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Transition states for the modeled reactions of tempo with hydrogen atom

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ABSTRACT

Theoretical calculations at the DFT/UB3-LYP/6-311+G(3df,2p)/(U)AM1 level revealed three transition states for the reaction of TEMPO with H atom leading to combination of reagents, abstraction of H atom from methyl group of TEMPO and abstraction of oxygen atom from TEMPO.

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KEYWORDS

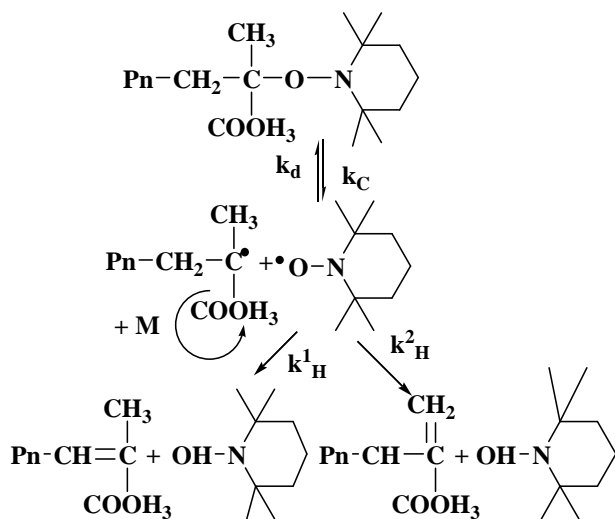
Hydrogen atom;
TEMPO;
Transition state;
AM 1 theory.

INTRODUCTION

Free radical reactions have become increasingly important and a very attractive tool in organic synthesis, e.g. cyclizations, additions, hydrogen-atom abstractions, decarboxylation reactions, due to their powerful and specific abilities to reactions under mild conditions^[1]. Lately, numerous efforts have been aimed at establish-

ing the role of the H-atom migration in the controlled radical polymerization process. In the nitroxide-mediated polymerization (NMP)^[2,3] the reversible trapping of propagating carbon-centered radicals by stable nitroxide species (k_d and k_c for homolytic dissociation and combination reaction, respectively) is disturbed by β -H atom transfer from the growing polymer chain end to the nitroxide (k_H^1) or abstraction of H-atom from α -methyl group of methyl methacrylate (M) (k_H^2)^[4], for example by 2,2,6,6-tetramethyl-1-piperidinyloxy radical (TEMPO)^[5,6] (SCHEME 1).

These reactions depend on structures of the nitroxide and carbon-centered radical species and result in a dead polymer chain containing an unsaturated chain end and increased polydispersity of polymer^[7-11]. Recently, we have found some additional theoretical proofs supporting these effects^[12-13]. Given the importance of the problem, an investigation was undertaken on the H-atom capture by TEMPO. The present study was performed by use of quantum chemistry calculations, probably the only method to evaluate geometries of transition structures and corresponding activation energies for short-lived reaction intermediates.



SCHEME 1

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TABLE 1: Selected geometrical parameters, activation energy (ΔE_0^\ddagger , kcal mol⁻¹) and enthalpy of activation (ΔH_{298}^\ddagger , kcal mol⁻¹) for TS calculated from at the (U)AM1 and (U)B3-LYP/6-31G(d) level of theory. For numbering of atoms see figure 1

Species/TS	Bond length, (Å)				Bond angle (°)		Dihedral angle (°)	P-y of N-atom ^a , (Å)	Thermo-dynamics	
	OH ₃	ON	H ₃ H ₄	C ₅ H ₄	NOH ₃	C ₅ H ₄ H ₃	C ₁ NC ₂ O		ΔE_0^\ddagger ^b	ΔH_{298}^\ddagger ^c
TEMPO ^d		1.216		1.117			152.6	0.195		
I ^d	1.765	1.225		1.117	113.0		154.0	0.335	11.2	10.4
II ^d	0.951	1.773		1.116	105.1		173.6	0.101	-16.4	-24.7
III ^e	1.703	1.216	0.777	1.544	109.2	142.0	-130.2	0.381	81.6	83.8

^aPyramidity measured as the distance (Å) of the out-of-plane N- atom from the plane defined by C₁C₂O; ^bCalculated according

to $\Delta E_0^\ddagger = (E_0 + \varepsilon_{ZPE})_{TS} - \sum_j (E_0 + \varepsilon_{ZPE})_j$; ^cCalculated according to $\Delta H_{298}^\ddagger = (E_0 + \varepsilon_{ZPE} + H_{corr})_{TS} - \sum_j (E_0 + \varepsilon_{ZPE} + H_{corr})_j$ where

H_{corr} is the correction to the enthalpy due to internal energy at 298 K from gaussian outputs calculated as a difference between the sum of electronic and thermal enthalpies, and the sum of electronic and zero-point energies, and ε_{ZPE} zero point energy; ^dDetermined at the UAM1 level; ^eDetermined at the AM1 level.

EXPERIMENTAL

The geometry of TEMPO used in the subsequent search for transition states (TS) was first fully optimized with the density functional theory (DFT) including Becke functional^[14] and functional correlations given by Lee et al.^[15] in the standard basis set UB3-LYP/6-31g(d). Generally, this level of theory is accepted for optimization of geometries for large organic systems^[16-18]. The search for TS has been carried out by use the following methods: DFT theory with the basis set up to 6-31G(d), Hartree-Fock theory and semi-empirical theory using PM1 and AM1 Hamiltonian, all with restricted and unrestricted treatments. In addition, the reaction path through the discovered TS were verified by the intrinsic reaction coordinate calculations (IRC)^[19]. All computational work presented in this article was performed with the Gaussian 98 suite of programs^[20].

RESULTS AND DISCUSSION

It was found that from all theoretical methods used in search for TS geometry only the semi-empirical Austin Model 1 (AM1) theory^[21] was successful, in spite of the fact that there were earlier reports in literature, however very few, on the effective use of the B3-LYP/6-31g(d) for reactions of carbon centered radicals, e.g. the ethyl, *n*-propyl, and *sec*-propyl free radicals^[22] as well as a ring opening reaction of the cyclopropylcarbinyl radical^[23]. Numerous attempts with (U)AM1 calculations revealed three TS corresponding to three differ-

ent reactions: combination of TEMPO with H atom (TS I), and two more complex chemical changes: combination of TEMPO with H atom concerted with simultaneous abstraction of OH radical (TS II), and abstraction of H atom from methyl group of TEMPO combined with cleavage of the piperidinyloxy ring (TS III) (Figure 1).

All structures were true transition states characterized by one, and only one imaginary vibrational frequency -572.02 cm⁻¹, -257.27 cm⁻¹ and -1296.83 cm⁻¹ for TS I, TS II and TS III, respectively. The piperidine ring for all TS demonstrated a chair conformation, a pyramidal geometry of the nitrogen atom and nearly equatorial position of the N...O bond. However, the pyramidity of the N-atom considerably differs for all discovered TS. Activation energies calculated as the energy of the transition structure relative to the reactants are given in TABLE 1.

The estimated activation energy ΔE_0^\ddagger for combination of TEMPO with H-atom (TS I) was found to be 11.2 kcal mol⁻¹. In literature, various experimental and theoretical values of activation energy for radical combination are reported: -6.1 and -7.8 kcal mol⁻¹^[24], 1 kcal mol⁻¹^[25], 1.7 kcal mol⁻¹^[26], 1.9-3.3 kcal mol⁻¹^[13], 3.4 kcal mol⁻¹^[27], 0-1 kcal mol⁻¹^[28-30], and 2.0-6.9 kcal mol⁻¹^[13]. Thorough analysis of these data indicates that the energy of activation for the coupling reaction with TS I is probable slightly overestimated when compared to the data given above. However, one should remember that the published activation energies depend on numerous parameters including structure of radicals,

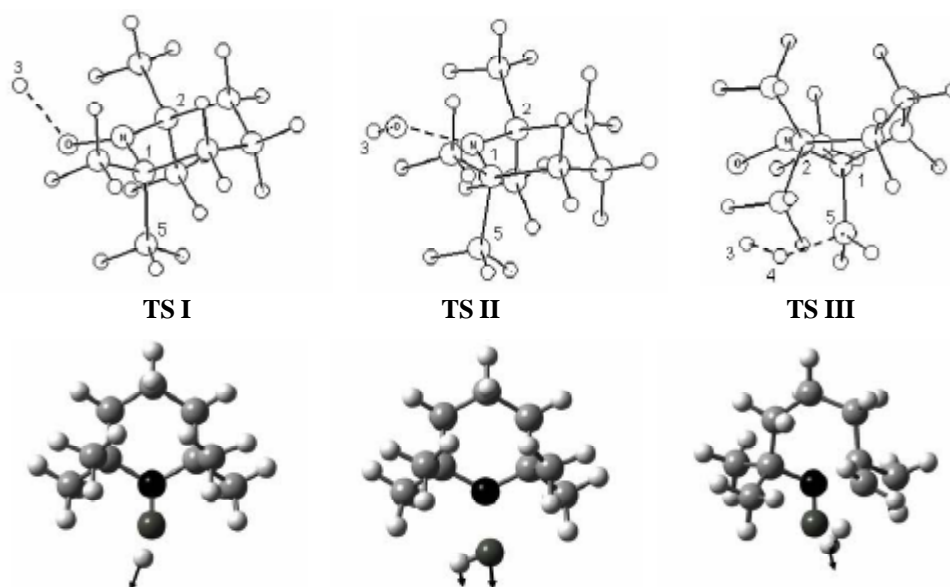
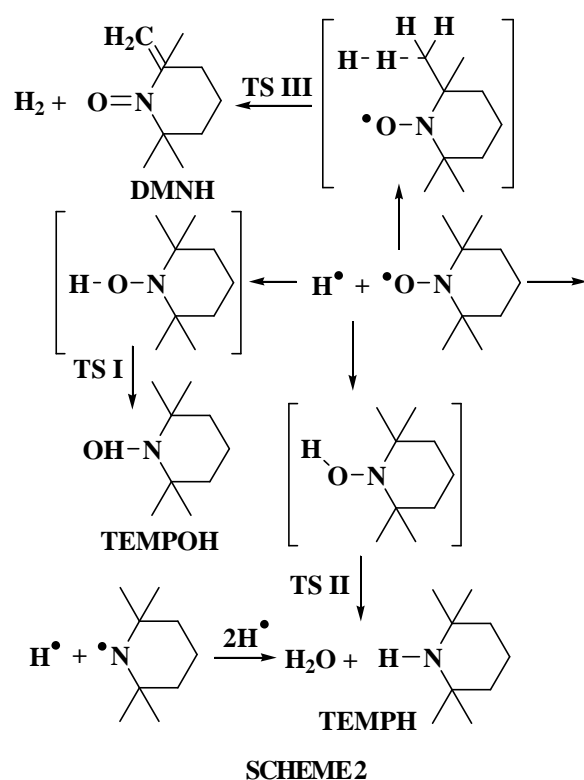


Figure 1: The optimized TS geometries: (TS I) - combination of TEMPO with H atom; (TS II) - combination of TEMPO with H atom concerted with abstraction of OH radical; (TS III) - abstraction of H atom from methyl group of TEMPO concerted with cleavage of the piperidinyloxy ring. Above: numbering of relevant atoms in TS; below: TS from different point of view together with transition vectors illustrating motion of structures away from the TS along the reaction coordinate.



environment of the reaction and investigation techniques. Therefore, they are not always comparable^[31].

TS II is characterized by a negative activation energy. The negative activation energy for radical reactions is in general explained by an existence of some

pre-reactive complex^[32-34]. This assumption was tested in the IRC part of calculations however, in our case, they have not showed any additional local maximum geometry. Nonetheless, the negative activation energy, TS II geometry and vectors illustrating the motion of the hydrogen atom bound to O-atom (Figure 1) suggest that the reaction path aiming at abstraction of OH radical is complex and probably consists of more than one chemical transformation. Unfortunately, there is no experimental data to be direct compared with the results presented here, however, reactions and products similar to those proposed in SCHEME 2 can be found in literature. For example, metal hydrides with relatively weak metal-hydrogen bond, like Ph_3GeH and Bu_3SnH , reduced TEMPO to the corresponding hydroxylamine, 2,2,6,6-tetramethyl-1-piperidinol (TEMPOH), while using tris(trimethylsilyl)silane, $(\text{TMS})_3\text{Si-H}$ a major product was an amine^[35,36]. Furthermore, at temperatures above 380 K TEMPO converts in the presence of a hydrogen donor like 1,4-cyclohexadiene or 9,10-dihydroanthracene into TEMPOH, thus, a compound obtained in our theoretical experiment on combination of TEMPO with H atom (TS I).

Additionally, it has been also suggested that TEMPOH is the intermediate for deoxygenation mechanism of TEMPO that, subsequently, can be reduced to

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the corresponding amine 2,2,6,6-tetramethylpiperidine (TEMPH)^[25], thus, a final product of the hypothetical reaction pathway passing through TS II. A secondary amine is also the major product of deoxygenation of nitroxide in cells^[37-38]. In another search, Heidbrink et al. reported gas-phase radical-radical combination reactions of nitroxides with phenyl radicals that leads to abstraction of H atom from cyclic nitroxides accompanied by fragmentation of the nitroxide^[39].

According to the present results, a hydrogen atom abstraction from methyl group (TS III, SCHEME 2) is followed by forming 2,6-dimethyl-6-nitrosohept-1-ene (DMNH).

This compound, being a stable, although highly reactive tert-alkyl nitroso compound^[40], was proposed to explain formation of a radical identical with that being an oxidized form of DMNH (SCHEME 2)^[41]. The activation energy for the H-atom abstraction from the methyl group of TEMPO was estimated to be 27.0 kcal mol⁻¹. Unfortunately, neither theoretical nor experimental reference data could be found in literature adequate for H-atom abstraction from C-H groups by hydrogen atom. However, this result is in comparatively good agreement with the activation energy estimated with the AM1 approach (24.06 kcal mol⁻¹) for the reaction of the ethyl radical and a hydrogen molecule^[42]. The semiempirical methods, including the AM1 calculations, strongly overestimate the barrier height as the activation energy for the reduction of methyl radical with methane, CH₃-H + CH₃ was experimentally determined to be 14.5 kcal mol⁻¹^[43]. This behavior is common to the semi-empirical methods.

In conclusion, we summarize that according to the theoretical analysis of the reactive system build-up from TEMPO radical and H atom, at least three final products, TEMPOH, TEMPH and DMNH can be expected as result of the reactions passing through three different transition states.

The results presented in this work were obtained using the computational resources of the Interdisciplinary Center for Mathematical and Computational Modeling at Warsaw University.

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