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Stable free radical polymerization—acrylate alkoxyamine synthesis☆

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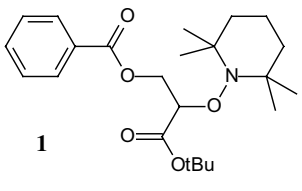
Abstract—An efficient synthesis of the alkoxyamine containing a benzoyl peroxide fragment, one *tert*-butyl acrylate monomer unit and TEMPO via an oxymercuration reaction followed by an oxidative demercuration reaction is reported. The formation of significant amounts of an undesired reduced product with the latter reaction was overcome by using a milder reducing agent ($NaBH_3CN$) than those ($NaBH_4$, $LiBH_4$) reported to work well in other systems.

1. Introduction

The synthesis of alkoxyamines and their subsequent uses as initiating species and model compounds to study the kinetics of the stable free radical polymerization (SFRP)[1] process has been a significant area of research for polymer chemists working in the living-radical polymerization arena.[2,3] Noticeably absent from the list of alkoxyamines that have been synthesized is the alkoxyamine **1**, the acrylate analogue of the alkoxyamine **2** derived from styrene, which has been synthesized and reported on extensively.[4]



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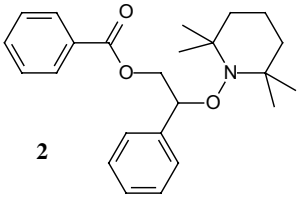

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We recently reported the use of alkoxyamine **2** to initiate the polymerization of *n*-butyl acrylate[5] in the presence of ascorbic acid to give a poly(*n*-butyl acrylate) polymer containing a penultimate styrene unit at the initiating end. As an extension to this work we were interested in performing the same polymerization with alkoxyamine **1** but found that the synthesis of this compound by the direct reaction of benzoyl peroxide (BPO) and *tert*-butyl acrylate (*t*-BuA) in the presence of TEMPO at temperatures ranging from 80 to 120 °C was fraught with problems.[6] Yields of alkoxyamine **1** were typically less than 5%. Attempts to prepare **1** by a recently developed low temperature procedure[7] that works well for **2** did not provide any significant improvement in yield. In this paper we report on the use of an oxymercuration reaction, followed by oxidative demercuration in the presence of TEMPO, for the synthesis of **1** in moderate yields.

2. Results and discussion

Alkoxyamine **1** was synthesized according to the reaction sequence outlined in Scheme 1. The route is short and relatively efficient, providing an overall yield of 45% in two steps. Oxymercuration of *t*-BuA provided the mercury(II) acetate intermediate **3**, which reacted with TEMPO in the presence of oxygen and a reducing agent to give the nitroxide-trapped product. Steric effects typically determine the regiospecificity of an oxymercuration reaction with the mercuric acetate becoming attached to the least sterically hindered carbon.[8] In the case of acrylates it was anticipated that the steric bias would be secondary to the electron withdrawing effect of

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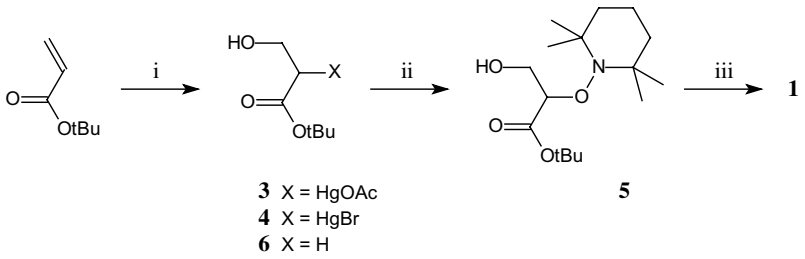


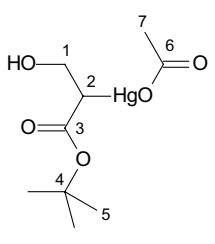
Scheme 1. Reagents and conditions: (i) H_2O, $Hg(OAc)_2$. (ii) DMF, TEMPO, 5 °C; O_2, then $NaBH_3CN$, 2 h. (iii) CH_2Cl_2, pyridine, 5 °C; then benzoyl chloride, 5–25 °C.

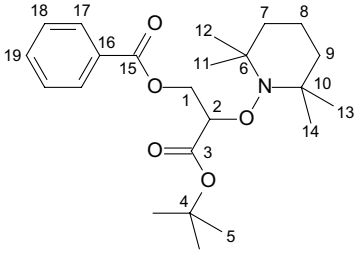
the carbonyl group, which would direct the mercuric acetate to the more highly substituted carbon of the double bond in the substrate, giving the desired anti-Markovnikov addition product.[9] In fact, the regioselectivity of the oxymercuration of *t*-BuA yielding **3** was greater than 95%, as determined by ^{1}H NMR.

Initially, the mercuric acetate intermediate **3** was converted into the corresponding bromomercury(II) derivative (**4**) with KBr, followed by oxidative demercuration with O_2 and $NaBH_4$ in the presence of TEMPO.[10] Under a variety of reaction conditions, which included changes in the reaction temperature, the order of addition of the reagents and the amounts of the various reagents, the major product was always the reduced compound **6**, with only trace amounts of the desired nitroxide-trapped product **5**. $LiBH_4$[11] again provided only the reduced product **6**. However, $NaBH_3CN$ proved to be a more effective reagent. The reaction of $NaBH_3CN$ with the organomercuric bromide **4** was not particularly successful but a significant improvement was observed with the organomercuric acetate intermediate **3**. Initial oxidation reactions at room temperature gave modest yields of 18%, which improved to 27% at 10 °C and 45% at 5 °C. Benzoylation of **3** gave the desired alkoxyamine **1**.

3. General procedure for the synthesis of 3[12]

Mercuric acetate (9.8 g, 31 mmol) was dissolved in water (100 mL) in a 250 mL beaker and *t*-BuA (4.8 mL, 33 mmol) added to the stirred solution at room temperature. Stirring was continued for 7 h, after which the solution was evaporated to dryness to yield a colourless, viscous oil. ^{1}H NMR (20 °C): δ 4.13 (dd, $^2J = 11.6$ Hz, $^3J = 3.5$ Hz, $^3J_{HgH} = 290$ Hz, 1H1); 3.82 (dd, $^2J = 11.6$ Hz, $^3J = 5.8$ Hz, $^3J_{HgH} = 123$ Hz, 1H1); 3.60 (vbr s, OH); 3.44 (dd, $^3J = 5.8$ Hz, $^3J = 3.5$ Hz, $^2J_{HgH} = 337$ Hz, 1H2); 2.05 (s, 3H7); 1.47 (s, 9H5). ^{13}C NMR (20 °C): δ 177.50 (C6); 173.59 ($^2J_{HgC} = 118$ Hz, C3); 82.00 (C4); 61.13 ($^2J_{HgC} = 107$ Hz, C1); 49.48 ($^1J_{HgC} = 1585$ Hz, C2); 28.17 (3C5); 22.93 (C7).





4. General procedure for the synthesis of 1[13,14]

TEMPO (7.55 g, 48 mmol), **3** (4.82 g, 12 mmol) and DMF (25 mL) were combined in a three-necked round bottom flask fitted with a sintered glass bubbler and thermometer. The solution was cooled to 5 °C, bubbled with oxygen for 15 min and $NaBH_3CN$ (2.27 g, 36 mmol) was then added. The reaction mixture was stirred for 2 h, after which it was poured into diethyl ether (50 mL). The resulting mixture was filtered through Celite to remove the mercury precipitate and the filtrate evaporated to dryness. The crude mixture containing **5** was dissolved in CH_2Cl_2 (80 mL), pyridine was added (11.5 mL) and the solution cooled to 5 °C. Benzoyl chloride (7.8 mL, 43 mmol) was added dropwise via a dropping funnel over 5 min. The solution was allowed to warm to room temperature and left at that temperature for 18 h. The reaction mixture was extracted with cold water, washed with cold dilute HCl (0.2 M), followed by cold dilute NaOH (0.2 M) and finally brine. The organic layer was dried over sodium sulfate, filtered, evaporated to dryness under vacuum and purified by flash chromatography (eluent: 20% ethyl acetate in hexane). The product was a colourless oil that crystallized on standing, mp 37–39 °C. ^{1}H NMR (−20 °C): δ 8.06 (m, $^3J = 8.4$ Hz, $^4J = 1.3$ Hz, 2H17); 7.60 (m, $^3J = 7.4$ Hz, $^4J = 1.3$ Hz, 1H19); 7.46 (m, $^3J_{av} = 7.8$ Hz, 2H18); 4.72, 4.56, 4.53 (ABX spin system, $^2J = -11.0$ Hz, $^3J = 6.8$ Hz, $^3J = 4.5$ Hz, 1H1, 1H2, 1H1); 1.56 (m, 1H8); 1.46 (m, 2H7, 2H9); 1.41 (s, 9H5); 1.32 (m, 1H8); 1.23, 1.18, 1.15, 1.12 (4s, 3H12, 3H14, 3H13, 3H11). ^{13}C NMR (−20 °C): δ 170.23 (C3); 166.06 (C15); 133.19 (C19); 129.62 (C17); 129.33 (C16); 128.34 (C18); 82.76 (C2); 81.67 (C4); 63.90 (C1); 59.99, 59.90 (C10, C6); 39.95, 39.92 (C9, C7); 33.51, 33.15, 20.04, 20.04 (C12, C13, C11, C14); 27.81 (C5); 16.91 (C8). EI MS: M^+ not observed; $M^+ - OtBu$, m/z 332; major fragment ions: 193, 156, 105, 249. HR MS: $M^+ - OtBu$, m/z 332.1863; calculated for $C_{19}H_{26}NO_4$: 332.1862.

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13. NMR spectra of compound **1** were recorded at −20 °C in order to 'freeze-out' the complex conformational rotation–inversion process associated with the N–O bond and the tetramethylpiperidine ring.[4a,15] CH_2 proton chemical shifts were measured from the gHSQC spectrum; accurate values of the H1 and H2 chemical shifts and the associated coupling constants were obtained by iterative simulation of the ABX spin system.
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