Journal of Molecular Graphics and Modelling 30 (2011) 10–14

Contents lists available at ScienceDirect

Journal of Molecular Graphics and Modelling

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

Determination of the optimal position of adjacent proton-donor centers for the activation or inhibition of peptide bond formation – A computational model study

Miroslav A. Rangelov[a], Galina P. Petrova[b], Vihra M. Yomtova[a], Georgi N. Vayssilov[b,*]

[a] Laboratory of BioCatalysis, Institute of Organic Chemistry, Bulgarian Academy of Sciences, Sofia 1113, Bulgaria
[b] Faculty of Chemistry, University of Sofia "St. Kliment Ohridski", 1, James Bourchier Ave., Sofia 1126, Bulgaria

ARTICLE INFO

Article history:
Accepted 24 May 2011
Available online 22 June 2011

Keywords:
Ester ammonolysis
Catalytic map
Hydrogen bond
Activation
Inhibition

ABSTRACT

The study reports a computational analysis of the influence of proton donor group adjacent to the reaction center during ester ammonolysis of an acylated diol as a model reaction for peptide bond formation. This analysis was performed using catalytic maps constructed after a detailed scanning of the available space around the reaction centers in different transition states, a water molecule acting as a typical proton donor. The calculations suggest that an adjacent proton donor center can reduce the activation barrier of the rate determining transition states by up to 7.2 kcal/mol, while no inhibition of the reaction can be achieved by such a group.

1. Introduction

Protein biosynthesis is an aminolysis reaction in which the amino group of an amino acid in the ribosome attacks the carbonyl of an amino acid esterified to the 3′-ribose of tRNA [1]. In a series of papers based on various experimental and computational approaches [2–11] it was shown that the elementary act of peptide bond formation includes a crucial catalytic influence of the vicinal OH group in ribose. This catalytic activation is accomplished via the so-called "proton shuttle" mechanism in which the vicinal OH directly participates in the proton transfer via hexagonal transition states [2,6,7]. Herein, we present a model study exploring the additional catalytic effect of an external group adjacent to the reaction center on the aminolysis reaction barriers. We modeled the effect of a water molecule (as proton donor) forming a hydrogen bond with the O center of the vicinal OH group. The influence of water molecules on peptide bond synthesis via formation of hydrogen bonds both with the nucleobase of the 3′ adenosine and with the 2′ vicinal hydroxyl has already been explored computationally [12] by inclusion of one or two additional water molecules in the rate determining transition state of the proton transfer that reduced the activation enthalpy of the reaction.

Our present modeling extends the analysis of the influence of an additional water or another adjacent proton donor group on the reaction to a detailed scanning of the available space around the vicinal OH in different transition states as obtained in our previous simplified model study of peptide bond formation based on the ammonolysis of monoacylated ethanediol [7]. We propose an alternative approach that allows us to evaluate the effect of such groups not only from a specific position but to map the whole available space around the reaction center using water as a typical proton donor model. To achieve this we calculated the difference between the interaction energies of the adjacent water and the Ov atom from the vicinal hydroxyl in the initial reaction complex and in the corresponding transition state of a concerted or a stepwise mechanism. Graphical representation of such a difference can be regarded as a *catalytic map* and can be used in determining the influence of adjacent groups in enzymes [13] and especially in the construction of theozymes or compuzymes [14,15]. In addition, such maps provide a convenient tool to design drug molecules with functional groups oriented appropriately for the activation or inhibition of the modeled processes.

2. Computational details and model

All quantum chemical calculations were performed with the Gaussian03 program suite [16]. The structures of the reaction complex (1-O-formyl-1,2-ethanediol + NH_3) and the transition states were initially optimized at the B3LYP/6-31+G* level [17–22] which has previously proved to provide adequate description of the geometry of the model system including formation of hydrogen bonds [23]. For each transition state about 100 structures with different orientation of the water molecule were studied.

* Corresponding author.
E-mail addresses: mran@orgchm.bas.bg (M.A. Rangelov), gnv@chem.uni-sofia.bg (G.N. Vayssilov).

1093-3263/$ – see front matter © 2011 Elsevier Inc. All rights reserved.
doi:10.1016/j.jmgm.2011.05.004

Catalytic maps for the ammonolysis reaction of formylethanediol as a mimic of the ribosomal peptide synthesis reaction were constructed. Various possible structures of different modeled transition states are described in detail in Ref. [7]. The current investigation was carried out for the most stable transition state structures only (according to Ref. [7]) of the rate determining steps of the different reaction pathways – concerted and stepwise mechanisms via tetragonal and hexagonal transition states, TSc^4, TS1^4 and TSc^6, TS1^6 [24] (for the reaction scheme see Refs. [7,23]).

Since the effect of a catalyst is to change the energy barrier of the rate determining reaction step, in order to estimate the catalytic effect of any factor on a studied process, it is necessary to calculate the difference in the energy change due to this factor for the reactants, on the one hand, and for the transition states, on the other. Thus, the catalytic effect of hydrogen bond formation could be quantified by computing the difference in the energy of interaction between the proton acceptor and the adjacent proton donor (here a water molecule) according to the following equation:

$$E_{cat} = -\{[E_{TS+wat} - (E_{TS} + E_{wat})] - [E_{initail+wat} - (E_{initial} + E_{wat})]\} \quad (1)$$

In this equation $E_{initial}$, E_{TS}, and E_{wat} are the total electron energies of the reactant, the transition state, and the isolated water molecule, respectively. The terms E_{TS+wat} and $E_{initial+wat}$ correspond to the energy of the complexes formed via a hydrogen bond between the water molecule and the Ov atom from the vicinal hydroxyl (as proton acceptor) in the transition state structure or the reactant molecule. The position of the water molecule in both complexes was optimized at the same values of the angles A and D while the geometry of the transition state and the reactant was kept fixed. The definition of the angles A and D around the vicinal OH group is shown in Fig. 1 on the example of TS1^4. The first angle, A, is defined between the second carbon atom from the ethanediol fragment (C2), the vicinal oxygen atom (Ov) and the proton from the water molecule Hw participating in the new hydrogen bond with Ov. The dihedral angle D is between C1, C2, Ov, and Hw atoms. In order to map the catalytic effect of the hydrogen bond between the adjacent proton-donating group and Ov, we optimized 100 geometries of each species corresponding to 10 points for both angles the angles A and D being varied in the range 68–140° and 132–240°, respectively. Thus, we covered the whole available space around the vicinal OH. From the 200 points obtained for the reactant-transition state couple, the energy difference, E_{cat}, was calculated according to Eq. (1). By applying the method of Akima [25], the net of points obtained was further extrapolated to 3D NURBS (non-uniform rational basis spline) surface representing the catalytic effect. All figures are produced by MolRan program [23].

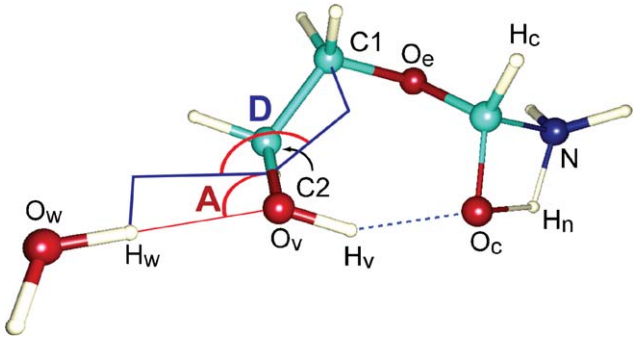

Fig. 1. Definition of the angles A and D, kept fixed during mapping the difference in the hydrogen bond strength in the reactant and transition – state structures. Designation of atoms is analogous to that in Ref. [7]: Oe, Oc, and Ov – oxygen atoms in the ester, carbonyl and vicinal OH groups, respectively; Hc, Hv, Hn – hydrogen atoms connected to the carbonyl C atom, the oxygen atom Ov from the vicinal OH group, and the N atom from the ammonia molecule, respectively; Hw and Ow – hydrogen and oxygen atoms from the coordinated water molecule.

A positive value of E_{cat} corresponds to activation of the reaction resulting from the stronger stabilization of the transition state due to the additional hydrogen bond, i.e. to a reduction of the activation barrier. On the other hand, a negative value of E_{cat} corresponds to inhibition of the reaction by the hydrogen bond with the proton donor.

3. Results and discussion

3.1. Tetragonal transition states

The modeled reaction of ester ammonolysis without external catalytic centers occurs in one or two steps by a concerted or stepwise mechanism (reaction scheme, shown in Refs. [6,7,23]). The concerted mechanism proceeds via the transition state TSc^4 which includes bonding of the N atom to the carbonyl carbon atom and simultaneous transfer of the proton Hn from ammonia to the Oe atom leading to a cleavage of the ester C–Oe bond. In the stepwise mechanism the Hn proton is initially transferred (transition state TS1^4) to the carbonyl Oc atom leading to the formation of an intermediate, I, and in the second step TS2^4, the intermediate is decomposed by proton transfer to the Oe atom and cleavage of the ester bond. The rate determining step in the stepwise mechanism is the formation of TS1^4 with an energy barrier of 52.7 kcal/mol, which is slightly higher than the barrier for the concerted mechanism, 51.5 kcal/mol [7]. When the reaction occurs via the same tetragonal transition states but with formylated ethanediol (as a simplified model of ribose) the vicinal OH group of the substrate can affect the process by formation of hydrogen bonds with Oe, Oc or N centers thus stabilizing the rate determining transition states TSc^4 and TS1^4 and reducing the corresponding barriers to 43.8 and 44.9 kcal/mol [7] (E_{act} in Table 1).

As mentioned above, we investigate here the effect of an additional proton-donor center (modeled as a water molecule) on the activation barriers by formation of a hydrogen bond with the oxygen center Ov of the vicinal hydroxyl of the substrate (Fig. 2). In this way the adjacent water molecule has only a secondary order influence on the reaction since it does not interact directly with any of the reaction centers, only increasing the acidity of the vicinal OH. Indeed, the catalytic map for the first tetragonal transition state TS1^4 of the stepwise mechanism (Fig. 2a) shows that the catalytic effect of the hydrogen bond formed with participation of an adjacent proton donor center is modest and does not exceed 1.7 kcal/mol. The observed result could be rationalized by the weak change of the charge at the carbonyl oxygen center Oc, which increases during the transition from reactants to the intermediate.

In the case of the tetragonal transition state of the concerted path of the ammonolysis reaction TSc^4 (Fig. 2b), the new HB(Ov-Hw) hydrogen bond strengthens the other two hydrogen bonds with participation of the vicinal OH, HB(Oc-Hv) and HB(Hn-Ov), formed with the atoms from the reaction ring (see Refs. [6,7]). The increase of the catalytic effect, observed when the water molecule approaches the N atom from the ammonia molecule, can be related to the formation of an additional hydrogen bond between a proton from the ammonia and the oxygen atom Ow from the water molecule. The formation of a second hydrogen bond with the water molecule results in a somewhat more pronounced catalytic effect of the water molecule on TSc^4 transition state, up to 5.7 kcal/mol, higher than in TS1^4. Here, however, we found some positions of the adjacent proton-donor that result in negative values of E_{cat} which corresponds to inhibition of the reaction, when it occurs via a concerted mechanism with a tetragonal transition state. Such effect appears when the water is at the A and D angles of 132° and 132°,

Table 1
Optimal position of the adjacent proton-donor center (angles in°, energies in kcal/mol, distances in Å) for different transition states.

TS	E_{act}[c]	Activation[a]				Inhibition[b]			
		A	D	E_{cat}	Ov-Hw[d]	A	D	E_{cat}	Ov-Hw[d]
TS1[4]	44.9	100	132	1.7	1.87	116	228	(0.3)	2.21
TSc[4]	43.8	140	228	5.7	1.80	132	132	−3.0	2.08
TS1[6]	31.2	140	228	7.2	1.82	68	240	(1.6)	3.10
TSc[6]	49.3	140	240	4.6	1.89	180	132	−2.8	2.18

[a] Position from the catalytic map with the highest value of E_{cat}.
[b] Position from the catalytic map with the highest (in absolute value) negative value of E_{cat}.
[c] Activation energy of the reaction with no adjacent proton-donor center [7].
[d] Hydrogen bond length in the corresponding optimal position.

respectively (Table 1). For this reason, the additional hydrogen bond increases the energy barrier of the reaction by up to 3.0 kcal/mol.

3.2. Hexagonal transition states

The vicinal hydroxyl group can also influence the mechanism of ester ammonolysis by the so-called proton shuttle mechanism when it is involved directly in the proton transfer via formation of hexagonal transition state cycles. In this way the vicinal OH stabilizes considerably the rate determining step of the stepwise mechanism TS1[6], by 21.5 kcal/mol to 30.0 kcal/mol, due to the more favorable angle for proton transfer. Unlike the tetragonal transition state, where the vicinal OH does not participate in the reaction cycle, in this case it participates in the proton transfer. Thus, the additional hydrogen bond of the adjacent proton-donor group to the Ov atom is expected to exert a stronger catalytic effect. As described below, this is indeed true in the case of TS1[6] but not in the case of TSc[6] transition state. Even after this reduction of the energy barrier to 30.0 kcal/mol the calculated value for our model is still rather high compared to the experimental barrier, 17.0 kcal/mol, reported by Johansson et al. [26]. This difference is due to the small model employed in the calculations and the lack of the surrounding effects. Indeed, the corresponding energy barriers obtained from calculations accounting for the environment of the peptidyl transferase center in the ribosome [12,27] are much closer to the experimental estimate.

The formation of a hydrogen bond between a water molecule and the vicinal hydroxyl results in a considerable catalytic effect, up to 7.2 kcal/mol, in the case of the first hexagonal transition state TS1[6] of the stepwise mechanism (Fig. 3a). The observed effect could be explained by a stronger interaction of the water in the transition state with the negatively charged Ov center as a result of the non-synchronous proton transfer of the two protons, Hv and Hn, interacting with the Ov center in this transition state: the Hn proton transfer from NH_3 is in an early stage while the proton Hv from the vicinal hydroxyl is almost transferred to the carbonyl oxygen center Oc. It should be noted that in all orientations of the adjacent proton-donor group the calculated catalytic effect, E_{cat}, is positive, i.e. the additional hydrogen bond only activates (strongly or weakly) but cannot inhibit the process via TS1[6].

The formation of a hydrogen bond between an additional water molecule and the vicinal hydroxyl of the ethanediol fragment results in a lower catalytic effect for the concerted hexagonal TSc[6] transition state, up to 4.6 kcal/mol. The weaker effect compared to the other hexagonal transition state TS1[6] could be explained with the smaller variations in the charge distribution in the TSc[6] transition state as a result of the more synchronous proton transfer. Similarly to the concerted tetragonal transition state, here, as well, the additional hydrogen bond has an inhibiting effect on the reaction for some orientations of the adjacent proton-donor since it increases the energy barrier for this reaction path by up to 2.7 kcal/mol (for the angles A = 68° and D = 240°).

3.3. Relevance to protein biosynthesis in the ribosome

The presence of a water molecule close to the reaction center for peptide bond formation of the ribosome is connected with the possibility for binding of this molecule to some proton donor or acceptor centers in the vicinity of the 3′ end of tRNA. The evolutionary conservatism of this 3′ nucleoside, which is adenosine in all organisms, supports the idea that adenine may be of importance for the aminolysis process. The nucleobase may influence the reaction by binding a water molecule via a hydrogen bond to the N3 atom of the nucleobase. This water molecule forms an addi-

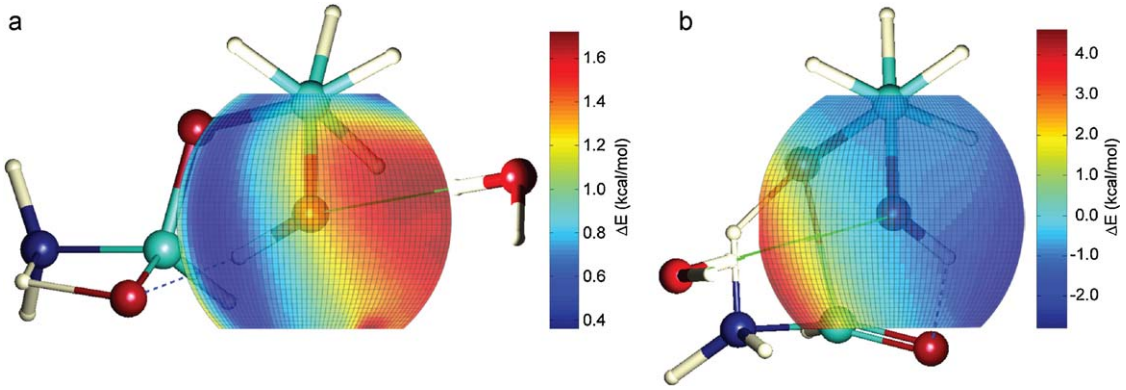

Fig. 2. Catalytic maps of the hydrogen bond with a proton donor for the tetragonal transition states with lowest energy for the stepwise, TS1[4] (a), and the concerted, TSc[4] (b), mechanisms of ammonolysis of 1-O-formyl-1,2-ethanediol.

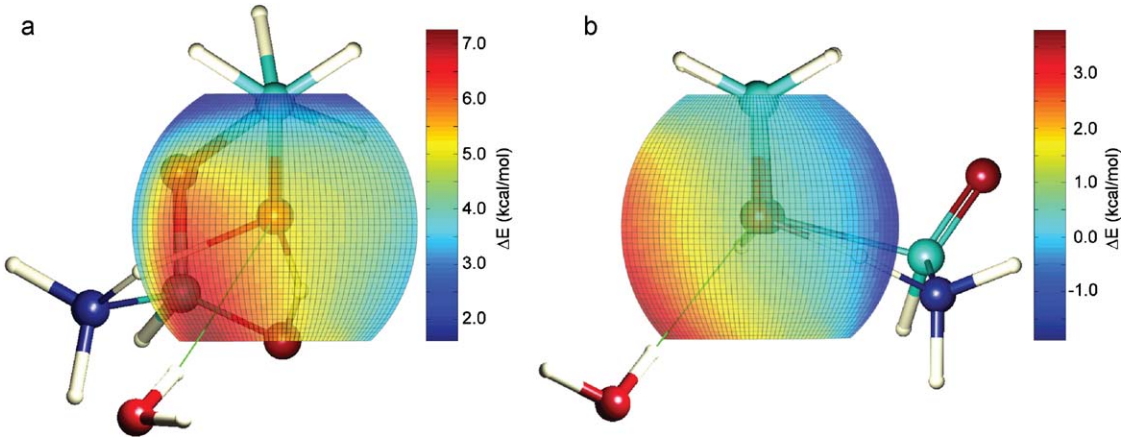

Fig. 3. Catalytic maps of the hydrogen bond with a proton donor for the hexagonal transition states with lowest energy for the stepwise, TS1[6] (a), and the concerted, TSc[6] (b), mechanisms of ammonolysis of 1-O-formyl-1,2-ethanediol.

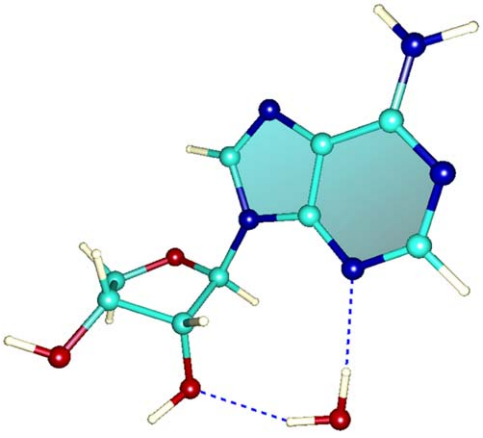

Fig. 4. Optimized structure of the complex of the adenosine analogue and a water molecule stabilized via hydrogen bonds to the N3 atom of the nucleobase and the oxygen atom of the vicinal hydroxyl OvHv.

tional hydrogen bond to the oxygen atom of the vicinal hydroxyl OvHv, thus activating the aminolysis process as described above. In connection with this idea we modeled computationally the interaction of the whole nucleoside, adenosine, with a water molecule (Fig. 4). In the obtained complex the water molecule is coordinated to the N3 atom of the adenine fragment and the vicinal hydroxyl OvHv. The obtained orientation of the water molecule in this complex can be used to analyze the effect of such proton donor center on the preference for attack of the amino group from the *re* or *si* face of the carbonyl group and formation of pro-*R* and pro-*S* transition states. In order to do this we considered the catalytic maps for the hexagonal transition state TS1[6] for the ammonolysis of formylated cis-tetrahydrofurandiol (possessing the same heterocyclic ring as ribose) for the structures with pro-*R* and pro-*S* attack (Fig. 5). Comparing the orientation of the water molecule, hydrogen bonded to 2′OH and the nucleobase in 3′ terminal adenosine of tRNA in Fig. 4, we can conclude that such water molecule is located suitably to facilitate a pro-*S* attack by about 7 kcal/mol. On the other hand, the location of such a water molecule is not particularly favorable in the case of a pro-*R* attack, where the stabilization of the transition state is about 3 kcal/mol. This result is in agreement with experimental data that show preference for pro-*S* attack in the ribosome peptidyltransferase center [4].

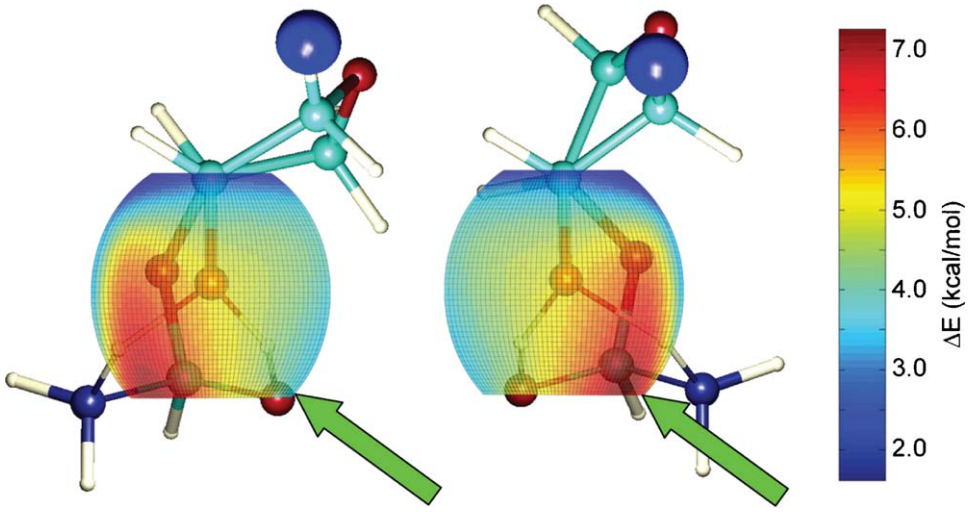

Fig. 5. Catalytic maps of the hydrogen bond with a proton donor for the hexagonal transition state TS1[6] for reactions with attack of the amino group from the *re* (a) and *si* (b) of the carbonyl group plane. The arrows point at the position of the water molecule stabilized in the complex shown in Fig. 4.

4. Conclusions

The catalytic maps for the influence of the adjacent proton donor group on the transition states for ammonolysis of acylated ethanediol, described in this study, suggest that participation of the Ov center of the vicinal hydroxyl in a hydrogen bond with an adjacent proton donor can reduce the activation energy of the reaction steps by up to 7.2 kcal/mol. The catalytic effect is most clearly pronounced for the rate-limiting step of the reaction, i.e. the first hexagonal transition state of the stepwise mechanism TS1[6]. For all orientations of the adjacent group the hydrogen bond has a positive catalytic effect, i.e. the additional proton-donor group is only able to activate but cannot inhibit the process via the rate determining transition state.

The modeling of a water molecule stabilized within an extended model of adenosine by hydrogen bonds to 2′OH of ribose and the N3 atom of the nucleobase allowed us to conclude that such an adjacent proton donor center would facilitate a pro-*S* attack of the amino group by about 7 kcal/mol, while the effect in the case of a pro-*R* attack would be twice smaller. This result is in agreement with available experimental data.

In general, the catalytic maps, constructed in the way reported here, can be used to predict the optimal position of groups in hypothetic ribozyme or enzyme active sites. They can also help in the construction of new or in the modification of known drugs targeting enzyme active sites, as well as, for the prediction of drug activity targeting known receptors.

Acknowledgments

The work was supported by Bulgarian National Fund for Scientific Research (contract DO 02-210) and the Center for supercomputer applications Super CA++.

References

[1] M.V. Rodnina, M. Beringer, W. Wintermeyer, Mechanism of peptide bond formation on the ribosome, Q. Rev. Biophys. 39 (2006) 203–225.
[2] S. Trobro, J. Åqvist, Mechanism of peptide bond synthesis on the ribosome, Proc. Natl. Acad. Sci. U.S.A. 102 (2005) 12395–12400.
[3] M.D. Erlacher, K. Lang, B. Wotzel, R. Rieder, R. Micura, N. Polacek, Efficient ribosomal peptidyl transfer critically relies on the presence of the ribose 2′-OH at A2451 of 23S rRNA, J. Am. Chem. Soc. 128 (2006) 4453–4459.
[4] T.M. Schmeing, K.S. Huang, D.E. Kitchen, S.A. Strobel, T.A. Steitz, Structural insights into the roles of water and the 2′ hydroxyl of the P site tRNA in the peptidyl transferase reaction, Mol. Cell 20 (2005) 437–448.
[5] M.M. Changalov, G.D. Ivanova, M.A. Rangelov, P. Acharya, S. Acharya, N. Minakawa, A. Földesi, I.B. Stoineva, V.M. Yomtova, C.D. Roussev, A. Matsuda, J. Chattopadhyaya, D.D. Petkov, 2′/3′-*O*-Peptidyl adenosine as a general base catalyst of its own external peptidyl transfer: Implications for the ribosome catalytic mechanism, Chembiochem 6 (2005) 992–996.
[6] M.A. Rangelov, G.N. Vayssilov, V.M. Yomtova, D.D. Petkov, The syn-oriented 2-OH provides a favorable proton transfer geometry in 1,2-diol monoester aminolysis: implications for the ribosome mechanism, J. Am. Chem. Soc. 128 (2006) 4964–4965.
[7] M.A. Rangelov, G.P. Petrova, V.M. Yomtova, G.N. Vayssilov, Catalytic role of vicinal OH in ester aminolysis: proton shuttle versus hydrogen bond stabilization, J. Org. Chem. 75 (2010) 6782–6792.
[8] W. Yang, D.G. Drueckhammer, Computational studies of the aminolysis of oxoesters and thioesters in aqueous solution, Org. Lett. 2 (2000) 4133–4136.
[9] S. Chalmet, W. Harb, M.F. Ruiz-Lopez, Computer simulation of amide bond formation in aqueous solution, J. Phys. Chem. A 105 (2001) 11574–11581.
[10] S. Ilieva, B. Galabov, D.G. Musaev, K. Morokuma, H.F. Schaefer III, Computational study of the aminolysis of esters. The reaction of methylformate with ammonia, J. Org. Chem. 68 (2003) 1496–1502.
[11] B. Galabov, S. Ilieva, B. Hadjieva, Y. Atanasov, H.F. Schaefer III, Predicting reactivities of organic molecules. Theoretical and experimental studies on the aminolysis of phenyl acetates, J. Phys. Chem. A 112 (2008) 6700–6707.
[12] G. Wallin, J. Åqvist, The transition state for peptide bond formation reveals the ribosome as a water trap, Proc. Natl. Acad. Sci. U.S.A. 107 (2010) 1888–1893.
[13] T. Dudev, C. Lim, Principles governing Mg, Ca, and Zn binding and selectivity in proteins, Chem. Rev. 103 (2003) 773–788.
[14] D.J. Tantillo, J. Chen, K.N. Houk, Theozymes and compuzymes: theoretical models for biological catalysis, Curr. Opin. Chem. Biol. 2 (1998) 743–750.
[15] Y.M. Lee, C.S. Babu, Y.C. Chen, M. Milcic, Y. Qu, C. Lim, Conserved structural motif for recognizing nicotinamide adenine dinucleotide in poly(ADP-ribose) polymerases and ADP-ribosylating toxins: implications for structure-based drug design, J. Med. Chem. 53 (2010) 4038–4049.
[16] M.J. Frisch, G.W. Trucks, H.B. Schlegel, G.E. Scuseria, M.A. Robb, J.R. Cheeseman, J..A. Montgomery Jr., T. Vreven, K.N. Kudin, J.C. Burant, J.M. Millam, S.S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G.A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J.E. Knox, H.P. Hratchian, J.B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R.E. Stratmann, O. Yazyev, A.J. Austin, R. Cammi, C. Pomelli, J.W. Ochterski, P.Y. Ayala, K. Morokuma, G.A. Voth, P. Salvador, J.J. Dannenberg, V.G. Zakrzewski, S. Dapprich, A.D. Daniels, M.C. Strain, O. Farkas, D.K. Malick, A.D. Rabuck, K. Raghavachari, J.B. Foresman, J.V. Ortiz, Q. Cui, A.G. Baboul, S. Clifford, J. Cioslowski, B.B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R.L. Martin, D.J. Fox, T. Keith, M.A. Al-Laham, C.Y. Peng, A. Nanayakkara, M. Challacombe, P.M.W. Gill, B. Johnson, W. Chen, M.W. Wong, C. Gonzalez, J.A. Pople, Gaussian 03, Revision E.01, Gaussian, Inc., Wallingford, CT, 2004.
[17] R. Ditchfield, W.J. Hehre, J.A. Pople, Self-consistent molecular-orbital methods. IX. An extended Gaussian-type basis for molecular-orbital studies of organic molecules, J. Chem. Phys. 54 (1971) 724–728.
[18] W.J. Hehre, R. Ditchfield, J.A. Pople, Self-consistent molecular orbital methods. XII. Further extensions of Gaussian-type basis sets for use in molecular orbital studies of organic molecules, J. Chem. Phys. 56 (1972) 2257–2261.
[19] P.C. Hariharan, J.A. Pople, Accuracy of AH_n equilibrium geometries by single determinant molecular orbital theory, Mol. Phys. 27 (1974) 209–214.
[20] M.S. Gordon, The isomers of silacyclopropane, Chem. Phys. Lett. 76 (1980) 163–168.
[21] P.C. Hariharan, J.A. Pople, The influence of polarization functions on molecular orbital hydrogenation energies, Theor. Chim. Acta 28 (1973) 213–222.
[22] A.D. McLean, G.S. Chandler, Contracted Gaussian basis sets for molecular calculations. I. Second row atoms, $Z = 11–18$, J. Chem. Phys. 72 (1980) 5639–5648.
[23] M.A. Rangelov, G.P. Petrova, V.M. Yomtova, G.N. Vayssilov, Hierarchical approach to conformational search and selection of computational method in modeling the mechanism of ester ammonolysis, J. Mol. Graphics Modell. 29 (2010) 246–255.
[24] The applied notation for the stationary points along concerted and stepwise reaction pathways is analogous to that in Ref. [7]: TSc – transition state of concerted; TS1 and TS2 – first and second transition states of the stepwise path; I – intermediate of the stepwise path. The superscript (4 or 6) denotes the number of atoms participating in the cycle of the corresponding transition states.
[25] H. Akima, A method of bivariate. Interpolation and smooth surface fitting for irregularly distributed data points, ACM Trans. Math. Softw. 4 (1978) 148–159.
[26] M. Johansson, E. Bouakaz, M. Lovmar, M. Ehrenberg, The kinetics of ribosomal peptidyl transfer revisited, Mol. Cell 30 (2008) 589–598.
[27] J. Kästner, P. Sherwood, The ribosome catalyzes peptide bond formation by providing high ionic strength, Mol. Phys. 108 (2010) 293–306.