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The reactivity of nitroxides towards alkenes

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Abstract

At elevated temperatures, nitroxides (e.g. 1,1,3,3-tetramethyl-2,3-dihydroisoindol-2-yloxyl) undergo a slow addition reaction with acrylonitrile, methyl acrylate and styrene to give the bis-nitroxide adducts. With alkenes containing an allylic hydrogen such as methyl methacrylate and 6-methylene-1,4-oxathiepan-7-one, the major reaction observed was hydrogen abstraction. The resulting hydroxylamines can be trapped as Michael addition products. © 2000 Elsevier Science Ltd. All rights reserved.

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1. Introduction

As the trapping of carbon-centred radicals by nitroxides is more efficient than their addition to monomers, we investigated the mechanism of the AIBN-initiated polymerization of the ring-opening monomer, 6-methylene-1,4-oxathiepan-7-one 2,¹ by carrying out the reaction of 2 (0.6 mmol) with alkoxyamine 3 (0.1 mmol) under vacuum, in benzene (2 ml) at 105°C for 6 hours. Upon heating, the alkoxyamine 3 undergoes reversible homolysis to generate cyanoisopropyl radicals and the nitroxide, 1,1,3,3-tetramethyl-2,3-dihydroisoindol-2-yloxyl (TMIO) 1.² Thus, 3 behaves as an analogue of AIBN, while at the same time providing a low concentration of nitroxide 1.



To our surprise, there was no evidence of the addition of cyanoisopropyl radicals to 2. The only products observed by HPLC/MS analysis were the nitroxide 1 (59%), compound 5 (36%) and the

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alkoxyamine 3(5%). Product 5 is formed as a result of hydrogen abstraction by the nitroxide 1 (confirmed in a separate experiment employing only 1 and 2) followed by trapping of the resultant allylic radical at the least hindered position (Scheme 1).



It is clear that cyanoisopropyl radical addition to the monomer double bond is not competitive with reactions such as hydrogen abstraction from 2. We were unable to determine the precise fate of the cyanisopropyl radicals, which probably either dimerized or underwent hydrogen transfer to nitroxide 1 to give methacrylonitrile. The other product of hydrogen abstraction is hydroxylamine 4, which was not detected by HPLC/MS presumably as it underwent rapid oxidation back to nitroxide 1 upon exposure to air during product analysis. In order to provide some supporting evidence for the formation of 4, we carried out a separate experiment in which 1 (0.3 mmol) was heated with 2 (1.0 mmol) in the presence of a good Michael acceptor (acrylonitrile, 3 ml). After 18 hours at 105°C under vacuum, HPLC/MS analysis showed the formation of 5 (28%), 7a (57%) and 8a (15%) (Scheme 2). The formation of 7a provides undergo facile Michael addition reactions to acrylonitrile). The formation of the di-TMIO adduct 8a was unexpected and prompted an investigation into the addition reactions of nitroxides with some common monomers.



2. Addition of nitroxides to alkenes

Evacuated solutions of TMIO 1 (1.3 mol 1^{-1}) in distilled neat monomer were heated at 110°C for 5 days. The results obtained are summarized in Table 1. Nitroxide addition to styrene proved the most facile, and it is interesting to note that the analogous di-TEMPO adduct of styrene was recently reported by Connolly and Scaiano,³ when TEMPO (2,2,6,6-tetramethylpiperidine-1-oxyl) was heated in styrene at 120°C for 2 hours. This suggests that resonance stabilization of the intermediate radical **6** is important for the formation of the bis-nitroxide adducts **8** (Scheme 2). The concurrent formation of significant amounts of adducts **7a** and **7b** suggests that the intermediate radical **6** also takes part in a hydrogen abstraction

 Table 1

 Percentage yields of products as a result of heating TMIO 1 in monomer at 110°C for 5 days

Monomer	Products	
Acrylonitrile	7a, 8%	8a , 13%
Methyl acrylate	7b , 1%	8b , 6%
Styrene	7c ,<1%	8c , 32%
Vinyl acetate	7d , 0%	8d ,<1%

or that some hydroxylamine **4** is formed, and that it undergoes a Michael addition to the respective monomers (as described later). Interestingly, HPLC/MS analysis did show molecular ions equivalent to putative intermediates **9** and **10**, which can be formed as a consequence of hydrogen abstraction from **8a** and **8b**. The yields of compounds **9** and **10** appeared to be low (<1%). Hydrogen abstraction (under the same reaction conditions) was faster in the case of methyl methacrylate (MMA) to predominantly give the previously described hydrogen abstraction product **11** in 13% yield.⁴



3. Addition of hydroxylamines to Michael acceptors

The hydroxylamines of TMIO, TEMPO and 4-oxo-TEMPO were prepared in situ via a simple hydrogenation over Adams catalyst (PtO_2) in dichloromethane at ambient temperature and pressure. After 1–3 hours the yellow/red colouration of the nitroxide had disappeared indicating that the hydrogenation had reached completion. The solution was filtered, evaporated to dryness, evacuated and stirred in monomer for 3 hours at ambient temperature. The Michael adducts (Scheme 3) were all isolated in quantitative or near-quantitative yields. When the reactions were carried out under analogous conditions but in the presence of 1 equivalent of sodium ethoxide, the reaction reached completion in half an hour, and no reaction was observed with styrene. It follows that these reactions are proceeding via a regular Michael addition rather than a radical-catalyzed Michael addition.

The addition of *N*,*N*-dialkylhydroxylamines to activated double bonds was first described by Zinner et al.,⁵ and more recently by Pastor and Hessell.⁶ The addition of these sterically hindered compounds is probably facilitated by the α -effect; however, the corresponding Michael adducts with MMA and methacrylonitrile were not formed. It is interesting to note that compounds **12** (the formal Michael adduct of TMIOH and MMA) and **13**, previously isolated from the reaction of isopropoxyl radicals with MMA, may be formed by a radical-catalyzed Michael addition process.⁴



4. Significance and conclusions

Nitroxides are finding increasing use as mediators for 'living' free radical polymerizations² so it is important to be aware of side-reactions involving nitroxides and alkenes. The bis-nitroxide compounds **8**, and the hydroxylamine Michael addition products described above, also have potential as unimolecular initiators for such 'living' polymerization processes. It is clear that any hydroxylamine formed during the polymerization of acylonitrile or acrylates will undergo rapid hydrogen transfer and addition reactions. This will slow down the polymerization process, and broaden the molecular weight distribution of the resulting polymers.⁷ Although the radical addition of nitroxides to various monomers is slow at the elevated temperatures at which such 'living' polymerizations generally take place, addition and hydrogen abstraction reactions by nitroxides are significant.

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