Novel Amide-Based Chain Transfer Agent for Reversible Addition Fragmentation Chain Transfer Polymerization

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Introduction. Reversible addition−fragmentation chain transfer (RAFT)[1,2] polymerization and macromolecular architecture design by interchange of xanthates (MADIX)[3,4] are the two of the youngest living radical polymerization (LRP) techniques. Like the two other main LRP techniques (transition-metal-mediated LRP, also known as atom transfer radical polymerization, ATRP, and nitroxide mediated polymerization, NMP), RAFT and MADIX produce polymers with predictable molecular weight, narrow molecular weight distribution, and specific architectures. Furthermore, both RAFT and MADIX tolerate various functionalities and therefore can polymerize an extensive range of monomers.[5,6] Moreover, they are effective over a vast range of temperatures (from ambient temperature to 150 °C) and are generally performed under conventional radical polymerization processes such as in bulk or emulsion.

RAFT and MADIX are based on a similar process which involves of a small amount of dithioester of the generic formula **I** (Scheme 1) (chain transfer agent, CTA) in a classic free radical polymerization system (monomer + initiator). Scheme 1 illustrates the principle behind the generally accepted mechanism.[7,8] The radical species issued from the decomposition of the radical initiator reacts with the monomer (**1**). Rapidly, this growing polymer chain adds onto the reactive C=S bond of the CTA to form a radical intermediate (**2**). The radical intermediate can fragment reversibly toward either the initial growing chain or the reinitiating group (R) and a macro-chain-transfer agent (macroCTA) (**3**). The R group can then reinitiate polymerization by reacting with monomer starting a new polymer chain. Once the entire initial CTA has been consumed, only the macroCTA is present in the reaction medium, which enters the equilibrium. This is considered to be the main equilibrium.

The choices of the R and Z groups are the key to obtaining good control of the polymerizations.[7,9−13] The Z group will help to stabilize the intermediate radical, facilitating the reaction of addition on the CTA, key to the living process. On the other hand, the R group needs to be stable enough to be formed by fragmentation of the intermediate radical but also reactive enough to reinitiate a growing polymeric chain, key to controlling polymerization. The use of esters as the leaving group R have raised very little interest to date due to their low efficiency in reinitiating polymerization and their limitation to specific monomers (mainly styrene and acrylate derivatives).[7,9−13] Recently, we used a methyl phenylacetate group to control the polymerization of styrene, acrylate, and acrylamide derivatives.[7] In this case, the R group forms a secondary radical, in which low steric hindrance favors addition to monomer, and the stabilization of the leaving group is achieved by the presence of a phenyl group on the α-C of the radical. The use of such a leaving group makes it possible to transform any hydroxyl bearing molecules into a CTA by esterification, giving the potential for an almost infinite number of possible polymeric chain-end functionalities.[7]

Surprisingly, amide leaving groups have received even less interest. McCormick's group was the first and, to the best of our knowledge, the only group to have used an R group based on an amide for RAFT polymerization.[10] By using an R group that mimics the propagating radical of acrylamide monomers, they successfully controlled the living radical polymerization of *N,N*-dimethylacrylamide. Acrylate radicals are more stabilized compared to acrylamide radicals due to the stronger electron withdrawing effect of the ester compared to amide group; therefore, the ester radical should be less reactive.[14]

In this communication, we report a novel CTA, *S*-diethylcarbamoylphenylmethyl dithiobenzoate (DCPDB), based on an amide functionality, to mediate the polymerization of styrene, acrylate, and acrylamide derivatives. We compare its reactivity in the polymerization of styrene, methyl acrylate, and *N,N*-dimethylacrylamide with that of its ester counterpart *S*-methoxycarbonylphenylmethyl dithiobenzoate (MCPDB).

Synthesis of *S*-Diethylcarbamoylphenylmethyl Dithiobenzoate (DCPDB).[15] *S*-Diethylcarbamylphenylmethyl dithiobenzoate was prepared by a simple three-step methodology (Scheme 2), by which 2-chloro-2-phenylacetyl chloride was reacted with *N,N*-diethylamine, and the resulting amide reacted with dithiobenzoic acid magnesium chloride salt[7] to give *S*-diethylcarbamoylphenylmethyl dithiobenzoate (DCPDB) (see Supporting Information for synthetic method). Although *N,N*-diethylamine was used as a model compound, any primary[16] and secondary amine can be used to produce a functional chain transfer agent. The full characterization, including the single-crystal X-ray structure, of the solid chain transfer agent is reported in this communication.

Polymerizations. Figure 1 shows the pseudo-first-order plots for the polymerization of *N,N*-dimethylacrylamide, methyl acrylate, and styrene, mediated by MCPDB and DPCDB. Both CTAs show relatively linear plots for all cases, to high conversion, indicating that the systems are in a stationary state with respect to concentrations of the propagating chain radicals, which remain constant (k_p[P•]). Figure 2 shows the linear evolution of molecular weight with conversion for all monomers, as expected from a living system.

***N,N*-Dimethylacrylamide Polymerization.** Figure 1 illustrates the respective kinetic plots for the polymerizations of DMA with DCPDB and MCPDB. In both cases, the polymerization of *N,N*-dimethylacrylamide is faster than that of styrene and methyl acrylate, with similar rates of polymerizations (18% conversion in 8 h

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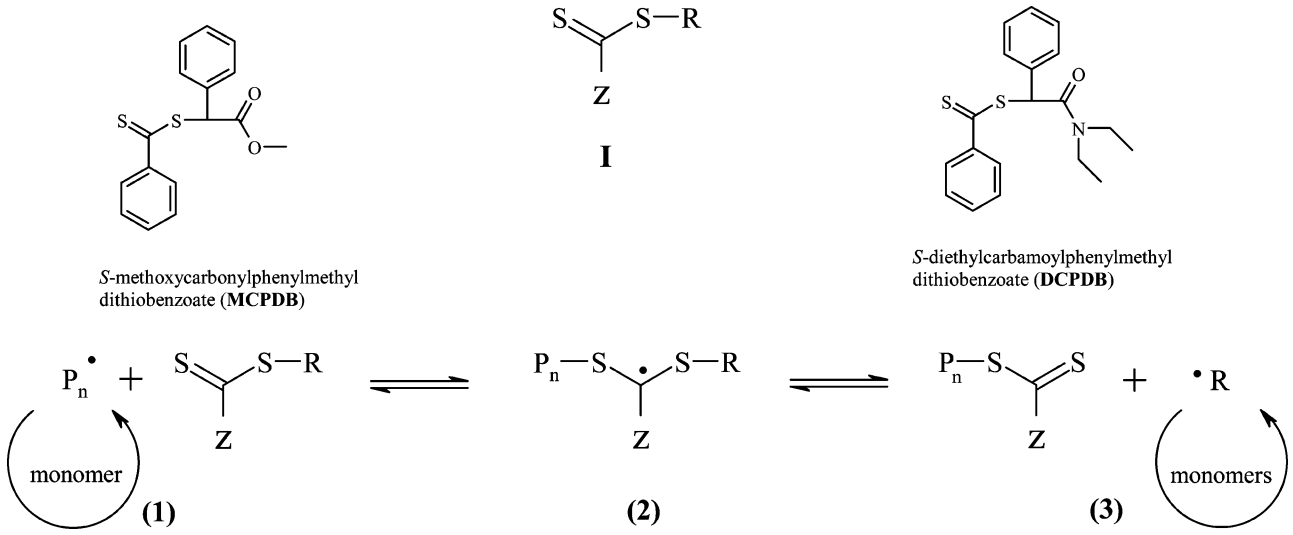
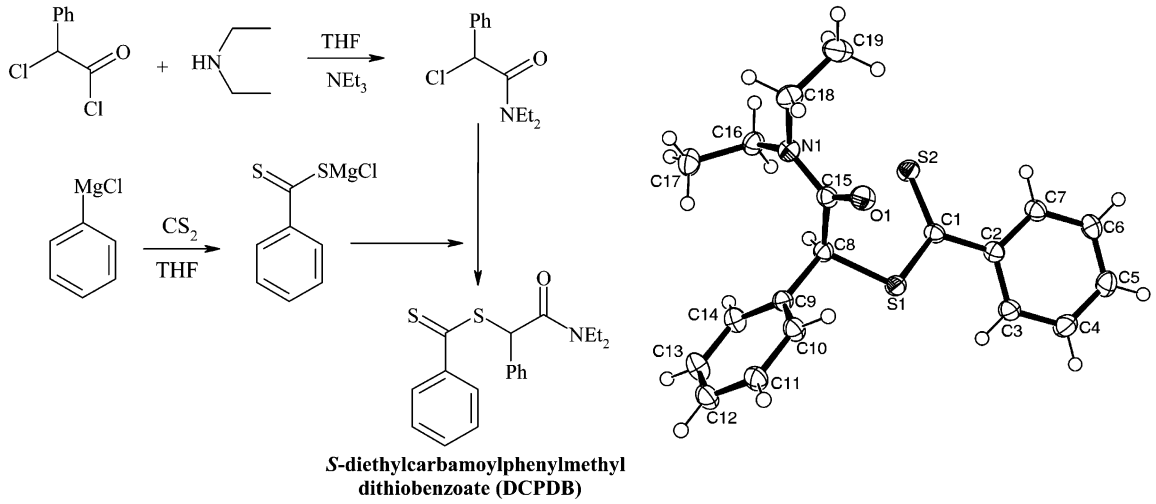
Scheme 1. General Reaction Scheme for Reversible Addition−Fragmentation Chain Transfer (RAFT) Polymerization



Scheme 2. Synthetic Methodology and Single-Crystal X-ray Structure[21] of *S*-Diethylcarbamoylphenylmethyl Dithiobenzoate (DCPDB)



when using MCPDB, 24% in 9 h for DCPDB). The modification of the R group is not expected to influence the propagation step, but only the reinitiating step, when the original CTA is consumed. The RAFT-mediated polymerization of *N,N*-dimethylacrylamide has been reported to show various degrees of inhibition, depending on the chain transfer agent utilized.[10] Such behavior has been reported for many fast propagating monomers, and its origin is still uncertain. Potential explanations are either slow fragmentation of the intermediate radical[9] or slow initiation of the expelled reinitiating group (R).[10] In this study, we modify the reinitiating group by replacing an ester functionality by an amide functionality on the α-C of the radical, with the assumption that this should enhance the reactivity of the expelled radical toward radical addition, in a similar manner as what Donovan et al. have previously reported.[10] Indeed, in their communication, the authors observe that the inhibition effect is minimized, which supports the theory of slow reinitiation. However, in the present investigation, the inhibition time for DCPDB is similar to that of MCPDB (approximately 1 h). Although this result is unexpected, we do not feel it is conclusive enough toward any of the proposed theories. Indeed, the presence of a phenyl group on the α-C of the radical would also greatly contribute to its reactivity, and it is likely that it overrides any effects from the ester/amide functionality. Figure 2 shows the evolution of molecular weight with conversion. As expected from a living system, the values increase linearly with conversion, but they are slightly higher than predicted (M_n = 56 400 g/mol at 96.4% conversion while $M_{n,theo}$ = 47 800 g/mol). Such results could be credited to the fact that not all CTAs have reacted and initiated polymeric chains and/or to a small amount of termination reactions. Also, the PMMA-calibrated size exclusion chromatography overestimates the real molecular weight of the samples. Nevertheless, the linear increase in molecular weight with conversion, with reasonable deviations from predicted values, and the polydispersity remaining below 1.2 are good indications of the living and controlled characteristics of the polymerization.

Methyl Acrylate Polymerization. The polymerization of methyl acrylate mediated by DCPDB follows a similar rate as that of the polymerization mediated by its ester equivalent (90% conversion reached in 150 h). As observed in the case of *N,N*-dimethylacrylamide polymerizations, the inhibition period is similar for both polymerizations (approximately 2 h), confirming the strong effect of the phenyl group over the ester/amide

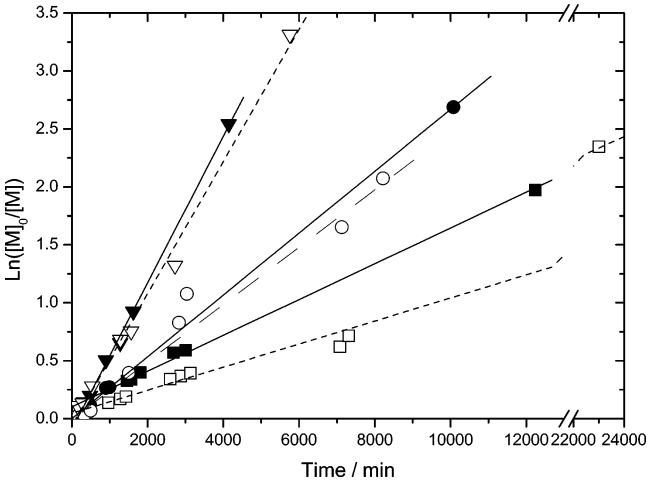


Figure 1. Pseudo-first-order rate plot for the bulk polymerization of styrene (■), methyl acrylate (●), and *N,N*-dimethylacrylamide (▼) mediated by *S*-methoxycarbonylphenylmethyl dithiobenzoate (MCPDB) and styrene (□), methyl acrylate (○), and *N,N*-dimethylacrylamide (▽) mediated by *S*-diethylcarbamoylphenylmethyl dithiobenzoate (DCPDB) in bulk, at 60 °C.

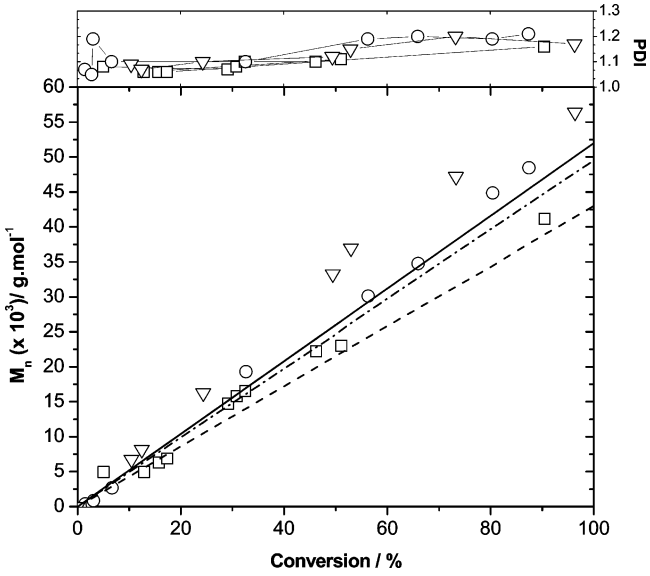


Figure 2. Molecular weight and PDI evolution with monomer conversion for the bulk polymerization of styrene (□), methyl acrylate (○), and *N,N*-dimethylacrylamide (▽) mediated by *S*-diethylcarbamoylphenylmethyl dithiobenzoate (DCPDB) in bulk, at 60 °C. The lines show the theoretical evolution of M_n with conversion[19] for the polymerization of styrene (—), methyl acrylate (– –), and *N,N*-dimethylacrylamide (– · –) (poly(methyl acrylate) and poly(*N,N*-dimethylacrylamide) molecular weights determined using poly(methyl methacrylate) standards).

functionality. The molecular weight increases linearly with conversion, with values slightly higher than predicted (M_n = 48 500 g/mol at 87.4% conversion while $M_{n,\,theo}$ = 37 600 g/mol), as observed in the case of DMA polymerization, and polydispersities typically below 1.2 (Figure 2). Overall, the polymerization is reasonably controlled.

Styrene Polymerization. Styrene is one of the most widely used monomers in RAFT polymerizations. The control of the polymerization mediated by DCPDB is similar to that mediated by MCPDB, up to high conversion. Styrene polymerization is the slowest of all monomers for both CTAs, and surprisingly, DCPDB mediates a much slower polymerization compared to that mediated by MCPDB (29% conversion in 44 h using DCPDB compared to 29% conversion in 26 h with MCPDB[7]). Although we do not have any explanations for this behavior at the present time, our experimental values are reproducible, and we are currently investigating the matter further. The molecular weight increases linearly with conversion and stays close to the predicted values. At high conversions, the experimental molecular weights deviate from the theoretical values (M_n = 41 200 g/mol at 90.4% conversion while $M_{n,theo}$ = 47 000 g/mol); we attribute this variation to a few side reactions of chain transfer. However, the polydispersity remains below 1.2, with values as low as 1.05 (Figure 2), characterizing a living and controlled polymerization.

The living character of the polymerization was further confirmed by the production of a diblock copolymer of PS and PMA. The first block was produced by polymerization of styrene mediated by DCPDB M_n = 25 450 g/mol, PDI = 1.23 (M_n = 28 300 g/mol),[17] and isolated. The PS macroCTA was then used to mediate MA polymerization and led to a diblock copolymer of M_n = 42 000 g/mol, PDI = 1.27 (M_n = 45 000 g/mol).[17]

The use of DCPDB to mediate RAFT/MADIX polymerization opens up a whole new area for functional polymers. Until recently, atom transfer radical polymerization (ATRP) was the technique of choice to introduce chain-end functionalities in polymers by the use of functional initiators.[18−20] Recently, we reported the use of *S*-methoxycarbonylphenylmethyl dithiobenzoate (MCPDB) to mediate RAFT/MADIX polymerizations.[7] MCPDB offers similar advantages as ATRP initiators, as it allows the easy transformation of any hydroxyl group into a CTA and the incorporation of functional molecules at the end of a polymeric chain. However, to date, ATRP has been unsuccessful in using a similar process to convert amine functionalities into initiators. In this communication, we have shown that the use of 2-chloro-2-phenylacetyl chloride allows the transformation of an amine group into CTA and therefore leads to a whole new area of amine functional molecules used as chain-end functionalities, so far inaccessible to living radical polymerization.

Unlike most CTAs reported to date, DCPDB is a solid, and it is therefore easy to handle safely. All polymerizations mediated by DCPDB show the characteristics of living polymerizations, with molecular weights increasing linearly with conversion and low PDIs (<1.20). We are currently investigating the synthesis and use of other amide functional CTAs with structures based on DCPDB to produce specific end-functional polymers, including polypeptides. In addition, we are currently investigating the modification of the Z group in the DCPDB structure in order to increase the rate of polymerization of most monomers, while controlling molecular weight and polydispersities.

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Supporting Information Available: Synthesis and full characterization of DCPDB, including single-crystal X-ray structure,[21] polymer synthesis, and description of equipment.

This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) Le, T. P.; Moad, G.; Rizzardo, E.; Thang, S. H. WO 9801478, 1998.
(2) Chiefari, J.; Chong, Y. K.; Ercole, F.; Krstina, J.; Jeffery, J.; Le, T. P. T.; Mayadunne, R. T. A.; Meijs, G. F.; Moad, C. L.; Moad, G.; Rizzardo, E.; Thang, S. H. *Macromolecules* **1998**, *31*, 5559−5562.
(3) Corpart, P.; Charmot, D.; Biadatti, T.; Zard, S.; Michelet, D. WO 9858974, 1998.
(4) Charmot, D.; Corpart, P.; Adam, H.; Zard, S. Z.; Biadatti, T.; Bouhadir, G. *Macromol. Symp.* **2000**, *150*, 23−32.
(5) Matyjaszewski, K., Ed. *Controlled/Living Radical Polymerization. Progress in ATRP, NMP, and RAFT; ACS Symp. Ser.* **2000**, 768.
(6) Matyjaszewski, K., Ed. *Advances in Controlled/Living Radical Polymerization; ACS Symp. Ser.* **2003**, 854.
(7) Perrier, S.; Takolpuckdee, P.; Westwood, J.; Lewis, D. M. *Macromolecules* **2004**, *37*, 2709−2717.
(8) Moad, G.; Mayadunne, R. T. A.; Rizzardo, E.; Skidmore, M.; Thang, S. H. *Macromol. Symp.* **2003**, *192*, 1−12.
(9) Perrier, S.; Barner-Kowollik, C.; Quinn, J. F.; Vana, P.; Davis, T. P. *Macromolecules* **2002**, *35*, 8300−8306.
(10) Donovan, M. S.; Lowe, A. B.; Sumerlin, B. S.; McCormick, C. L. *Macromolecules* **2002**, *35*, 4123−4132.
(11) Chong, Y. K.; Krstina, J.; Le, T. P. T.; Moad, G.; Postma, A.; Rizzardo, E.; Thang, S. H. *Macromolecules* **2003**, *36*, 2256−2272.
(12) Farmer, S. C.; Patten, T. E. *J. Polym. Sci., Part A: Polym. Chem.* **2002**, *40*, 555−563.
(13) Lebreton, P.; Ameduri, B.; Boutevin, B.; Corpart, J. M. *Macromol. Chem. Phys.* **2002**, *203*, 522−537.
(14) March, J. *Advanced Organic Synthesis*: *Reactions, Mechanisms, and Structure*, 4th ed.; Wiley-Interscience: New York, 1992.
(15) Further experimental details and products characterizations are given in the Supporting Information.
(16) Shanahan, S. E.; Byrene, D. D.; Inglis, G. G. A.; Alam, M.; Macdonald, S. J. F. *Chem. Commun.* **2002**, 2554−2555.
(17) Calculated using the following formula: $M_{n,theo}$ = [monomer]/[DCPDB] × M × c, where M is the monomer molecular mass and c the fractional conversion.
(18) Zhang, X.; Xia, J.; Matyjaszewski, K. *Macromolecules* **2000**, *3*, 2340−2345.
(19) Zhang, X.; Matyjaszewski, K. *Macromolecules* **1999**, *32*, 7349−7353.
(20) Haddleton, D. M.; Waterson, C. *Macromolecules* **1999**, *32*, 8732−8739.
(21) Sheldrick, G. M. *SHELXL97, Program for crystal structure determination*; University of Gottingen: Gottingen, Germany, 1997.

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