

Theoretical evaluation of the order of reactivity of transfer agents utilized in RAFT polymerization: group Z

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Abstract In the present study we report theoretical calculations, by means of density functional theory (DFT), for 28 transfer agents used in reversible addition-fragmentation chain transfer (RAFT) polymerization. Functional PBE1PBE and 3–21G* theory levels with Gaussian 03 software were used to determine the order of reactivity of RAFT agents through the evaluation of reactivity parameters such as global softness, global hardness and global philicity. It was found that the global softness of the agent was more favored when it contained benzyl or phenyl groups as the Z group, than in RAFT agents with Z groups based on oxygen, nitrogen, or sulfur. On the one hand, when the Z group is based on oxygen or nitrogen, the tendency to form zwitterionic bonds with the adjacent radical center is very high, causing reactivity reduction in these kinds of compounds (e.g., dithiocarbamates) in comparison with compounds that do not experience this type of event; on the other hand, with Z groups based on sulfur, two fragmentation paths are possible, which reduces the fragmentation rate since both Z and R can function as leaving groups. With this investigation we contribute to the understanding of RAFT-mediated polymerization mechanisms by proposing an order of reactivity based on evaluating the importance of the Z group.

Keywords Living polymerization · RAFT · Group Z · Density functional theory

Introduction

Reversible addition-fragmentation chain transfer polymerization mechanism

Living radical polymerization has proved a versatile tool for preparing well-defined polymeric structures [1]. The basic principle behind living processes is to protect the growing polymeric chains of bimolecular termination through the use of molecular traps in order to obtain dormant species [2]. In recent years, some systems such as nitroxide-mediated polymerization (NMP), degenerative transfer (DT), atom transfer radical polymerization (ATRP), and reversible addition-fragmentation chain transfer (RAFT) polymerization have been studied widely [3]. The RAFT mechanism, first reported by Rizzardo et al. in 1998 [4], has been established as illustrated in Scheme 1 [5]. A lot of work reported during the last decade has demonstrated the versatility of RAFT, in particular due to (1) the wide availability of monomers that polymerize through this mechanism, (2) the low sensitivity towards oxygen and other potential poisoning agents present in the polymerization system, (3) the possibility of obtaining complex polymeric architectures, (4) the applicability either in one phase or in dispersed media, and (5) the potential for industrial applications [6–12].

The RAFT polymerization mechanism involves a series of reversible addition-fragmentation steps; i.e., the addition of a propagating radical (P_n^\bullet) to the thiocarbonyl compound in the agent $[S=C(Z)S-R]$ and generation of an adduct radical, which fragments to form a polymeric thiocarbonyl compound, $[P_n-S-C(Z)=S]$, and a new radical, R^\bullet . The reaction of R^\bullet with the monomer (M) generates a new propagating radical P_m^\bullet . Subsequent addition-fragmentation steps allow a dynamic equilibrium that establishes itself

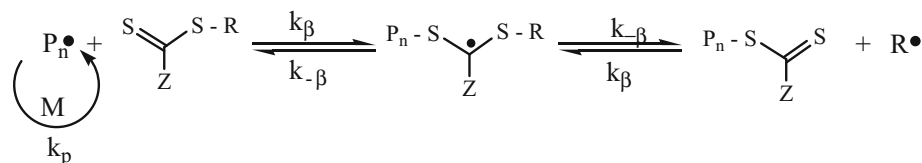
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Scheme 1 Mechanism of reversible addition-fragmentation chain transfer (RAFT) polymerization

Initiation



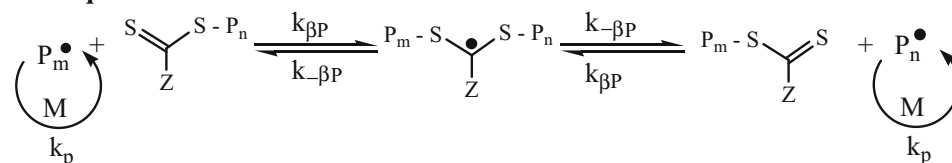
Reversible chain transfer, pre-equilibrium



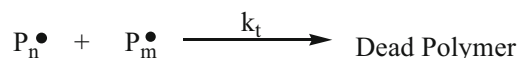
Reinitiation



Chain equilibration



Termination



between the active propagating radicals (P_n^\bullet and P_m^\bullet) and the dormant polymeric thiocarbonyl compounds [$\text{P}_n-\text{S}-\text{C}(\text{Z})=\text{S}$ and $\text{P}_m-\text{S}-\text{C}(\text{Z})=\text{S}$]; both the propagating radicals and the dormant chains have an equal probability of growth, permitting a narrow molecular weight distribution [5, 13, 14].

Both the reactive double bond $\text{C}=\text{S}$ and the simple weak $\text{S}-\text{R}$ bond are the structural keys of RAFT transfer agents based on thiocarbonyl compounds. Thus, by changing Z and/or R groups it is possible to determine the addition and fragmentation rate and, therefore, the activity of the RAFT agent. This is possible because the reacting propagating species as well as the partitions between reactants, monomer and agent are included inside the radicals. It is worth mentioning that the RAFT agent can be modified in such a way that it can be consumed quickly during the initial stages of polymerization, considering that the activity of the RAFT agent is controlled by a complex set of polar, steric, strain, and stereoelectronic effects [11] in a manner similar to that occurring in free radical reactions.

Conceptual density functional theory framework

The dependence of the activity of the RAFT agent on Z and R groups can be qualitatively predicted by low-level

molecular orbital calculations; that is, it is possible to obtain reactivity orders without performing excessive or expensive calculations [15]. This provides an idea of kinetic and chemical factors; although for more quantitative predictions, it is suggested that ab initio calculations of a higher level should be used. These kinds of studies will help to identify tendencies in the activity of a RAFT agent with Z and R substituents, which is a good reason to evaluate whether or not the ab initio simulation is a useful tool for designing RAFT agents [11]. Density functional theory (DFT) [16–18] is one of most widely used computational strategies for performing theoretical calculations; this tool is commonly used for the evaluation of organic molecules, and uses electronic density $\rho(x, y, z)$ instead of the wave functions used in calculations based on Hartree Fock (HF) formalism [19]. One reason why DFT is preferred is because it is a method that depends only on electronic distribution; i.e., it is a position function based on three variables (x, y, z). On the other hand, the wave function uses $4n$ variables and thus calculation difficulty increases as the number of electrons in the molecule increases, while the difficulty for DFT remains the same [18].

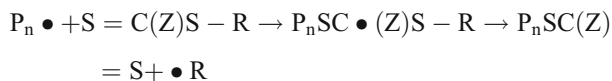
In contrast to experimental activity, ab initio molecular orbital calculations offer direct access to barriers, enthalpies and rate coefficients for individual reactions and should

provide a powerful tool for probing reaction mechanisms [20]. In addition, such theoretical calculations make it possible to understand the RAFT polymerization mechanism and to determine the reactivity tendency of the transfer agents. Coote and Radom [20] developed studies on RAFT polymerization kinetics using DFT/B3LYP/6–31G(d) in Gaussian 98 and 03 and G3(MP2)–RAD with MOLPRO 2000; they explained the inhibition periods that occur in these sorts of polymerizations in terms of the low fragmentation rate of the adduct radical [2, 20, 21]. Izgorodina and Coote [15] reported the calculation of β -scission reaction enthalpies for RAFT agents by means of the DFT, MP2 and ONION methods; they evaluated different basis sets and found that the RAFT process is a complex system for theoretical calculations. Nevertheless, they suggested that it is possible to develop new computational strategies to provide more information about the kinetics of this process. With the present study we attempt both to provide new information about RAFT process kinetics and to contribute to the understanding of RAFT polymerization by a theoretical evaluation of the role of the Z group in transfer agents.

Computational procedures

Gaussian 03 [22] is a chemical computation program used for evaluating chemical and structural properties by means of electronic structure. Among the properties that can be predicted are: molecular energy and structure, reaction energies, molecular atomic charges, vibrational frequencies, thermochemical properties, and reaction routes. Gaussian is supported by a graphic interface designed to help prepare input files and for graphically examining the output files that Gaussian generates.

DFT calculations were evaluated for 28 organic structures (Table 1), which were employed experimentally in polymerization via RAFT according to the addition-fragmentation reaction in pre-equilibrium as follows:



To evaluate the importance of the Z group, these 28 structures were optimized using the PBE1PBE [50] functional with 3–21G* basis set [51]. Before this computational procedure, the molecules were first optimized using SE/PM3, afterwards with HF/STO–3G* and HF/3–21G*, and finally by DFT/PBE1PBE/3–21G*. These optimizations were carried out with the objective of obtaining closer approximations for minimum energy as well as determining frequency calculations. Global reactivity descriptors, such as softness, hardness, electronegativity and philicity, were determined by ionization potential and electronic affinity calculations [52].

Absolute electronegativity was defined by Mulliken, in the sense that it does not depend on the molecular environment and can be obtained directly in terms of ionization potential and electron affinity, i.e.,: $\chi = (I + A)/2$. Electronegativity depends on the hybridization of atoms present in a molecule. In order to calculate the power of an atom to attract electrons to itself, one has to consider the charge effect on that atom. Hardness is another important parameter for understanding structure and reactivity, and the absolute hardness is given as $\eta = (I - A)/2$, which is the energy change of species in a disproportionation reaction of the type: $A^\bullet + A^\bullet \rightarrow A^+ + A^{\bullet\bullet-}$, $\Delta E = I - A$. The inverse of hardness is softness, which is given as $S = 1/2 \eta$. The concept of softness is associated with polarizability. The larger the chemical system, the softer it will be. This correlation of softness with polarizability can be found directly from a bond charge model where softness is found to be proportional to the internuclear distance of a molecule. Parr et al. [53] defined the electrophilicity index, $w = \mu^2/2 \eta$, which measures the propensity of electrophilic attack. This is the concept of by far the most powerful and general reactivity and selectivity index [52, 54].

On the other hand, the ionization potential, I , and electron affinity, A , can be approximated as the negative of energies of the highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO), respectively, using Koopmans' theorem. In this framework, the electronegativity is the negative of HOMO–LUMO energy average and is written as $-\chi = \mu = 1/2 (\epsilon_{\text{HOMO}} + \epsilon_{\text{LUMO}})$; the hardness becomes half of the energy gap between HOMO and LUMO as: $\eta = 1/2 (\epsilon_{\text{HOMO}} - \epsilon_{\text{LUMO}})$. This definition, like ours, has a direct consequence on reactivity theories as a large HOMO–LUMO gap signifies reluctance of the system to take or give up electrons [19, 52].

The efficacy of a RAFT agent is related strongly to the efficiency of the Z group in stabilizing the double C=S bond by allowing the addition step and the readiness of R to be both a good leaving group and a prompt polymerization reinitiator. The Z group was modified by taking into account the following substituents: $-\text{CH}_3$, $-\text{CH}_2\text{Ph}$, $-\text{Ph}$, $-\text{OEt}$, $-\text{OPh}$, $-\text{OC}_6\text{H}_5$, $-\text{Pyrrol}$, $-\text{Npyrrol}$, $-\text{Noxipyrrol}$, $-\text{N}(\text{Et})_2$. The R group was modified in the following way: $-\text{CH}_2\text{Ph}$, $-\text{CH}_2\text{COOH}$, $-\text{CH}(\text{CH}_3)\text{Ph}$, $-\text{CH}(\text{CH}_3)\text{CO}_2\text{CH}_3$, $-\text{CH}(\text{CH}_3)\text{CO}_2\text{Et}$, $-\text{CH}(\text{CH}_3)\text{CON}(\text{CH}_3)_2$, $-\text{C}(\text{CH}_3)\text{Ph}$, $-\text{C}(\text{CH}_3)_2\text{CN}$, $-\text{C}(\text{CH}_3)_2\text{CONH}_2$, $-\text{C}(\text{CH}_3)_2\text{CO}_2\text{Et}$, $-\text{C}(\text{CH}_3)\text{C}_6\text{H}_8\text{OCH}_3$, $-\text{C}(\text{CH}_3)(\text{CN})(\text{CH}_3)_2\text{OH}$, $-\text{C}(\text{CH}_3)(\text{CN})(\text{CH}_3)_2\text{COOH}$, $-\text{C}(\text{CH}_3)_3$.

Results and discussion

Radical polymerization via RAFT is based on an equilibrium between active and dormant species generated by a

Table 1 Twenty-eight reversible addition-fragmentation chain transfer polymerization (RAFT) agents evaluated with DFT/PBE1PBE/3–21G*. *DT* Dithioesters, *DC* dithiocarbamates, *X* xanthates, *T* trithiocarbonate, *Ph* phenyl

| RAFT agent | Molecules | Z group | R group | References |
|------------|--|---|--|----------------|
| DT-1 | Benzylthioacetate | –CH ₃ | –CH ₂ Ph | 2, 4, 15, 23 |
| DT-2 | Benzylthiobenzoate | –Ph | –CH ₂ Ph | 24–27 |
| DT-3 | S-Thiobenzoylthioglycolic Ac. | –Ph | –CH ₂ COOH | 28–30 |
| DT-4 | 1-Methoxy carbonylethylthiobenzoate | –Ph | –CH(CH ₃)COOCH ₃ | 31 |
| DT-5 | N, N-Dimethyl S-thiobenzoyl thiopropionamide | –Ph | –CH(CH ₃)CON(CH ₃) ₂ | 27, 32 |
| DT-6 | 1-Phenyl ethylthiobenzoate | –Ph | –CH(CH ₃)Ph | 4, 23, 25, 31 |
| DT-7 | 1-Butylthiobenzoate | –Ph | –C(CH ₃) ₃ | 25, 27, 33, 34 |
| DT-8 | 2-Cyanoprop-2-ylthiobenzoate | –Ph | –C(CH ₃) ₂ CN | 8, 11, 27, 35 |
| DT-9 | S-Thiobenzoylthioglycolic Ac. (2) | –Ph | –C(CH ₃) ₂ CONH ₂ | 28 |
| DT-10 | 2-(Ethoxycarbonyl)prop-2ylthiobenzoate | –Ph | –C(CH ₃) ₂ COOCH ₂ CH ₃ | 1, 6, 25, 33 |
| DT-11 | 2-Phenylprop-2-ylthiobenzoate | –Ph | –C(CH ₃) ₂ Ph | 11, 27, 36, 37 |
| DT-12 | 1, 4 Methylcyclohexan-2-onyl 1-methylethylthiobenzoate | –Ph | –C(CH ₃) ₂ C ₆ H ₈ OCH ₃ | 30 |
| DT-13 | 4-Cyano-1-hydroxypent-4-ylthiobenzoate | –Ph | –C(CH ₃)(CN)CH ₂ CH ₂ CH ₂ OH | 4, 11, 33 |
| DT-14 | 4-Cyano 4-thiobenzoylsulfanylpentanoic Ac. | –Ph | –C(CH ₃)(CN)CH ₂ CH ₂ COOH | 11, 27, 35, 38 |
| DT-15 | 1-Phenylethylphenylthioacetate | –CH ₂ Ph | –CH(CH ₃)Ph | 39, 40 |
| DT-16 | 2-Phenylprop-2-ylthioacetate | –CH ₂ Ph | –C(CH ₃) ₂ Ph | 39, 41–43 |
| DC-1 | S (2 Cyanoprop-2-yl) N,N dimethylthiocarbamate | –N(CH ₃) ₂ | –C(CH ₃) ₂ CN | 24 |
| DC-2 | S-Benzyl N, N-diethylthiocarbamate | –N(CH ₂ CH ₃) ₂ | –CH ₂ Ph | 24, 25, 44 |
| DC-3 | 2-Cyanoprop-2-yl 1-pyrrolicarbodithioate | –Pyrrole | –C(CH ₃) ₂ CN | 8, 11, 24, 44 |
| DC-4 | S-Benzyl N-pyrrolicarbodithioate | –Pyrrole | –CH ₂ Ph | 24, 25, 27, 44 |
| DC-5 | Benzyl 1-imidazolyncarbodithioate | –Imidazolylene | –CH ₂ Ph | 24 |
| DC-6 | Benzyl 2-pyrrolidone 1-carbodithioate | –Pyrrolidone | –CH ₂ Ph | 11, 25, 44 |
| X-1 | O-Ethyl S-benzylthiocarbonate | –OCH ₂ CH ₃ | –CH ₂ Ph | 25, 27, 44 |
| X-2 | Xanthate 1 | –OCH ₂ CH ₃ | –CH(CH ₃)COOCH ₂ CH ₃ | 8 |
| X-3 | 1-O-Ethylxathylethylbenzene | –OCH ₂ CH ₃ | –CH(CH ₃)Ph | 27, 45–47 |
| X-4 | O-Phenyl-S-benzylxanthate | –OPh | –CH ₂ Ph | 25, 44 |
| X-5 | O-Pentafluorophenyl S-benzylxanthate | –OC ₆ F ₅ | –CH ₂ Ph | 8, 11, 25, 44 |
| T-1 | Dibenzyltrithiocarbonate | –SCH ₂ Ph | –CH ₂ Ph | 11, 27, 48, 49 |

reversible process of addition-fragmentation [30], in which the transfer agent is a thiocarbonyl compound with the generic structure S=C(Z)S–R, frequently dithioesters [2, 5, 55, 56], xanthates [57], dithiocarbamates [44] or trithiocarbonates [44]. Thus, the efficiency of a RAFT agent in conferring living properties is attributed to its transfer constant, which ensures the interchange rate between dormant species and living chains. Selection of the Z and R groups in the transfer agent is decisive in polymerization performance; so, in order to obtain a high transfer constant, Z should activate (or at least not deactivate) the double C=S bond for the addition of the initiating radical [4, 33, 44]. At present, it is possible to control polydispersity and molecular weight under certain reaction conditions, which depend on the nature of the Z and R groups and the monomer used in the system. R is a homolytic leaving group that has the ability to efficiently reinitiate polymerization and generate transference between chains. Z is a

group that modifies the reactivity of the thiocarbonylthio compounds and radical adduct derivatives [44].

In living/controlled polymerization, the effectiveness of the equilibrium between active and dormant species generates the reversible addition-fragmentation process. Furthermore, its efficiency depends on the Z and R substituents as well as the monomer type used in the reaction. The addition step is related mainly to the Z group which, at the same time, is governed by the reactivity of the double C=S bond. On the other hand, the R group is affected mainly by the fragmentation process. Therefore, a good leaving group (which must be favored by steric hindrance and radical stability) often makes the S–R bond weaken and, as a result, the discharged R• radical should be a good chain reinitiator [30].

The results obtained for the minimum energy (neutral radical), negative ion and positive ion, HOMO and LUMO are presented in Table 2. Using these results, the global

Table 2 Calculation of neutral energies, positive ion energies, negative ion energies, highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) of 28 agents employed in RAFT polymerization with density functional theory (DFT)/PBE1PBE/3–21G*

| RAFT agent | E0 Ev | E+1 | E-1 | HOMO eV | LUMO |
|------------|------------|------------|------------|------------|---------|
| DT-1 | -30,994.31 | -30,985.90 | -30,994.17 | -6.1495 | -1.6651 |
| DT-2 | -36,176.93 | -36,169.15 | -36,177.49 | -6.1327 | -2.1236 |
| DT-3 | -35,028.89 | -35,020.87 | -35,029.19 | -6.2162 | -2.0101 |
| DT-4 | -37,154.22 | -37,146.36 | -37,154.87 | -6.1607 | -2.2485 |
| DT-5 | -37,679.72 | -37,671.88 | -37,680.42 | -6.2415 | -2.2782 |
| DT-6 | -37,239.73 | -37,232.02 | -37,240.36 | -6.0995 | -2.1845 |
| DT-7 | -33,119.80 | -33,112.07 | -33,120.34 | -6.0225 | -2.1527 |
| DT-8 | -34,550.23 | -34,542.13 | -34,551.13 | -6.4214 | -2.5056 |
| DT-9 | -36,617.43 | -36,609.50 | -36,618.33 | -6.2851 | -2.5010 |
| DT-10 | -39,279.99 | -39,272.18 | -39,280.54 | -6.1479 | -2.0999 |
| DT-11 | -38,302.29 | -38,294.68 | -38,302.92 | -6.0124 | -2.1388 |
| DT-12 | -41,464.43 | -41,456.76 | -41,465.23 | -6.1057 | -2.3372 |
| DT-13 | -38,708.65 | -38,700.71 | -38,709.46 | -6.2970 | -2.3780 |
| DT-14 | -40,710.33 | -40,702.24 | -40,711.31 | -6.4413 | -2.5519 |
| DT-15 | -38,302.26 | -38,294.63 | -38,302.19 | -5.9912 | -1.5837 |
| DT-16 | -39,365.09 | -39,357.45 | -39,365.08 | -5.9969 | -1.6009 |
| DC-1 | -31,926.80 | -31,918.73 | -31,925.89 | -6.1754 | -0.8025 |
| DC-2 | -35,678.93 | -35,671.38 | -35,678.15 | -5.6396 | -0.9195 |
| DC-3 | -33,953.59 | -33,945.08 | -33,954.25 | -6.7936 | -2.2651 |
| DC-4 | -35,580.19 | -35,572.18 | -35,580.70 | -6.3403 | -2.1070 |
| DC-5 | -36,013.70 | -36,005.39 | -36,014.54 | -6.6364 | -2.4735 |
| DC-6 | -37,647.75 | -37,639.94 | -37,647.86 | -6.0984 | -1.6958 |
| X-1 | -34,090.72 | -34,082.59 | -34,090.07 | -6.4018 | -1.0403 |
| X-2 | -36,130.84 | -36,122.48 | -36,130.30 | -6.4902 | -1.2025 |
| X-3 | -35,153.52 | -35,145.43 | -35,152.91 | -6.3893 | -1.0523 |
| X-4 | -38,210.54 | -38,202.46 | -38,210.14 | -6.4524 | -1.2482 |
| X-5 | -51,625.89 | -51,617.43 | -51,626.66 | -6.8565 | -2.4330 |
| T-1 | -48,020.69 | -48,012.79 | -48,020.87 | -6.4081 | -1.7266 |

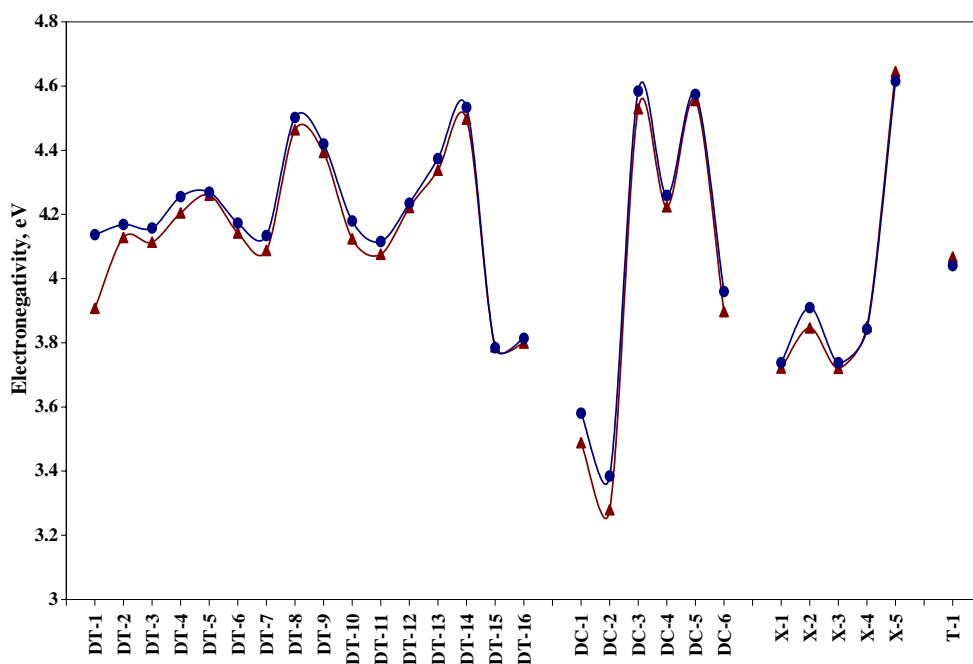
reactivity descriptors were evaluated for all the structures, taking into account the electronic affinities and ionization potentials, using the Mulliken scale and Koopmans' theorem.

Electronegativity [54] and hardness [58] are two important descriptors of global reactivity. Electronegativity is defined as the ability of an atom in a molecule to attract electrons; absolute electronegativity, as defined by Mulliken, does not depend on the environment to which the molecule is subject and can be obtained from two experimentally measurable variables: ionization potential and electronic affinity. In some cases, the difference in electronegativity by itself cannot be taken into account for determining the stability of the molecule. For this reason, Pearson [59] introduced two useful parameters: hardness and softness, corroborating the hard-soft acid-base (HSAB)

principle. This principle establishes that a reaction site with large softness values could prefer to react with soft species or with the softest site of a species, and a hard reaction site should be involved with hard–hard interactions. The HSAB principle has been used to understand the selective sites of a molecule. Because of this, it is suggested that soft molecules are more reactive in comparison to their hard counterparts [52].

Figure 1 shows the electronegativity of the 28 transfer agents evaluated with Gaussian. Even though electronegativity is a relative concept, that is, it can be measured only by comparing two elements, it provides an estimation of the ability of a compound to accept electrons, which in the present case was favored for dithioesters and dithiocarbamates. In generally, dithioesters are divided into two families according to their Z group: dithioacetates and

Fig. 1 Global electronegativity calculated with density functional theory (DFT)/PBE1PBE/3–21G*. *DT* Dithioesters, *DC* dithiocarbamates, *X* xanthates, *T* trithiocarbonate. ● Mulliken's scale, ▲ Koopmans' theorem



dithiobenzoates. As can be observed, the dithiobenzoates DT-8 and DT-14 presented the best ability for accepting electrons, while the dithioacetates DT-1, DT-15, and DT-16 showed negative electronic affinity, indicating that its electron-attracting strength is limited. This is due likely to the presence of the methyl in the $-\text{CH}_2\text{Ph}$ group, which stabilizes the adjacent radical center and prevents the acceptance of electrons inside the group; therefore, electronegativity was lower than in the dithiobenzoates.

Electronegativity was higher for the dithiocarbamates with pyrrol groups, DC-3 and DC-5, than for the groups $-\text{N}(\text{CH}_3)$ or $-\text{N}(\text{CH}_2-\text{CH}_3)$, DC-1 and DC-2, respectively, due to electron delocalization in the aromatic compound. It can also be observed that X-5 presented a higher value of electronegativity than X-1, even though the latter has the Z group $\text{O}-\text{CH}_2\text{CH}_3$, which is a more selective group to form free radicals (by minimizing reactivity) contrary to the O-pentafluorophenyl group of X-5, which presented a higher reactivity due to the presence of fluoride atoms, and therefore, a considerable capacity to attract electrons [60].

When Z groups contain dialkylamines or alkoxy radicals, i.e., dithiocarbamates and xanthates, respectively, the RAFT agents presented low transfer constants and were relatively ineffective [4]. The dissociation energies of the C–H bond for this type of compound presented a low activity of dithiocarbamate [$\text{Z} = \text{N}-(\text{alkyl})$] and xanthate ($\text{Z} = \text{O}-\text{alkyl}$) derivatives [44]. It has been reported that this low relative activity of dithiocarbamates and xanthates could be due to a phenomenon called zwitterionic canonical forms (Fig. 2) [44], which arises from interaction between pairs of electrons from oxygen or nitrogen with the double $\text{C}=\text{S}$

bond. A zwitterion is an ionic species that carries a total net charge of 0; however, it carries formal positive and negative charges in different atoms. This term refers to compounds with non-adjacent positive and negative charges. Zwitterions are polar and are usually water-soluble, but poorly soluble in most organic solvents. This factor reduces the reactivity of the double $\text{C}=\text{S}$ bond of dithiocarbamate and xanthate towards the addition of free radicals. This phenomenon led to the expectation that substituents that accept electrons, or those that have the ability to delocalize the pair of electrons only, could increase the activity of these compounds [25, 44]. The low activity of dithiocarbamates and xanthates could be due to their ability to stabilize an adjacent center radical more than aliphatic substituents or adjacent sulfide [44]. This behavior was also exhibited by the capability of accepting electrons from other elements, i.e., the electronic affinity of the molecule, which was lower in these compounds. Likewise, the xanthates and

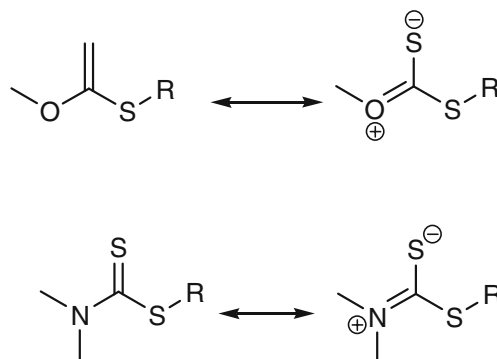


Fig. 2 Zwitterionic canonical schemes

dithiocarbamates studied here presented similar electronegativities, probably due to the same effect. Compound X-5 showed the highest electronegativity, which was attributed to the presence of the highly electronegative fluor atoms in the molecule.

By comparing the chemical structures of the different families, it was possible to figure out that the compound with highest electronegativity was X-5, a xanthate, followed by DC-3 and DC-5, which are dithiocarbamates; these were then followed by two dithiobenzoates, DT-8 and DT-14, and finally, the trithiocarbonate T-1. This sequence could be explained in terms of the molecules' ability to attract electrons; however, it seems more a consequence of the number of electrons prompted to react inside the molecules.

Figure 3 shows the results of philicity—a reactivity descriptor that allows a quantitative classification of the global electrophilic nature of a molecule in a relative scale where philicity is a measurement of the energy lost due to the maximum flow between a donor and an acceptor [61]. These results kept the same tendency as electronegativity. It is known that when a molecule is formed, atomic electronegativity switches to molecular electronegativity, which is constant anywhere within the molecule. For this reason, it has been suggested that electronegativity cannot appropriately take into account all aspects of a chemical process; therefore, it is necessary to include another parameter: softness. Hardness is defined as the resistance of a given compound to any change in its electronic distribution and is a global property system. On the contrary, softness, which is the inverse of hardness, then predicts the affinity that has a particular chemical system to modify its electronic structure as well as to react to a

particular external chemical potential [52]. The results of global softness are shown in Fig. 4. It can be observed that the dithioacetates were less susceptible to electron exchange, i.e., their softness was lower than in the rest of the dithioesters. This corroborates the fact that the benzyl group stabilizes the agent more strongly by obstructing its reaction. Additionally, it can be observed that reactivity with respect to the R group was higher for the dithiobenzoates than for the dithioacetates even though both contain tri-substituted groups with aromatic rings. This characteristic suggested, in general, that the inclusion of an aromatic ring, i.e., a planar group with a high molecular mass, generates higher steric hindrance and, consequently, higher stability than other groups such like alkyl radicals. Among tri-substituted compounds, softness competes with aromatic groups such as DT-11 and DT-12. The slight increase in softness of the DT-12 group was due to the fact that its R was comparatively larger than that of the other compounds. It was clear that any tri-substituted group presented higher softness with respect to mono- and bi-substituted groups. Softness was affected by aromatic rings because these provide higher susceptibility to function as effective leaving groups.

The Z group has a strong effect on the stability of the RAFT adduct radical, and is positioned directly towards the carbon of the unpaired electron in the adjacent radical center. It is believed that phenyl substituents, like dithiobenzoates, stabilize the adduct properly due to their ability to dislocate an unpaired electron inside the aromatic ring. In this case, the large exothermic event produced by the addition reaction between the substituted agents and benzyls could be an indication of the high ability of freeing steric forces inside the reaction [2].

Fig. 3 Global philicity calculation using DFT/PBE1PBE/3-21G*. DT Dithioesters, DC dithiocarbamates, X xanthates, T trithiocarbonate. ● Mulliken's scale, ▲ Koopmans' theorem

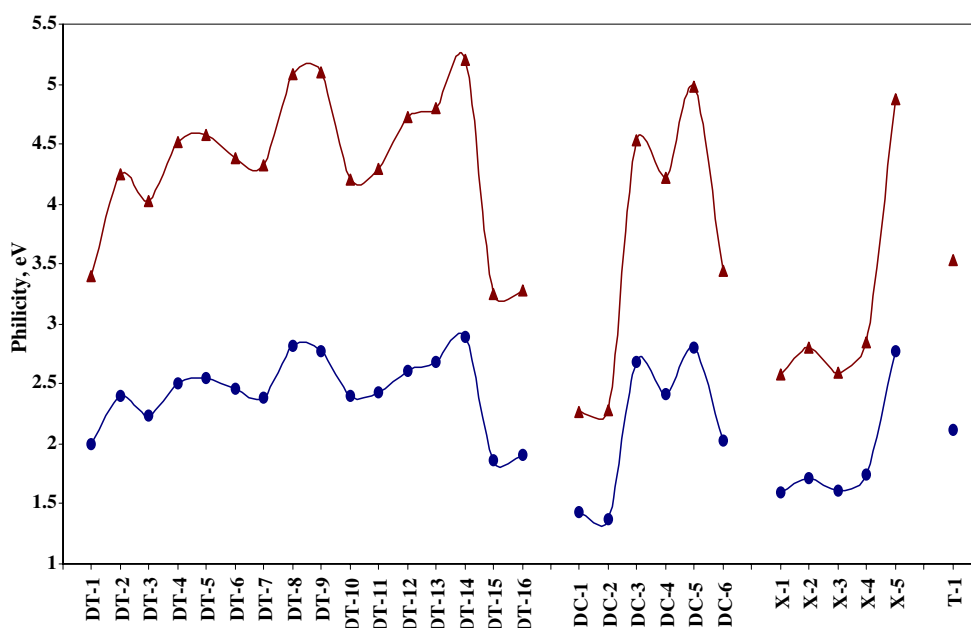
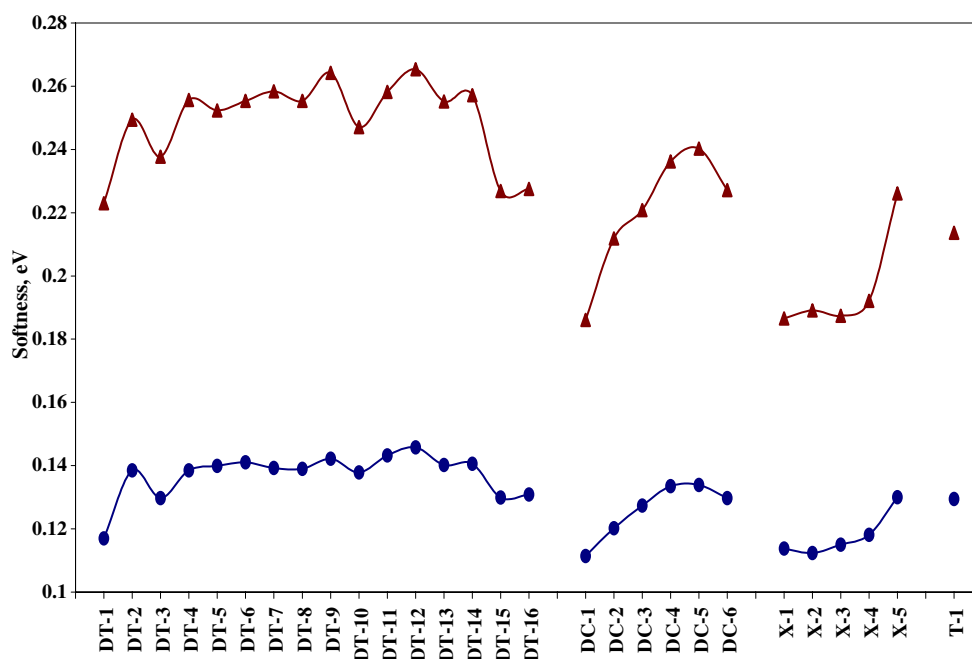


Fig. 4 Global softness calculated by DFT/PBE1PBE/3–21G*. *DT* Dithioesters, *DC* dithiocarbamates, *X* xanthates, *T* trithiocarbonate. ● Mulliken's scale, ▲ Koopmans' theorem



The change between benzyl or cyanoisopropyl groups produced differences in transfer coefficients, due mainly to the influence of the Z group on the addition rate of the free radical on the double C=S bond. The partition of the adduct radical between the initial compounds and products could be determined by the ability of the leaving R group and polymeric radical as well as their constants [44].

With regard to dithiocarbonates, when R was a benzyl group, softness was preferably higher. Although in this case, there was competition with the bi-substituted group of X-3. From among these compounds, X-1, X-2 and X-3 had the same Z group: $-\text{O}-\text{CH}_2\text{CH}_3$. It is possible to observe the preference of softness in groups with a higher number of substituents in the central carbon of the R group.

Despite the fact that DC-1 and DC-3 agents (dithiocarbamates) contain tri-substituted leaving R groups, the $-\text{CH}_2\text{Ph}$ group resulted in lower softness compared to other dithiocarbamates, which was attributed to the planarity and high molar mass of the phenyl group, which in turn increases the steric hindrance. Additionally, T-1, the only trithiocarbonate studied, was the second least reactive or hard compound, which was attributed to the fact that its leaving groups are identical (R and Z). Thus, the influence on their susceptibility to react could be expected to be the same. Nevertheless, these leaving R (or Z) groups had a lower molar mass and were more stable; therefore, they did exhibit anything like the hindrance produced in compounds with higher molar masses, such as DT-12 [49, 62, 63].

Global softness as a reliable reactivity descriptor resulted in the following order of reactivity: dithioesters (dithiobenzoates) > dithioacetates > dithiocarbamates > dithiocarbon-

ates (xanthates) > trithiocarbonates. Thus the influence of the different Z groups can be described as follows:

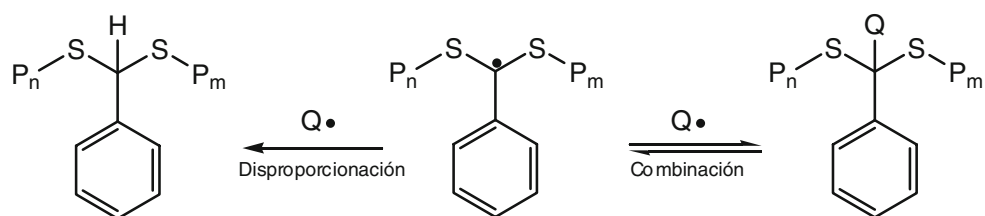


The Z group has a strong effect on the stability of the RAFT adduct radical and is positioned towards the carbon of the unpaired electron. It is believed that phenyl substituents, such as dithiobenzoates, stabilize the adduct properly due to a higher ability to dislocate an unpaired electron inside the aromatic ring. In this case, the large exothermic event produced by the addition reaction between the substituted agents and benzyls could be an indication of the high ability of freeing steric forces in the addition-fragmentation steps [2], i.e., easy breakage of the S-R link.

The exchange of benzyl for cyanoisopropyl groups in the transfer agent produced differences in transfer coefficients, which were due mainly to the influence of the Z group on the addition rate of the free radical on the double C=S bond. Partition of the adduct radical between the initial compounds and products could be determined by the ability of the leaving R group and polymeric radical as well as their constants [44].

Recently, Chong et al. [33] reported that polymerizations with styrene carried out with dithiobenzoate derivatives showed a marked retardation even at very high DT-11 concentrations, but found that retardation is much lower utilizing DT-8 under the same conditions. It is believed that a possible reaction route of the adduct with small propagating radicals existed through combination or disproportionation, inhibition of which is possibly generated by these potential parallel reactions (Fig. 5) [33].

Fig. 5 Potential parallel reactions in the RAFT process



In particular, in order to explain the retardation rate of DT-11, some researchers [18, 56] have postulated the existence of an auto-terminating reaction, where the radical RAFT adduct terminates by itself or with a propagating radical. Nevertheless, experimental evidence for the kinetic significance of this reaction has been contradictory [2].

Based on the transfer mechanism of addition-fragmentation, there are four factors that could influence the effectiveness of dithiobenzoates as transfer agents: (1) the rate constant or the reaction of dithiobenzoate with the propagating radicals or radicals derived from the initiator; (2) the partition of the adduct radical between initiating compounds and products determined by the relative magnitude of the addition constant and the fragmentation constant; (3) the rate constants for the fragmentation of intermediate radicals, and (4) the ability of the expelled radical to reinitiate polymerization [33].

Factors (1) and (2) could be manifested directly in the magnitude of the transfer coefficient of the dithiobenzoate. Factor (3) does not directly affect the transfer coefficient. Nevertheless, if the fragmentation is especially low or the reinitiation of polymerization is slow with respect to propagation, then polymerization could be retarded and the probability that the R• and/or adduct radicals could undergo parallel reactions producing the increment of some degree of inhibition increases. This retardation can be observed in RAFT polymerizations with certain dithiobenzoate derivatives when agent concentrations are very high [33].

As transfer agents, the trithiocarbonates have two identical leaving groups, i.e., both benzyl groups, which act at the radical adjacent center. These compounds can have a transfer constant higher than a monobenzyl compound, as they can follow two fragmentation routes towards the intermediate adduct [44]. Usually, the trithiocarbonates are the simplest bifunctional agents to obtain polymers in triblocks, and are useful as precursors for obtaining polymeric arms of the same size and composition [8]. However, it has also been reported that trithiocarbonates function like effective RAFT agents. Their notable characteristic is that they can be prepared in different fashions and present good leaving homolytic groups and, consequently, form copolymers in ABA triblocks [61], which are obtained from a monomer addition sequence in two steps. These compounds effectively control the

polymerization of styrene, methylmetacrylate and methyl acrylate, developing very low polydispersities, which can be obtained at high conversions [48].

Transfer agents with benzyl and phenyl groups are the most studied and exhibit quite acceptable answers when simulation and experimental results are compared. This study has determined that transfer agents that form with the benzyl group, such as the Z group, exhibited higher susceptibility to react; i.e., their global softness was more pronounced than that of the other compounds. Results for xanthates and dithiocarbamates agreed with those already reported [24, 47, 64]; nevertheless, contrary to our results, trithiocarbonates have been reported as effective transfer agents. It is possible that the low reactivity of the trithiocarbonate studied, T-1, was due to its Z and R groups being identical. Their reactivity was therefore apparently divided between both leaving groups, consequently reducing the possibility of reaction.

With respect to the Z group, some important factors must be considered when determining the addition rate of the free radical to the thiocarbonylthio compound. It is clear that the stability of the generated radicals, or, better yet, the ability of the Z group to stabilize an adjacent radical center, is not, in itself, a predictive tool for estimating transfer coefficients [44].

RAFT agents with phenyl and benzyl substituents in the Z position (but with methyl groups as the R substituent) exhibited a vigorous retardation rate; however, methyl groups in the Z position did not exhibit this feature. This fact notwithstanding, it was clear that RAFT agents with larger R groups had equilibrium constants considerably lower than those with methyl groups. Therefore, it is possible that the use of non-methyl, phenyl, or benzyl R groups in RAFT agents could result in the observed retardation rates. In order to determine if low fragmentation contributes to the retardation rate in real RAFT systems, it is necessary to consider the effects of R and Z substituents acting together [2].

Nevertheless, despite the experimental agreement reported in this study, and the computational procedures performed, it can be seen that softness as a global reactivity descriptor yielded very close results (Fig. 4), i.e., the difference between the first five agents was small and did not guarantee that the first one is the most reactive compound. Furthermore, another descriptor of global

reactivity, electrophilicity, indicated that an S–thiobenzoyl thioglycolic acid derivate, DT–9, had the highest reactivity. Thus, it is necessary to use local reactivity descriptors in order to obtain clearer results to suggest environments informing an agent's reactivity by using electronic charge distribution mathematical formalisms such as Fukui indices.

Conclusions

Through the theoretical studies performed here, by using DFT methods, it was possible to predict the order of reactivity for the Z group of a series of RAFT agents. The results showed that substituents that were better able to stabilize the transfer agent were those containing benzyl groups, as in the case of dithiobenzoates (dithioesters), followed, in order of reactivity, by the dithiocarbamates and xanthates, and finally trithiocarbonate. Although the global reactivity descriptors (softness, hardness, electronegativity and philicity) provided information about the reactivity of the Z group, it is necessary to extend the study by evaluating the importance of the R group, since information on the Z group itself was not enough to predict the efficiency of a transfer agent in a given RAFT polymerization.

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