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Nicholas S Hill, Melinda J. Fule, Jason C. Morris, Jean-louis Clément, Yohann Guillaneuf, et al.. Mesolytic versus Homolytic Cleavage in Photochemical Nitroxide Mediated Polymerization. *Macromolecules*, 2020, 53 (5), pp.1567-1572. 10.1021/acs.macromol.0c00134 . hal-03007478

HAL Id: hal-03007478

<https://hal.science/hal-03007478>

Submitted on 16 Nov 2020

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Mesolytic versus Homolytic Cleavage in Photochemical Nitroxide Mediated Polymerization

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ABSTRACT: Time-dependent density functional theory calculations have been performed to study the photocleavage reactions of chromophore-functionalized alkoxyamines in nitroxide-mediated photopolymerization. Two case studies were considered: azaphenylene derivatives and benzophenone-based alkoxyamines. For the azaphenylene derivatives, we show that the expected homolysis pathway is actually inaccessible. Instead, these alkoxyamines exhibit low-lying $n_N\pi^*$ excited states that exhibit an electronic structure about the nitroxide moiety similar to that of the formally oxidized radical cation. As a result, the cleavage of these alkoxyamines can be described as mesolytic-like, rather than homolytic. As with formally oxidized species, mesolytic cleavage can result in the production of either carbon-centered radicals or carbocations, with only the former resulting in radical polymerization. Here, the cleavage products are found to be dependent on the respective radical/cation stabilities of the monomer units of choice (styrene, ethyl propanoate, and ethyl isobutyrate). In contrast to the azaphenylene derivatives, in the benzophenone-based alkoxyamines, conjugation between the nitroxide and chromophore moieties appears to facilitate homolysis, due to the ideal alignment of singlet and triplet states of different symmetries.

INTRODUCTION

Methods for controlling the molecular weight and architecture in free-radical polymerization have broad applications in the synthesis of smart materials for use in applications ranging from drug delivery to lithography.^{1,2} One such technique is nitroxide mediated polymerization (NMP).³⁻⁵ In this process, control is achieved through a dynamic equilibrium between the dormant alkoxyamine and active propagating radical (Scheme 1). By minimizing the concentration of active propagating radicals with respect to the population of dormant alkoxyamines, bimolecular termination is minimized with respect to chain growth while imparting a synthetically useful nitroxide functionality on the chain end. However, a key drawback of NMP is the requirement for elevated temperatures, which can lead to side reactions that deactivate the dynamic equilibrium upon NMP depends.⁶

Scheme 1. Controlling equilibrium for NMP where an alkoxyamine is thermally cleaved into the active transient carbon centered radical and persistent nitroxide radical.

To address this problem the use of light, rather than heat, to activate the alkoxyamine has been explored.⁷⁻⁹ However, while so-called photo-nitroxide-mediated polymerization (PNMP) has shown extremely promising results in certain systems, overall the results have been mixed, with some systems displaying control, others displaying non-controlled polymerization and some displaying no reaction at all. For example, while azaphenylenes are effective PNMP agents for styrene polymerization, alkoxyamines containing chromophores such as 9,10-diphenylanthracene and 9,10-

bis(phenylethynyl) anthracene undergo fluorescence instead.¹⁰ A better understanding of the photochemical processes involved and their dependence on chemical structure is essential to the design of more effective PNMP agents.

To date it has been assumed that PNMP occurs via energy transfer from the chromophore to the breaking NO–R bond on the triplet surface, so as to cause homolysis in the same manner as standard NMP.^{7,11} This reactive process is in competition with various non-reactive processes, as represented in Figure 1. However, mesolytic cleavage (Scheme 2) is a conceivable alternative which could help to explain some of the unexpected failures of PNMP agents. The excited state capable of leading to mesolytic cleavage is the $n_N\pi^*$ state, on either the singlet or triplet surface. This excited state results in the transfer of a non-bonding electron from the nitrogen atom into the π^* -system of the chromophore, resulting in a biradical charge-separated state. The radical cation centered on the nitrogen therefore possesses the valency necessary for mesolysis.

Figure 1. A simplified Jablonski diagram showing the photochemical processes leading to homolytic cleavage and the competing non-reactive relaxation processes.

As shown in Scheme 2 mesolytic cleavage results in the formation of a radical and a cation, with the ultimate location of these species dependent on their respective stabilities, i.e. nitroxide radical and carbocation versus oxoammonium cation and carbon-centered radical. In these situations, it is unclear if the propagating species and nitroxide can recouple to reform the dormant species. However, it is likely that if a carbon

centered radical is formed, the zwitterionic nitroxide fragment could relax back to a nitroxide allowing controlled radical polymerization to proceed. If, however, a carbocation is formed, cationic polymerization may occur with fate of the nitroxide radical anion dependent on protic impurities.

Scheme 2. Alternative homolysis (black) and mesolysis (blue) pathways demonstrated for an azaphenylene. Mesolytic cleavage can result in either a carbocation or a carbon-centered radical depending on their relative stabilities and those of the nitroxide and oxoammonium.

Interestingly, the local $[\text{NO-R}]^{++}$ environment in the $n_N\pi^*$ state directly resembles that of formally oxidized alkoxyamines, which have recently been shown to undergo mesolytic cleavage. Experiments have shown that the exact specific cleavage behavior depends on the leaving group and the presence or absence of nucleophiles including coordinating solvents such as acetonitrile (see Scheme 3).^{12–15} As seen in Scheme 3, in the oxidized species at least, cleavage to a carbon-centered radical is expected for acrylate and methacrylate polymerizations, but not for styrene which will produce carbocations.

Scheme 3. Effect of R on the oxidation behavior of TEMPO-based alkoxyamines. Included among the R groups are models of the propagating species in polymerizations of vinyl acetate (VA,

CH₂OCOCH₃), styrene (STY, CH(CH₃)Ph), methyl acrylate (MA, C(CH₃)COOCH₃), methyl methacrylate (MMA, C(CH₃)₂COOCH₃), and acrylonitrile (AN, CH(CH₃)CN).¹²

Summing up, while it has been assumed until now that PNMP proceeds via energy transfer and standard homolytic cleavage, the possibility of mesolytic cleavage and its implications has not been explored. If it occurs, this has significant implications for the success or failure of PNMP as it can lead to species other than carbon-centered propagating radicals being produced. In this work we use computational chemistry to study the cleavage pathways in two key PNMP families, azaphenalenenes (**1**) and benzophenone-based nitroxides (**2**), with a view to better informing reagent design.

Scheme 1. Test set considered

COMPUTATIONAL METHODOLOGY

All electronic structure calculations were performed with density functional theory (DFT) or its excited state extension, time-dependent DFT (TD-DFT), using the Gaussian 16.C01 software package.¹⁶ The M06-2X functional¹⁷ was used for both types of calculation, as it has been shown to perform well when describing free-radical processes, and the excited states of organic chromophores. The 6-31+G(d,p) basis set was employed for all calculations, and the SMD universal solvent model¹⁸ was used for solvent-phase electronic energies. The solvent used was ethyl ethanoate, as it is a solvent that will exhibit similar properties to that of bulk acrylate monomer. TD-DFT was chosen for investigating the excited states of the alkoxyamines as multireference calculations, requiring a large active space that includes

$n_{N/O}$, π and π^* , and σ orbitals for a proper description of the dissociation pathways, are too expensive for these systems. M06-2X has, however, been shown to give good agreement with respect to predicting the ordering of states of differing symmetries, as well as at predicting singlet-triplet gaps.¹⁹ Whilst accurate excited state free energies are not possible with TD-DFT, enough information about the character and therefore reactivity of the excited states is possible.

RESULTS AND DISCUSSION

Azaphenalenenes (1). To explore the likelihood of homolytic versus mesolytic cleavage, TD-DFT calculations were first used to construct Jablonski diagrams for a family of 6-azaphenalenenes (Figure 1). 6-Azaphenalenenes have been shown to be effective PNMP agents for styrene polymerization, but not for (meth)acrylates, though this latter result was attributed to side reactions rather than problems in the photodissociation. In the present work styrene, methyl acrylate and methyl methacrylate were modelled using unimeric R-groups of styrene (STY), ethyl propanoate (EP) and ethyl isobutyrate (EIB), respectively. Qualitative results for each of the three leaving groups are shown in Figure 2; the low-lying states are localized to the chromophore and the character of these states are found to be independent of the R-group, and the vertical excitation energies change only minimally.

Figure 2. Simplified Jablonski diagram for azaphenalenenes functionalized with R groups shown in Scheme 1. The characters of the low-lying states are found to be independent of the R group, as they are localized on the azaphenalene moiety. Radiative processes are

not shown but they can be expected to compete with radiationless processes.

In the azaphenalenenes, the first singlet excited state is a $\pi\pi^*$ transition centered on the chromophore. However, the accompanying triplet state nearest in energy (average $\Delta E_{S-T}(\pi\pi^*) = -0.07$ eV between R-groups) is also, of $\pi\pi^*$ character rather than $n_N\pi^*$ character. Intersystem crossing between the singlet and triplet states of the same symmetry does not occur,²⁰ and so the reactive $^3\pi\pi^*$ state is inaccessible. Thus, populating the bright $^1\pi\pi^*$ would not result in any reaction, as the valency around the nitroxide moiety will remain unchanged. Instead, for dissociation to occur, only mesolytic cleavage from S_3 (average $\Delta E_{S-T}(n_N\pi^*) = -0.05$ eV) is available. In the azaphenalenene derivatives, population of the dark $n_N\pi^*$ state is likely possible by first populating the bright $S_4(\pi\pi^*)$ state which lies relatively close in energy to the $S_3(n_N\pi^*)$ state (average $\Delta E = +0.3$ eV). As a result, mesolysis, if it occurs, is the only possible reactive outcome in this family of reagents.

While TD-DFT is sufficiently reliable to draw this qualitative conclusion, it is not sufficiently accurate for predicting quantitative reaction energies. As described above, accurate alternatives such as multireference methods are cost prohibitive for these large systems. To qualitatively assess the likely mesolytic cleavage behavior we can instead examine the ground state formally oxidized species. Figure 3 shows the computed bond dissociation Gibbs free energies for mesolytic cleavage to a nitroxide radical and a carbocation, and cleavage to an oxoammonium and a carbon-centered radical.

Figure 3. Bond dissociation Gibbs free energies for the (ground state) oxidized 6-azaphenalenenes, showing results as a function of leaving group for mesolytic cleavage to a nitroxide radical and a carbocation, and cleavage to an oxoammonium and a carbon-centered radical.

From Figure 3, it is seen that the styrene-derivative of oxidized 6-azaphenalenene prefers to undergo cleavage to a carbocation, while the (meth)acrylates prefer to cleave to a radical. Moreover, the energetic cost of cleavage is least for the styrene leaving group and most for the acrylate leaving group, as one might expect based both radical and carbocation stability considerations. This is consistent with experimental observations for the oxidative cleavage of the corresponding TEMPO-based analogues.¹²⁻¹⁵ If the results above were to apply also to corresponding the excited state mesolytic cleavage, it would suggest styrene actually undergoes photo-initiated cationic polymerization with this PNMP agent (which would still be consistent with the observed control), and the acrylates in particular struggle to undergo cleavage at all, which could help to explain the failed experiments with this monomer.

While most of the trends in the calculations of Figure 3 would be mirrored in the excited state mesolysis energies, there are two important differences: (1) the excited states are higher in energy and this additional energy can help to overcome the otherwise unfavorable Gibbs free energies requirements; (2) the chromophore bears a remote negative charge which is able to electrostatically interact with the nitroxide functionality. This latter effect would preferentially stabilize the oxoammonium over the nitroxide and systematically reduce the mesolytic cleavage energies for carbon-centered radical production.

In order to assess the potential impact of the negative charge that will be present in the charge-separated, biradical $n_N\pi^*$ excited state, a negatively charged BF_4^- ion was introduced to the azaphenalenene-styrene radical cation system. The difference in reaction free energies for styrene/azaphenalenene radical/cation formation with and without the BF_4^- salt is shown in Table 1. Table 1 clearly shows how the electrostatic interaction between the negative BF_4^- salt and positive

radical cation stabilizes the formation of the oxoammonium and styrene radical.

One could consider the formally oxidized species, and the zwitterionic BF_4 salt as limiting cases, with the true behavior somewhere in between the two. While quantitative results are not possible without prohibitive multireference calculations, one can conclude that mesolysis is the only available pathway for these systems. For (meth)acrylates carbon-centered radicals are preferred over carbocations, while for styrene the two pathways are in reasonably close competition and cations should not be ruled out.

Table 1. Reaction free energies (kJ mol^{-1}) for azaphenylene-styrene mesolysis with and without BF_4 present

Product	STY radical	STY cation	$\Delta\Delta G^0_{\text{rad-cat}}$
No BF_4	+35.0	-12.5	+47.4
With BF_4	+55.7	+70.5	-14.8

Benzophenone Derivatives (2). The benzophenone-based alkoxyamines have been shown to initiate photopolymerization of n-butyl acrylate with partial living character. In contrast to the azaphenalenenes, the chromophore is directly bonded to the nitroxide moiety making them a better candidate for direct homolysis via energy transfer.

Figure 4. Simplified Jablonski diagram for R-functionalized benzophenone derivatives.

Indeed, examining the excited states from TD-DFT highlights some clear differences between the benzophenone and azaphenylene derivatives. In Figure 2, TD-DFT predicts singlet and triplet states of the same symmetry close in energy, suggesting that ISC to the triplet manifold would be uncompetitive, relative to reactivity from the singlet states. In Figure 4, however, this is not the case, with singlet and triplet states of different symmetries predicted to be near degenerate in energy. In contrast to azaphenylene derivatives, this would allow for efficient population of low-lying triplet states, resulting in triplet photoreactivity like that of acetophenone. As well as this, population of the $^1n_N\pi^*$ state, which would possess the correct valency for mesolysis, is:

1. Difficult to populate, due to the transition being symmetry-forbidden and no other singlet states being close in energy (slow internal conversion)
2. Likely unreactive; Figure 5 shows the BDFEs for mesolysis of the formally oxidized benzophenone derivatives suggests that even upon oxidation, cleavage to either a nitroxide or oxoammonium is unfavourable (except for with styrene as an R group).

Summing up, in contrast to the azaphenalenenes, for the benzophenone derivatives the triplet $\pi\pi^*$ state can be populated, while the $n_N\pi^*$ state is difficult to populate and likely to be in any case unreactive. Hence triplet reactivity and bond homolysis, rather than mesolysis, is the preferred pathway for these systems.

Figure 5. Bond dissociation Gibbs free energies for cleavage of oxidized benzophenone nitroxide and oxoammonium species.

CONCLUSION

Theoretical calculations have been performed which highlight the potential role of mesolytic cleavage in describing the cleavage pathways of photoactive NMP agents. Mesolytic cleavage can be used to explain the monomer-dependent performance of PNMP. The radical rearrangement upon mesolytic-like cleavage can regenerate the nitroxide radical (when mesolysis produces R•) or the hydroxylamine (when mesolysis produces R⁺). However, analogous to Type II photoinitiators such as anthraquinones, electron transfer reactions with additives (or impurities) such as amines, halides and so forth can compete, and negatively impact the radical-radical recombination required for “living” polymerization reactions.

The consequences of this study are as follows:

1. Conjugation between the nitroxide and chromophore moieties appears to facilitate homolysis, due to the ideal alignment of singlet and triplet states of different symmetries. However, it must be noted that such conjugation can also promote side reactions such as N-O homolysis or beta-fragmentation (on the second alkyl group bearing by the nitroxide).
2. When there is no conjugation between the nitroxide and the chromophore, a low-lying, charge-separated $n_N\pi^*$ excited state is accessible, which possesses the valency around the nitroxide to undergo mesolytic, rather than homolytic cleavage.
3. The choice of monomer remains important when designing PNMP agents: as with thermally-initiated NMP, acrylate derivatives still suffer with side-reactions and poor “living” behavior.
4. The mesolytic pathway may lend itself to other synthetically useful photoreactions, outside that of NMP applications, analogous to our recent use of formally oxidized alkoxyamines as in situ methylation agents.¹⁴

ASSOCIATED CONTENT

Supporting Information

Supplementary figures and complete computational details. The Supporting Information is available free of charge on the ACS Publications website.

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Funding Sources

Australian Research Council (CE140100012, FL170100041)

CONFLICTS OF INTEREST

There are no conflicts to declare.

ACKNOWLEDGMENT

The authors acknowledge financial support from the Australian Research Council (ARC) Centre of Excellence for Electromaterials Science, an ARC Laureate Fellowship (to M.L.C.), and generous supercomputing time from the National Computational Infrastructure.

REFERENCES

- (1) Matyjaszewski, K.; Spanswick, J. Controlled/Living Radical Polymerization. *Mater. Today* **2005**, *8* (3), 26–33. [https://doi.org/https://doi.org/10.1016/S1369-7021\(05\)00745-5](https://doi.org/https://doi.org/10.1016/S1369-7021(05)00745-5).
- (2) Matyjaszewski, K. Architecturally Complex Polymers with Controlled Heterogeneity. *Science* **2011**, *333* (6046), 1104 LP – 1105. <https://doi.org/10.1126/science.1209660>.
- (3) Hawker, C.; Bosman, A.; Harth, E. New Polymer Synthesis by Nitroxide Mediated Living Radical Polymerizations. *Chem. Rev.* **2001**, *101* (12), 3661–3688.
- (4) Grubbs, R. B. Nitroxide-Mediated Radical Polymerization: Limitations and Versatility. *Polym. Rev.* **2011**, *51* (2), 104–137. <https://doi.org/10.1080/15583724.2011.566405>.
- (5) Bertin, D.; Gimes, D.; Marque, S. R. A.; Tordo, P. Kinetic Subtleties of Nitroxide Mediated Polymerization. *Chem. Soc. Rev.* **2011**, *40* (5), 2189–2198. <https://doi.org/10.1039/C0CS00110D>.
- (6) Gryn'ova, G.; Lin, C. Y.; Coote, M. L. Which Side-Reactions Compromise Nitroxide Mediated Polymerization? *Polym. Chem.* **2013**, *4* (13), 3744.

- <https://doi.org/10.1039/c3py00534h>.
- (7) Chen, M.; Zhong, M.; Johnson, J. A. Light-Controlled Radical Polymerization: Mechanisms, Methods, and Applications. *Chem. Rev.* **2016**, *116* (17), 10167–10211. <https://doi.org/10.1021/acs.chemrev.5b00671>.
 - (8) Guillauneuf, Y.; Bertin, D.; Gigmes, D.; Versace, D. L.; Lalevée, J.; Fouassier, J. P. Toward Nitroxide-Mediated Photopolymerization. *Macromolecules* **2010**, *43* (5), 2204–2212. <https://doi.org/10.1021/ma902774s>.
 - (9) Morris, J.; Telitel, S.; Fairfull-Smith, K. E.; Bottle, S. E.; Lalevée, J.; Clément, J.-L.; Guillauneuf, Y.; Gigmes, D. Novel Polymer Synthesis Methodologies Using Combinations of Thermally- and Photochemically-Induced Nitroxide Mediated Polymerization. *Polym. Chem.* **2015**, *6* (5), 754–763. <https://doi.org/10.1039/C4PY01270D>.
 - (10) Bottle, S. E.; Clement, J.-L.; Fleige, M.; Simpson, E. M.; Guillauneuf, Y.; Fairfull-Smith, K. E.; Gigmes, D.; Blinco, J. P. Light-Active Azaphenylene Alkoxyamines: Fast and Efficient Mediators of a Photo-Induced Persistent Radical Effect. *RSC Adv.* **2016**, *6* (83), 80328–80333. <https://doi.org/10.1039/C6RA18500B>.
 - (11) Huix-Rotllant, M.; Ferré, N. Theoretical Study of the Photochemical Initiation in Nitroxide-Mediated Photopolymerization. *J. Phys. Chem. A* **2014**, *118* (25), 4464–4470. <https://doi.org/10.1021/jp501773n>.
 - (12) Hammill, C. L.; Noble, B. B.; Norcott, P. L.; Ciampi, S.; Coote, M. L. Effect of Chemical Structure on the Electrochemical Cleavage of Alkoxyamines. *J. Phys. Chem. C* **2019**, *123* (9), 5273–5281. <https://doi.org/10.1021/acs.jpcc.8b12545>.
 - (13) Noble, B. B.; Norcott, P. L.; Hammill, C. L.; Ciampi, S.; Coote, M. L. Mechanism of Oxidative Alkoxyamine Cleavage: The Surprising Role of the Solvent and Supporting Electrolyte. *J. Phys. Chem. C* **2019**, *123* (16), 10300–10305. <https://doi.org/10.1021/acs.jpcc.9b01832>.
 - (14) Norcott, P. L.; Hammill, C. L.; Noble, B. B.; Robertson, J. C.; Olding, A.; Bissember, A. C.; Coote, M. L. TEMPO–Me: An Electrochemically Activated Methylating Agent. *J. Am. Chem. Soc.* **2019**, *141* (38), 15450–15455. <https://doi.org/10.1021/jacs.9b08634>.
 - (15) Zhang, L.; Laborda, E.; Darwish, N.; Noble, B. B.; Tyrell, J. H.; Pluczyk, S.; Le Brun, A. P.; Wallace, G. G.; Gonzalez, J.; Coote, M. L.; et al. Electrochemical and Electrostatic Cleavage of Alkoxyamines. *J. Am. Chem. Soc.* **2018**, *140* (2), 766–774. <https://doi.org/10.1021/jacs.7b11628>.
 - (16) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Petersson, G. A.; Nakatsuji, H.; et al. Gaussian 16 Revision C.01. 2016.
 - (17) Zhao, Y.; Truhlar, D. G. The M06 Suite of Density Functionals for Main Group Thermochemistry, Thermochemical Kinetics, Noncovalent Interactions, Excited States, and Transition Elements: Two New Functionals and Systematic Testing of Four M06-Class Functionals and 12 Other Function. *Theor. Chem. Acc.* **2007**, *120*, 215–241. <https://doi.org/10.1007/s00214-007-0310-x>.
 - (18) Marenich, A. V.; Cramer, C. J.; Truhlar, D. G. Universal Solvation Model Based on Solute Electron Density and on a Continuum Model of the Solvent Defined by the Bulk Dielectric Constant and Atomic Surface Tensions. *J. Phys. Chem. B* **2009**, *113*, 6378–6396.
 - (19) Jacquemin, D.; Perp, E. A.; Ciofini, I.; Adamo, C.; Electrochimie, L.; Cnrs-enscp, U. M. R. Assessment of Functionals for TD-DFT Calculations of Singlet-Triplet Transitions. *J. Chem. Theory Comput.* **2010**, *6*, 1532–1537.
 - (20) McNaught, A. D.; A., W. *IUPAC. Compendium of Chemical Terminology*, 2nd Editio.; Blackwell Scientific Publications, 1997.

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