Supplementary Information

Methylthiodeoxynivalenol (MTD): Insight into chemistry, structure and toxicity of thia-Michael adducts of trichothecenes

Philipp Fruhmann,[a#] Theresa Weigl-Pollack,[a#] Hannes Mikula,*[a]
Gerlinde Wiesenberger,[b] Gerhard Adam,[b] Elisabeth Varga,[c] Franz Berthiller,[c] Rudolf Krska,[c]
Christian Hametner,[a] Johannes Fröhlich[a]

[a] *Institute of Applied Synthetic Chemistry, Vienna University of Technology (VUT), Getreidemarkt 9/163, 1060 Vienna, Austria.*
E-mail: hannes.mikula@tuwien.ac.at

[b] *Department of Applied Genetics and Cell Biology, University of Natural Resources and Life Sciences, Vienna (BOKU), Konrad Lorenz Str. 24, 3430 Tulln, Austria.*

[c] *Christian Doppler Laboratory for Mycotoxin Metabolism and Center for Analytical Chemistry, Department for Agrobiotechnology (IFA-Tulln), University of Natural Resources and Life Sciences, Vienna (BOKU), Konrad Lorenz Str. 20, 3430 Tulln, Austria.*

Table of Contents

1. NMR spectra of compounds 6b, 8, 9 and 11

Figure S1: ^{1}H NMR spectrum of compound **6b**

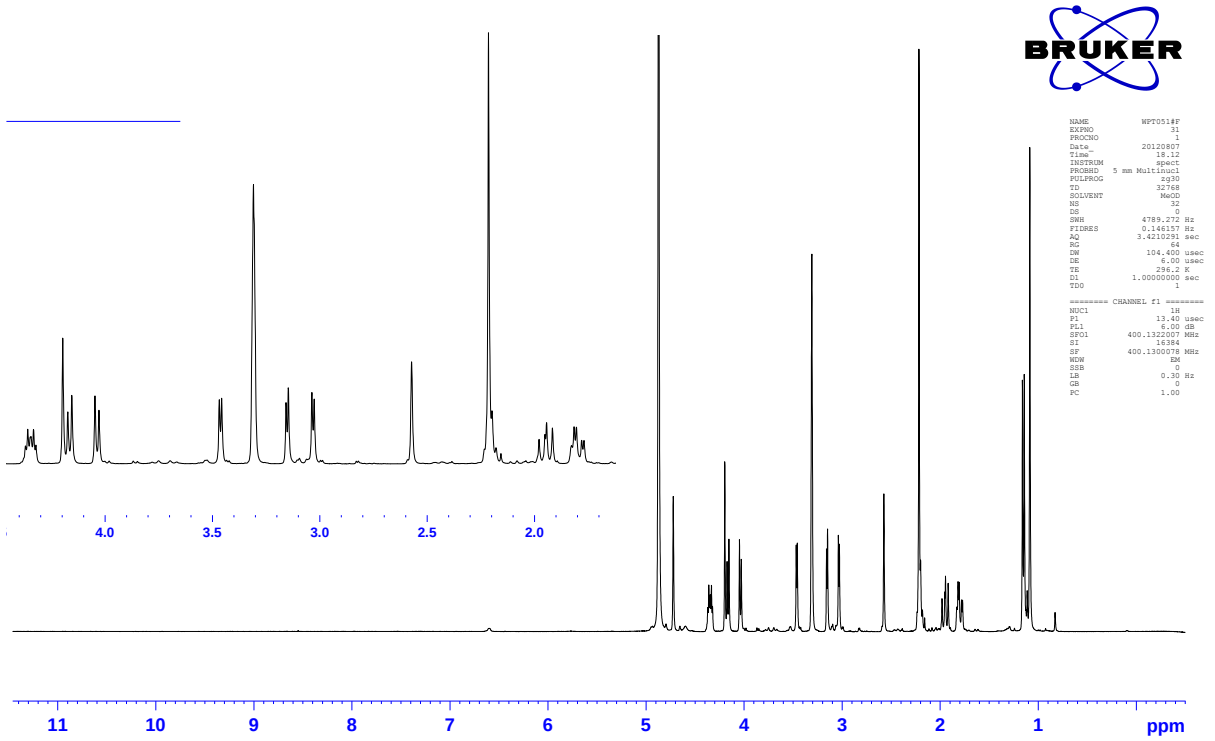


Figure S2: ^{13}C NMR spectrum of compound **6b**

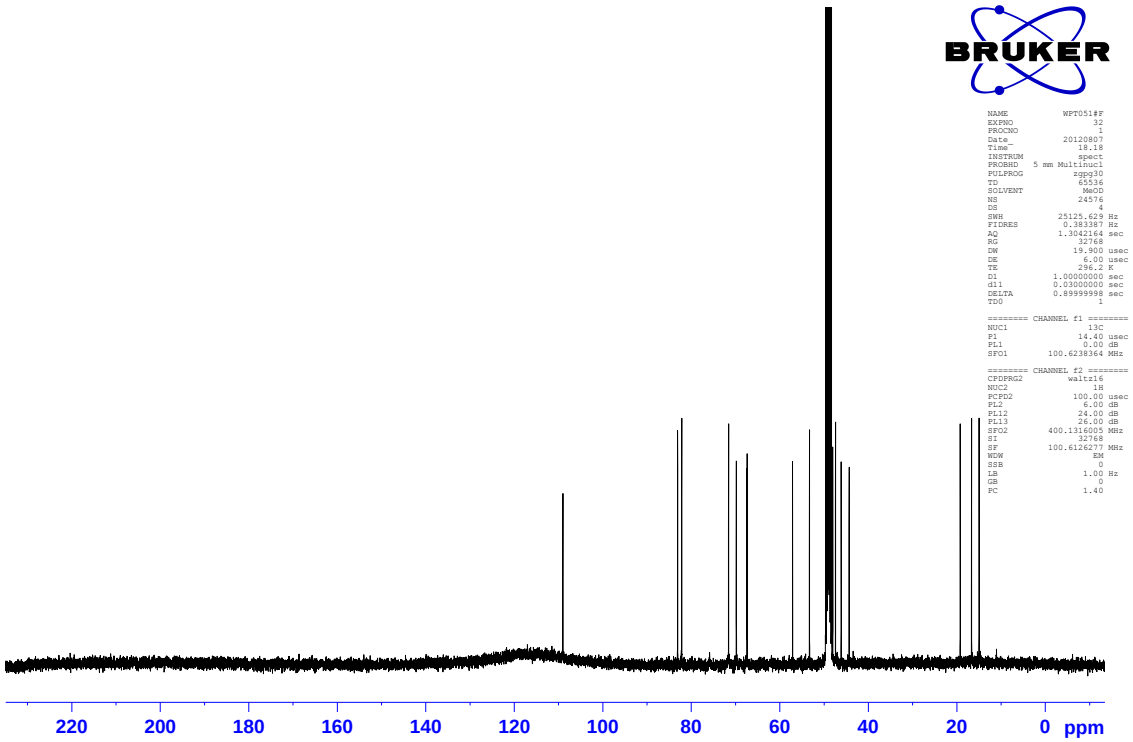


Figure S3: COSY spectrum of compound **6b**

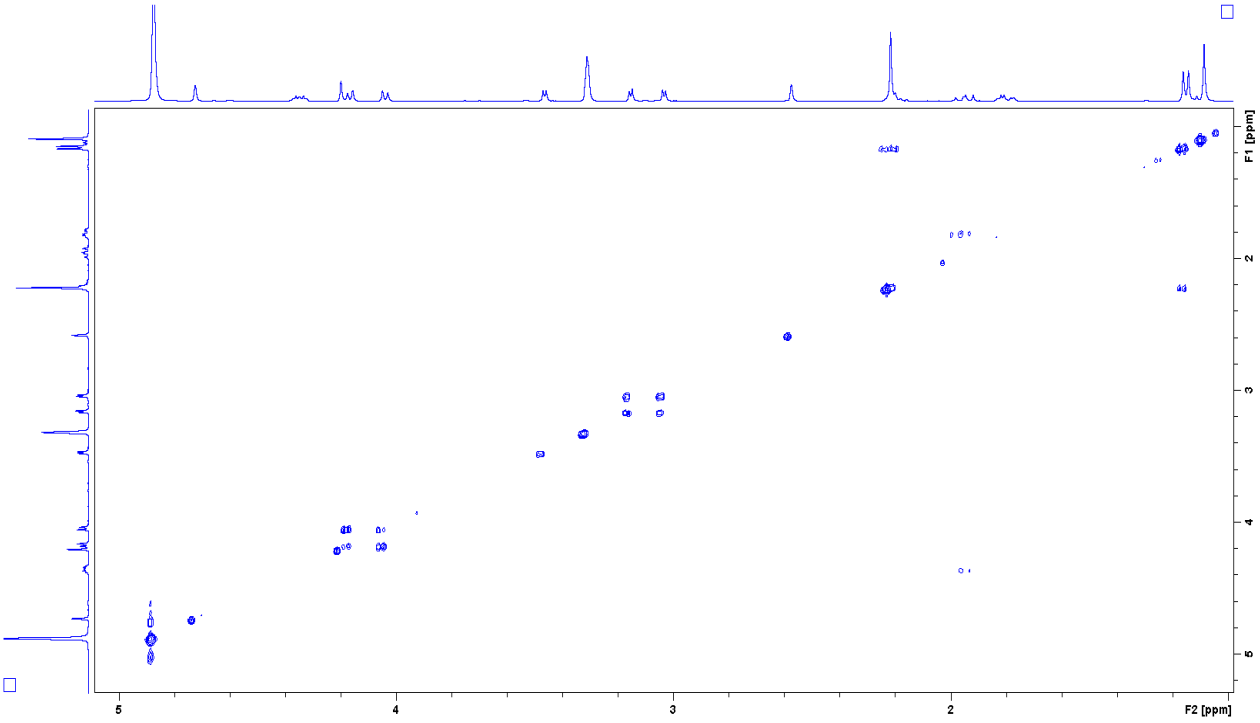


Figure S4: HSQC spectrum of compound **6b**

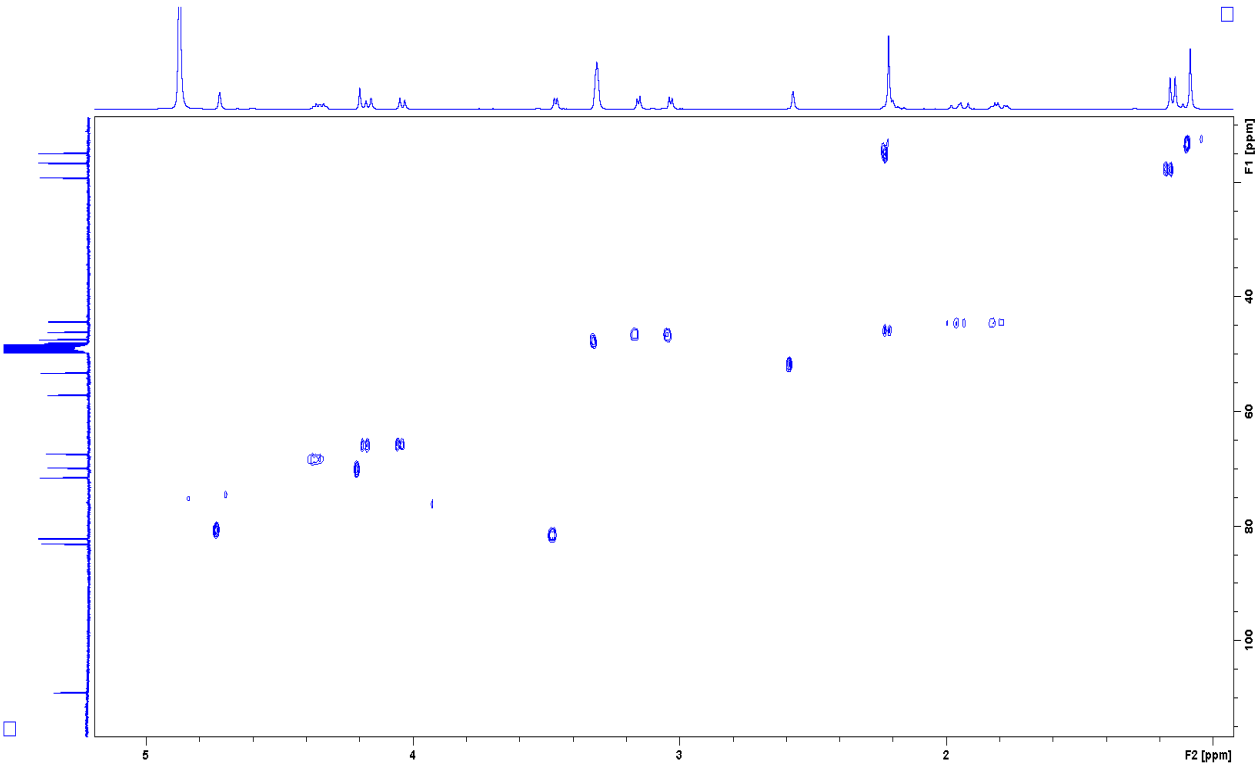


Figure S5: HMBC spectrum of compound **6b**

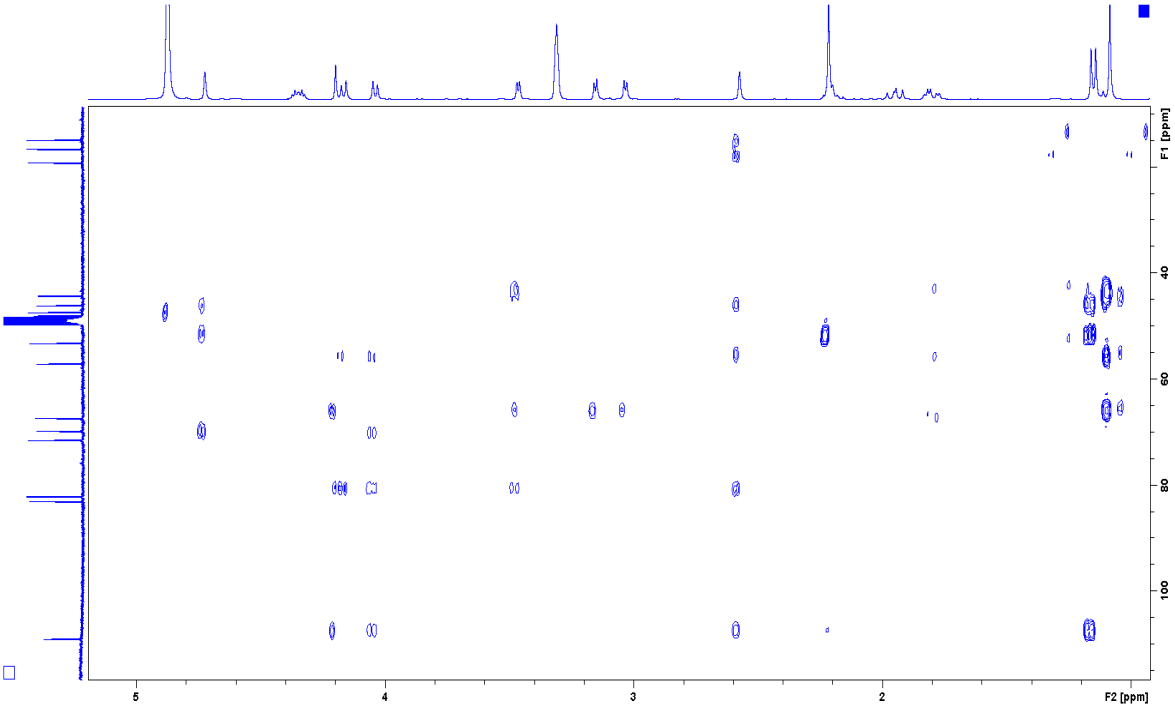


Figure S6: HR-MS spectra of compound **6b**

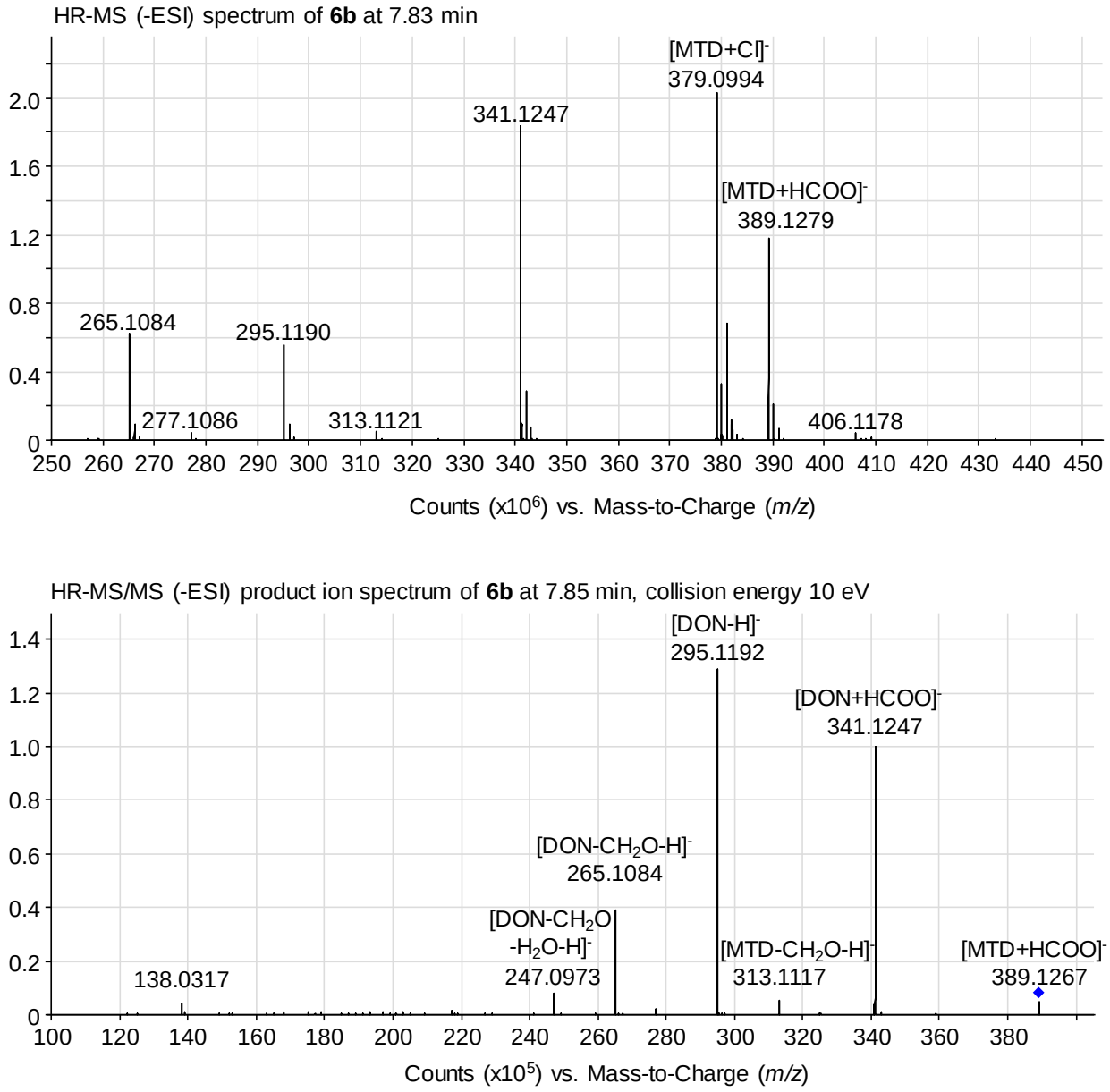
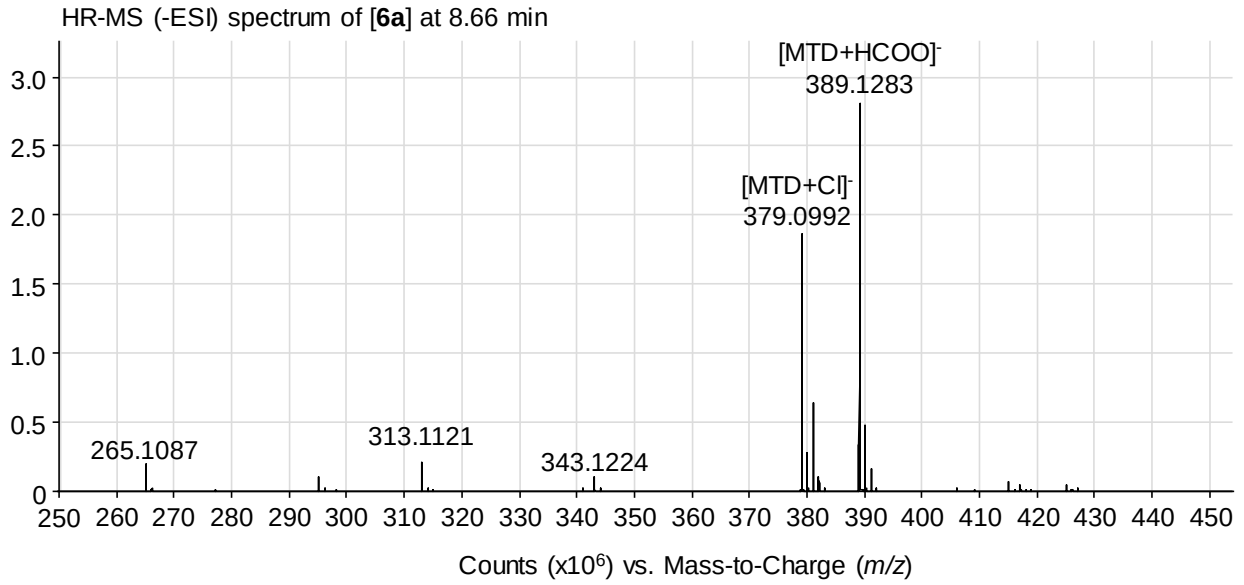


Figure S7: HR-MS spectra of compound [**6a**]



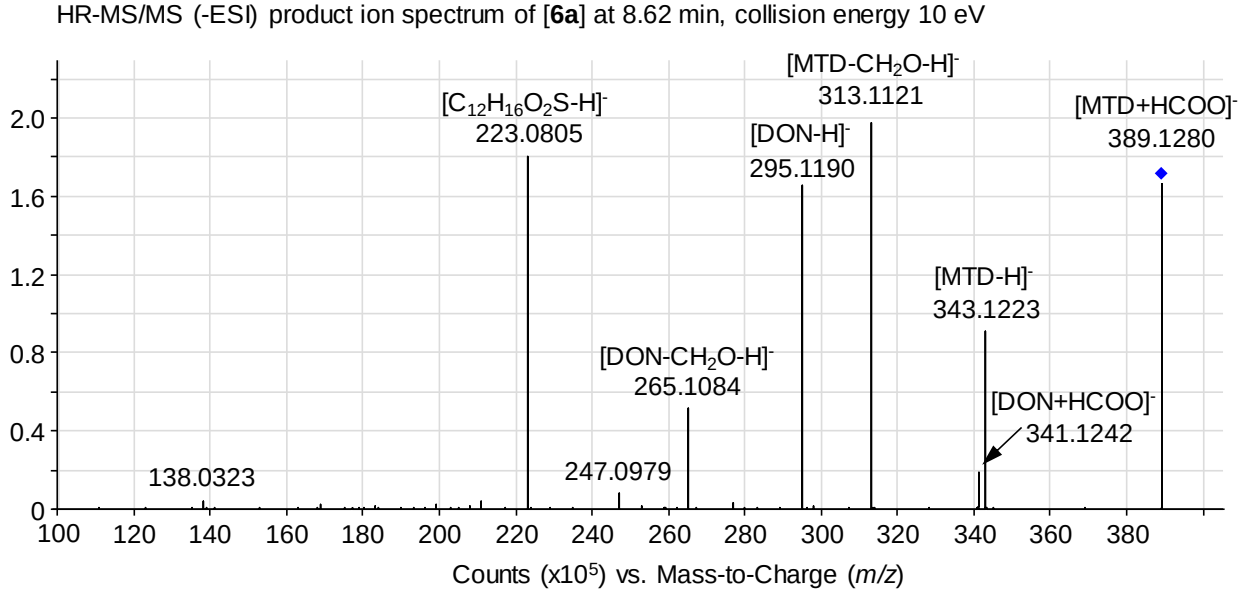


Figure S8: ^{1}H NMR spectrum of compound **8**

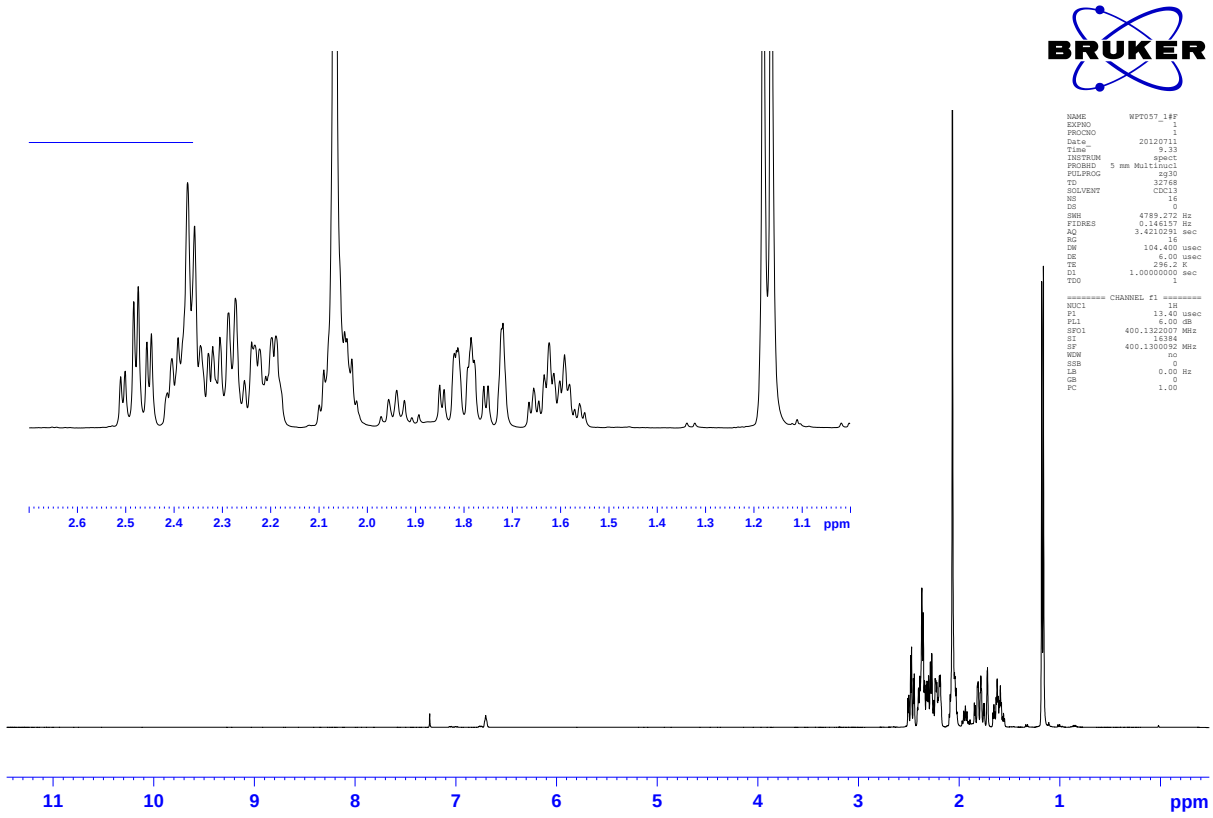


Figure S9: ^{13}C NMR (APT) spectrum of compound **8**

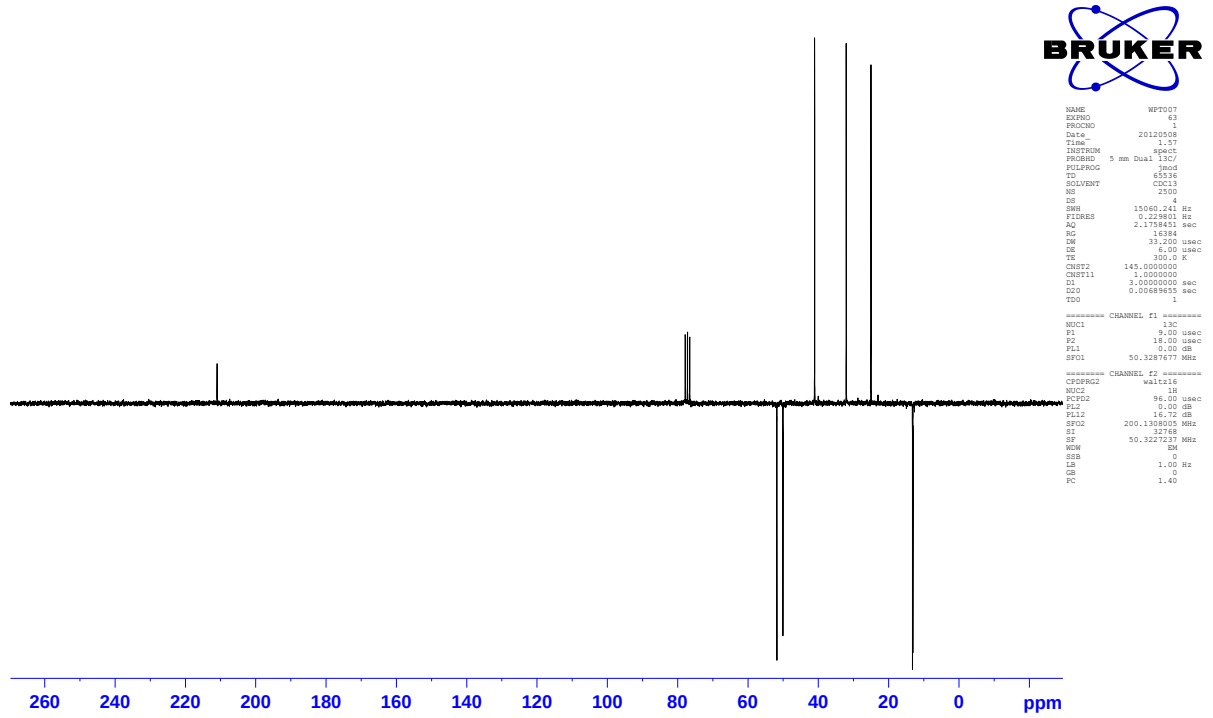


Figure S10: ^{1}H NMR spectrum of compound **9**

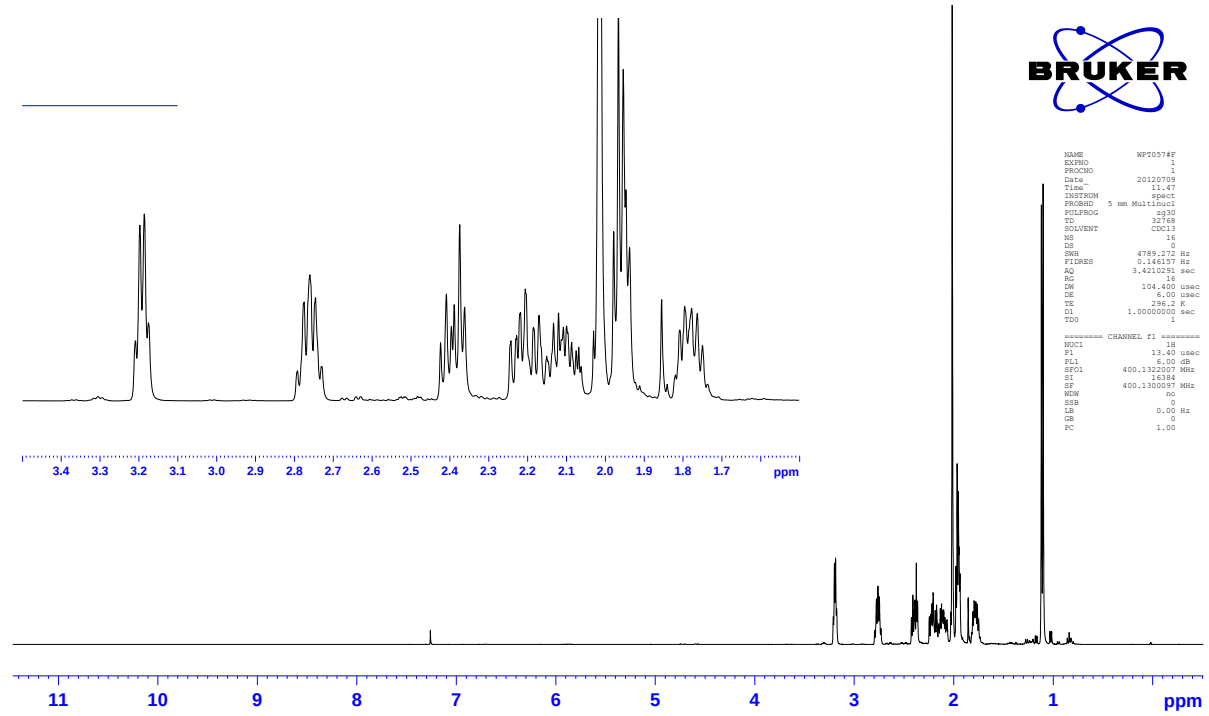


Figure S11: ^{13}C NMR (APT) spectrum of compound **9**

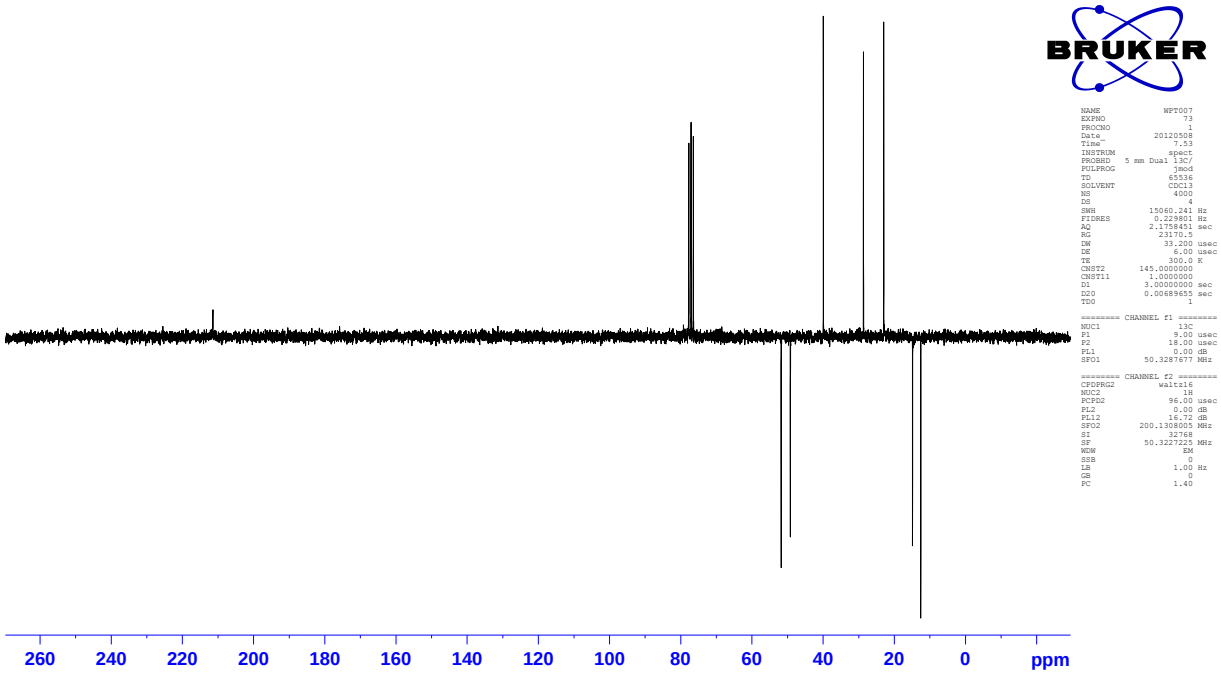


Figure S12: ^{1}H NMR spectrum of compound **11**

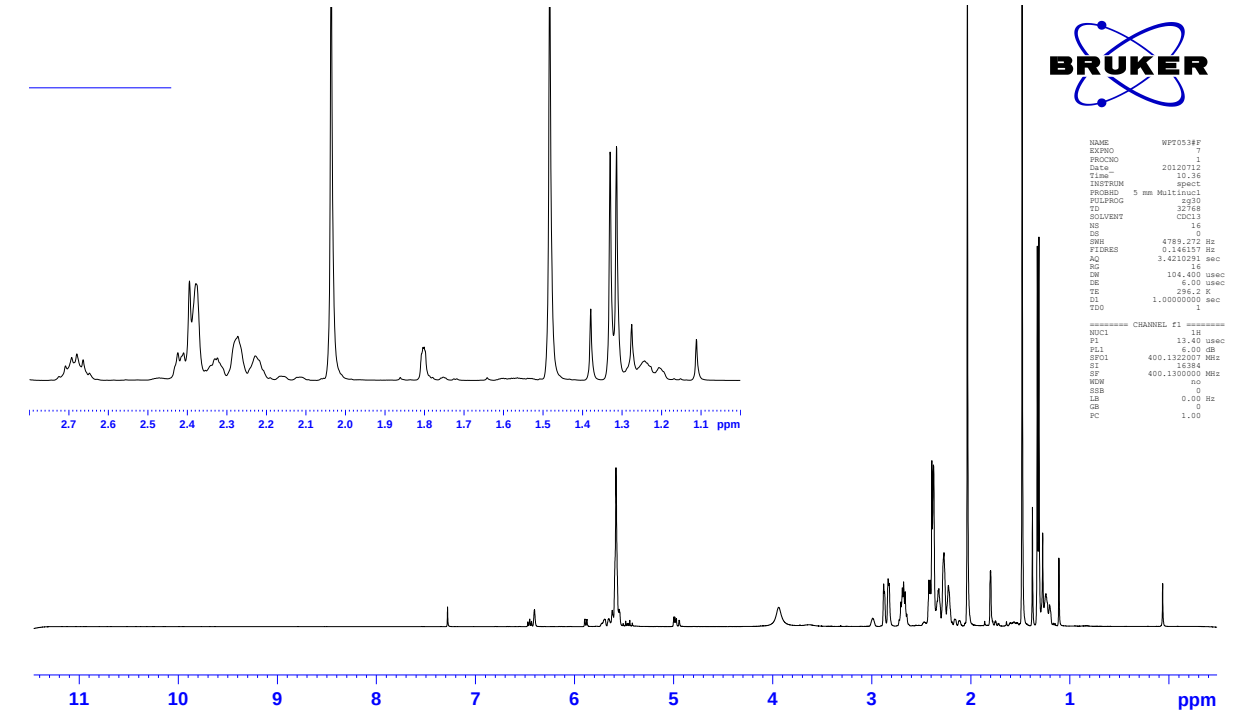
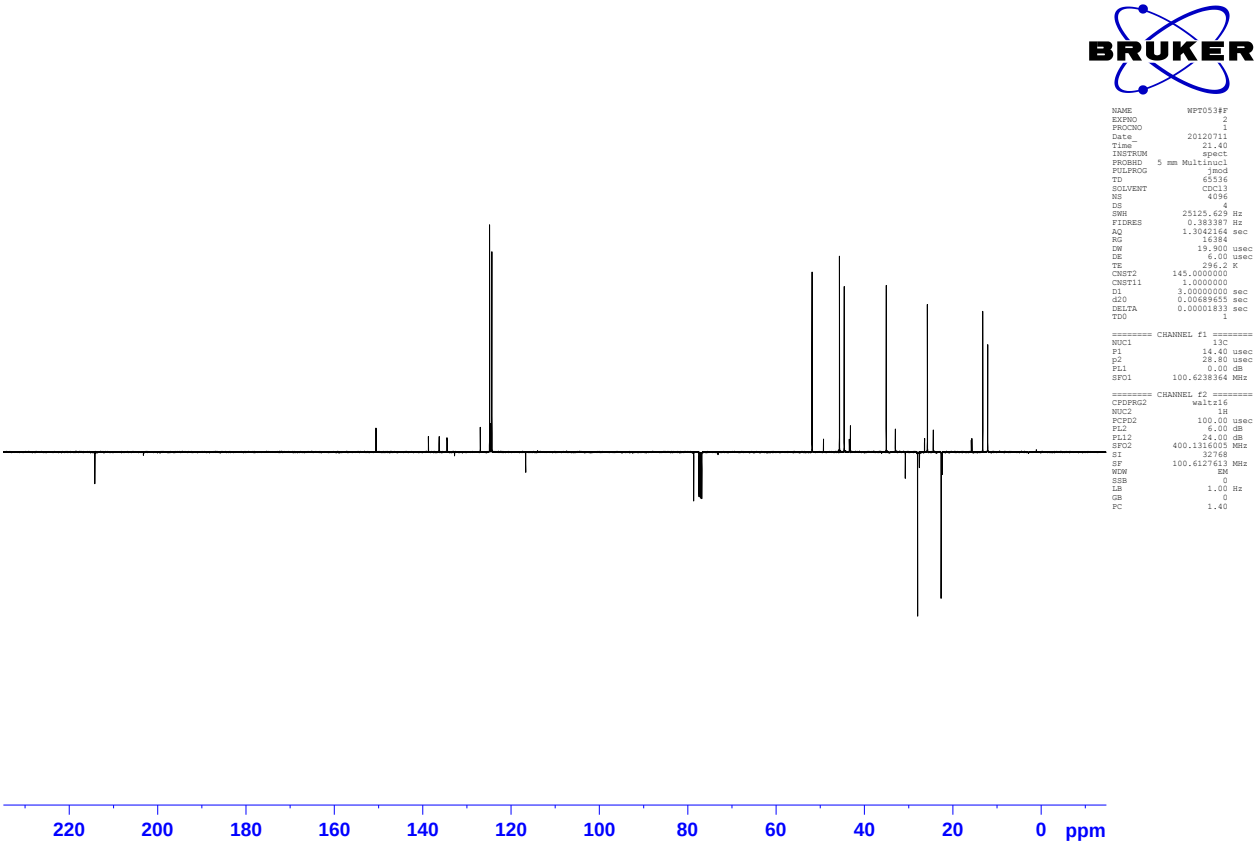


Figure S13: ^{13}C NMR (APT) spectrum of compound **11**



2. Quantum Chemical Calculations

Computational methods

Geometry optimisations to energy minima as well as subsequent frequency analyses of all considered starting geometries were achieved applying the PM6 semiempirical method[1] followed by DFT calculations[2] at the level 6-311++G(d,p),[3] using the B3LYP hybrid functional,[4] as implemented in the Gaussian 09 (Revision A.1) program package.[5] For calculations in methanol and water the polarisable continuum model (PCM)[6] using the integral equation formalism variant (IEFPCM) was applied. Data analysis was done using GaussView 5 (Gaussian, Inc.).

Modelling of hemiketalisation

Table S1: Calculated energies for all compounds in gas phase and water.

Reaction	Compound	E_{keto}(a) [Hartree]		$E_{hemiacetal}$(b) [Hartree]	
		gas phase	water	gas phase	water
i	**I**	-423.3149	-423.3270	-423.3034	-423.3120
ii	**II**	-424.5429	-424.5525	-424.5385	-424.5464
iii	**III**	-769.2026	-769.2139	-769.1934	-769.2029
iv	**IV**	-1207.9545	-1207.9667	-1207.9547	-1207.9648
v	**1**	-1035.1823	-1035.1993	-1035.1748	-1035.1903
vi	**6**	-1473.9344	-1473.9506	-1473.9357	-1473.9509

[1] Stewart, J. P. *J. Mol. Model.* **2007**, *13*, 1173-1213.
[2] (a) Kohn, W.; Sham, L. J. *Phys. Rev.* **1965**, *140*, A1133-A1138. (b) Parr, R. G.; Yang, W. *Density Functional Theory of Atoms and Molecules*. Oxford University Press: London, **1989**.
[3] Krishnan, R.; Binkley, J. S.; Seeger, R.; Pople, J. A. *J. Chem. Phys.* **1980**, *72*, 650-654.
[4] Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648-5652.
[5] Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J., J. A.; ; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, Ö.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J., *Gaussian 09, Revision A.1*. Gaussian Inc: Wallingford CT, 2009.
[6] Tomasi, J.; Mennucci, B.; Cammi, R. *Chem. Rev.* **2005**, *105*, 2999-3094.

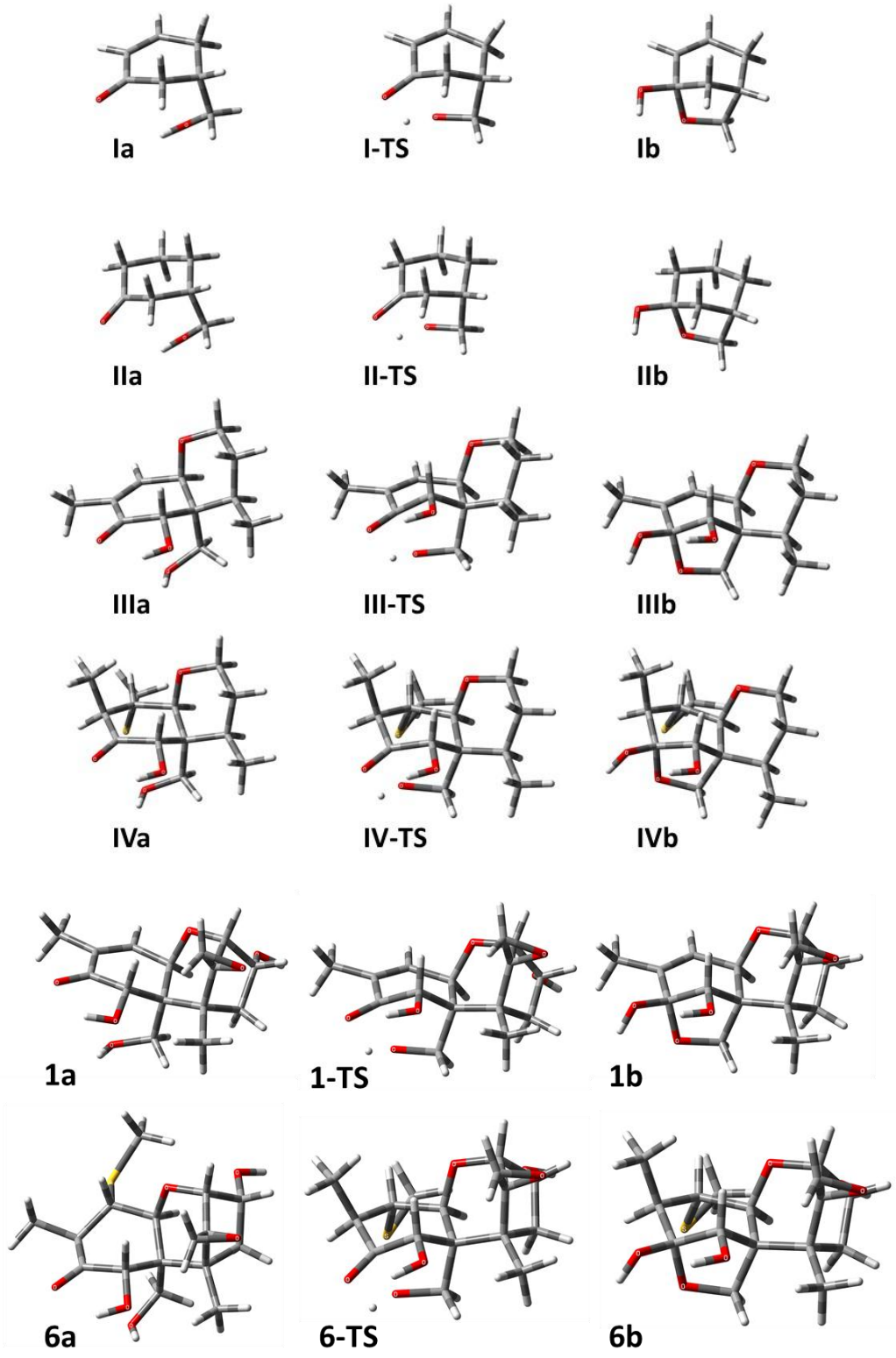


Figure S14: Optimised geometries for hemiketalisation of model compounds **I-IV**, DON (**1**) and MTD (**6**)

Conformation of MTD (6b) in solution

On the basis of the observed NOESY correlations several starting geometries of MTD were optimised in gas phase applying PM6 and DFT calculations. Lowest total energy was obtained for conformation **6b**, which was subsequently optimised in solution (MeOH, see Figure 2 in the manuscript).