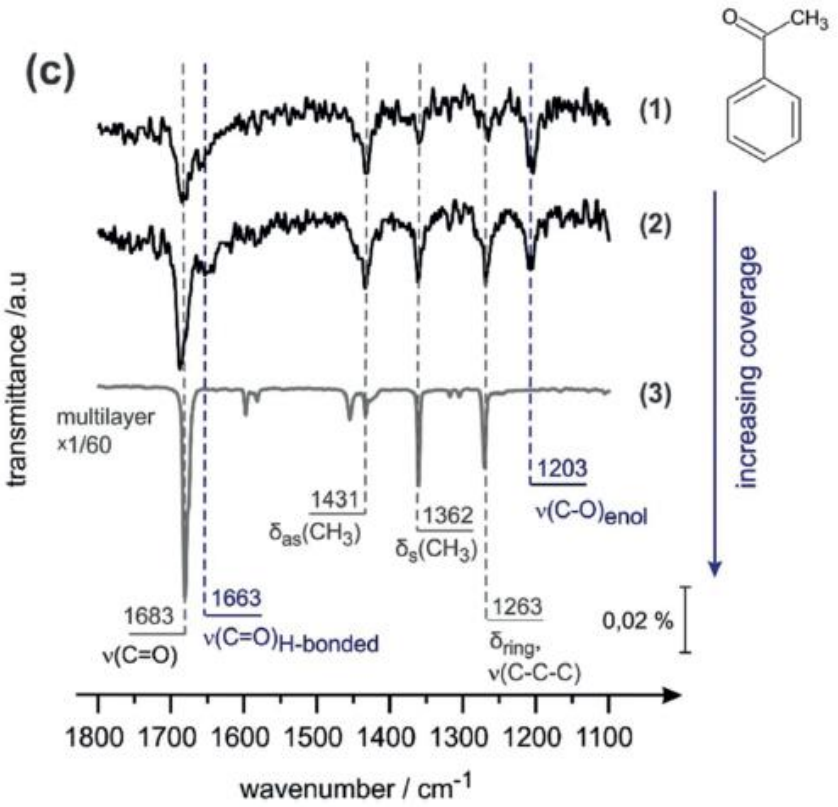




F. Turecek, S. Vivekananda, M. Sadilek, M. Polasek, *J. Am. Chem. Soc.* **2002**, *124*, 13282-13289.

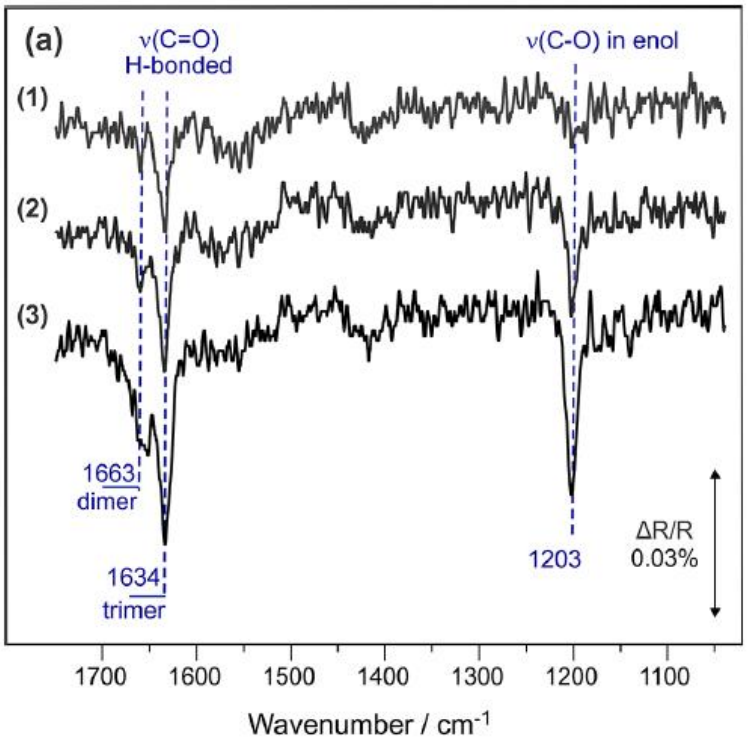
Surface-Driven Keto–Enol Tautomerization

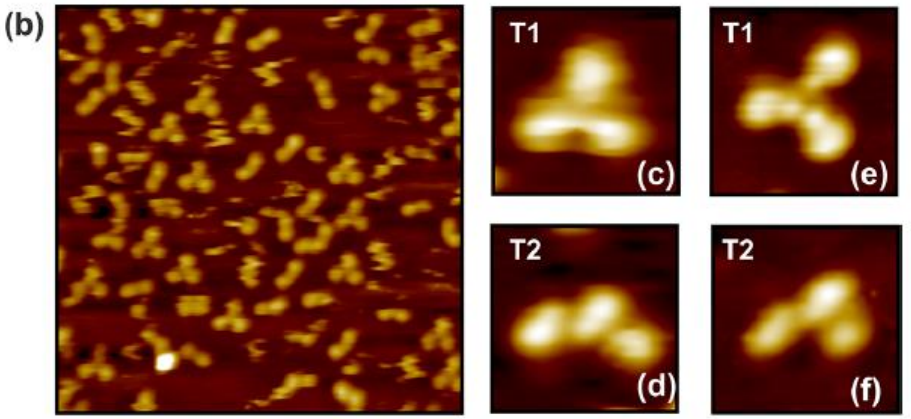


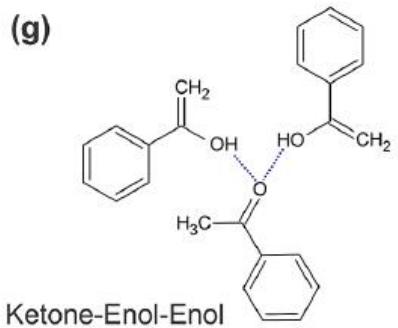


S. Attia, M.-C. Schmidt, C. Schroeder, P. Pessier, S. Schauermann, *Angew. Chem., Int. Ed.* **2018**, *57*, 16659-16664.

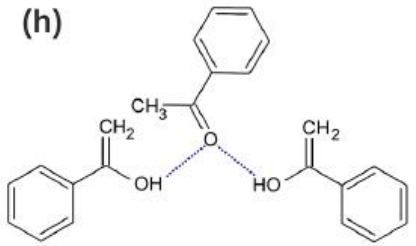
Formation and Stabilization Mechanisms of Enols on Pt through Multiple Hydrogen Bonding







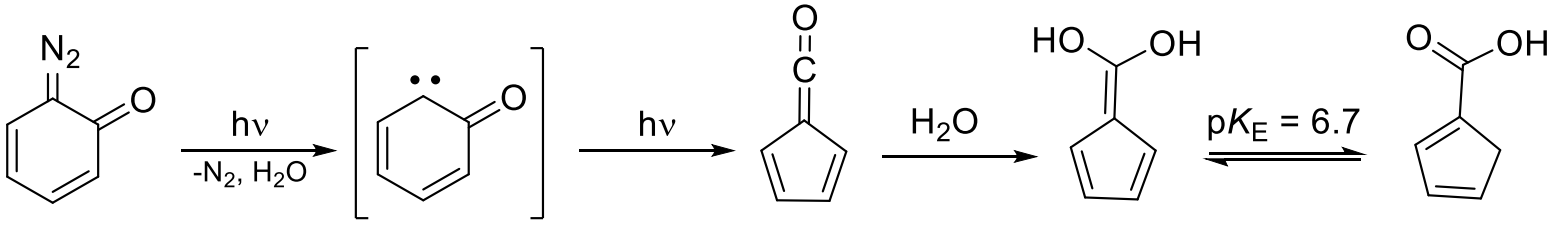
Ketone-Enol-Enol
Trimer **T1**

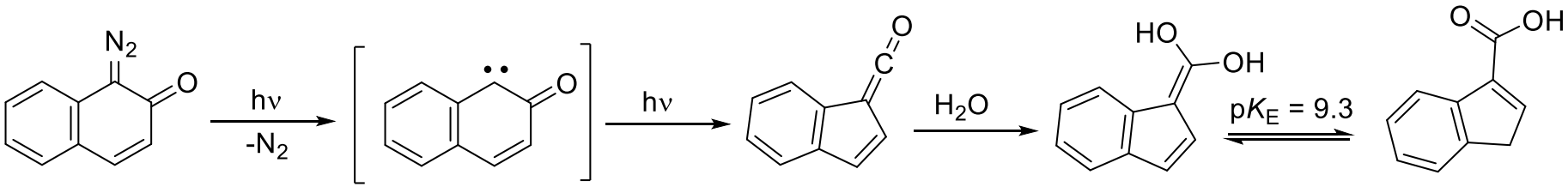


Ketone-Enol-Enol
Trimer **T2**

S. Attia, M. C. Schmidt, C. Schröder, and S. Schauermann, *ACS Catal*. **2019**, 9, 6882−6889.

Conjugated Enols – Time Resolved Spectroscopy

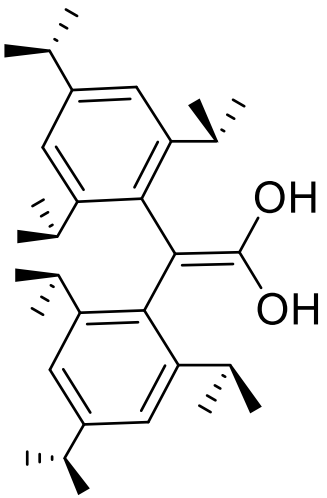


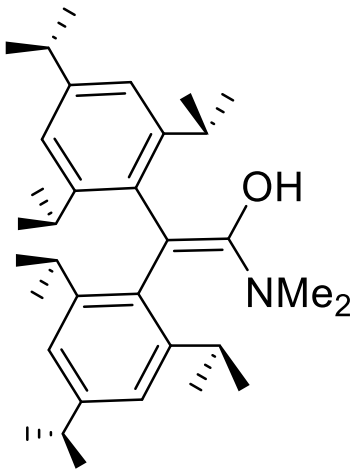


(1) B. Urwyler, J. Wirz, *Angew. Chem.* **1990**, *102*, 790-792. (2) Y. Chiang, A. J. Kresge, P. Pruszynski, N. P. Schepp, J. Wirz, *Angew. Chem. Int. Ed.* **1990**, *29*, 792-794. (3) J. I. K. Almstead, B. Urwyler, J. Wirz, *J. Am. Chem. Soc.* **1994**, *116*, 954-960. (4) J. Andraos, Y. Chiang, A. J. Kresge, V. V. Popik, *J. Am. Chem. Soc.* **1997**, *119*, 8417-8424.

Observation of Kinetically Stabilized Enols

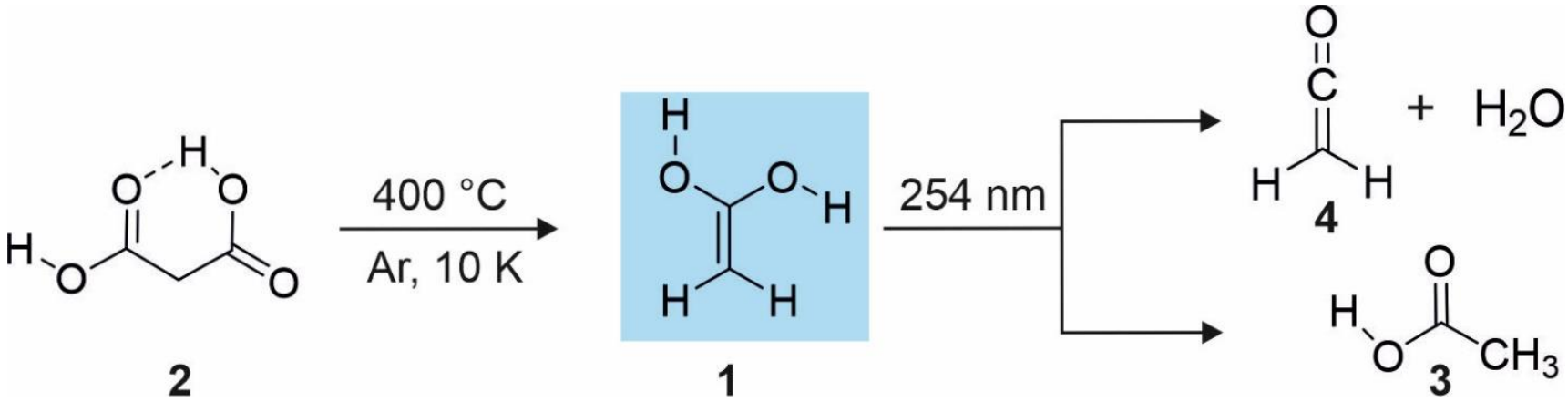
$Tip_2C{=}C{=}O$





(1) J. Frey, Z. Rappoport, *J. Am. Chem. Soc.* **1995**, *117*, 1161. (2) J. Frey, Z. Rappoport, *J. Am. Chem. Soc.* **1996**, *118*, 5182-5191.

1,1-Ethenediol - The Enol of Acetic Acid



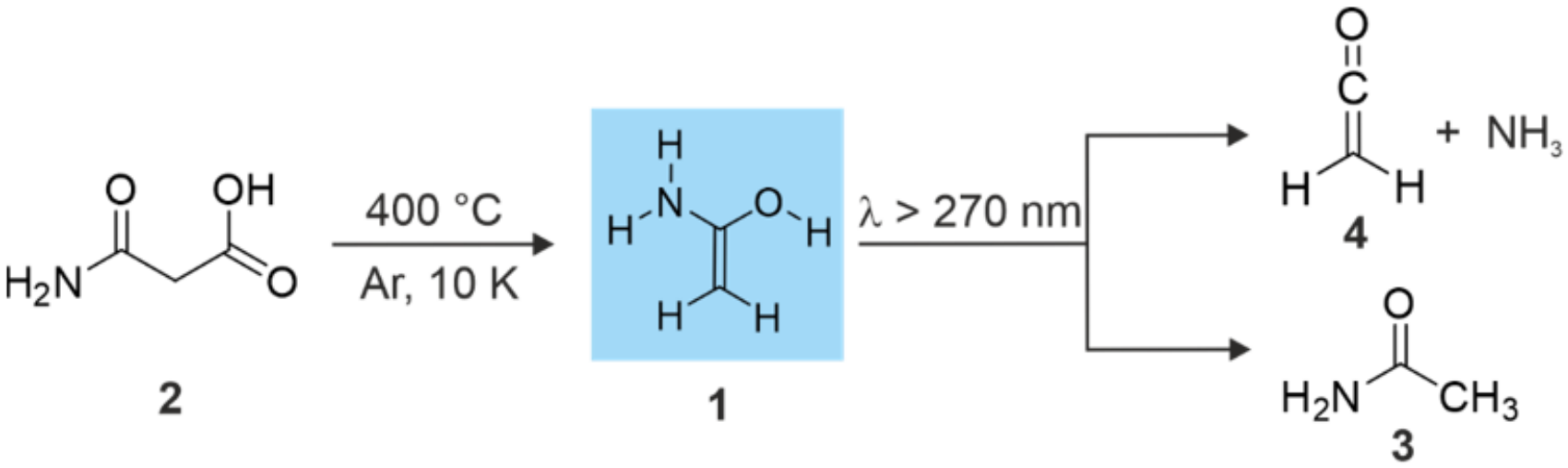
A. Mardyukov, A. Eckhardt, P. R. Schreiner, *Angew. Chem. Int. Ed*. 2020, 59, 5577-5580.

About 200 molecules have been found in the interstellar medium and there is evidence for the existence of far larger molecular species

2 atoms	CS	HCO^+	KCN	H_3O^+	HCOOH	*l*-HC_4N	CH_2CHCHO	CH_3OCH_2OH
H_2	HF	HCS^+	FeCN	NH_3	H_2CNH	*c*-H_2C_3O	CH_2CCHCN	11 atoms
AlF	SH	HOC^+	HO_2	c-SiC_3	H_2C_2O	C_5N^-	H_2NCH_2CN	HC_9N
AlCl	SH^+	H_2O	TiO_2	CH_3	H_2NCN	E-HNCHCN	CH_3CHNH	CH_3C_6H
C_2	FeO	H_2S	C_2N	C_3N^-	HNC_3	SiH_3CN	CH_3SiH_3	C_2H_5OCHO
CH	O_2	HNC	SiCSi	PH_3	SiH_4	CH_2CNH	C_2H_5N	$CH_3OC(O)CH_3$
CH^+	CF^+	HNO	S_2H	HCNO	H_2COH^+	C_5S	$(NH_2)_2CO$	12 atoms
CN	PO	MgCN	HCS	HOCN	C_4H^-	7 atoms	9 atoms	*c*-C_6H_6
CO	AlO	MgNC	HSC	HSCN	HC(O)CN	C_6H	CH_3C_4H	C_3H_7CN
CO^+	CN^-	N_2H^+	NCO	H_2O_2	HNCNH	CH_2CHCN	CH_3CH_2CN	*t*-$C_2H_5OCH_3$
CP	HCl^+	N_2O	OCN^-	l-C_3H^+	CH_3O	HC_5N	$(CH_3)_2O$	>12 atoms
CSi	TiO	NaCN	4 atoms	HMgNC	H_2NCO^+	CH_3CHO	CH_3CH_2OH	C_{60}
HCl	ArH^+	OCS	C_3H^*	HCCO	$NCCNH^+$	NH_2CH_3	HC_7N	C_{60}^+
KCl	N_2	SO_2	*l*-C_3H^+	CH_3Cl	NH_3D^+	*c*-C_2H_4O	C_8H	C_{70}
NH	NO^+	*c*-SiC_2	C_3N	CNCN	6 atoms	H_2CCHOH	$CH_3C(O)NH_2$	c-C_6H_5CN
NO	NS^+	CO_2	C_3O	MgCCH	C_5H	C_6H^-	C_8H^-	$CO(CH_2OH)_2$?
NS	LiH	NH_2	C_3S	NCCP	*l*-C_4H_2	CH_3NCO	C_3H_6	$C_{14}H_{10}$?
NaCl	CrO	H_3^+	C_2H_2	5 atoms	C_2H_4	HC_5O	CH_3CH_2SH	$C_{14}H_{10}^+$
OH	3 atoms	SiCN	HC_2N	C_5	CH_3CN	8 atoms	CH_3NHCHO	C_6H_5OH
OH^+	C_3	AlNC	$HCNH^+$	C_4H	CH_3NC	CH_3C_3N	HC_7O	
PN	C_2H	SiNC	HNCO	C_4Si	CH_3OH	$HC(O)OCH_3$	10 atoms	
SO	C_2O	HCP	HNCS	*c*-C_3H_2	CH_3SH	CH_3COOH	CH_3C_5N	
SO^+	C_2S	CCP	$HOCO^+$	CH_2CN	HC_3NH^+	C_7H	$(CH_3)_2CO$	
SiN	CH_2	AlOH	H_2CO	CH_4	HC_2CHO	H_2C_6	$(CH_2OH)_2$	
SiO	HCN	H_2O^+	H_2CN	HC_3N	NH_2CHO	CH_2OHCHO	CH_3CH_2CHO	
SiS	HCO	H_2Cl^+	H_2CS	HC_2NC	C_5N	*l*-C_6H_2	CH_3CHCH_2O	

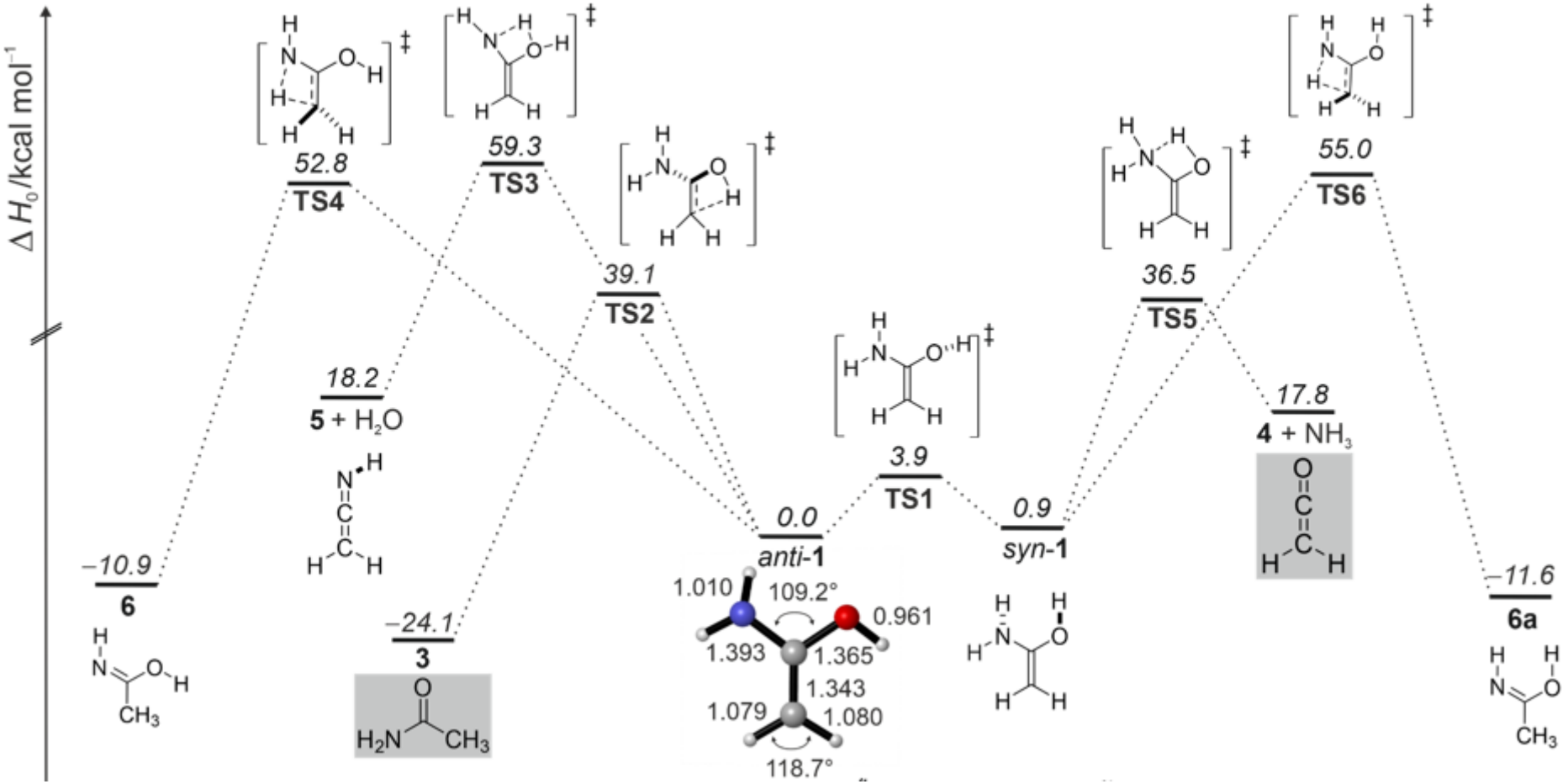
C. R. Arumainayagam, *et al.*, *Chem. Soc. Rev.* 2019, 48, 2293–2314.

1-Aminoethenol - The Enol of Acetamide



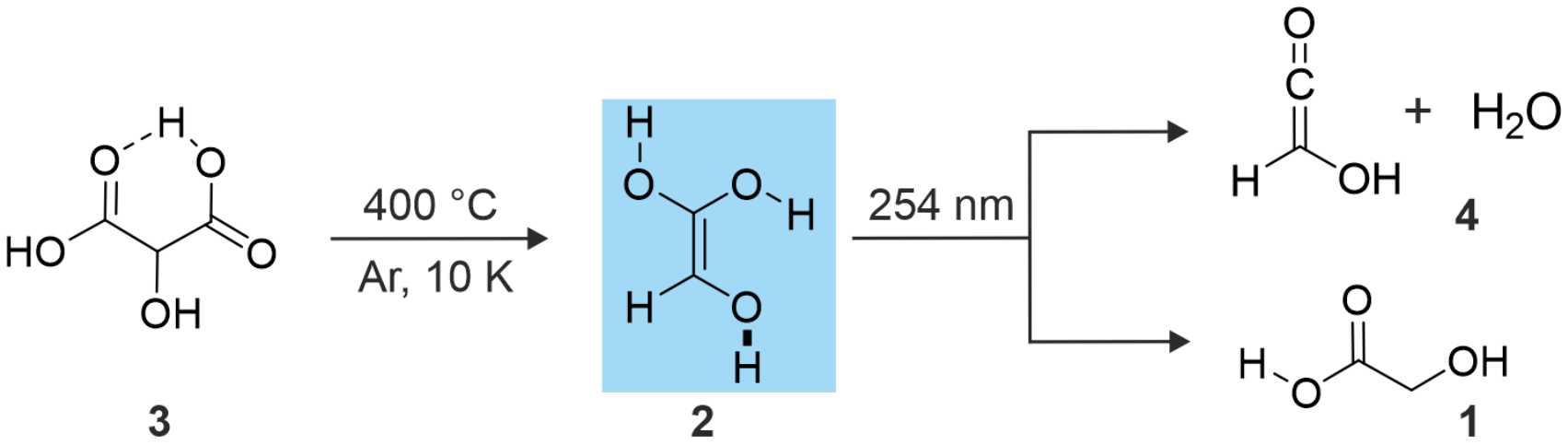
A. Mardyukov, F. Keul, P. R. Schreiner, *Chem. Sci*. 2020, 11, 12358–12363.

Potential Energy Profile



Potential energy profile (ΔH_0) in kcal mol^{-1} of the reactions of enol **1** at AE-CCSD(T)/cc-pVTZ + ZPVE

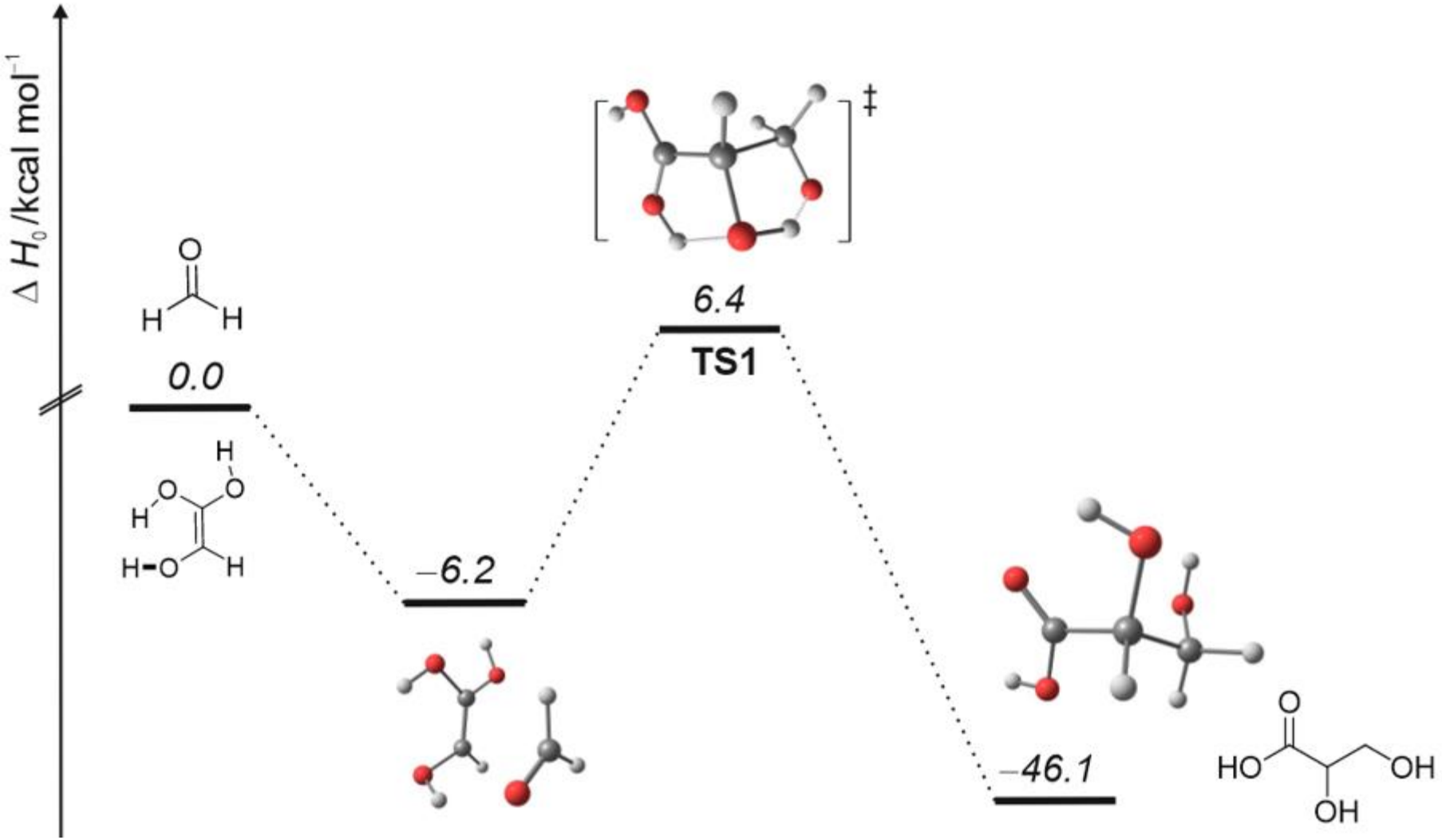
1,1,2-Ethenetriol – The Enol of Glycolic Acid



3 **2** **4** **1**

A. Mardyukov, F. Keul, P. R. Schreiner, *Angew. Chem. Int. Ed.* 2021, 60, 15313-15316.

Reaction of Triol with Formaldehyde



Organic compounds on comet 67P/Churyumov-Gerasimenko revealed by Cometary Sampling and Composition (COSAC) mass spectrometry (Rosetta's Philae lander)

Table 1. The 16 molecules used to fit the COSAC mass spectrum.

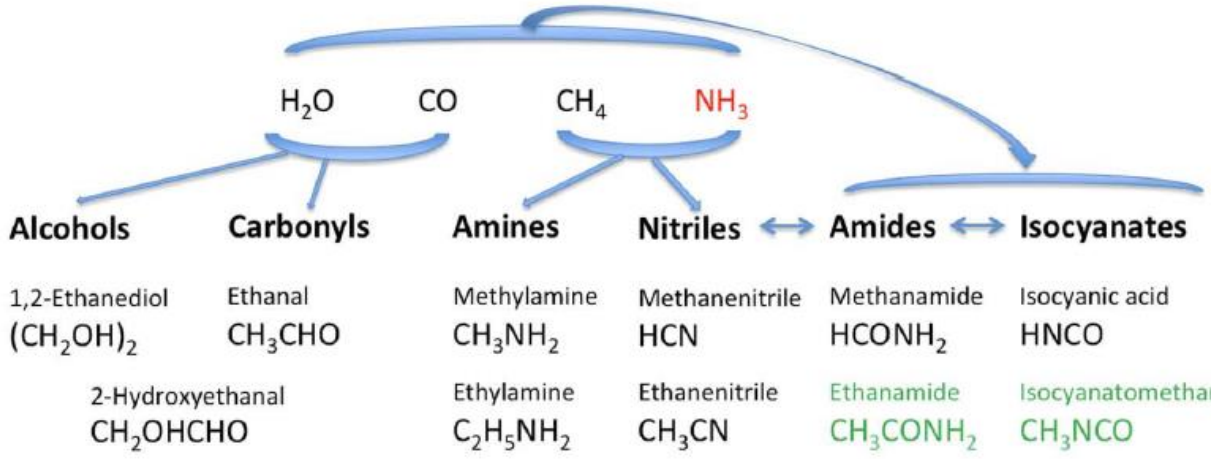
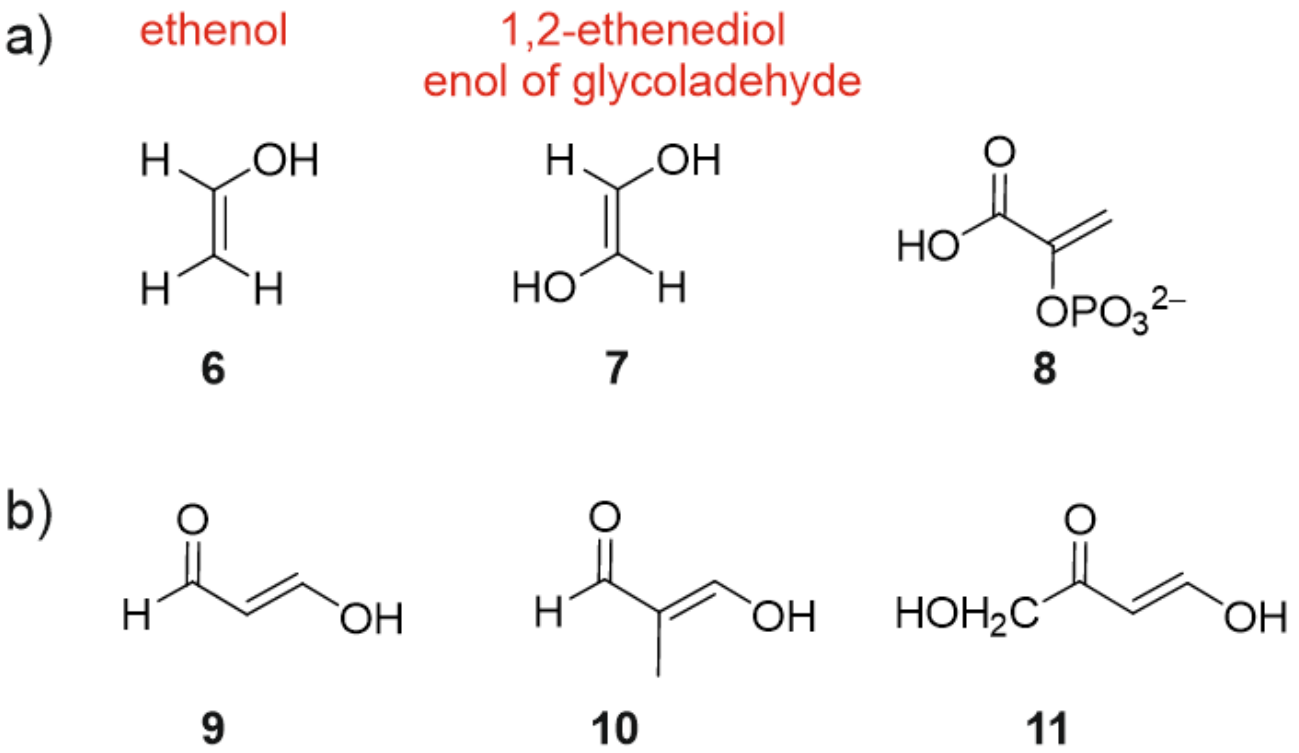


Fig. 3. Possible formation pathways of COSAC compounds. Species in red are not confidently identified; species in green are reported for the first time in comets by COSAC.

Fred Goesmann et al., *Science* 2016, 349, 6247, aab0689.

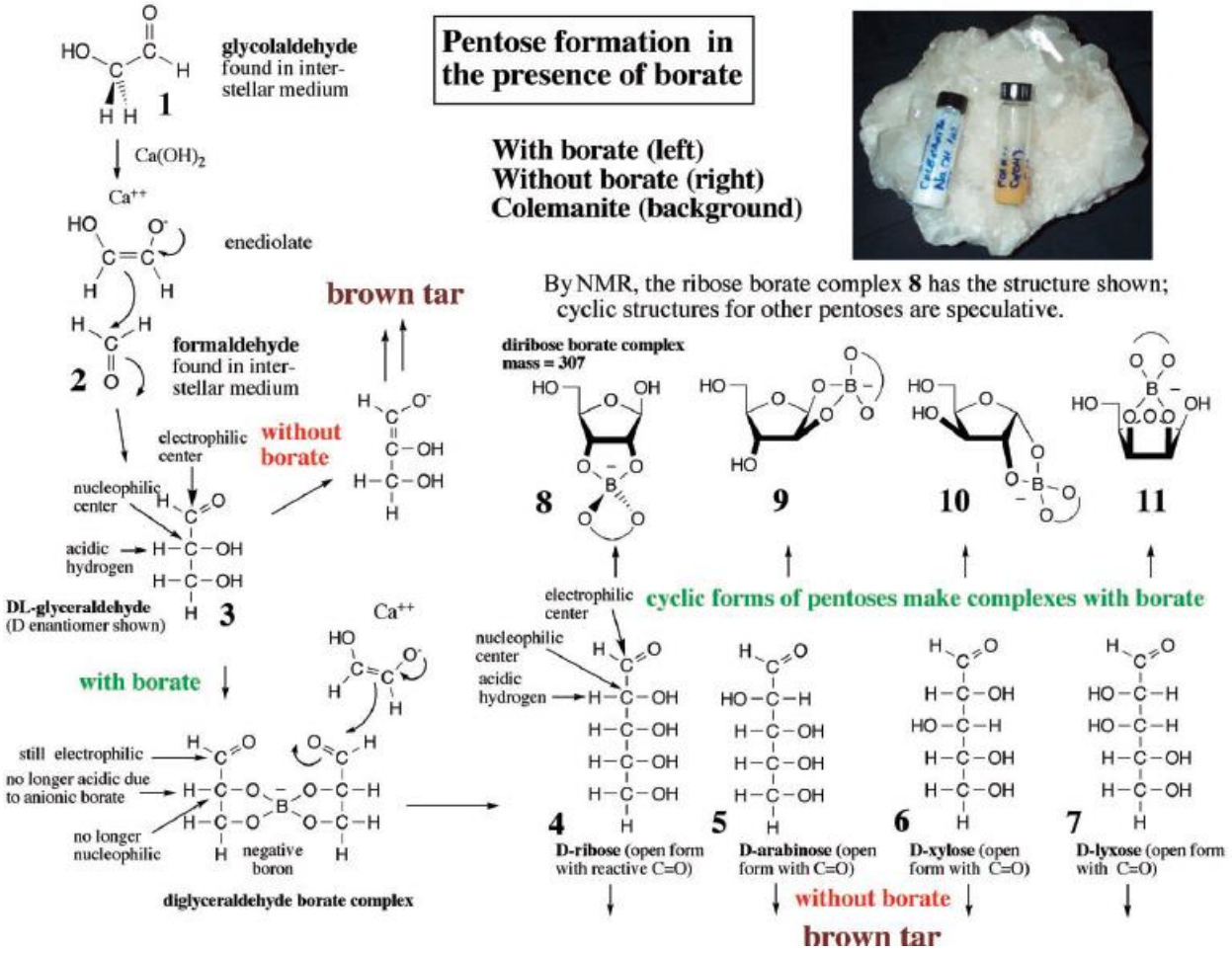
Enols as Intermediates for Prebiotic and Atmospheric Implications



(b) Enols suggested as intermediates in the photooxidation of isoprene.

(1) F. Paulot, J. D. Crounse, H. G. Kjaergaard, J. H. Kroll, J. H. Seinfeld, P. O. Wennberg, Atmos. Chem. Phys. **2009**, 9, 1479. (2) A. J. Coggins, M. W. Powner, *Nat. Chem.* **2017**, *9*, 310-317. (3) D. U. Andrews, B. R. Heazlewood, A. T. Maccarone, T. Conroy, R. J. Payne, M. J. T. Jordan, S. H. Kable, *Science* **2012**, *337*, 1203-1206. (4) A. E. Clubb, M. J. T. Jordan, S. H. Kable, D. L. Osborn, *J. Phys. Chem. Lett.* **2012**, *3*, 3522-3526.

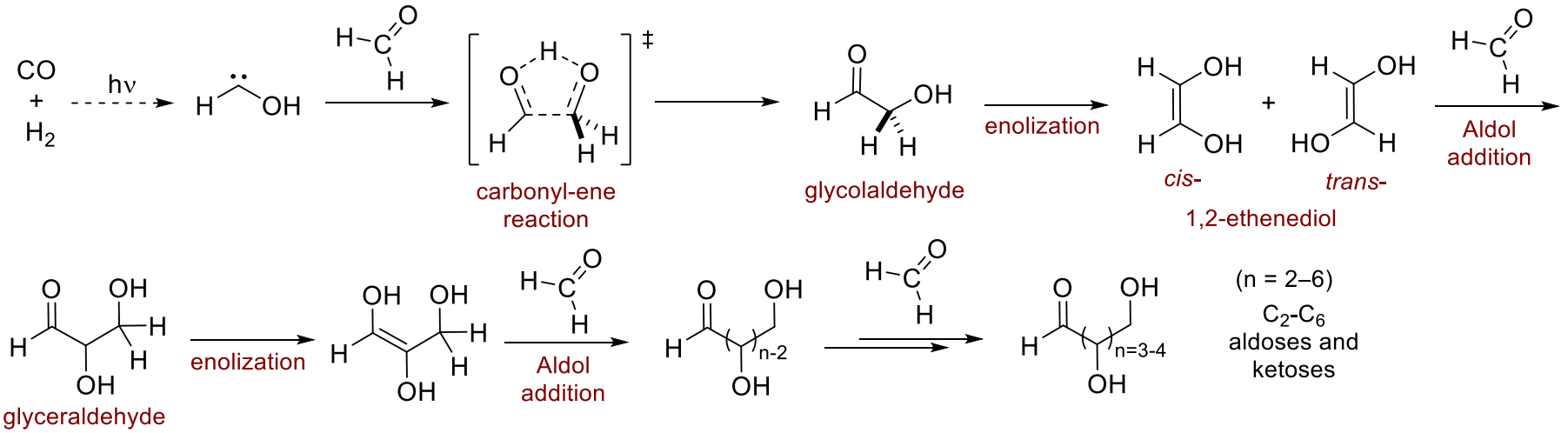
Borate Minerals Stabilize Ribose



Pentose formation in the presence of borate.

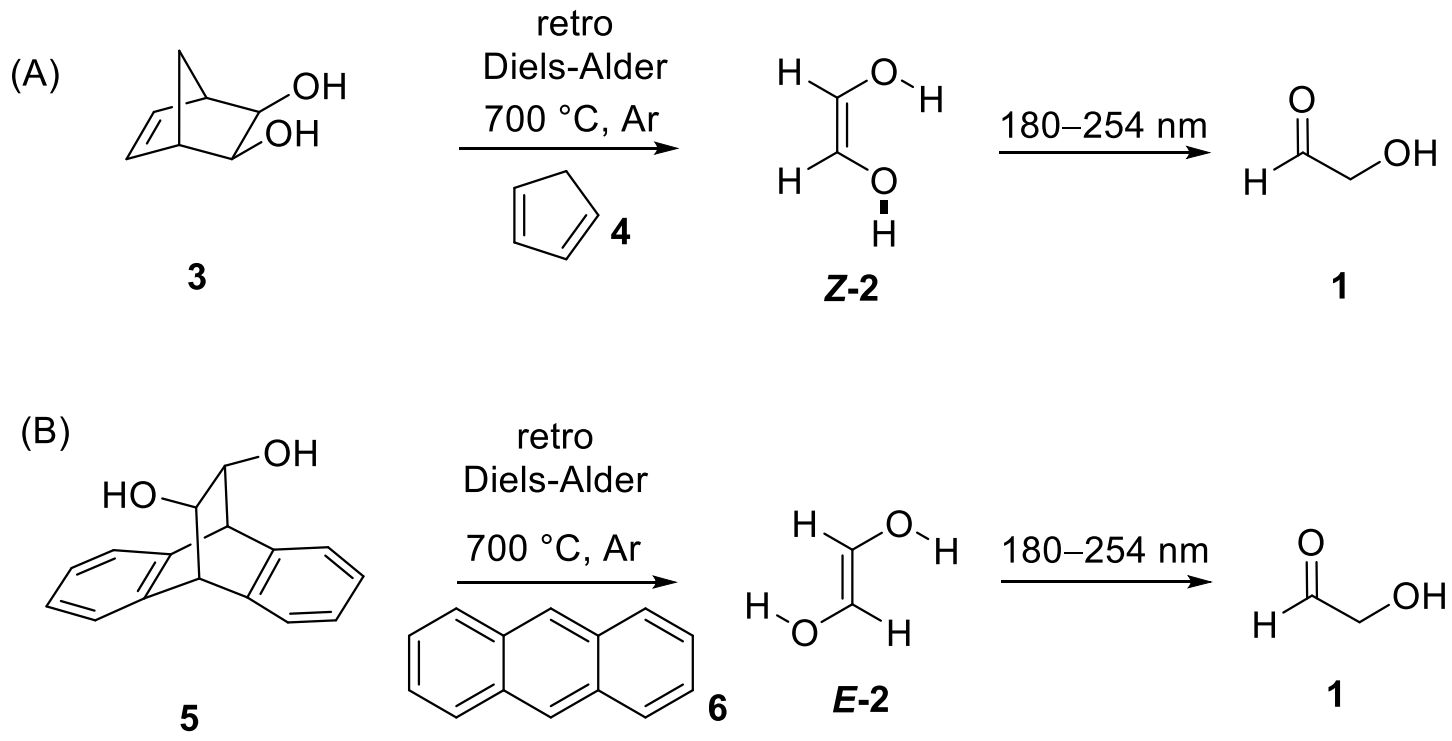
A. Ricardo, M. A. Carrigan, A. N. Olcott, S. A. Benner, *Science* **2004**, *303*, 196

Previously proposed mechanism for mineral-driven prebiotic synthesis of carbohydrates. Formation of glycolaldehyde from hydroxymethylene as the reactive formaldehyde isomer. Generation and subsequent reaction of 1,2-ethenediol with formaldehyde in the presence of minerals.



(1) H.-J. Kim, A. Ricardo, H. I. Illangkoon, M. J. Kim, M. A. Carrigan, F. Frye, S. A. Benner, *J. Am. Chem. Soc.* **2011**, *133*, 9457-9468. (2) A. K. Eckhardt, M. M. Linden, R. C. Wende, B. Bernhardt, P. R. Schreiner, *Nat. Chem.,* **2018**, *10*, 1141-1147.

1,2-ethenediol – The Enol of Glycolaldehyde



1,2-Ethenediols (**2**) generated from **3** and **5** through pyrolysis and trapping in an argon matrix. Subsequent photorearrangement to glycolaldehyde (**1**).

(1) M.-C. Lasne, J.-L. Ripoll, *Tetrahedron Lett.* **1982**, *23*, 1587-1588. (2) F. Turecek, *Tetrahedron Lett.* **1984**, *25*, 5133. (3) F. Turecek, L. Brabec, J. Korvola, *J. Am. Chem. Soc.* **1988**, *110*, 7984.

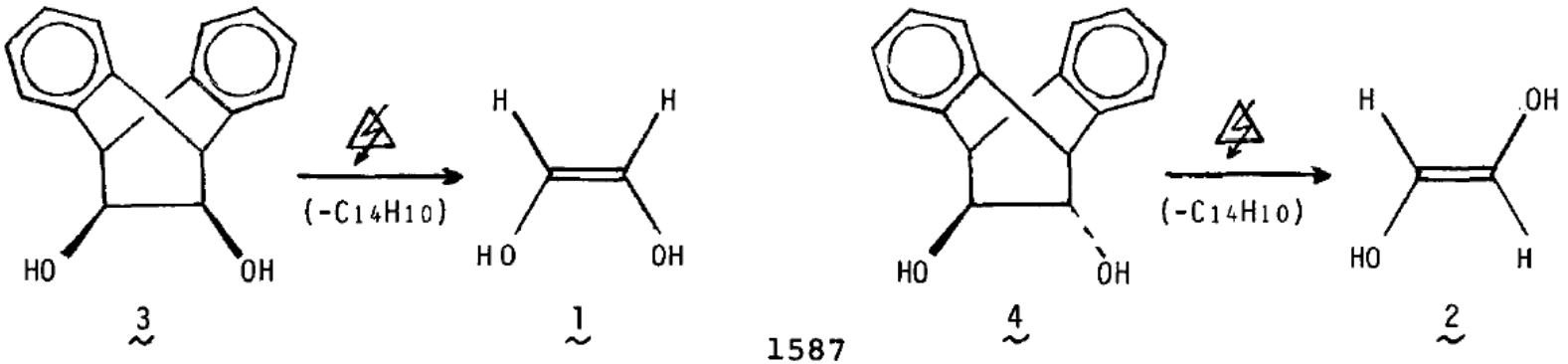
Tetrahedron Letters,Vol.23,No.15,pp 1587-1588,1982 0040-4039/82/151587-02$03.00/0
Printed in Great Britain

REACTIONS RETRODIENIQUES XIII‡ - THERMOLYSE ECLAIR DES (Z) et (E) DIHYDROXY-11, 12 ETHANO-9,10 DIHYDRO-9,10 ANTHRACENES : SYNTHESE DES (Z) et (E) ETHENEDIOLS-1,2.

Marie-Claire Lasne et Jean-Louis Ripoll *

ERA CNRS 391, ISMRA, Université de Caen, 14032 Caen, France.

The flash vacuum thermolysis of diols 3 and 4 affords, via a retro-Diels-Alder cleavage, the simplest enediols 1 and 2 for which the NMR and IR spectra as well as their thermal evolution are reported.



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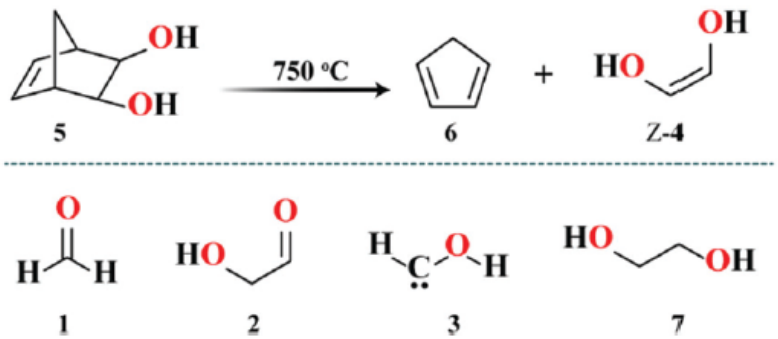
Gas-phase identification of (*Z*)-1,2-ethenediol, a key prebiotic intermediate in the formose reaction†

Mattia Melosso, *[ab] Luca Bizzocchi,[ac] Houda Gazzeh,[de] Francesca Tonolo, [ac] Jean-Claude Guillemin, [d] Silvia Alessandrini, [ac] Víctor M. Rivilla,[fg] Luca Dore, [a] Vincenzo Barone [c] and Cristina Puzzarini *[a]



Scheme 1 (*Z*)-1,2-Ethenediol (*Z*-**4**) and cyclopentadiene (**6**) generated in the flash vacuum pyrolysis of bis-*exo*-5-norbornene-1,2-diol (**5**). Other molecules of interest are reported for the sake of clarity: formaldehyde (**1**), glycolaldehyde (**2**), hydroxymethylene (**3**), and ethylene glycol (**7**).

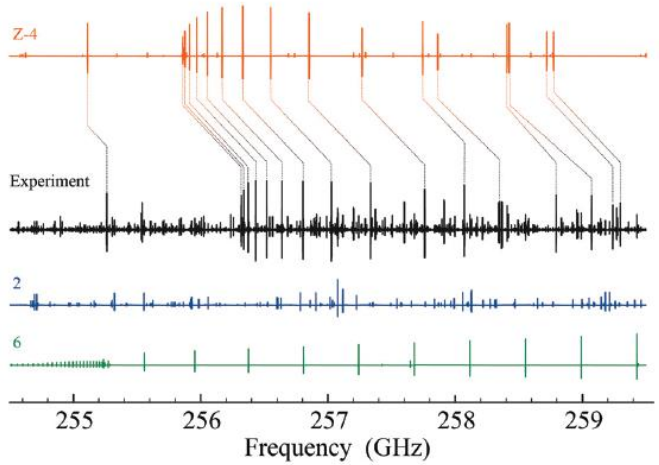
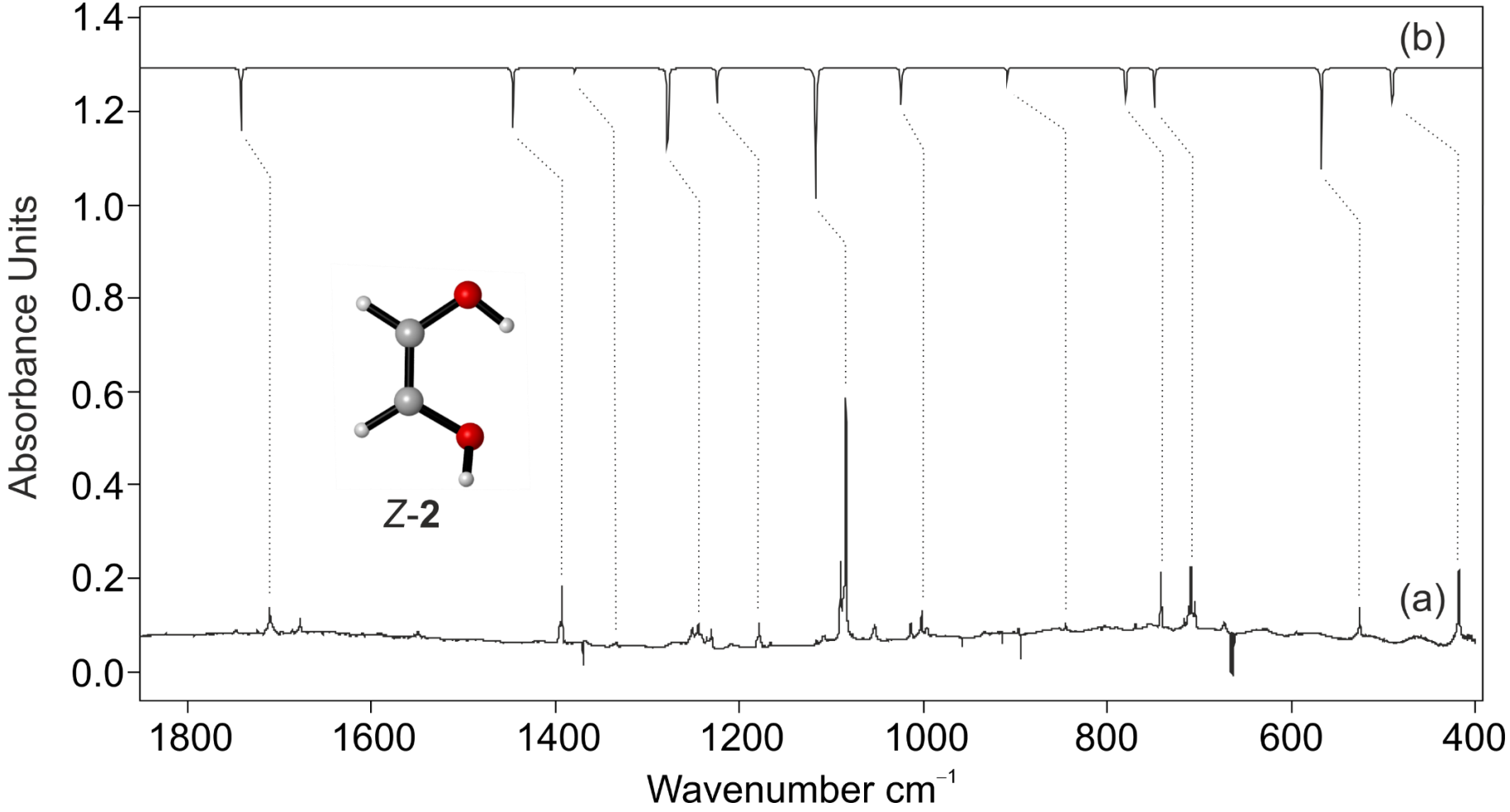


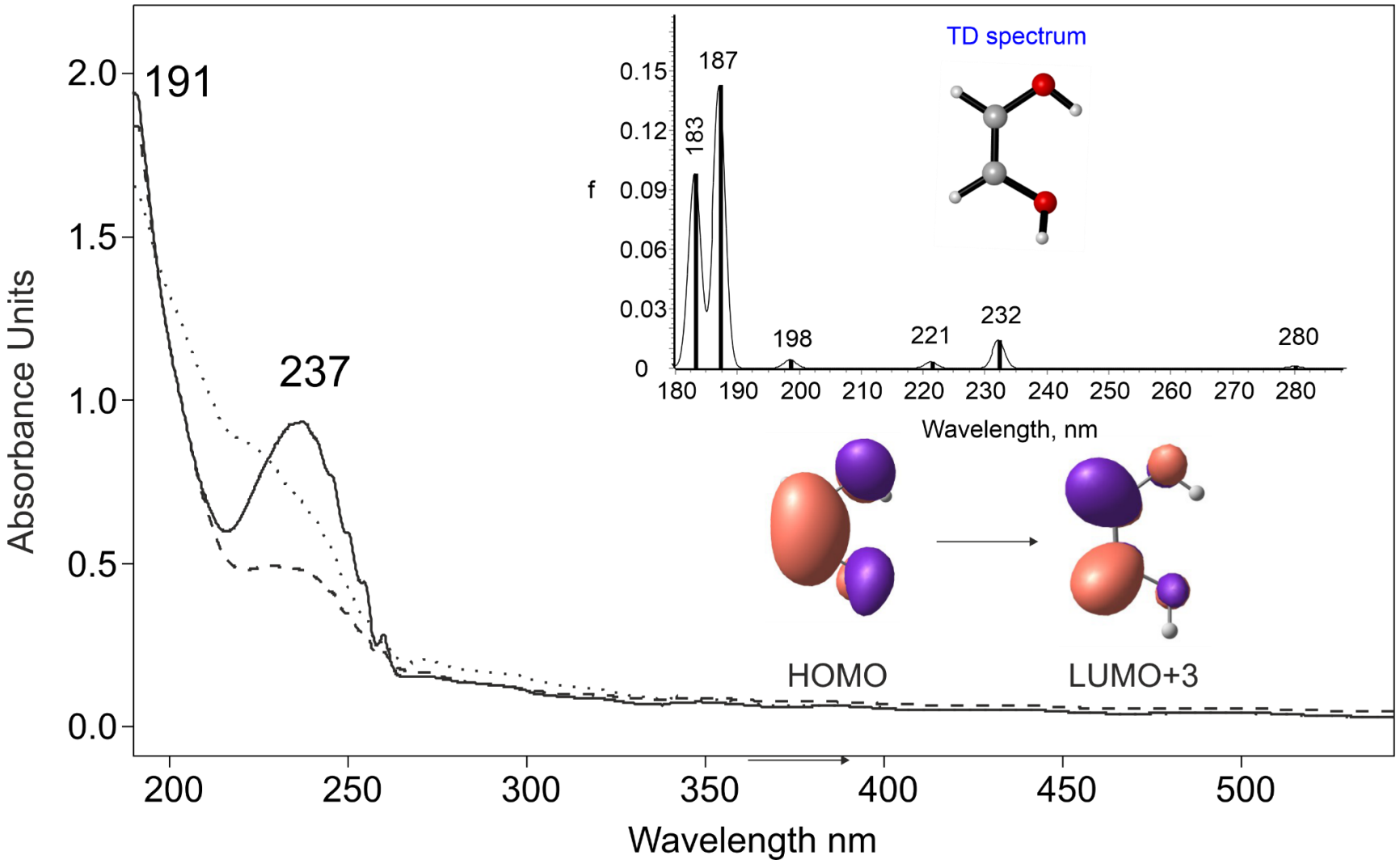
Fig. 1 Portion of the millimeter-wave spectrum around 257 GHz. The experimental spectrum (black trace) is compared with the spectral simulation of glycolaldehyde (**2**, blue trace), cyclopentadiene (**6**, green trace), and the computational guess obtained for 1,2-ethenediol (*Z*-**4**, orange trace). The intensities of the simulated spectra have been adjusted in order to match roughly the experimental spectrum.

Cis-1,2-ethenediol



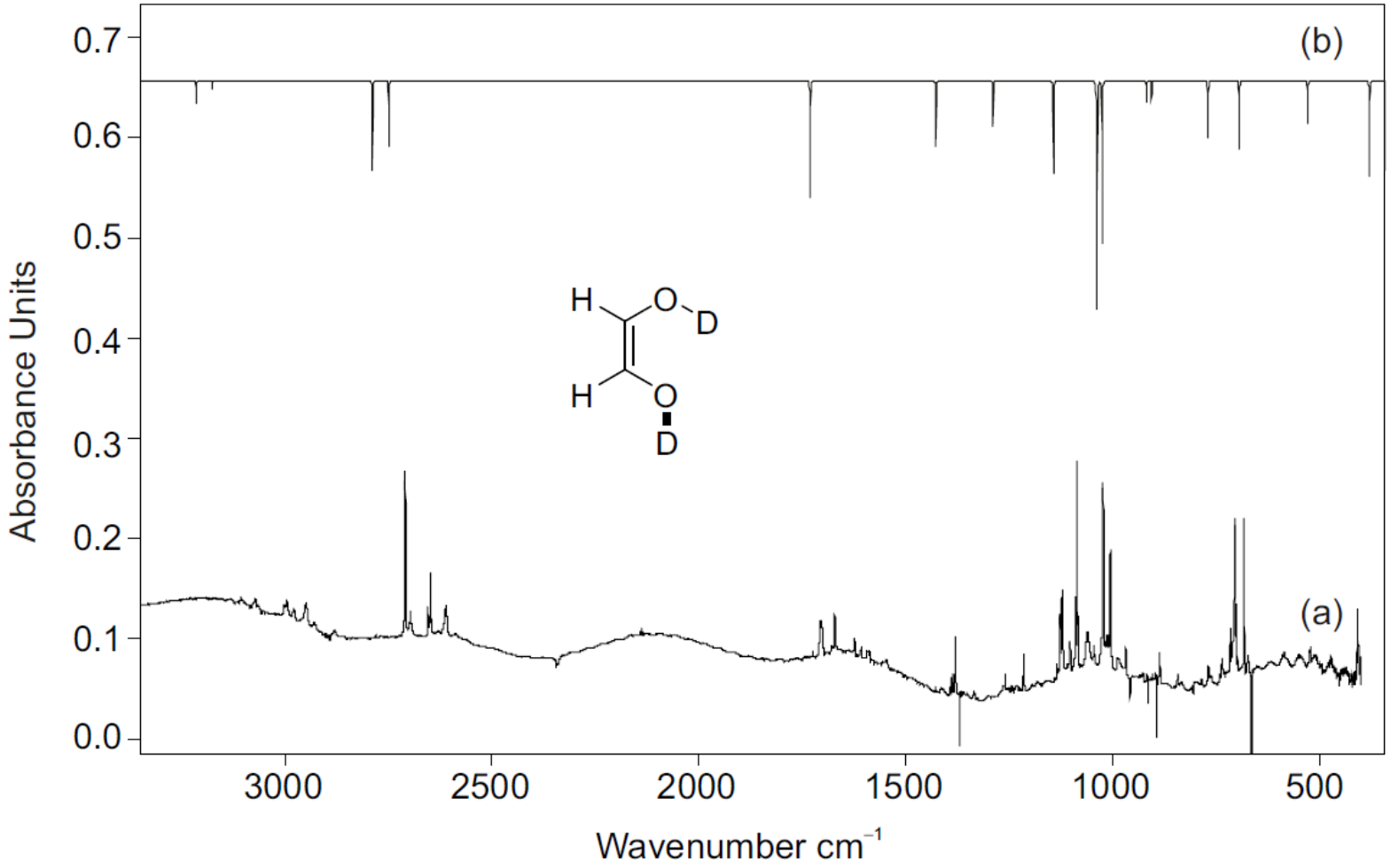
(a) IR spectrum showing the pyrolysis products of **3** with subsequent trapping in an argon matrix at 10 K. The matrix isolation spectrum of **4** was subtracted (downward bands). (b) IR spectrum of *Z*-**2** computed at AE-CCSD(T)/cc-pVTZ (unscaled).

Cis-1,2-ethenediol



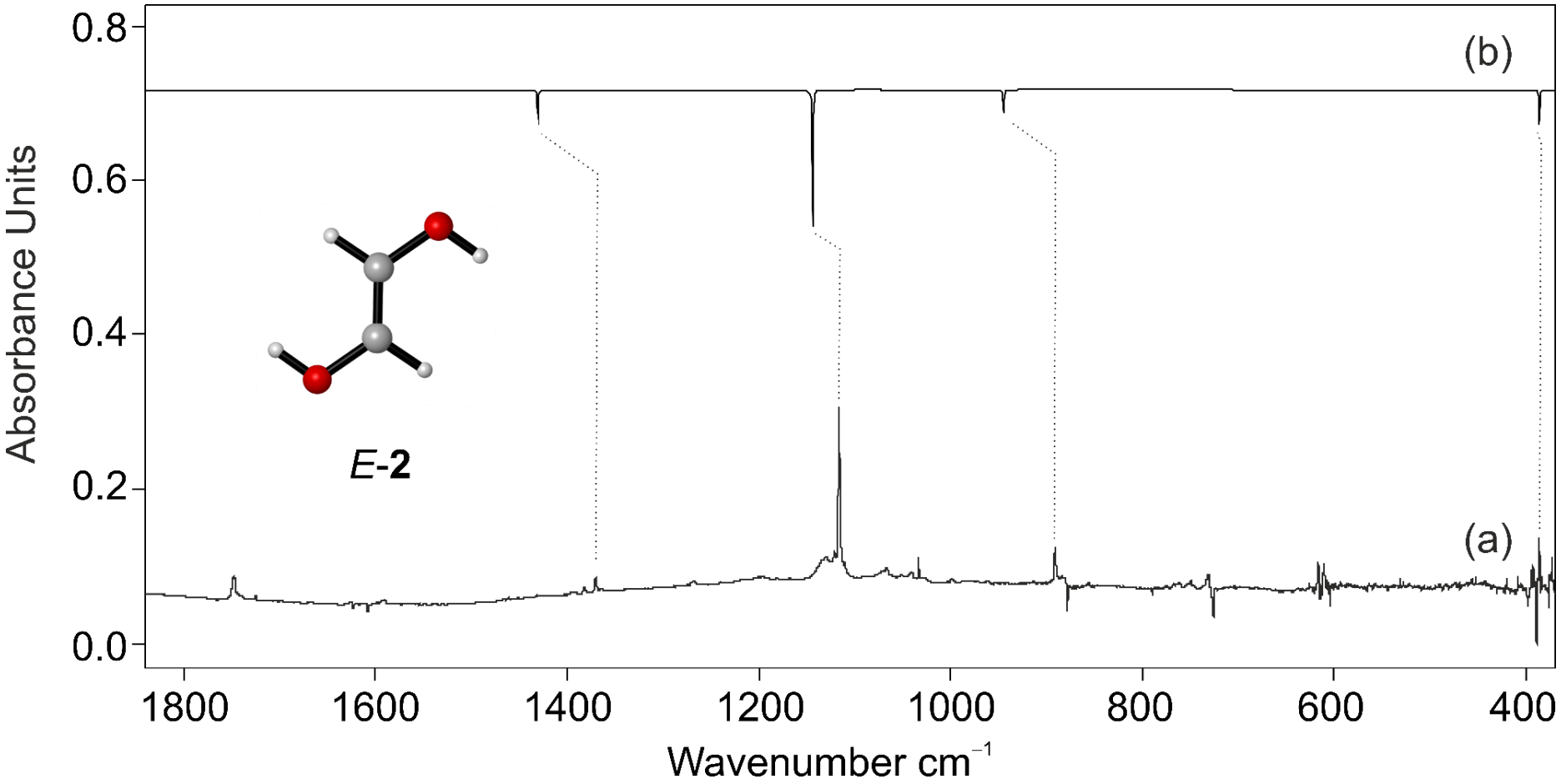
Solid line: UV/vis spectrum showing the pyrolysis product of **3** with subsequent trapping in an argon matrix at 10 K. Dashed line: after irradiation at $\lambda > 200$ nm for 30 min in argon at 10 K. Dotted line: after irradiation at λ =180-254 nm for 30 min in argon at 10 K. Inset: computed [TD-B3LYP/6-311++G(2d,p)] electronic transitions for *Z*-**2**.

Cis-1,2-ethenediol



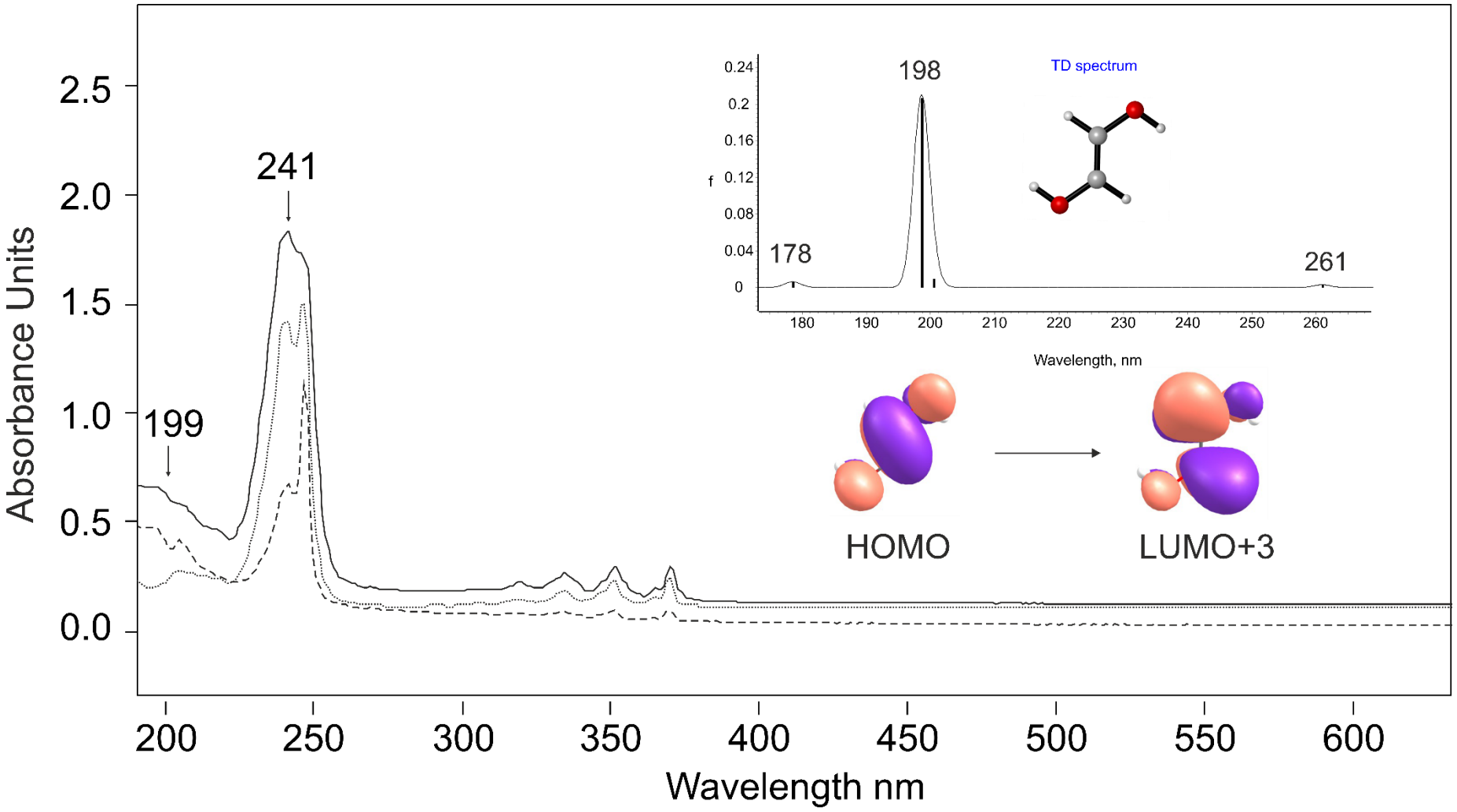
(a) IR spectra showing the product of pyrolysis (700 °C) of d_2-**3** in argon matrix with subsequent trapping in an argon matrix at 10 K. The matrix isolation spectrum of **4** was subtracted (downward bands). (b) IR spectrum of d_2-*Z*-**2** computed at AE-CCSD(T)/cc-pVTZ (unscaled).

Trans-1,2-ethenediol



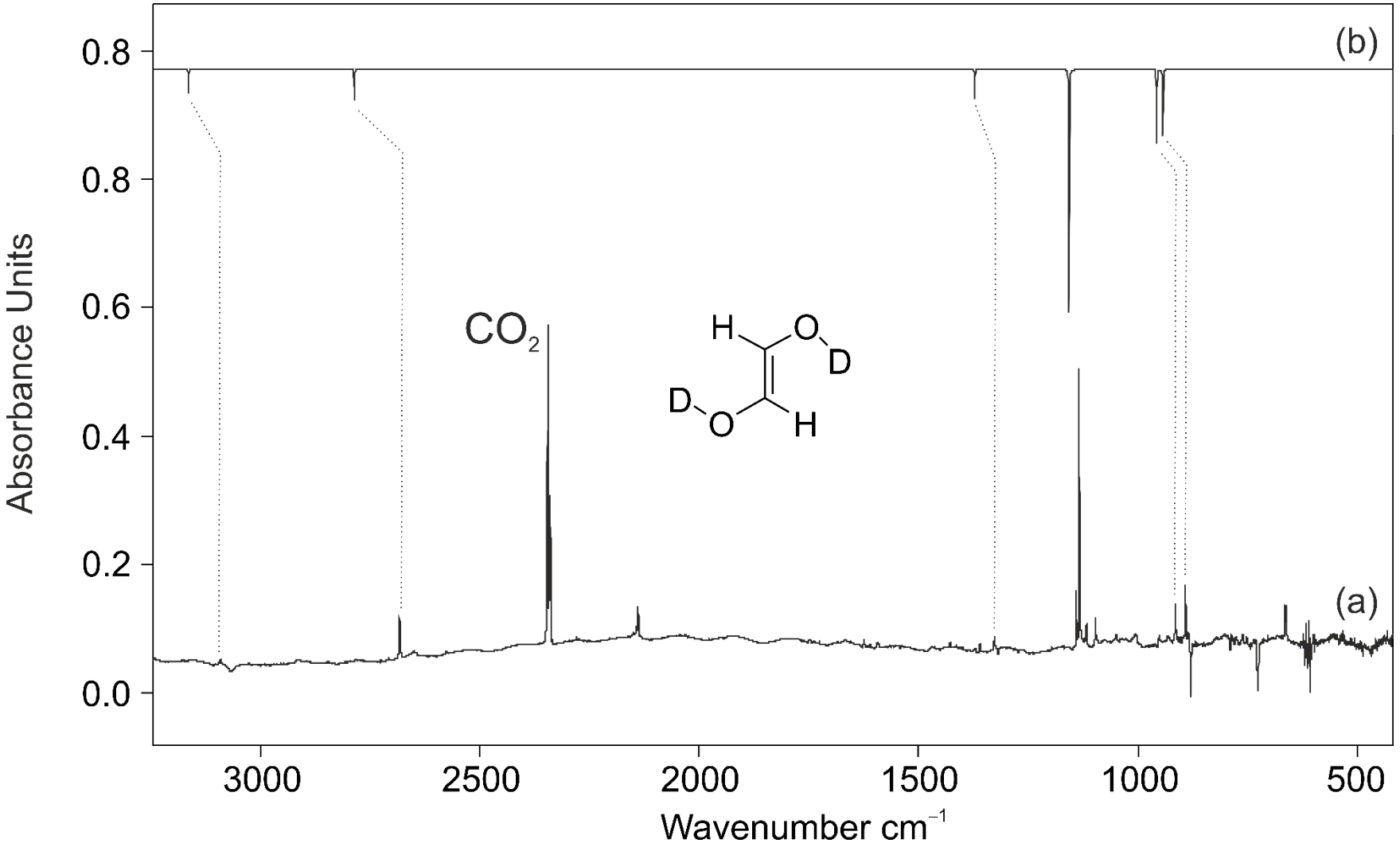
(a) IR spectrum showing the pyrolysis product of **5** with subsequent trapping in an argon matrix at 10 K. The matrix isolation spectrum of cycopentadiene was subtracted (downward bands). (b) IR spectrum of *E*-**2sa** computed at AE-CCSD(T)/cc-pVTZ (unscaled).

Trans-1,2-ethenediol



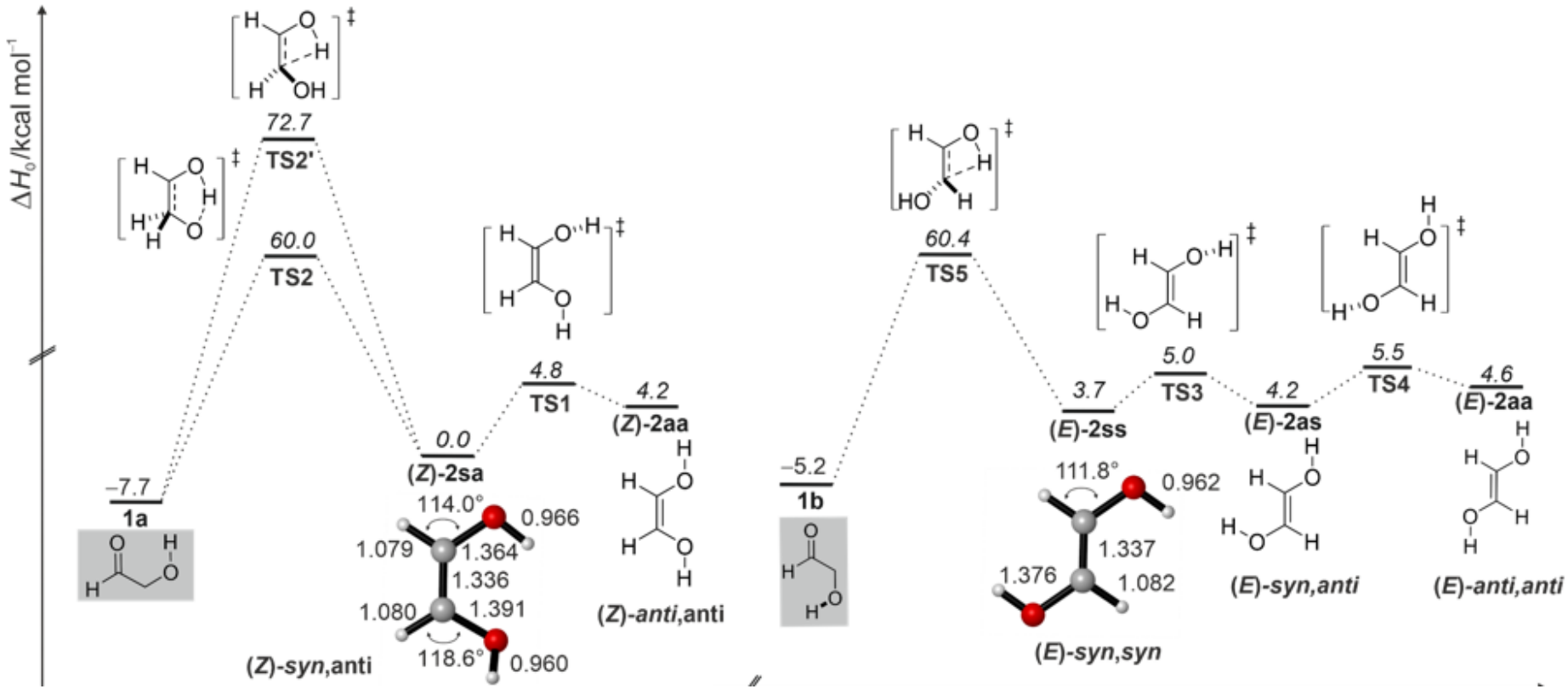
Solid line: UV/Vis spectrum showing the pyrolysis product of **5** with subsequent trapping in an argon matrix at 10 K. Dashed line: after irradiation at l = 254 nm for 30 min in argon at 10 K. Dotted line: UV/Vis spectrum of matrix-isolated **6** in argon at 10 K. Inset: computed [TD-B3LYP/6-311++G(2d,p)] electronic transitions for *E*-**2**.

Trans-1,2-ethenediol



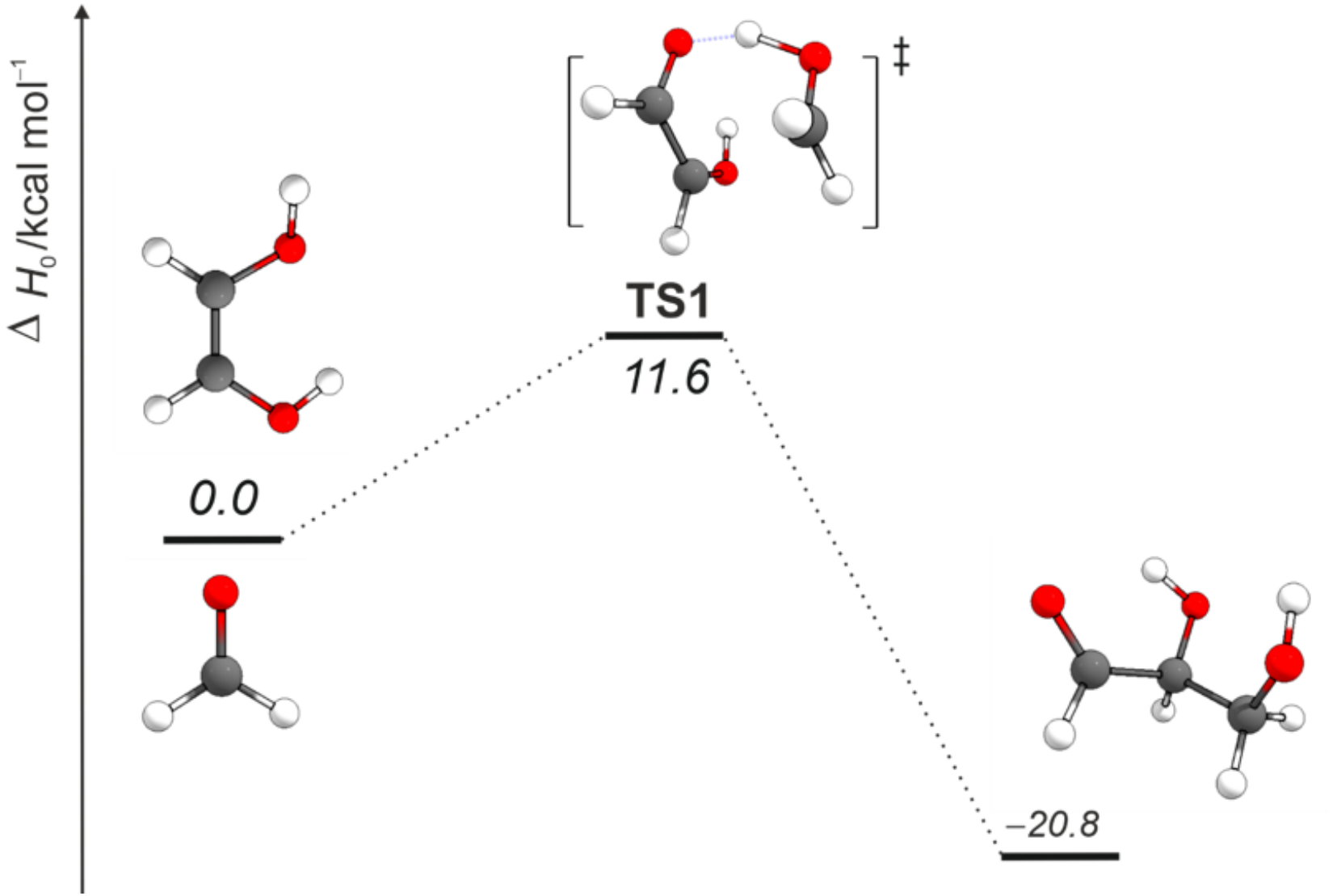
(a) IR spectra showing the product of pyrolysis (700 °C) of d_2-**5** in argon matrix with subsequent trapping in an argon matrix at 10 K. The matrix isolation spectrum of antracene was subtracted (downward bands). (b) IR spectrum of d_2-E-**2** computed at AE-CCSD(T)/cc-pVTZ (unscaled).

Potential Energy Profile

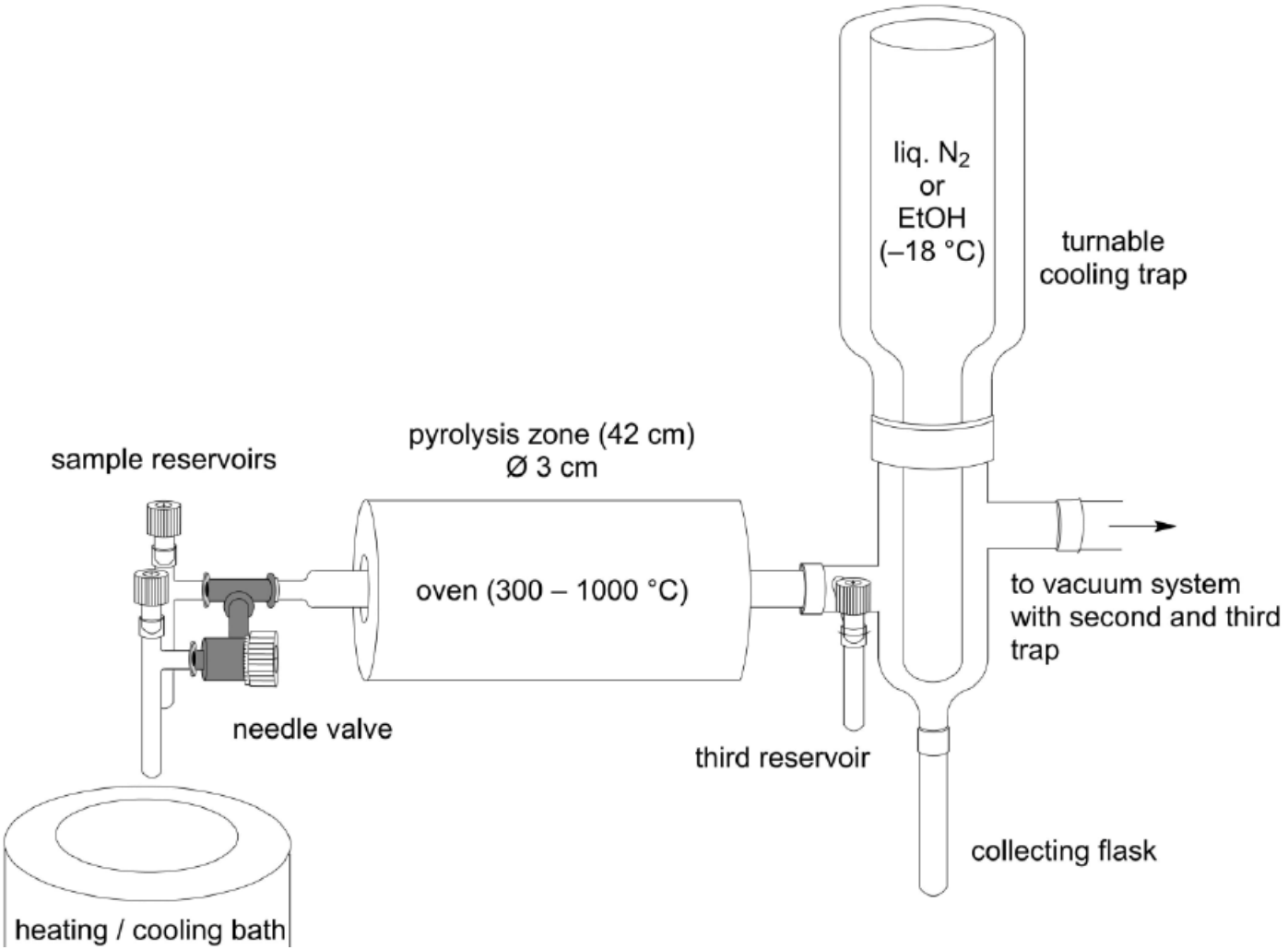


Potential energy profile (ΔH_0) in kcal mol^{-1} of the reactions of enols **2** at AE-CCSD(T)/cc-pVTZ + ZPVE at 0 K.

Formation of glyceraldehyde through enol-CH_2O reaction

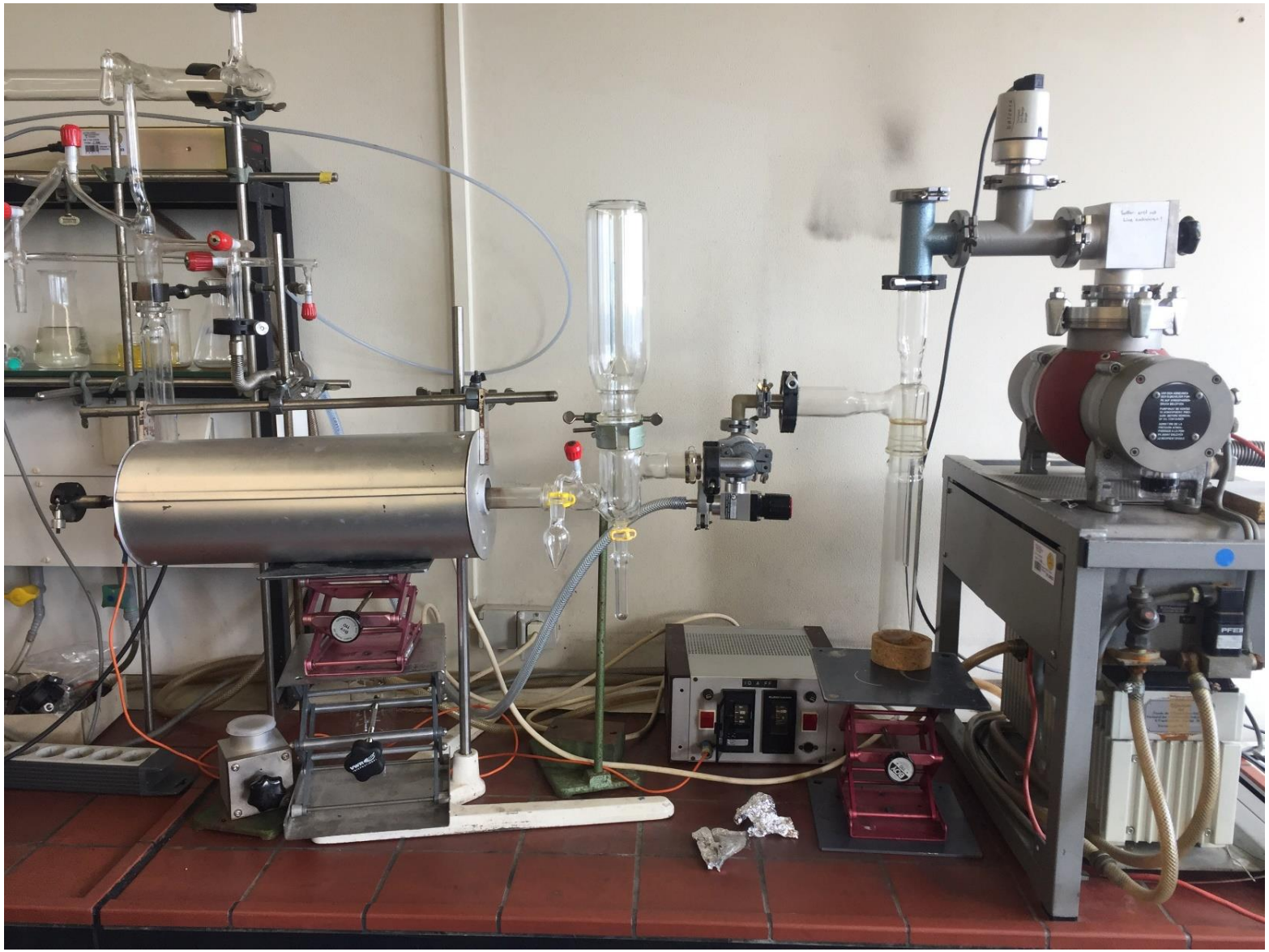


Preparative Flash Vacuum Pyrolysis – Flow Pyrolysis



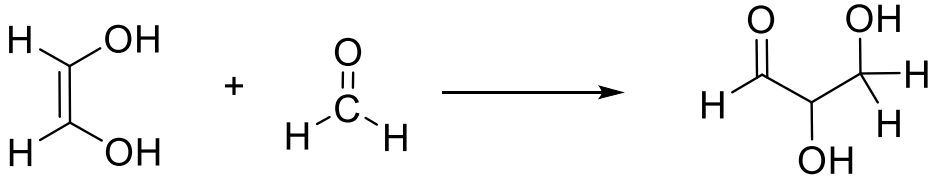
C. Wentrup, *Angew. Chem. Int. Ed.* **2017**, *56*, 14808

Preparative Flash Vacuum Pyrolysis – Flow Pyrolysis



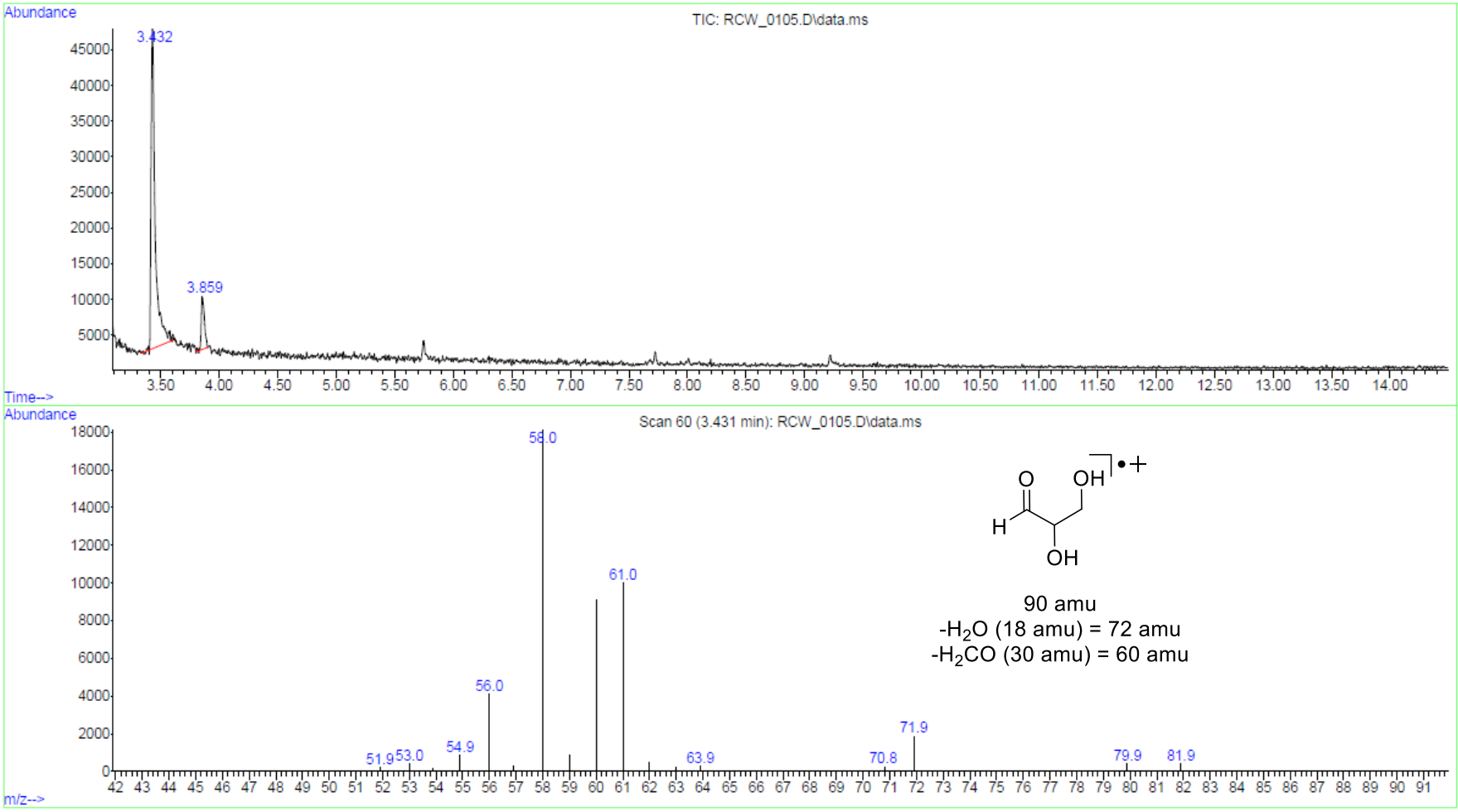
C. Wentrup, *Angew. Chem. Int. Ed.* **2017**, *56*, 14808

Gas Phase Aldol Reaction



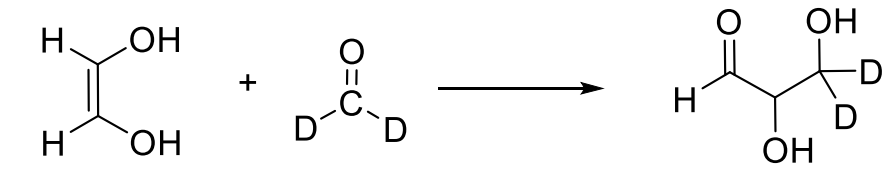
cis-
1,2-ethenediol

glyceraldehyde



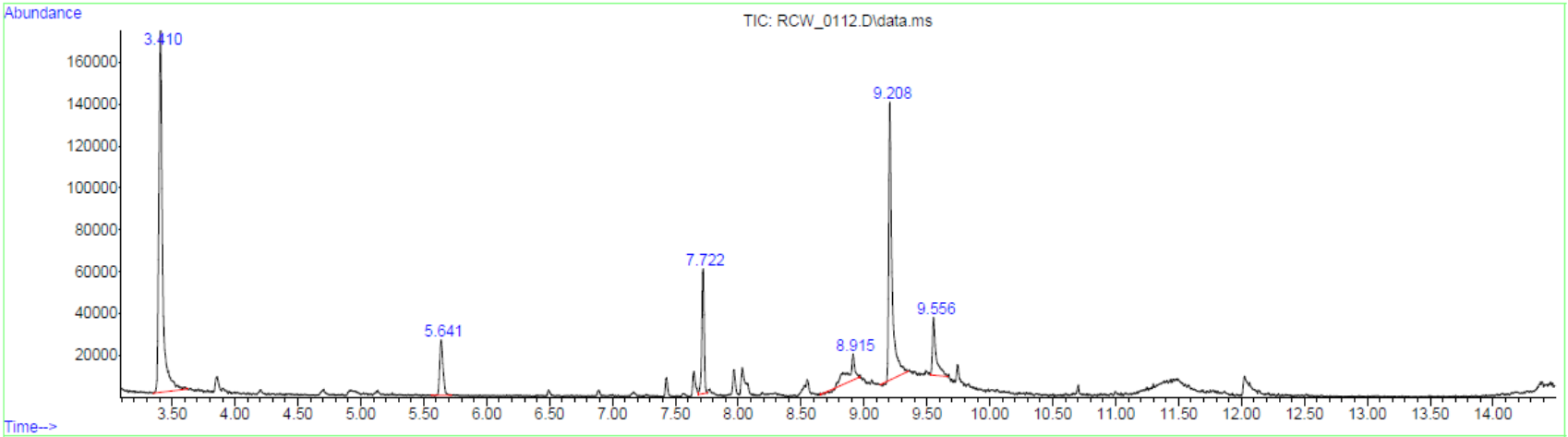
90 amu
-H_2O (18 amu) = 72 amu
-H_2CO (30 amu) = 60 amu

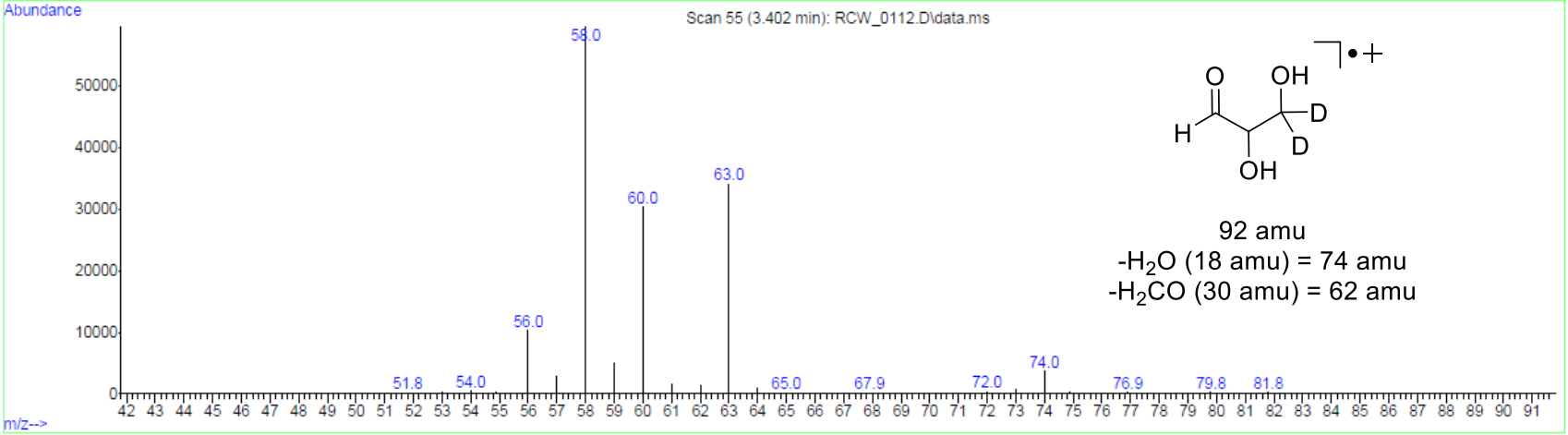
Gas Phase Aldol Reaction – Isotope Labelling



cis-
1,2-ethenediol

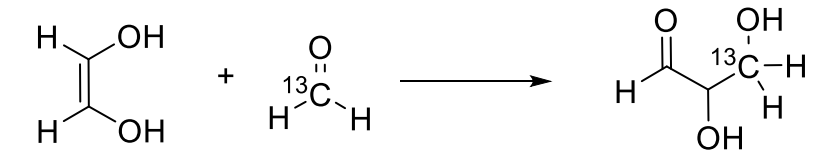
glyceraldehyde





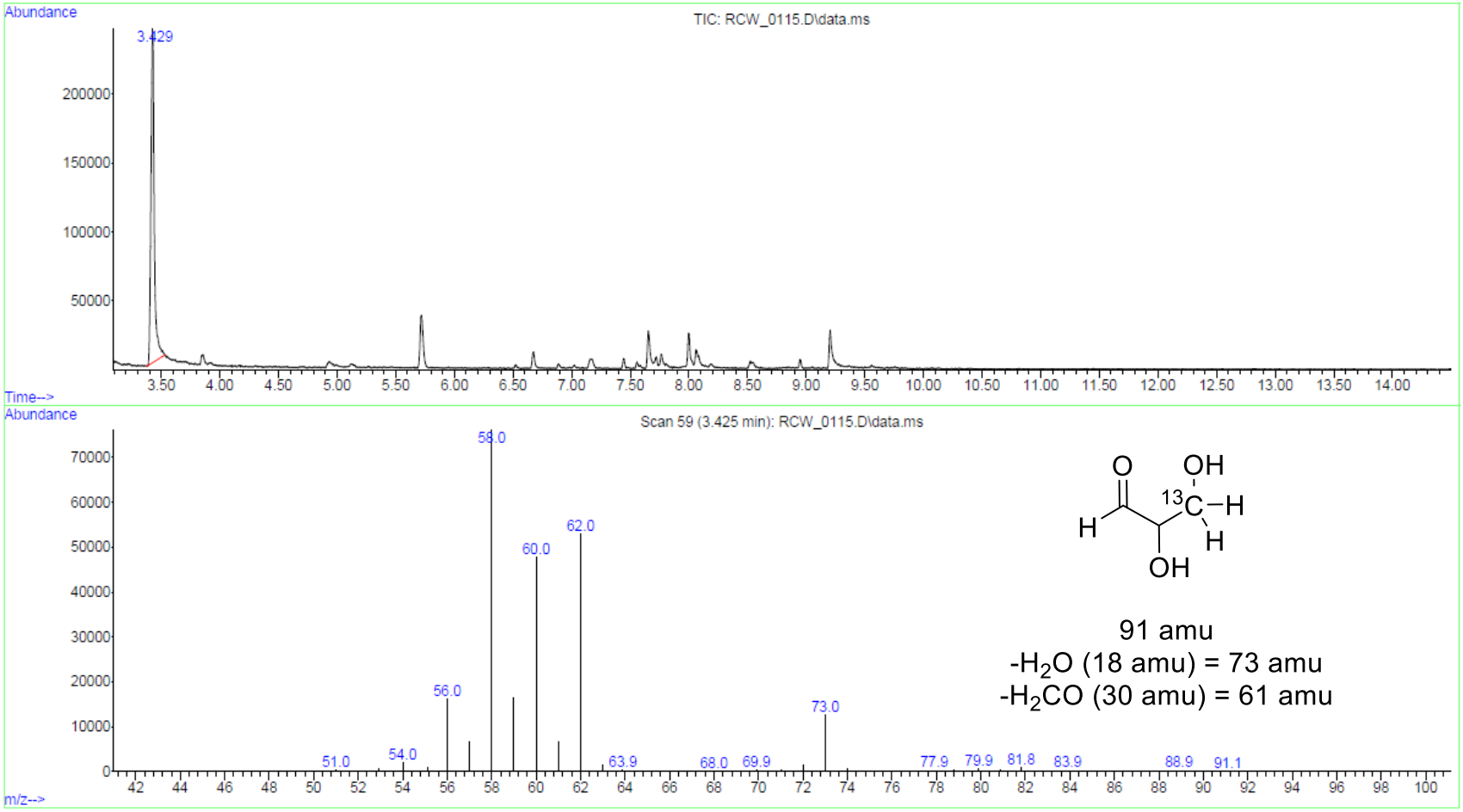
92 amu
-H_2O (18 amu) = 74 amu
-H_2CO (30 amu) = 62 amu

Gas Phase Aldol Reaction – Isotope Labelling



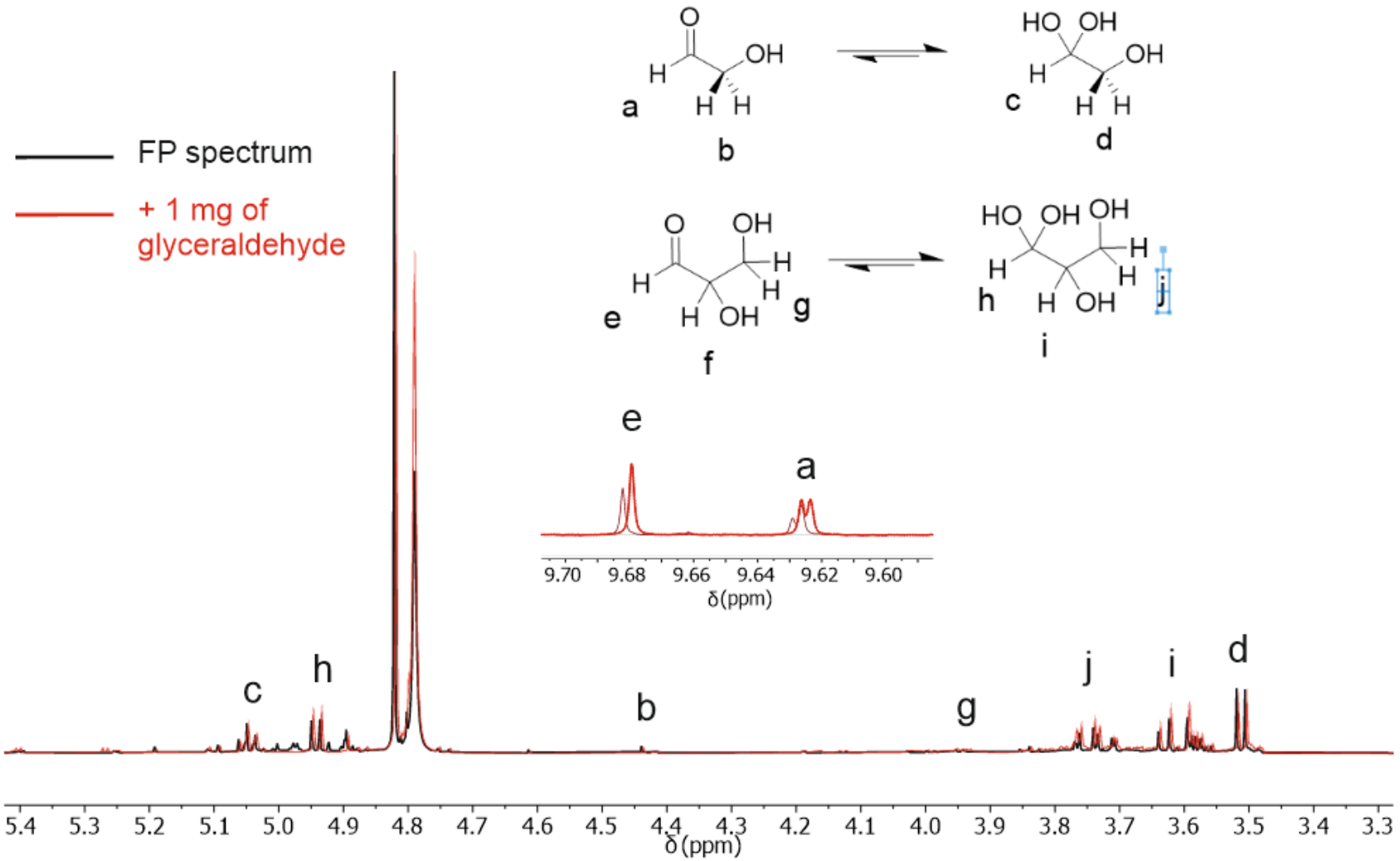
cis-
1,2-ethenediol

glyceraldehyde



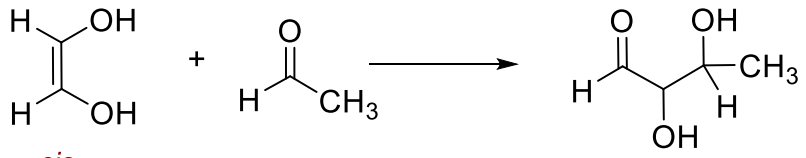
91 amu
-H_2O (18 amu) = 73 amu
-H_2CO (30 amu) = 61 amu

Gas Phase Aldol Reaction – NMR

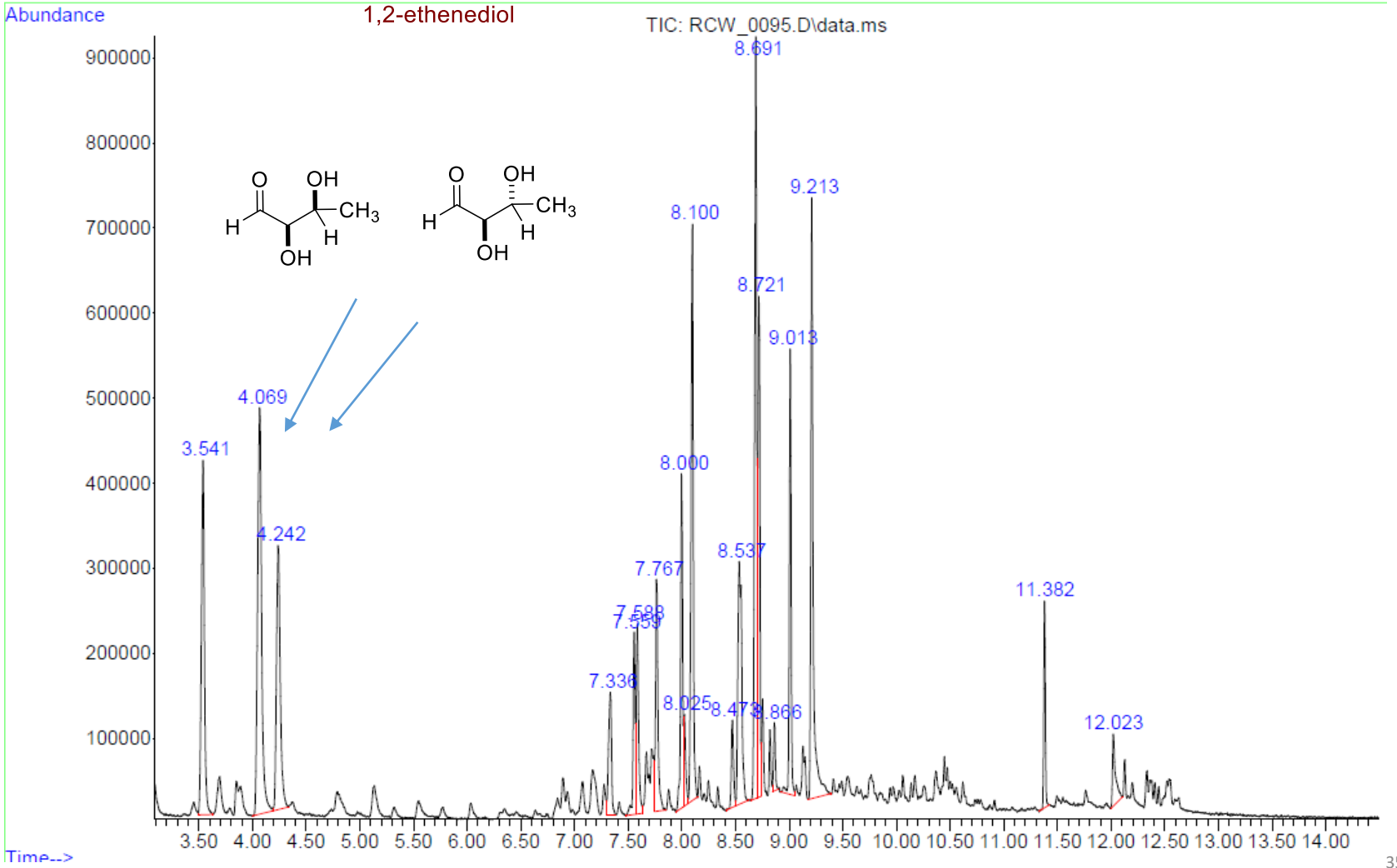


^{1}H NMR (400 MHz; D_2O) spectrum immediately taken after 100 min flow pyrolysis of the diol and formaldehyde.

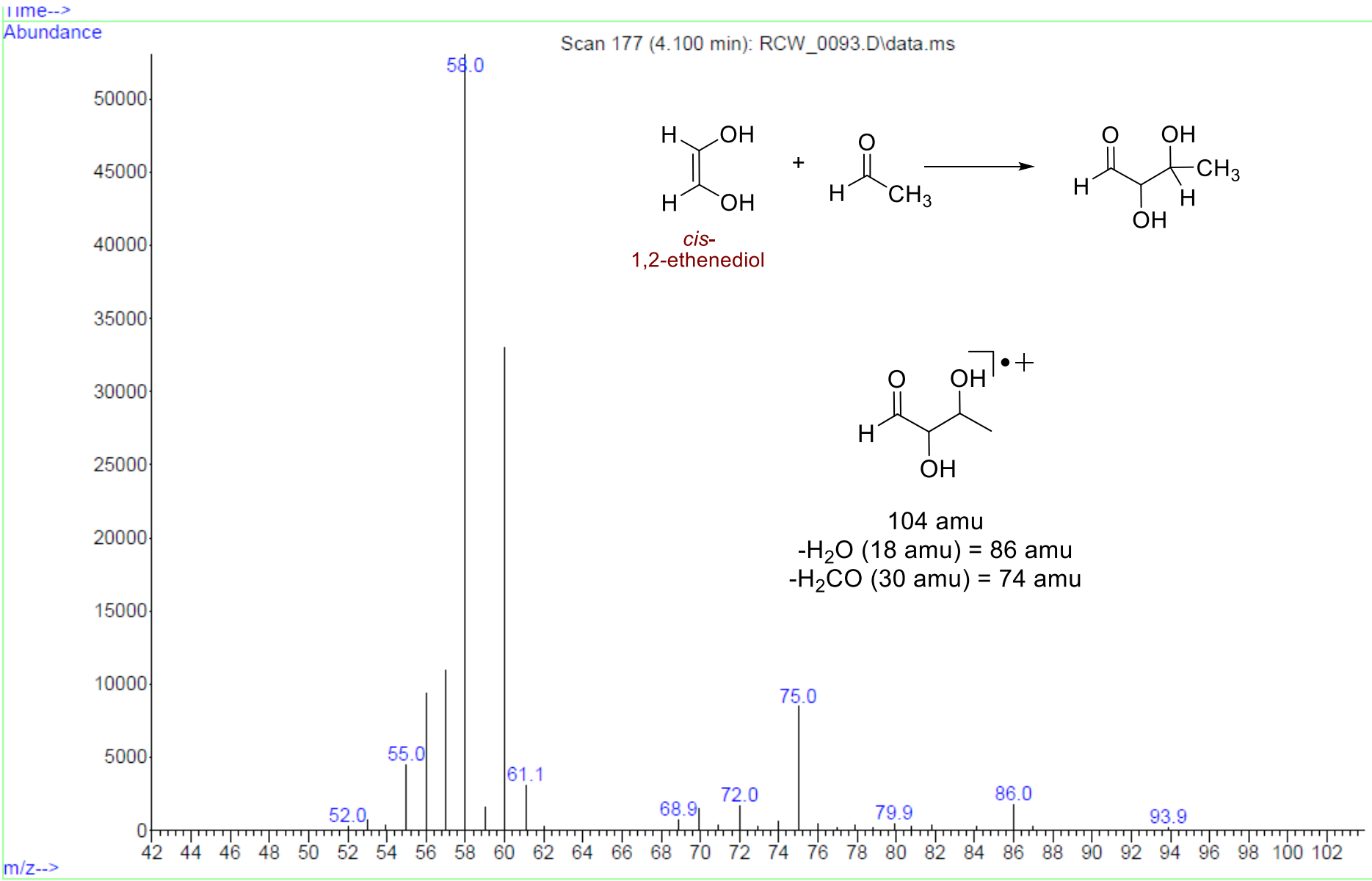
Gas Phase Aldol Reaction with Acetaldehyde



cis-
1,2-ethenediol



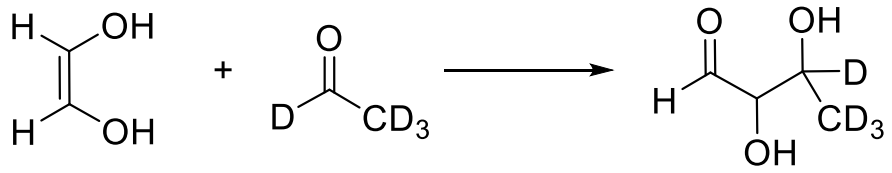
Gas Phase Aldol Reaction – Acetaldehyde



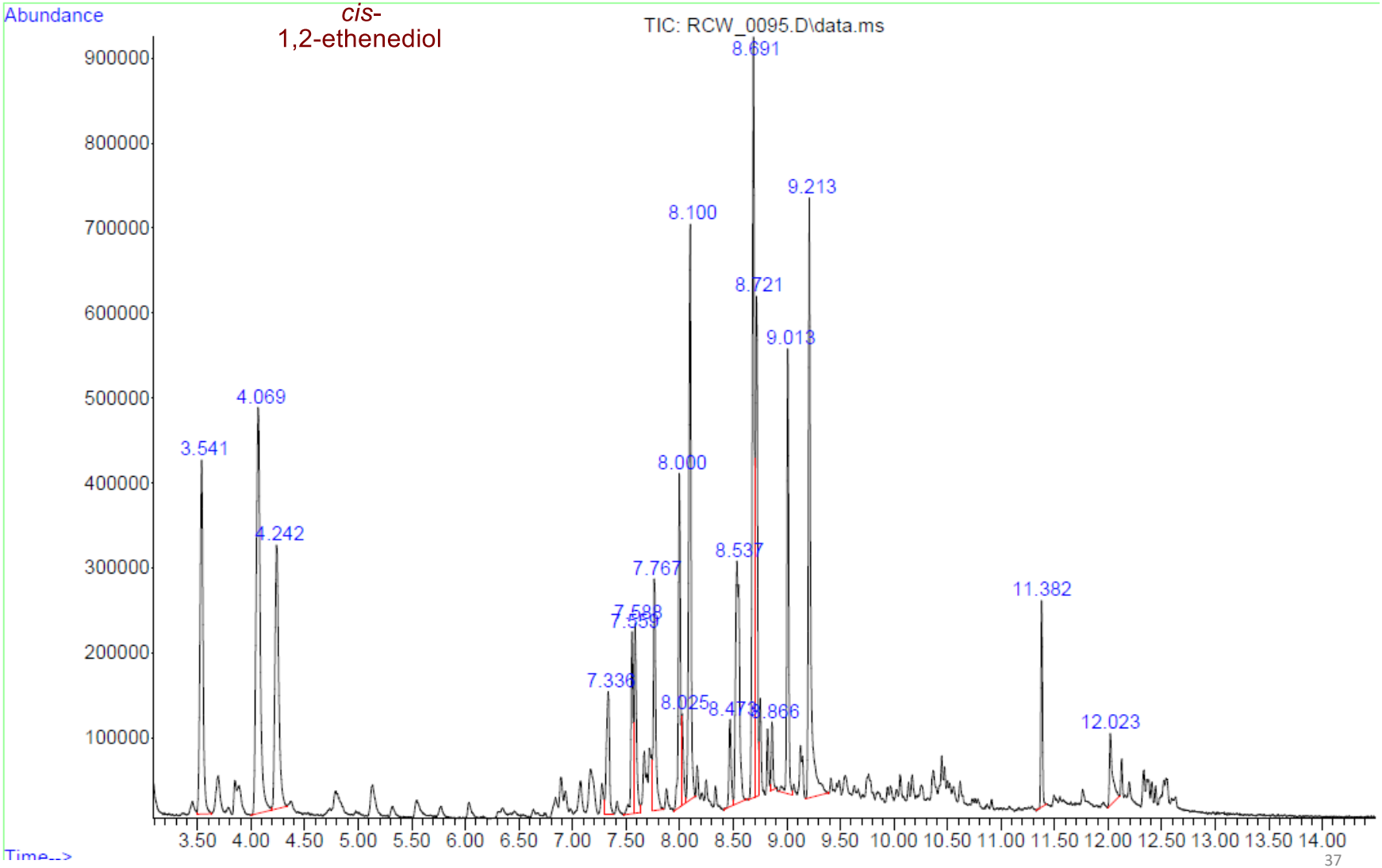
cis-
1,2-ethenediol

104 amu
-H_2O (18 amu) = 86 amu
-H_2CO (30 amu) = 74 amu

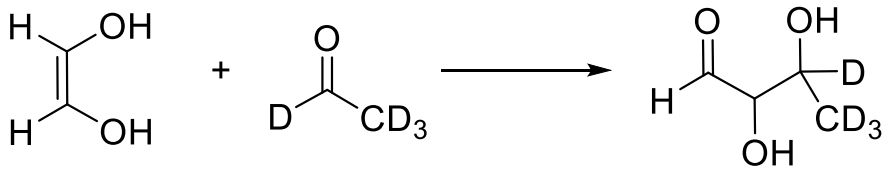
Gas Phase Aldol Reaction with Acetaldehyde-d_4



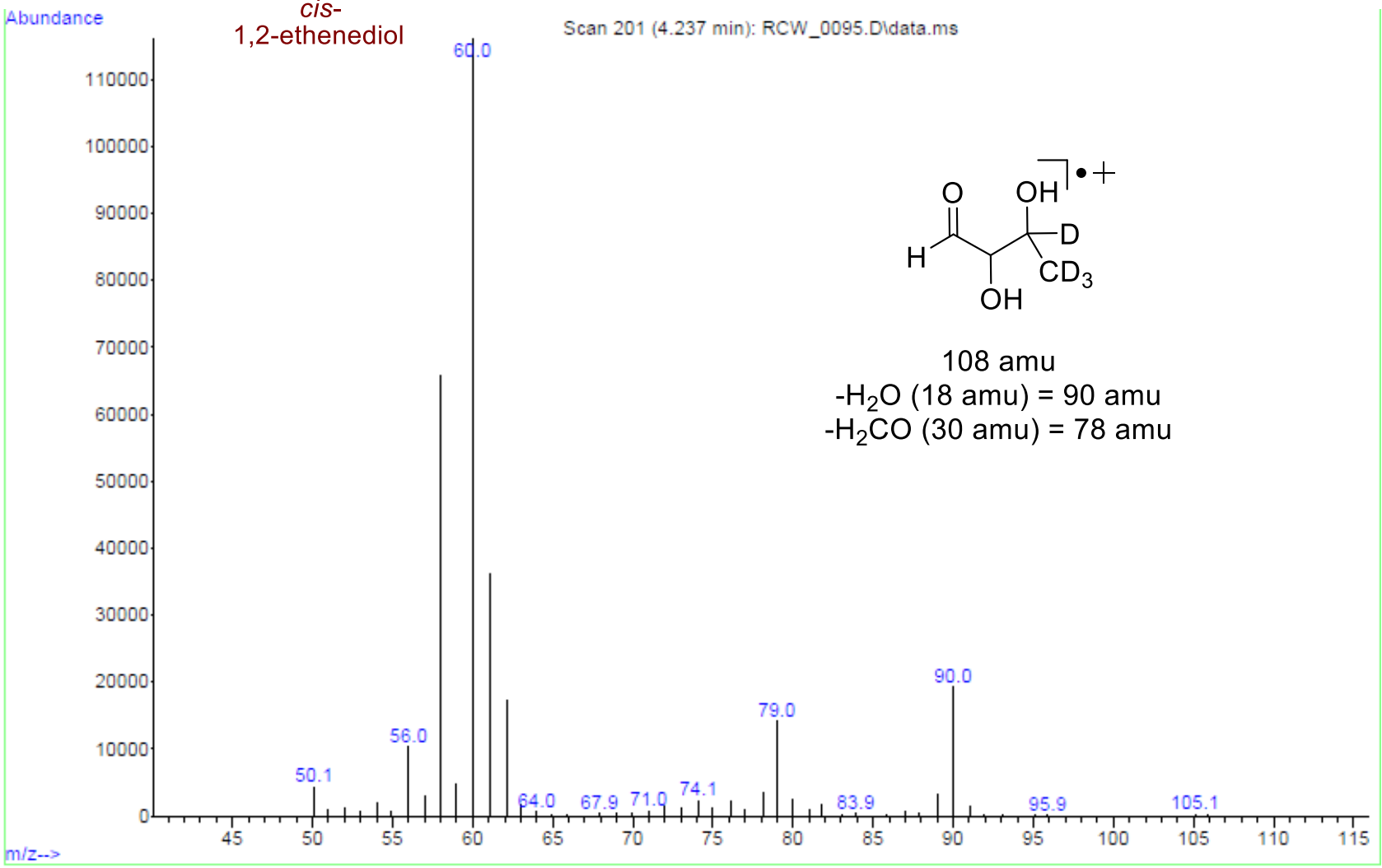
cis-
1,2-ethenediol



Gas Phase Aldol Reaction – Acetaldehyde-d_4

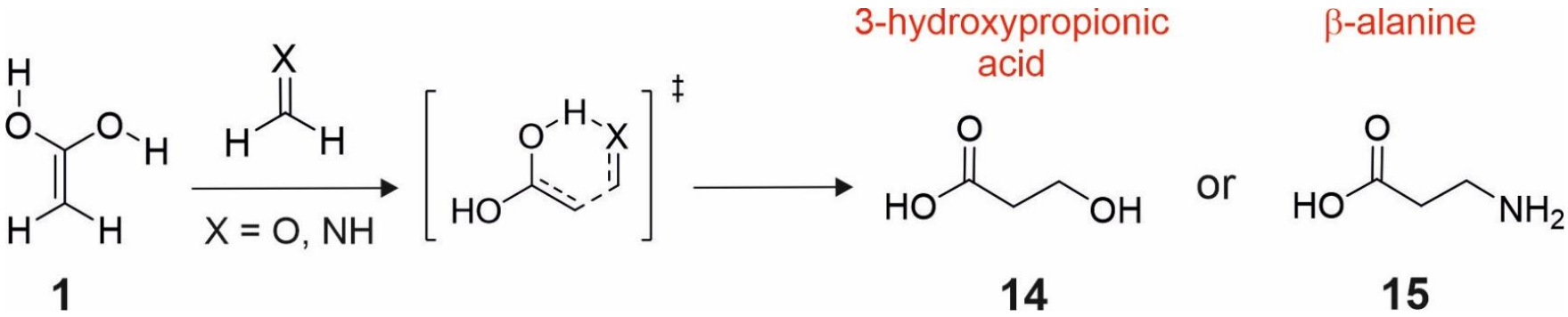


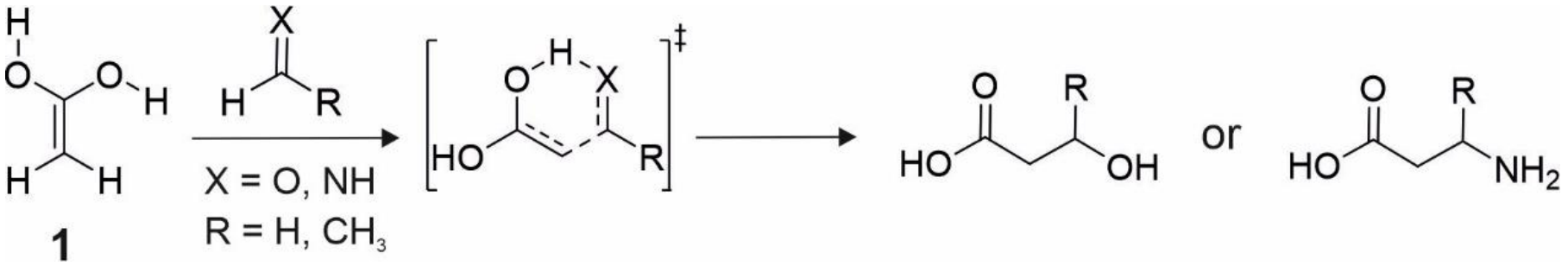
cis-
1,2-ethenediol



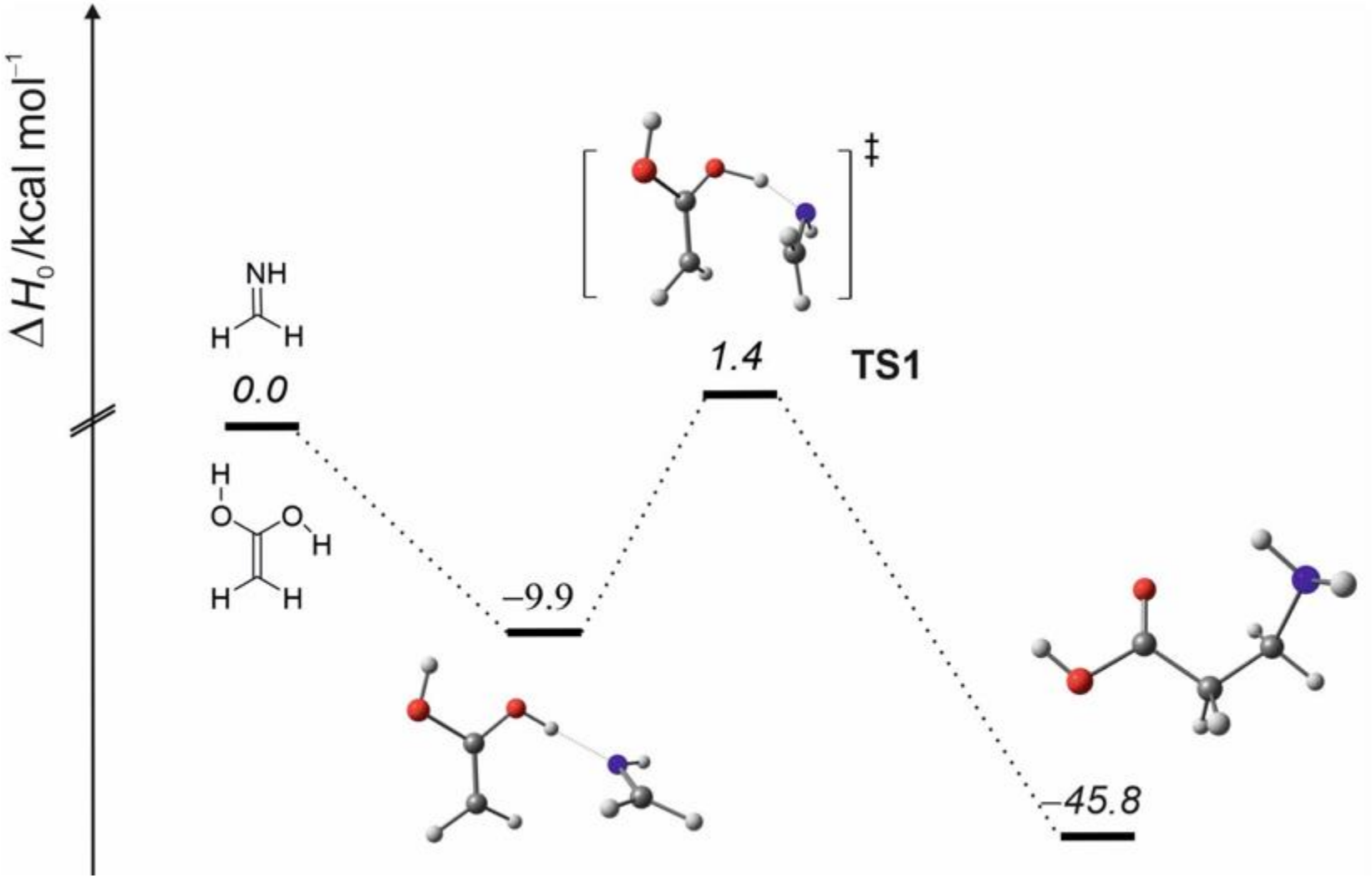
108 amu
-H_2O (18 amu) = 90 amu
-H_2CO (30 amu) = 78 amu

Formation of prebiotic amino acid(s) through enol-molecules reactions

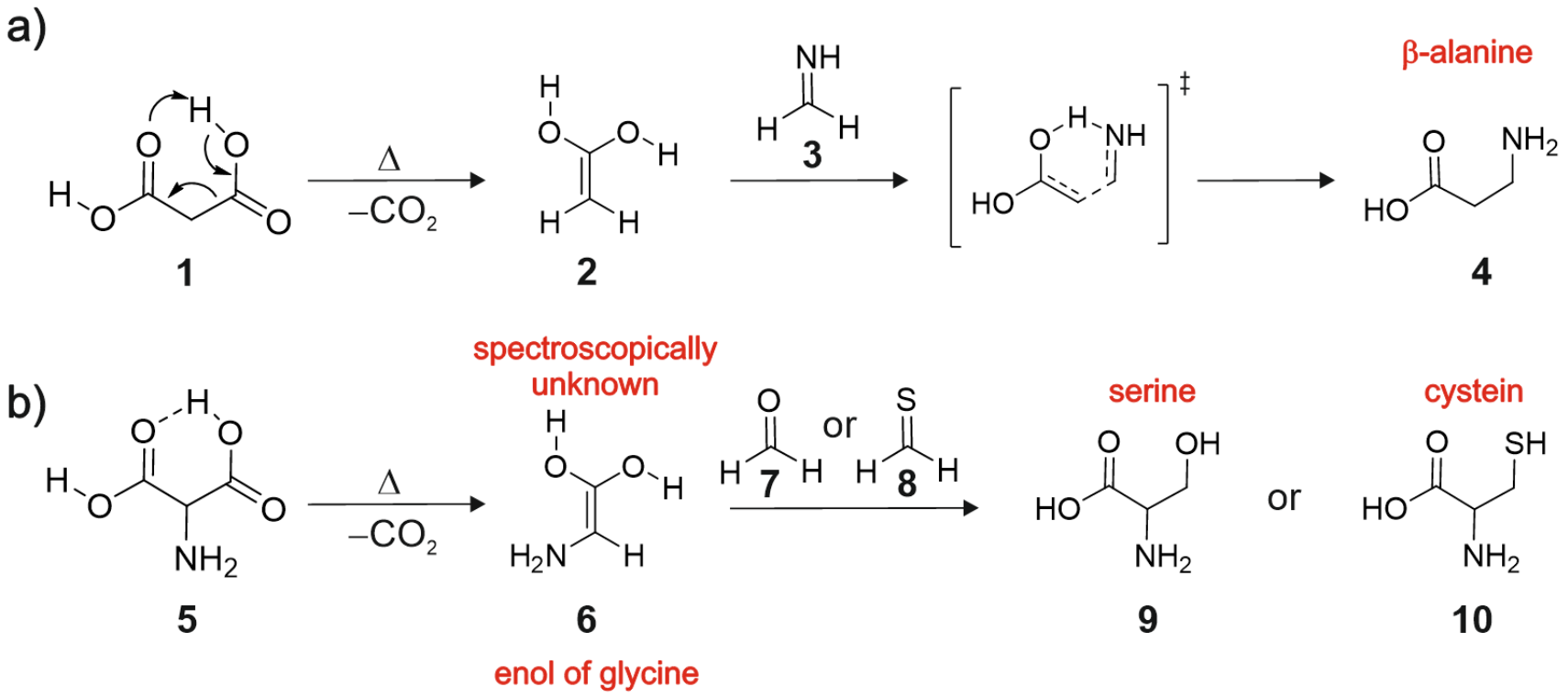




Formation of β-alanine through 1,1-ethenediol – CH_2NH reaction



The Enol of Glycine



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