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Photochemical Synthesis of TEMPO-capped Initiators for "Living" Free Radical Polymerization

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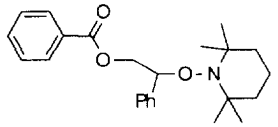
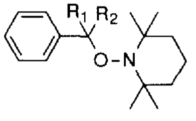
Abstract: Two photochemical routes to stoichiometric initiators used in living free radical polymerizations are presented. These routes offer the advantages of higher yields and allow for the preparation of initiators not accessible using current methodology. All initiators gave detectable carbon centered radicals (laser flash photolysis) and promoted the polymerization of styrene. Copyright © 1996 Elsevier Science Ltd

High polydispersities generally characterize resins obtained by free radical polymerization. Georges et al. have recently shown that polymers (particularly polystyrene) obtained by free radical polymerization in the presence of TEMPO (2,2,6,6-tetramethyl-1-piperidinyloxy free radical) can have polydispersities well below the theoretical limit of 1.5, an observation that has led to considerable interest in the subject.[1,2] These polymerizations have been described as "living" free radical polymerizations reflecting that the weak bond formed upon trapping of the growing polymer by TEMPO is believed to cleave upon heating, thus allowing further polymer growth by addition of monomer to the chain terminus.

It is of interest to develop initiators that contain the initiating radical and TEMPO in the correct (usually 1:1) stoichiometry, so as to control the number of chains initiated. Recent reports have dealt with the synthesis and properties of **I** and **II**, both typical representatives of this type of initiator.[3,4] Their decomposition can be triggered either thermally or photochemically.



I



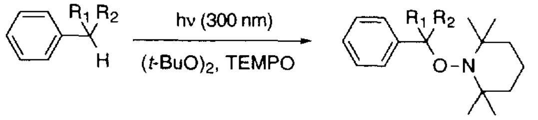
II : R_1=R_2=H
III : R_1=CH_3; R_2=H
IV: R_1=Et; R_2=H
V: R_1=R_2=CH_3
VI: R_1=H;R_2=Ph

Quite recently, Hawker, Barclay and coworkers reported the synthesis and evaluation of several stoichiometric initiators.[5] One series of initiators was prepared by extending the recently reported methodology of Priddy and Howell.[6] Hydrogen abstraction from alkylbenzenes, followed by radical trapping by TEMPO led to the initiators in fair to moderate yields. The benzylic radicals were formed by hydrogen abstraction by *tert*-butoxyl radicals formed by thermal decomposition of di-*tert*-butyl peroxide at temperatures around 125 °C. The reaction works well with toluene and ethylbenzene, moderately with propylbenzene (where some attack at the non-benzylic methylene group occurs), and fails with cumene, in spite of its weak C-H bond.

In this paper, we report on the successful attempts to generate several initiators photochemically, including one example of a bifunctional initiator. Photochemical routes present a major advantage in these systems, since the synthesis can be performed at room temperature. This is particularly important, given that efficient initiators need to have a weak bond to the TEMPO moiety. The labile oxygen-carbon bond makes thermal synthesis a "catch-22" route, since the temperature required to prepare these compounds are in the same range as those employed to fragment them in order to promote polymerization.

Results and Discussion.

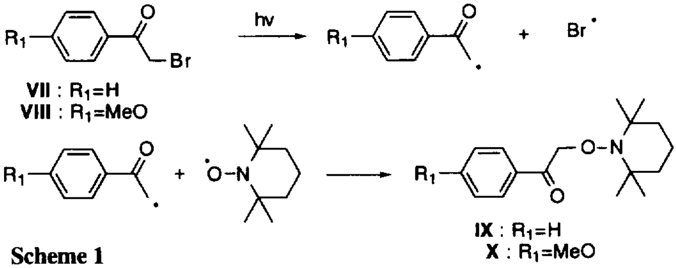
Our strategy for the synthesis of TEMPO-capped initiators consists of the photodecomposition of a radical precursor in the presence of TEMPO. The generated carbon radical is trapped by TEMPO to give an initiator which has the initiating radical and TEMPO in the correct (usually 1:1) stoichiometry.



The "alkoxy route" takes advantage of the fact that oxygen-centered radicals tend to be unreactive towards nitroxides.[7-10] Thus, *tert*-butoxyl radicals generated from the peroxide tend to react with the substrate or solvent, rather than with TEMPO. By using toluene, ethylbenzene, propylbenzene or cumene as solvents in the presence of TEMPO (typically 0.13 M) and di-*tert*-butyl peroxide (typically 0.50 M), it was straightforward to prepare the corresponding adducts.

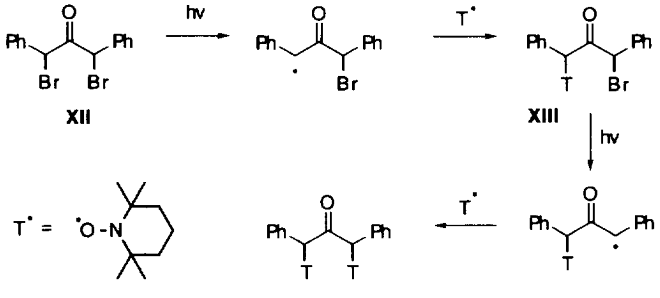
The color of TEMPO provides an efficient indicator of the reaction. Irradiation (300 nm) of the red-orange TEMPO solutions until the TEMPO color fades to pale yellow (typically 12-36 h) affords the desired compounds in excellent yields (90% for **II**, 91% for **III** and over 95% for **IV** and **V**). In the case of cumene, we presume that the success of this photochemical technique, compared with the thermal method, reflects the thermal instability of the adduct V. In the case of n-propylbenzene, the photoinduced method gave excellent selectivity in favor of the benzylic position (40:2:1 for α:β:γ) in contrast with the thermal method. Although Hawker et al. report a 19:1 ratio for reaction at the α vs. β center of n-propylbenzene and do not mention any reaction at the γ center, in our hands, the same thermal synthesis (~130 °C) gives essentially an equi-molar mixture of adducts resulting from reaction at all three centers. The difference may be a reflection of thermal instability of **IV** then of actual site selectivity.

Another photochemical route that proved valuable involves photoinduced cleavage of the C-Br bond (Scheme 1). Thus, irradiation (350 nm) of phenacyl bromides **VII-VIII** in acetonitrile (typically 0.10 - 0.15 M) leads to the corresponding TEMPO derivatives **IX** and **X** in yields of 58 and 92% respectively. Optimum results were obtained when solid sodium thiosulfate was added to the reaction mixture. Adsorption of generated bromine results in the reaction medium remaining transparent, and consequently higher conversions and yields.



Scheme 1

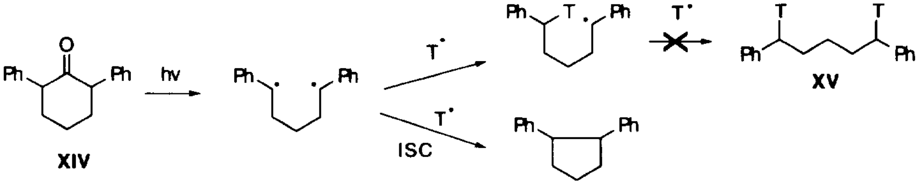
The photodebromination route proved effective even where other techniques failed. For example, it was possible to prepare the difunctional derivative **XI** by sequential debromination and trapping of 1,3-dibromo-1,3-diphenylacetone **XII** as illustrated in Scheme 2.



Scheme 2

The fact that photodecomposition of **XII** proceeds with loss of bromine atoms was verified by carrying out its photodecomposition (308 nm) in acetonitrile containing 0.1 mM tetrabutylammonium bromide. Under these conditions bromine atoms are trapped in a diffusion-controlled process to yield $Br_2^{\bullet-}$. Under laser flash photolysis conditions, the spectrum recorded showed a strong maximum at 370 nm, consistent with $Br_2^{\bullet-}$, thus confirming that photolysis of **XII** involves C-Br cleavage.[11] It is clear that formation of **XI** must be a stepwise process. It is thus interesting that **XIII** *appears* to prefer C-Br over C-TEMPO cleavage. In fact, even if C-TEMPO cleavage occurs, we expect the radical to be trapped by the excess TEMPO to reform **XIII**. Thus, only events leading to C-Br cleavage from **XIII** are actually irreversible and lead to product formation.

The synthesis shown in Scheme 2 is a useful strategy, particularly in view of the failure of biradical trapping routes to yield the corresponding adducts (Scheme 3). For example, irradiation of 2,6-diphenylcyclohexanone (**XIV**) in the presence of TEMPO does not yield the adduct **XV**.



Scheme 3

The photochemistry of **XIV** yields the corresponding 1,5-biradical from the triplet state. The biradical has a lifetime of 900 ns in methanol[12], and is thus sufficiently long-lived for TEMPO scavenging. While it is well known that paramagnetic quenchers can interact with biradicals via assisted intersystem crossing (ISC)[13], we had hoped that (just as in the case of oxygen) sufficient chemical trapping would take place to result in a convenient (even if rather inefficient) synthesis of initiator **XV**. Unfortunately, it is clear that assisted ISC predominates. Initiator **XV** was produced in yields of only ~2%, as estimated by NMR spectroscopy.

The C-Br photocleavage route should be favored in the case of multifunctional initiators, since the corresponding precursors (e.g. **XII**) can be readily prepared. These initiators (e.g. **XI**) provide an interesting way to incorporate specific chromophores at approximately the center of a polymer chain. For example, one would anticipate that a polymer containing the moiety from **XI** at the center of the chain will undergo photocleavage efficiently just as its low molecular weight analogue, dibenzyl ketone, does in the case of small molecules.[14]

All the initiators prepared were subjected to two tests. First, laser flash photolysis of all of them gave readily detectable signals from the corresponding radicals. Benzylic radicals were monitored at ~320 nm, and p-methoxyphenacyl at 512 nm. The laser flash photolysis of **I** has been examined in detail earlier.[4,15] The second test involved the initiation of styrene polymerization. Following the optimal conditions described by Hawker and Barclay, addition of 3 mL of distilled styrene to 50-75 mg of the appropriate initiator, followed by heating, in the absence of a cosolvent, at 125 °C for 72 hours led to crude polystyrene which was purified via standard methods to afford polystyrene as a bright white solid, with yields being 85-95% of theory.

In summary, we have shown two photochemical routes to efficient initiators that may be used in the free radical mediated living polymerization of styrene. Our methods show improved yields over existing methods, and allow for the preparation of initiators not accessible using current protocol. Clearly, other thermal, yet low temperature routes to alkoxyl radicals may be worth exploring, such as di-*tert*-butyl hyponitrite and di-*tert*-butyl peroxyoxalate.

Experimental

All substituted aromatics, including styrene, were distilled under reduced pressure immediately prior to use. All solvents used for synthesis and laser flash photolysis studies were of the highest grade commercially available (BDH, Omnisolv grade) and were used without further purification. TEMPO was purchased from Sigma, and was used as received. *Tert*-butylperoxide was obtained from Aldrich and was purified by passing through a plug of activated alumina just before use. All reactions using TEMPO were carried out under the strict exclusion of oxygen. Steady state irradiations were performed at 30-32 °C with a Rayonet photoreactor. Laser flash photolysis were carried on solutions contained in 7x7 mm^2 Suprasil quartz cuvettes using the system described elsewhere.[16]

II-V were prepared using the same procedure. In a typical experiment, a solution of *t*-butylperoxide (1.18 g, 8.08 mmol) in the appropriate aromatic solvent (15 mL) was placed in a quartz test tube and was deaerated with nitrogen for 15 min. TEMPO (300 mg, 1.92 mmol) was then added, and the resulting red-orange solution was deaerated a further 10 min. The reaction vessel was then placed in a Rayonet photoreactor and irradiated with nine RPR-300 nm lamps until the color of TEMPO faded to colorless or pale yellow. The reaction mixture was concentrated, and the resulting residue purified via column chromatography.

(2',2',6',6'-Tetramethyl-1'-piperidinyloxymethyl)benzene (II): Same as that prepared previously.[4]

1-Phenyl-1-(2',2',6',6'-Tetramethyl-1'-piperidinyloxy)ethane (III): Spectral properties identical to reported values. (mp: 42 °C, lit[5]: 46-47 °C). **1-Phenyl-1-(2',2',6',6'-Tetramethyl-1'-piperidinyloxy)propane (IV)**: The clear oil obtained after chromatography slowly solidified on standing, and was recrystallized from methanol to afford white prisms (mp 46 °C, lit:[5] oil). ^{1}H-NMR (500 MHz, $CDCl_3$): δ 0.51 (bs, 3H), 0.65 (t, 3H, J = 7.5 Hz), 1.00 (bs, 3H), 1.10 (bs, 3H), 1.25 (bs, 3H), 1.40 (m, 6H), 1.75 (m, 1H), 2.15 (m, 1H), 4.50 (dd, 1H, J = 9.5, 4.0 Hz), 7.20 (m, 5H) ppm. **1-Methyl-1-phenyl-1-(2',2',6',6'-Tetramethyl-1'-piperidinyloxy)ethane (V)**: Column chromatography (hexanes) afforded the title compound as a white solid which was recrystallized from methanol to afford white needles (mp 50 °C). ^{1}H-NMR (500 MHz, $CDCl_3$): δ 0.83 (s, 6H), 1.08 (s, 6H), 1.2-1.5 (m, 6H), 1.60 (s, 6H), 7.18 (t, 1H, J = 7.5 Hz), 7.28 (t, 2H, J = 7.5 Hz), 7.48 (d, 2H, J = 7.5 Hz) ppm. ^{13}C-NMR (125 MHz, $CDCl_3$): δ 17.07, 20.55, 28.18, 33.86, 40.82, 59.42, 79.65, 125.32, 126.01, 127.59, 150.83 ppm. IR (CH_2Cl_2): 2923, 1376, 1137 cm^{-1}.**Diphenyl-(2',2',6',6'-Tetramethyl-1'-piperidinyloxy)methane (VI)**: A deaerated solution of 1,1-diphenylacetone (105 mg, 0.50 mmol) and TEMPO (62.4 mg, 0.40 mmol) in n-pentane (10 mL) was irriadiated (300 nm) for 30 min. The solvent was evaporated and the residue was chromatographed (CH_2Cl_2) affording **VI** in a yield of 20%. ^{1}H-NMR (200 MHz, $CDCl_3$): d 0.70 and 1.20 (bs, 12H), 1.40 (m, 6H), 5.70 (s, 1H), 7.20-7.40 (m, 10 H) ppm. Anal. for $C_{22}H_{35}NO$ Calcd: C, 81.73; H, 8.98; N, 4.33. Found: C, 81.94; H, 8.74; N 4.16.**(4-**

Methoxybenzoyl)-1-(2',2',6',6'-Tetramethyl-1'-piperidinyloxy)methane (X): A deaerated solution of 4-methoxyphenacylbromide (500 mg, 2.18 mmol), sodium thiosulfate (150 mg) and TEMPO (425 mg, 2.72 mmol) in CH_3CN (50 mL) was irradiated at 350 nm for 16 h. The resulting mixture was filtered, concentrated under reduced pressure, and the resulting yellow oil was purified via column chromatography (8:1 hexanes:EtOAc) affording **VIII** as a white crystalline solid (610 mg, 92%). Recrystallization (MeOH) afforded white needles (mp 120 °C). ^{1}H-NMR: (500 MHz, $CDCl_3$): δ 1.16 (s, 12 H), 1.4-1.6 (m, 6H), 3.86 (s, 3H), 5.03 (s, 2H), 6.92 (d, 2H, J = 8.5 Hz), 7.93 (d, 2H, J = 8.5 Hz) ppm; ^{13}C-NMR (125 MHz, $CDCl_3$): 17.06, 20.27, 32.84, 39.75, 55.46, 60.10, 81.35, 113.73, 128.60, 130.39, 163.56, 194.42 ppm; IR (CH_2Cl_2): 1601, 2918 cm^{-1}; EI-MS (m/z, (%)): 305 (3.2), 290 (31.1), 222 (4.9), 156 (100); HRMS: Calc. for $C_{18}H_{27}NO_3$: 305.19909; Found: 305.20023. **Benzoyl-1-(2',2',6',6'-Tetramethyl-1'-piperidinyloxy)methane (IX):** Prepared as above except that phenacyl brominde was used as starting material. The product was isolated as a clear oil (58%) after column chromatography (20:1 hexanes: EtOAc). ^{1}H-NMR (500 MHz, $CDCl_3$): δ 1.15 (s, 12 H), 1.3-1.6 (m, 6H), 5.08 (s, 2H), 7.43 (t, 2H, J = 7.1 Hz), 7.52 (t, 1H, J = 7.1 Hz), 7.91 (d, 2H, J = 7.1 Hz) ppm; ^{13}C-NMR (125 MHz, $CDCl_3$): δ 17.04, 20.23, 32.81, 39.73, 60.12, 81.36, 127.97, 128.54, 133.17, 135.56, 195.71 ppm; IR (CH_2Cl_2): 1695, 2908 cm^{-1}; EI-MS (m/z, (%)): 275, (4.8), 260 (45.4), 192 (7.1), 156 (100); HRMS for $C_{17}H_{25}NO_2$ Calc: 275.18853; Found: 275.18847.**1,3-Diphenyl-1,3-bis(',2',6',6'-Tetramethyl-1'-piperidinyloxy)-2-propanone (XI):** A deaerated solution of 1,3-dibromo-1,3-diphenyl-2-propanone (110.4 mg, 0.30 mmol) and TEMPO (120.1 mg, 0.77 mmol) in n-pentane:dichloromethane (4:1, 5 mL) was irradiated at 254 nm for 12 h. Usual work-up and chromatography (CH_2Cl_2) afforded **XI** in a yield of 12%. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 1.0-1.3 (m, 24 H), 1.50 (m, 12 H), 5.10 (s, 2H), 7.4-7.7 (m, 10 H) ppm; ^{13}C-NMR (125 MHz, $CDCl_3$): δ 18.17, 31.42, 32.26, 40.74, 59.06, 60.12, 91.43, 129.29, 139.71, 192.34 ppm; IR (film): 1360, 1370, 1455, 1725, 2939 cm^{-1}; CI-MS (m/z, (%)): 209 (40), 156 (100), 142 (97).[17]

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