

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

Part 2: Group R

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Abstract Density functional theory, DFT, PBE1PBE functional and 6-31+G(d,p) basis set in Gaussian 03 software were used in order to determine the reactivity order of the R group in RAFT agents used in the radical addition-fragmentation transfer polymerization, through the evaluation of reactivity parameters such as: global and local electronegativity, hardness, softness, and philicity. It was found that the reactivity order is governed by both the number and the composition of the substituent group (primary, secondary or tertiary); that is, the larger those parameters are the larger factors like steric hindrance, polar effects and electronic interchanges are, which favors the breaking of the C–S bond from the adduct radical, permitting the exit of the leaving radical and allowing, as a consequence, the fragmentation step in RAFT polymerization. Trisubstituted dithioesters with structure $S=C(Z)S-R$, where $Z=Phenyl$ and $R=C(CH_3)_2CONH_2$, $C(CH_3)_2Ph$ or $(CH_3)_2C_6H_8OCH_3$, in accordance with the previously exposed, presented the most favorable reactivity parameters.

Keywords DFT · RAFT · Reactivity order · Softness-hardness · Transfer agent

Introduction

RAFT polymerization mechanism, Scheme 1 [1, 2], involves a series of reversible addition-fragmentation steps; *i.e.*, the addition of a propagating radical (P_n^\bullet) to the thiocarbonyl compound $S=C(Z)S-R$ 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 with the monomer (M) generates a new propagating radical P_m^\bullet . The subsequent addition-fragmentation steps allow a dynamic equilibrium which establishes itself between the active propagating radicals (P_n^\bullet and P_m^\bullet) and the dormant polymeric thiocarbonyl compounds [$P_n-S-C(Z)=S$ and $P_m-S-C(Z)=S$]; both having an equal probability of growing from all of the chains. This permits a narrow molecular weight distribution [1, 3, 4].

Radical polymerization *via* RAFT is based on an equilibrium between active and dormant species generated by a reversible process of addition-fragmentation [5, 6], in which the transfer agent is a thiocarbonylthio based compound with the generic structure $S=C(Z)S-R$, frequently called: dithioesters [1, 7–10], xanthates [11], dithiocarbomates [11, 12] or trithiocarbonates [12, 13].

The efficiency of RAFT agents in conferring living properties to polymers obtained is attributed to their transfer constants, which insure the interchange rate between dormant species and living chains; therefore, the selection of Z and R in transfer agents is crucial to polymerization success [12, 14, 15].

Recently some theoretical studies related to chain transfer agents used in RAFT polymerization have been developed with different computational strategies [16–18]. In a previous study we reported the importance of the Z

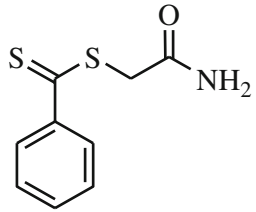
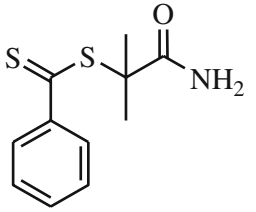
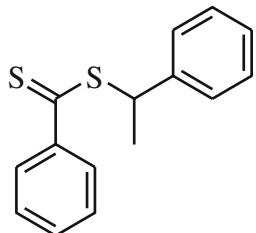
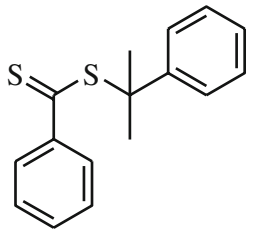
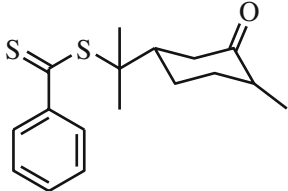
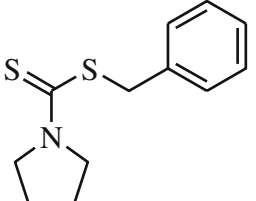
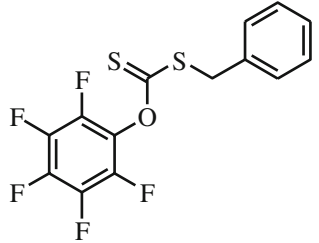
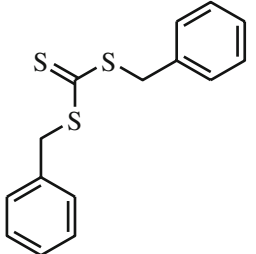
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environment and can be directly obtained in terms of two experimental quantities, ionization potential and electron affinity, such as: $\chi = (I + A)/2$. The electronegativity depends on the hybridization of atoms in which the atom is present in the molecule. In order to calculate the power of an atom to attract electrons to it one has to consider charge effects on it. In a chemical system of interest, electrons will be distributed in such a way that the electronegativity of orbitals will be equal to the electronegativity on the system. Electronegativity was defined by Allred and Rochow such that provides a direct physical interpretation of it as “the electron - attracting power of atoms”.

However, in many cases, electronegativity difference alone cannot account for the stability of the molecule [37].

Hardness is another important parameter for understanding structure and reactivity; 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 is, the softer it will be. This correlation of softness with polarizability can be found directly from a bond charge

Table 1 RAFT transfer agents evaluated with DFT/PBE1PBE/6-31+G**

 <p>D1: S-Dithiobenzoylthioglycolic ac. [5, 25, 26]</p>	 <p>D2: S-Dithiobenzoylthioglycolic ac. 2 [25]</p>
 <p>D3: 1-Phenylethyl dithiobenzoate [14,28-30]</p>	 <p>D4: Cumyl dithiobenzoate [2,27,31,32]</p>
 <p>D5: Mentonyl dithiobenzoate [5]</p>	 <p>DC1: S-Benzyl N-pyrrolcarbodithioate [2,12,33]</p>
 <p>X1: O-pentafluorophenyl S-benzylxanthate [12,27,29,34]</p>	 <p>T1: Dibenzyl trithiocarbonate [2,27,35,36]</p>

D: Dithioesters, DC: Dithiocarbamates, X: Xanthates, T: Trithiocarbonate.

model where softness is found to be proportional to the internuclear distance of a molecule. Parr *et al.* [38, 39] defined electrophilicity index, $w = \mu^2/2\eta$, which measures the propensity of electrophilic attack. Electrophilicity is by far the most powerful concept, as it contains almost all information obtainable from global and local reactivity and selectivity descriptors, in addition to the information regarding electrophilic and nucleophilic power of a given atomic site in a molecule [37, 40].

On the other hand, the ionization potential, I , and electron affinity, A , can be calculated as the negative energies of both the highest occupied molecular orbital, HOMO and lowest unoccupied molecular orbital, LUMO, respectively, by using Koopmans' theorem. In this framework, the electronegativity is the average negative energy of HOMO-LUMO and is written as $-\chi = \mu = \frac{1}{2}(\epsilon_{\text{HOMO}} + \epsilon_{\text{LUMO}})$; the hardness becomes half of the energy gap between HOMO and LUMO as: $\eta = \frac{1}{2}(\epsilon_{\text{HOMO}} - \epsilon_{\text{LUMO}})$. This definition has a direct consequence on the reactivity theory as a large HOMO-LUMO gap signifies reluctance of the system to take or give electrons [37, 41].

With the knowledge of global parameters, such as electronegativity and hardness it is possible to obtain information about the general reactivity. However, the reactivity of a particular site in molecular species would be explained by using local quantities; that is, electronic density, $\rho(r)$, Fukui indices, $f(r)$, local hardness or local softness, local electronegativity and local philicity. The dependence of these local quantities upon the reaction, show the utility of these local parameters in the prediction of selective sites of studied chemical reactions [37].

The second important derivative of the electronic chemical potential, $\mu[N, v]$, is the space-dependent (local) function, Eq. 1:

$$f(r) = \left[\frac{\delta\mu}{\delta v(r)} \right]_N = \left[\frac{\partial\rho(r)}{\partial N} \right]_v \quad (1)$$

which, for reasons that will shortly become clear, is called the Fukui function for the system. It is normalized: $\int f(r) dr = 1$. The physical meaning of $f(r)$ is implied by its definition as $[\delta\mu/\delta v(r)]_N$: it is a measure of how sensitive the chemical potential of a system is to an external perturbation at a particular point. The second formula for $f(r)$, written as $[\partial\rho(r)/\partial N]_v$, shows that it is a quantity involving atom or molecule electron density in its frontier, valence region. Assuming that it goes from N electrons to $N + \delta$ electrons, for some system, the only change in the electronic structure would be the addition of δ electrons to some density $\partial\rho$ normalized to unity. Under this "frozen core" assumption, $\Delta \int \sum [\partial\rho(r)/\partial N]_v$ would be just $\partial\rho$. The derivative $\partial\rho(r)/\partial N$ at some integral value of N will in general have one value from the right, one from the left, and an average. Consequently we have three indices or

Fukui functions: electrophilic, nucleophilic or radical attack at a particular reactions site. By using difference and frozen core approximations, these three Fukui functions that provide a correspondence between this local parameter and the frontier orbital theory of chemical reactions, justifies the nomenclature of Fukui (frontier) function. A large value of f^- , f^+ , or f^0 at a particular site denotes the high probability of electrophilic, nucleophilic or radical attack to take place at that site. The expression for condensed Fukui functions for the i atom in a molecule can be obtained by considering finite differences shows in Eq. 2 for nucleophilic attack, Eq. 3 for electrophilic attack, and Eq. 4 for radical attack: [37, 40, 42, 43]

$$f^+(\vec{r}) = \rho_{N+1}(\vec{r}) - \rho_N(\vec{r}) \quad \text{for nucleophilic attack} \quad (2)$$

$$f^-(\vec{r}) = \rho_N(\vec{r}) - \rho_{N-1}(\vec{r}) \quad \text{for electrophilic attack} \quad (3)$$

$$f^0(\vec{r}) = (\rho_{N+1}(\vec{r}) - \rho_{N-1}(\vec{r}))/2 \quad \text{for radical attack} \quad (4)$$

The expressions for condensed Fukui functions, local electronegativity, local softness, and local philicity are defined by Eqs. 5, 6 and 7, respectively.

$$f_k^\alpha \quad \text{condensed Fukui functions} \quad \text{where } \alpha \text{ are } +, - \text{ and } 0 \quad (5)$$

$$\chi_k^\alpha = f_k^\alpha \chi \quad \text{Local Electronegativity} \quad (6)$$

$$s_k^\alpha = f_k^\alpha S \quad \text{Local Softness} \quad (7)$$

$$\omega_k^\alpha = f_k^\alpha \omega \quad \text{Local Philicity} \quad (8)$$

In order to evaluate the importance of the R group, the eight structures were optimized by using the PBE1PBE [22] functional with 6-31+G**. The R group was modified in the following way: $-\text{CH}_2\text{Ph}$, $-\text{CH}_2\text{COOH}$, $-\text{CH}(\text{CH}_3)\text{Ph}$, $-\text{C}(\text{CH}_3)_2\text{CONH}_2$, $-\text{C}(\text{CH}_3)_2\text{Ph}$, $-(\text{CH}_3)_2\text{C}_6\text{H}_8\text{OCH}_3$, $-\text{SCH}_2\text{Ph}$.

Results and discussion

In living/controlled polymerization, the effectiveness of the equilibrium between active and dormant species generates

Table 2 Global properties of RAFT transfer agents evaluated with DFT/PBE1PBE/6–31+G**

Molecules	<i>I</i>	<i>A</i>	χ	η	<i>S</i>	ω
	eV					
D1	0.29570	0.03120	4.44774	3.59873	0.13894	2.74852
<i>D2</i>	0.29570	0.04570	4.64502	3.40145	0.14700	3.17162
<i>D3</i>	0.28450	0.03530	4.35113	3.39057	0.14747	2.79192
<i>D4</i>	0.28110	0.03610	4.31576	3.33342	0.15000	2.79379
<i>D5</i>	0.28510	0.03990	4.42189	3.33614	0.14987	2.93049
<i>DC1</i>	0.29520	0.03170	4.44774	3.58513	0.13947	2.75895
<i>X1</i>	0.31130	0.03930	4.77019	3.70078	0.13511	3.07432
<i>T1</i>	0.29980	0.01940	4.34297	3.81507	0.13106	2.47196

I: Potential ionization, *A*: Electronic affinity, χ : Electronegativity, η : Hardness, *S*: Softness, ω : Philicity.

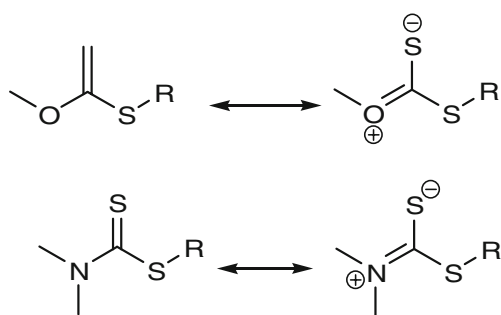
the reversible addition–fragmentation process. Furthermore, its efficiency depends on the Z and R substituents as well as the monomer type used in the reaction. The addition step is mainly related to the Z group which, at the same time, is governed by the reactivity of the double C=S bond. On the other hand, the R group is mainly affected 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 [5]. To know the performance of the transfer agents, in particular the R group, to consider the ability to reinitiate the polymerization is important. Just like a conventional chain transfer, the reinitiation rate could be equal or greater than the propagation rate in order to prevent retardation. In RAFT polymerization, it is also necessary to consider the reinitiation rate in relation to the reaction rate of R with the polymeric RAFT agent. If the reinitiation rate is small, the consumption rate of the initial RAFT agent could be reduced, which could make the transfer coefficient dependant on RAFT agent concentration and conversion [15].

The results obtained for the minimum energy (neutral radical), negative ion and positive ion, HOMO and LUMO with DFT/PBE1PBE/6–32+G**, were used to evaluate the global descriptors: electronegativity, hardness, softness and philicity, Table 2. These results were evaluated taking into

account the electronic affinities and ionization potentials by using the Mulliken scale.

Even though electronegativity is a relative concept; that is, it can only be measured by comparing two elements, it provides an estimation of the ability of a compound to accept electrons. In the present case electronegativity was favored for X1, that presented a higher reactivity, due to the presence of fluoride atoms, and therefore, a considerable capacity to attract electrons [44] D1 and DC1, with the same value, followed in this order; apparently this feature was induced by the presence of nitrogen atoms, which increased electronegativity. Finally, D3, D4 and T1 agents presented the lowest electronegativities; the presence of methyl groups and aromatic rings suggested that these compounds can not participate easily in electron interchange, because they have the tendency to develop alkyl reactions; *i.e.*, the occurrence of breaking bond reactions is quite probable due to radical events.

Hardness is defined as the resistance of a given compound to any change in its electronic distribution and is a global property of the system. On the contrary, softness, which is the inverse of hardness, predicts the affinity that a particular chemical system has to modify its electronic structure, as well as to react to a particular external chemical potential [37]. The results of global softness are shown in Table 2, it is observed that the value for the susceptibility of the dithioester D4 was higher than the value for the dithioester D5, because the cumyl group is more stable and a better leaving group, consequently, than mentonyl group in D5 [45]. These two compounds present tertiary R groups with elevated molar mass, both of them reported as efficient leaving groups and as readily reinitiators of polymerization *via* RAFT. Even though the dithioester D2 has also a trisubstituted R group, its softness value was more similar to the value of D3, that has a disubstituted R group and not to D5 or D4. This feature could be due to the so called *zwitterionic canonical forms* phenomenon, Fig. 1 [12, 29], which arises from interactions between the pairs of electrons of oxygen or nitrogen atoms with the double C=S bond. A zwitterion is a chemical

**Fig. 1** Zwitterionic canonical schemes

specie that carries a total net charge of 0; however, it carries formal positive and negative charges in different atoms. This term is referred to compounds with non-adjacent positive and negative charges that are both polar and usually water-soluble compounds, but poorly soluble in most organic solvents.

The dithioester D1 and the dithiocarbamate DT1 are presented lower softness than D2 and D3. This could be because both D1 and DT1 have monosubstituted R groups and low molar mass. Resonance events are also probable in these compounds due to the formation of dipolar ions inside of the molecules caused by the presence of an unpaired electron. The transfer agents with the lowest global softness were the xanthate X1 and the trithiocarbonate T1. The low values were attributed, in the case of X1, to the presence of *zwitterionic forms* [12, 29], whereas in the case of T1 to the similar leaving character of Z and R groups in this compound. Although for the transfer agents with $-\text{CH}_2-\text{Ph}$ groups small reactivity has been reported [45]. Nevertheless, these leaving R (or Z) groups had a lower molar mass and were more stable; therefore, they did not compete with the hindrance produced in compounds with higher molar masses, such as [46].

The electrophilicity index measures the propensity of electrophilic attack; that is, is 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 electronic flow between a donor and an acceptor [47]. Table 2 shows the results of global philicity, as can be seen the dithioester D2 has the lowest philicity, followed by the xanthate X1. The first one is a compound with tertiary R group and high capacity to donate/to accept electrons because of the presence of oxygen atoms. Something similar is observed for X1, although its R group is a monosubstituted group the presence of fluor or oxygen atoms give rise to high electronegativities. Dithioester D5, which has a tertiary R group and an oxygen atom, showed high philicity; the presence of the oxygen would elevate its capacity for electrons interchange. In the same context, the dithioesters D4 and D3 showed lower philicity than the previous one, as these contain bisubstituted and trisubstituted R groups, respectively. D1, DC1 and T1 had the lowest philicities, since these agents have primary R groups. It should be mentioned that primary groups are poorly appealing in RAFT polymerization, since they have low capacity to reinitiate polymerization.

The previous results suggested that the R group as good leaving group followed the order below:

Tertiary group > secondary group > primary group

It has been reported that agents with a benzyl R group are poorer leaving groups in respect to the polymeric group,

and this has been attributed to the influence of steric factors [12]. Thus, the relative stresses in structure conformation could increase from tertiary > secondary > primary. In accordance to this theory, oligomeric and polymeric radicals could be better leaving groups than the monomeric species. This is the reason why the initial transfer agents are not well suited for initiating polymerization [15]. It has been reported that the fragmentation reaction is very sensitive to the characteristics of the leaving group, and that the use of a methyl radical might not yield an appropriate model of a leaving group in experimental systems [7, 29].

Experimentally, the fragmentation rate of D4 varies significantly and reflects the difficulty of using kinetic experiments for studying the rates of individual stages in the RAFT process. Such rates can not be measured directly and could be deduced from relative quantities (such as the total rate of polymerization) assuming first a specific kinetic model and values for some of the coefficients of individual rates. Contrary to experiments, *ab initio* calculations of molecular orbitals offer a direct access to the barriers, enthalpies, and rate coefficients of individual reactions and could provide a useful tool for evaluating the reaction mechanism [48].

Despite the notable versatility of RAFT polymerization, the long inhibition and/or retardation periods represent a highly controversial aspect. Inhibition periods are governed by the ability of the leaving group to reinitiate the polymerization and the fragmentation rate of the RAFT radical in pre-equilibrium. As it turns out, it is difficult to separate the influence of both factors in a particular reaction. In experimental work when D3 was used inhibition was induced; meanwhile with $\text{C}(\text{CH}_3)_2\text{CN}$ dithiobenzoate inhibition in polymerizations with methylacrylate was reduced. This suggests that the radical RAFT groups in pre-equilibrium, which contain phenyl groups, are more stable than cianisopropyl radicals. On the other hand, it has been observed that a dithiobenzoate that contains the cumyl group as the R substituent inhibits completely the polymerization of methylmethacrylate, which indicates that these type of dithiobenzoates could be stable and suffers only from slow fragment [45]. Therefore, in accordance to the stabilizing effects for these three groups, the following order could be proposed: cumyl > phenylethyl > cianoisopropyl. If it is assumed that the stability of the species could be governed by the stabilizing effects of the Z group, which was the same in this study, it can be concluded that the cumyl group was the worst R group, followed by phenylethyl and finally, by cianoisopropyl. However, according to its ability to stabilize the RAFT species the cumyl group was the most stable radical of the three and, therefore, was the best leaving group, followed by cianoisopropyl and finally, by

phenylethyl [30]. In this study, by using the following R groups: $C(CH_3)_3$, $C(CH_3)C_6H_4OCH_3$, $C(CH_3)_2Ph$ y CH_2COOH this analogy was clearly shown.

Based on the reasonable assumption that the R group did not have a dramatic effect on the rate of addition to the thiocarbonyl group, the magnitude of the transfer constant was reflected in the partition of intermediates between initial materials and products and the ability of the leaving group. When compared to the benzyl and 1-phenylethyl groups in dithiobenzoates, it has been reported that steric factors are more important than radical stability in determining the ability of the leaving group [29, 30]. This directly applies to the comparison of D1 with D4 or D5 in this study. In dithioacetates family, cumyldithioacetate has a tertiary leaving group, cumyl and phenylethylphenyldithioacetate has a secondary leaving group, phenylethyl. This is why a tertiary leaving group forms a more stable radical than a secondary or primary, which makes the intermediate adduct radical fragmentation RAFT rate faster. On the other hand, a leaving group which is less effective could completely retard the conversion of the initial RAFT agent toward the macroradical and, consequently, delay the main pre-equilibrium of the process, thus generating an uncontrolled macroradical [49].

Although global reactivity descriptors are widely used to describe chemical behavior in a given system, it has been reported that local functions have information about the inherent reactivity of molecules and specific steric control associated with a chemical reaction. DFT suggests that the hardness-softness acid-base principle (HSAB) [39], which was initially formulated for the study of global changes inside a reaction, can also be applied to local interactions. The HSAB principle establishes that a reaction site, which has large softness values, could prefer to react with soft species or with the softest site of a species; whereas 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. It has been observed that soft-soft interactions are preferred in maximum Fukui functions and that minimum Fukui functions are sites preferred in hard-hard interactions. Calculated condensed Fukui functions from charges in neutral and ionic molecules provide information that is in agreement with the predictions carried out from the mapping of a local function. A local softness mapping depicts the variation in reactivity in different sites in a molecule, while global softness is only related to relative reactivity, which varies from a molecule to another [37].

Local reactivity descriptors, have been successfully used in studying the selective sites of a molecule, due to chemical reactions are dynamical processes the profiles dependant on time for these descriptors and the other dynamical side to the structural principles has been widely

used in order to predict a chemical reaction from the beginning to the end; thus, through these calculations some events could be predicted even before starting the chemical reaction [50, 51].

In order to determine the selective sites of a structure it is necessary to determine the local descriptors with Fukui indices and Hirshfeld population analysis, are showed in the Table 3 [52]. This is because these quantities measure the sensitivity of the chemical potential of a system in an external perturbation in order to perform energetic comparisons from charge distribution inside each structure [53–55]. The Hirshfeld population analysis has clearly demonstrated the superiority over other methods of population analysis, because the results for Fukui indeces always results as positive. The technique of charge partition was proposed by Hirshfeld and is defined as deformation of density, which is different among relaxed molecular atomic charges [52].

The local reactivity descriptors represent the electronic charge distribution into a chemical system. Figure 2 shows the local electronegativity results obtained for the eight transfer agents by Hirshfeld population analysis and Fukui indices. From this figure it is possible to say that a radical attack over the thiocarbonyl bond would be preferably on the $C=S$ bond, since it is a double bond. Double bonds consist of a strong σ bond and a weak π bond. So it was expected that the reaction imply the rupture of the weak bond. This was the reason why the characteristic reactions of these bonds were addition reactions. In these bonds, there exists a cloud of π electrons above and below the plane of the atoms. These π electrons are less involved than the σ electrons in keeping the atomic nuclei united and, therefore, they themselves are good electron releasers and are particularly available for species that look for electrons. So it is not surprising that in many reactions where double bonds are involved π bonds are a source electrons; that is, they act as a base. The kinds of compounds with which they react are electron deficient; *i.e.*, they are acids. Other types of reagents exist, such as free radicals, which look for electrons or better yet one electron. These are called reactions of free radical addition. Basically, the RAFT process occurs because of the transference of free radicals by means of addition. Therefore, it is possible to observe that the sulfur that forms the double bond is more susceptible to radical attack, since it is able to receive an electron to form simple or strong bonds, with the most interest placed on the suscceptibility of a radical attack due to the fact that polymerization *via* RAFT is carried out by means of the transference of free radicals. The results showed that three sites, which were the most selective, were the sites which form the thiocarbonyl bond of the transfer agent and varied according to the way as the Z and R groups were modified in the structure. Nucleophilic attack

Table 3 Local descriptors with Fukui indices to radical attack using DFT/PBE1PBE/6–31+G** for transfer agents

Molecules	Atoms	$f_k^{\alpha}\chi^a$	$f_k^{\alpha}\eta^b$	$f_k^{\alpha}S^c$	$f_k^{\alpha}\omega^d$
D1	S	1.683232	1.361930	0.052581	1.040168
	C	0.332395	0.268946	0.010383	0.205406
	S	0.588638	0.476276	0.018388	0.363754
	C	0.026033	0.021063	0.000813	0.016087
	C	0.097783	0.079118	0.003055	0.060426
D2	S	1.645473	1.204945	0.052073	1.123529
	C	0.331810	0.242977	0.010500	0.226560
	S	0.530457	0.388442	0.016787	0.362196
	C	0.020724	0.015176	0.000656	0.014150
	C	0.057789	0.042317	0.001829	0.039458
D3	S	1.497038	1.166548	0.050737	0.960580
	C	0.303509	0.236505	0.010286	0.194748
	S	0.488356	0.380545	0.016551	0.313355
	C	0.018582	0.014479	0.000630	0.011923
	C	0.062904	0.049017	0.002132	0.040363
D4	S	1.480200	1.143282	0.051445	0.958203
	C	0.298118	0.230261	0.010361	0.192986
	S	0.454024	0.350681	0.015780	0.293911
	C	0.011320	0.008744	0.000393	0.007328
	C	0.063312	0.048901	0.002200	0.040985
D5	S	1.479724	1.116395	0.050153	0.980649
	C	0.307056	0.231662	0.010407	0.203493
	S	0.462290	0.348780	0.015669	0.306371
	C	0.015342	0.011575	0.000520	0.010167
	C	0.058643	0.044244	0.001988	0.038864
DC1	S	1.400296	1.128718	0.043908	0.868609
	C	0.305491	0.246243	0.009579	0.189497
	S	0.509221	0.410461	0.015967	0.315872
	N	0.034875	0.028111	0.001094	0.021633
	C	0.081511	0.065703	0.002556	0.050562
X1	S	1.541426	1.195858	0.043658	0.993426
	C	0.357333	0.277223	0.010121	0.230296
	S	0.717408	0.556575	0.020319	0.462359
	O	0.109338	0.084826	0.003097	0.070466
	C	0.107441	0.083354	0.003043	0.069244
T1	S	1.144479	1.005363	0.034537	0.651423
	C	0.288562	0.253486	0.008708	0.164246
	S	0.537302	0.471990	0.016214	0.305825
	S	0.507804	0.446079	0.015324	0.289035
	C	0.068456	0.060135	0.002066	0.038964

a Local electronegativity, b Local hardness, c Local softness, d Local philicity.

was preferred in the central carbon atom and radical attack, which was in our interest, appeared in the sulfur atom which was bonded with the carbon atom with the double bond. This result was logical due to the presence of the double bond, which is easily broken due to a delocalization of electrons.

The sulfur atom that conform the S=C bond has higher value of local electronegativity than the other atoms. The dithioesters D1, D2, D3, D4, and D5 were favored with the highest electronegativity, followed by the xanthate X1, the dithiocarbamate, DC1 and finally by the trithiocarbonate, T1. This was an expected result, since the last three

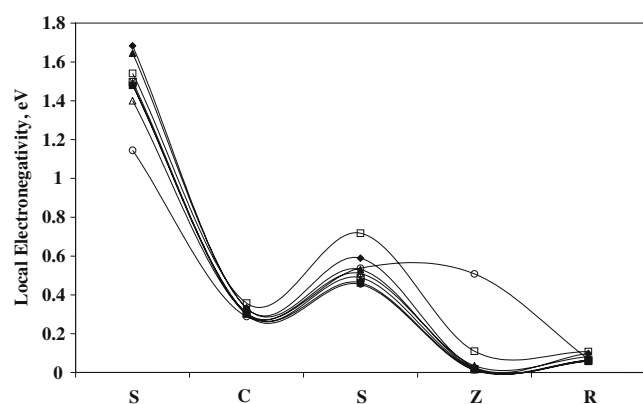


Fig. 2 Local electronegativity using DFT/PBE1PBE/6-31+G** for radical attack. (◆) D1, (▲) D2, (*) D3, (●) D4, (■) D5, (Δ) DC1, Z = N, (□) X1, Z = O, (○) T1, Z = S

compounds were favored by high electronic transfer or ionic attacks. The local electronegativity of the dithioesters decreased according to the degree of substitution of the R group, as in the case of the dithioesters D3, D4 and D5, respectively.

Another atom that has an important reactivity was the sulfur of the S–R bond for all the studied RAFT agents. The xanthate X1 presented the highest electronegativity perhaps because of the presence of highly electronegative atoms. Next, the dithioester D1, that has an R group constituted by $\text{CH}_2\text{C}=\text{ONH}_2$. Afterward, with similar local electronegativity, D2 and T1; it is possible that in these compounds the reactivity is shared among the three sulfur atoms in both Z and R groups that will work as leaving groups. It should be mentioned that D1 possess a trisubstituted R group, which contains oxygen and nitrogen atoms, which in turn induced the high electronegativity and thus the breaking of the S–C bond. The value of the local electronegativity for the dithiocarbamate DC1, with a pyrrol as the Z group, was lower than in the previous one, perhaps because the competition between groups R and Z for capturing electrons. Finally, the dithioesters D3, D4, and D5 showed the lowest electronegativity in the S–R bond, possibly it was derived by the presence of stable groups with the tendency to form chains that do not experience electron interchange or the local electronegativity is decreased.

The results of local softness for five atoms in the thiocarbonyl group of the eight RAFT agents with susceptibility to a radical attack are shown in Fig. 3. These results were evaluated by using the route: DFT/PBE1PBE/6-31+G**. The highest softness was for the double S=C bond, which was logical because this is a weak double bond with the capacity to suffer from radical attack. Thus the agents with the highest susceptibility to radical attack were the dithioesters with the order: D1, D2, D3, D4, and D5. The dithioesters D1 and D2 have oxygen and nitrogen

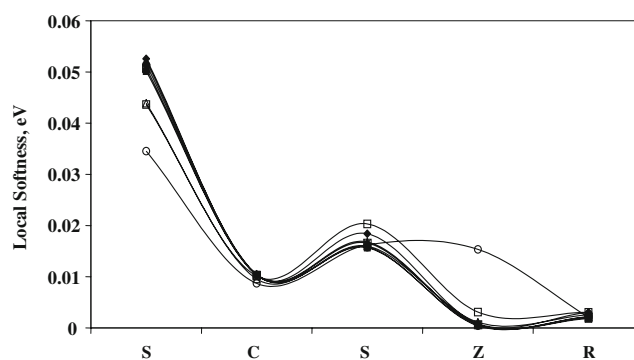


Fig. 3 Local softness using the charge distribution population of Hirshfeld. (◆) D1, (▲) D2, (*) D3, (●) D4, (■) D5, (Δ) DC1, Z = N, (□) X1, Z = O, (○) T1, Z = S

atoms as part of the compound; these would generate increments of steric hindrance inside the molecule making easier the addition step. Afterward, the dithioester D4 that also had a high local softness in the sulfur of the S=C bond, which was attributed to the tertiary R group. It is worth mentioning that trisubstituted groups have been reported to be good leaving groups [45, 49].

The lowest susceptibility to radical attack in S=C group for agents with Z groups with oxygen and nitrogen atoms would be due to the zwitterionic events. These transfer agents also present monosubstituted R groups. Even though the trithiocarbonate T1 had the lowest local softness, it is reported that the trithiocarbonates are good transfer agents, since they generate complex structures; however, in our study, the worst behaviours were those with the identical monosubstituted Z and R groups, whose capacity to reiniciate the polymerization was also low. The reactivity of radical attack of the S–R bond indicated that the xanthate X1 had the highest softness, although it is a monosubstituted group with fluorine and oxygen atoms. Coming immediately after the dithioester D1, with similar descriptors as X1. The dithioesters D2 and D3, the trithiocarbonate T1 have groups such like: tertiary, secondary and primary,

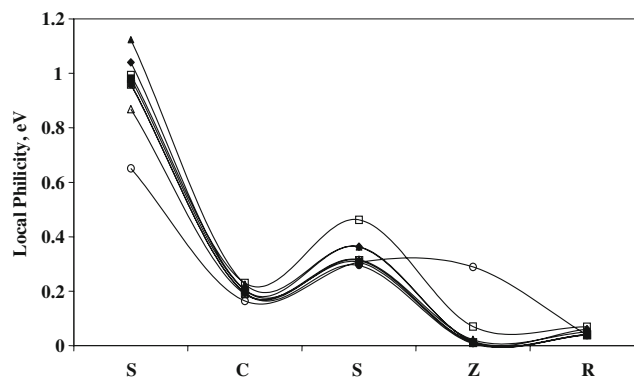


Fig. 4 Local philicity using the charge distribution population of Hirshfeld. (◆) D1, (▲) D2, (*) D3, (●) D4, (■) D5, (Δ) DC1, Z = N, (□) X1, Z = O, (○) T1, Z = S

respectively. Reaffirming the susceptibility to a chemical change can be influenced by the number of R substituents. Finally, the dithiocarbonate DC1, with pyrrol as the Z group, and the dithioesters D4 and D5, containing tertiary Z groups, with the lowest softnesses.

Local philicity was by far the most useful reactivity-selectivity function when compared to the global electrophilicity index, Fukui functions, local or global softness, since this parameter contained information about all global and local descriptors of selectivity and chemical reactivity [40]. The results of local philicity for five atoms of the thiocarbonyl compound for the eight transfer agents with the susceptibility to radical attack by using DFT/PBE1PBE/6-31+G** are shown in Fig. 4. In this figure it could be observed that the dithioesters D2 and D1 had the highest local philicity, where the R group in D2 is a trisubstituted group with oxygen and nitrogen atoms. The R group for D1 is a monosubstituted radical but also has oxygen and nitrogen atoms. Immediately after, the xanthate X1 and the dithioesters D5, D3 and D4, which had lower philicity than D2 and D1. In accordance with the substituent group, the local philicity in D5 was higher in the S=C bond than in the dithioester D4, although both have a tertiary R group. Nevertheless, these are good leaving groups and can reactivate the polymerization efficiently. The dithiocarbonate DC1 had lower philicity than the last mentioned. It could be caused by the presence of the pyrrol as the Z group. Finally, the trithiocarbonate T1 had the lowest local philicity, which could be attributed to the presence of monosubstituted R groups; this characteristic was in agreement with the previous local descriptors. The philicity in the weak S-C bond changed in the next order: $X1 > D1=D2 > DC1=D3 > D5=T1 > D4$. In agreement with the previous group of local descriptors this tendency indicated that the dithioesters had low capacity to experiment radical attack in this bond.

Steric factors, radical stability, and polar factors were important in determining the ability of the R• group (the more stable, electrophilic, and higher the molecular mass, the better the leaving group will be). The partition of R• between the added monomer (for initiating) and its addition to the polymeric RAFT agent could also have a significant effect on the consumption rate of the RAFT agent [15].

From a general point of view, steric hindrance contributed to the stability of the R• and plays a major role in the efficiency of the dithioester. Hence it was expected that MDB or D5 had a little higher fragmentation rate constant. Nevertheless, it presented a reinitiation efficiency a little lower than other studied agents such as CDB or D5. However, the menthonyl and tert-butyl radicals are both ternary centered carbons and were very good leaving groups as compared to other groups such as those generated by monomers (primary and secondary radicals), which explains their similarity in kinetics [5].

Conclusions

It was found that trisubstituted dithioesters were the most favored R groups to be used in RAFT agents, since they are stable groups with high capacity to reinitiate polymerization. The other R groups in the transfer agents would present modest efficiencies due to the occurrence of zwitterionic events. It is worth mentioning that the trithiocarbonate evaluated, which has been widely used experimentally, presented the lowest values in all reactivity descriptors; both the identical R and Z group and the resonance events in the radical center could be the reason for the poor performance.

Finally, it can be concluded that it was possible to propose an order of reactivity of the R group for eight RAFT agents. The presence of electronegative atoms as well as trisubstituted radicals in the R group promoted higher transfer rates. With these results and in combinations with a previous work, where the importance of Z group in these RAFT agents was determined, it would be possible to predict events of addition - fragmentation according to a combination of R and Z groups in the agent. Thus, with both studies we expect to provide certain valuable information, which permit to predict the performance of certain agents during the polymerization for future proposal in the practical field of polymerization *via* RAFT.

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