Ab initio study of in-situ Nitroxide Mediated Polymerization: level of theory study and assessment of nitrone structure influences on thermodynamics and kinetics

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A quantum chemical study is presented reporting thermodynamic and kinetic data obtained at various levels of theory for a set of compounds and reactions related to in-situ Nitroxide Mediated Polymerization (NMP). In-situ NMP is a newly developed method allowing the synthesis of well-defined polymer based on a reversible recombination/dissociation reaction. BMK/6-311G(d,p) is shown to be the most appropriate level of theory for the dissociation reactions involved. In particular, influences of the nitrone structure on reaction thermodynamics and kinetics can be described well. Furthermore, this study offers a basis on which other nitrone compounds may be evaluated for their use in in-situ NMP.

Keywords: NMP, in-situ, DFT, kinetics, thermodynamics

1. Introduction

Controlled radical polymerization (CRP) is a promising polymerization technique that enables to produce well-defined, end-functionalized polymers at less stringent experimental reaction conditions than living ionic polymerization. An interesting and polyvalent CRP method is Nitroxide Mediated Polymerization (NMP) [1]. The control of the NMP process is based on a reversible recombination between propagating species (P●) and nitroxide with the formation of alkoxyamine (see Figure 1), resulting in a low radical concentration and, hence, leading to a suppression of undesired termination reactions. A recently developed type of NMP is in-situ Nitroxide Mediated Polymerization (in-situ NMP) [2], in which the nitroxide and alkoxyamine are formed in the polymerization medium itself, based on precursors such as nitrones (RN(O)=CHR, R = alkyl group), nitroso compounds (RN=O, R = alkyl group) etc.

In this work, a quantum chemical study is presented reporting thermodynamic and kinetic data obtained at various levels of theory for a set of compounds and reactions related to in-situ NMP. The selection of a cost-efficient method to study these compounds and reactions was done by comparison of calculated ab initio data with experimental data or with values obtained from high level benchmark calculations. Subsequently, the most appropriate level of theory was applied to the calculation of nitroxide- and alkoxyamine-forming reactions of a typical initiating system comprising 2,2'-azobisisobutyronitrile (AIBN), styrene and a nitrone. Following nitrones were considered: N-tert-butyl-α-isopropylnitrone (iPBN), N-tert-butyl-α-tert-butylnitrone (BBN), C-phenyl-N-tert-butylnitrone (PBN), 5,5-dimethyl-1-pyrrolidin-N-oxide (DMPO). It is shown that the selected level of theory captures well the difference in reactivity of these nitrones.

2. Computational procedures

All calculations have been performed with either the *Gaussian03* suite of programs [3] or the *Turbomole* computational package [4, 5]. An extensive set of DFT functionals is applied. Generalized Gradient Approximation (GGA) functionals are considered: B3LYP, B3P86, BHandHLYP, BMK, MPW1PW91 and BB1K. The newly developed double hybrid exchange-correlation functional, B2-PLYP, and the dispersion-corrected method, B97-D, are also used. Owing to the scarceness of experimental data, calculations are also performed using high-level composite methods, G3B3, and complete basis set method CBS-QB3. Calculations on the B3LYP, B3P86, BHandHLYP, BMK, MPW1PW91, BB1K levels of theory are combined with various Pople split-valence basis sets: 6-311G, 6-311G(d,p) and are calculated with the Gaussian03 package (also applied for the composite methods). Turbomole is used for single point energy calculations with B2-PLYP (basis sets:

cc-pVQZ and QZVPP as suggested by Grimme [6]) and B97-D (with the TZVPP basis set) on B3LYP/TZVPP optimized structures.

For G3B3 and CBS-QB3, the default scaling factors used are 0.96 and 0.99. For the B2-PLYP method, a scaling factor of 0.97 is applied on the B3LYP/TZVPP calculated frequencies, as suggested by Grimme [6]. For all other DFT methods, a scaling factor of 0.99 is selected, which is close to the value of 0.9877 advised by Andersson and Uvdal [7] for scaling DFT/triple-ζ ZPVEs. Standard enthalpies of formation, molar entropies, bond dissociation enthalpies and rate coefficients are calculated.

3. Results and discussion

From the results of the level of theory study, an appropriate method is determined to describe compounds and reactions involved in in-situ NMP by comparing calculated data with experimental data and benchmark computational data, obtained with composite methods. The test set of the level of theory study consists of initiator-related compounds such as AIBN and benzoyl peroxide (BPO) and their radicals (structures 1-6 in Figure 2), nitrones, nitroxides and alkoxyamines (structures 7-13 in Figure 2), and also monomer- and polymer-related structures, such as styrene, benzene, ethyl benzene and corresponding radicals (structures 14-20 in Figure 2).

It was found that the standard enthalpies of formation are best described by the composite G3B3 method with a Mean Average Deviation from experiment, MAD_{exp}, of 4.2 kJ mol^{-1}. This composite method, however, is only applicable for the small molecules. Hence, G3B3 is used only as benchmark to extend the test set for the evaluation of the other methods. The Mean Average Deviations of the enthalpies of formation from benchmark G3B3 data are given in Figure 3. Considering only the DFT methods, the B2-PLYP/cc-pVQZ method is clearly the best performing with a

MAD_{exp} of 6.4 kJ mol^{-1} and a MAD from G3B3 benchmark results of 14.6 kJ mol^{-1}. For larger systems, however, the MP2 contribution to the B2-PLYP results scales with N^5 (N being the number of basis functions), whereas regular DFT methods scale with N^3. The order of increasing performance for the regular DFT methods is BMK/6-311G(d,p), MPW1PW91/6-311G(d,p), B97-D/TZVPP. Molar entropies have also been calculated and evaluated. It can be seen that the difference between the various methods is rather limited and will therefore not be discussed in further detail.

Considering dissociation (recombination) reactions, Bond Dissociation Enthalpies (BDEs) are calculated for the following reactions: C_6H_5COO-$OOCC_6H_5$, $NC(CH_3)_2C$-NN-$C(CH_3)_2CN$, CH_3COO-$OOCCH_3$, H_2NO-H, TEMPO-H, TEMPO-$CHCH_3C_6H_5$, H-$CHCH_3C_6H_5$, H-C_6H_5, H-$CH_2CH_3CHC_6H_5$. The Mean Average Deviations of the BDEs from experimental data are given in Figure 4. For reaction enthalpies, BMK/6-311G(d,p) is found to outperform all other methods with a MAD_{exp} of 9.5 kJ mol^{-1}.

As shown in Figure 1, the mechanism of NMP is based on a reversible recombination/dissociation reaction. Hence, it is extremely important to describe the thermodynamics of this kind of reactions well. For this, BMK/6-311G(d,p), the best performing DFT method for the prediction of BDE, is used.

Kinetic and thermodynamic data obtained with the BMK/6-311G(d,p) level of theory are reported on reactions typical for the initiating system of an in-situ NMP as proposed by Sciannamea et al. [8] In this study, the formation of a nitroxide by addition of an AIBN radical ($NC(CH_3)_2C\bullet$) to the following nitrones is reported: N-tert-butyl-α-isopropylnitrone (iPBN), N-tert-butyl-α-tert-butylnitrone (BBN), C-phenyl-N-tert-butylnitrone (PBN), 5,5-dimethyl-1-pyrrolidin-N-oxide (DMPO). In Table 1, the reaction enthalpy $\Delta_r H^0_{addition}$, the equilibrium coefficient *K* and kinetic

parameters (pre-exponential factor A, activation energy E_a and the rate coefficient $k_{forward}$ for the forward reaction) for the addition of $NC(CH_3)_2C\bullet$ to nitrones are given. Note that the rate of formation of the nitroxides has to be sufficiently high to obtain an amount of nitroxides that is able to trap present radicals reversibly and, hence, control the polymerization. From Table 2, it is clear that nitroxide formation increases in the series: BBN < iPBN < PBN < DMPO.

The recombination/dissociation reactions of the formed nitroxides with an AIBN radical ($NC(CH_3)_2C\bullet$) and with $C_6H_5C\bullet HCH_2C(CH_3)_2CN$ are also investigated. The reaction enthalpies and equilibrium coefficients are given in Table 2. A high value of the equilibrium coefficient corresponds with a stable alkoxyamine and leads to a slow polymer growth resulting in polymers with a low number average molar mass. Hence, a trade-off is required between a sufficiently fast nitroxide formation and a not too slow dissociation rate of the formed alkoxyamines. From Table 2, it can be seen that the nitroxides formed from DMPO are rapidly trapped but that the formed alkoxyamines decompose slowly as they are very stable. Polymerization with DMPO as precursor for the nitroxides can thus be expected to proceed slowly. For the other 2 nitrones (BBN and iPBN), in which the phenyl-substituent (PBN) is replaced by a tert-butyl group (BBN) or isopropyl group (iPBN), steric effects are more important than for the planar phenyl group in PBN. The higher steric constraints caused by substitution of the phenyl group by an isopropyl group in iPBN can be clearly seen in the kinetic and thermodynamic parameters: a less stable nitroxide is formed at a slower rate. This results in a lower amount of nitroxide (and thus also alkoxyamine) formed and in a polymer with a higher number average molar mass. This effect is even more pronounced in the case of the tert-butyl substituent in BBN as can be seen in Table 1. These steric effects are also seen in the stability of the

alkoxyamines: alkoxyamines formed from iPBN and BBN are less stable and decompose easily (Table 2).

From the set of molecules considered, PBN can be expected to offer the best trade-off between control and required polymerization time. Indeed the initiation efficiency corresponding with BBN and iPBN is too low, indicating that the amount of nitroxides present in the medium is not sufficient to reversibly capture the formed radicals, and the alkoxyamines corresponding with DMPO decompose too slowly.

In general, the structural effects on the kinetics and thermodynamics of these addition and recombination reactions are in agreement with the experimental findings of Sciannamea et al. [8]. These authors found that DMPO has the highest initiation efficiency, i.e. the highest yield of nitroxides but leads to polymers with a lower number average molar mass, relative to the use of PBN as a nitrone and that poor control is obtained with BBN and iPBN as nitrones. Hence, it can be expected that the selected computational procedure will allow to assess other nitrone compounds for their use in in-situ NMP.

4. Conclusions

A level of theory study has been performed on molecules and reactions related to in-situ Nitroxide Mediated Polymerization. The BMK/6-311G(d,p) level of theory is preferred for the description of reactions. Applying BMK to investigate the influence of the nitrone structure on elementary reactions involved in in-situ NMP, shows significant differences between the various nitrones in agreement with experimental findings.

Acknowledgements
The Research Foundation – Flanders (FWO) is acknowledged for a Ph.D. fellowship. This work is supported by the Belgian Government (IAP/IUAP/PAI P6/27: “Functional Supramolecular Systems”) and the E.C. (Network of Excellence IDECAT, NMP3-CT-2005-011730).

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Table 1. Formation of nitroxides (in-situ) at 298 K: addition of $NC(CH_3)_2C\bullet$ to nitrone.

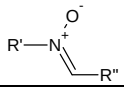
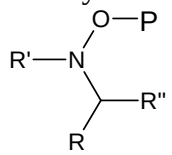
Nitrone 	Addition of $NC(CH_3)_2C\bullet$ to nitrone (formation of nitroxide)				
	$\Delta_r H^0_{addition}$ kJ mol^{-1}	K m^3 kmol^{-1}	log (A/m^{3}kmol^{-1}s^{-1})	E_a kJ mol^{-1}	$k_{forward}$ m^{3}kmol^{-1}s^{-1}
iPBN: R'=tB, R"=iP	-96.88	7.00 10^6	4.09	50.79	1.47 10^{-5}
BBN: R'=tB, R"=tB	-90.26	1.28 10^5	4.78	58.62	3.06 10^{-6}
PBN: R'=tB, R"=Ø	-112.21	1.66 10^{10}	4.58	28.50	3.67 10^{-1}
DMPO	-141.17	1.42 10^{15}	4.75	7.61	2.49 10^3

Table 2. Formation of alkoxyamines (in-situ) at 298 K: (1) recombination of nitroxides with $NC(CH_3)_2C\bullet$ and (2) recombination of nitroxides with $C_6H_5C\bullet HCH_2C(CH_3)_2CN$ (initiated styrene).

Alkoxyamine 	(1) P = $\bullet C(CH_3)_2CN$		(2) P = $C_6H_5C\bullet HCH_2C(CH_3)_2CN$	
	$\Delta_r H_1^0$	$K_{recomb1}=k_c/k_d$	$\Delta_r H_2^0$	$K_{recomb2}=k_c/k_d$
	kJ mol^{-1}	m^3 kmol^{-1}	kJ mol^{-1}	m^3 kmol^{-1}
R=$NC(CH_3)_2C\bullet$, R'=tB, R"=iP	-68.67	$1.58\ 10^0$	-94.65	$6.01\ 10^4$
R=$NC(CH_3)_2C\bullet$, R'=tB, R"=tB	-61.81	$9.71\ 10^{-1}$	-45.96	$3.20\ 10^{-4}$
R=$NC(CH_3)_2C\bullet$, R'=tB, R"=Ø	-85.03	$1.46\ 10^3$	-66.5	$3.01\ 10^{-1}$
DMPO	-116.7	$5.00\ 10^9$	-118.74	$7.79\ 10^9$

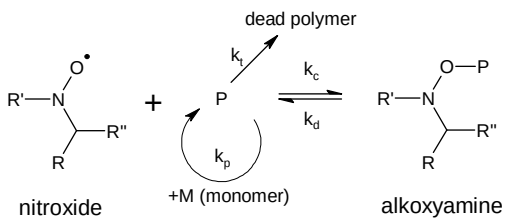


Figure 1. Basic principle of NMP: P = propagating radical; R, R’, R’’ = alkyl groups; M = monomer; k_p, k_d, k_c, k_t = rate coefficients for propagation, dissociation (activation), coupling (deactivation) and termination reactions respectively.

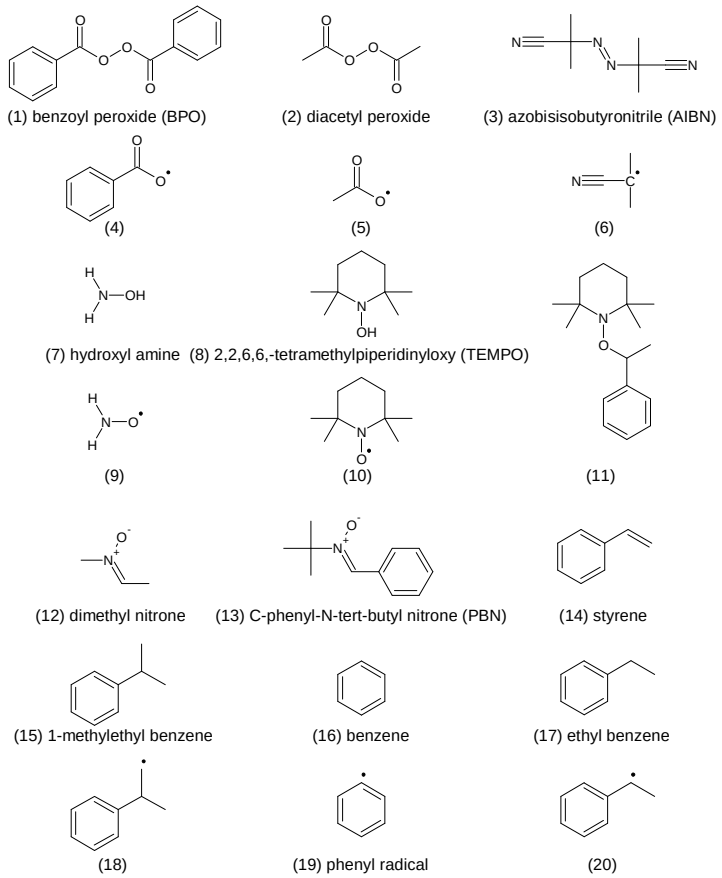


Figure 2. Test set: initiator-related structures (1-6), nitrone- and nitroxide-related structures (7-13) and monomer-related structures, i.e. hydrocarbons (14-20).

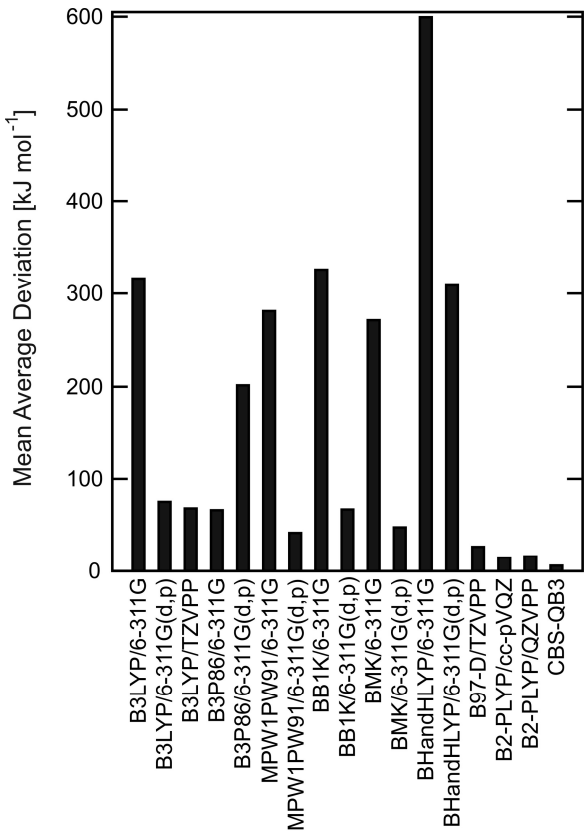


Figure 3. Mean Average Deviation of enthalpies of formation from G3B3 benchmark data.

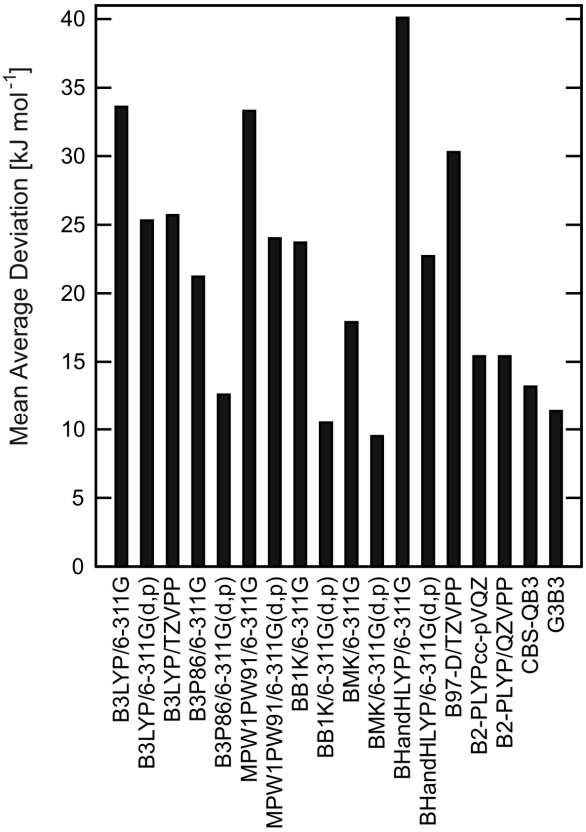


Figure 4. Mean Average Deviation of BDEs from experimental data.