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The reaction of α-phenethyl radicals with 1,4-benzoquinone and 2,6-di-*tert*-butyl-1,4-benzoquinone

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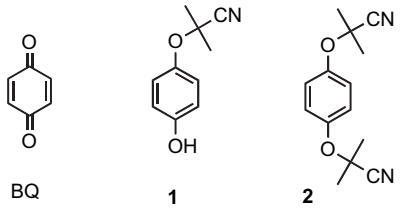
ABSTRACT

The absolute rate constant for 1,4-benzoquinone (BQ) irreversibly trapping α-phenethyl radicals (**3**) has been determined as 4.4×10^6 M^{-1} s^{-1} at 43 °C using acyclic *cis* azoalkane **9c** as a radical precursor. These reactants afford the hydroquinone mono ether **4** at 30 °C but a mixture of products at elevated temperature. 2,6-Di-*tert*-butyl-1,4-benzoquinone (DTBQ) also reacts with **3** but the cyclohexadienone products are thermally labile.

1. Introduction

Aside from their importance in biology,[1,2] quinones have been employed as free radical polymerization inhibitors for over 70 years. The reaction of benzoquinone (BQ) with free radicals was first reported by Wieland, who used phenylazotriphenyl-methane as the radical source.[3] The products were hydroquinone bis-triphenylmethyl ether, quinhydrone, and 2-phenyl benzoquinone, as confirmed by Betterton and Waters.[4] The first product represents radical attack on BQ oxygen while the last one arises from attack on a ring carbon, also called the nucleus. A few years later, Breitenbach et al.[5] showed that BQ inhibited the thermal polymerization of styrene while Foord examined a large number of potential inhibitors, including BQ.[6] Cohen studied the benzoyl peroxide initiated polymerization of styrene using BQ and other quinones as inhibitor.[7] He suggested that quinones react with two radicals to produce a phenol retarder arising from disproportionation of phenoxy radicals with growing chains or by nuclear substitution on BQ. Determining the nature of inhibition reactions is complicated by the small percentage incorporation of the inhibitor end group into the polymer structure. This point can be illustrated by the work of Yassin and El-Reedy,[8] who studied the quinone inhibited polymerization of styrene and reached the unlikely conclusion that the growing chains attacked BQ on the ring (vide infra). To surmount this problem, Waters' group[9,10] and later Gleixner et al.[11] studied the thermolysis of the common free radical initiator AIBN with BQ. The 2-cyanopropyl radicals serve as a model for propagating methacrylonitrile chains and produce low molecular weight compounds that are easier to characterize. The main products were the mono- and diethers of hydroquinone **1** and **2**, though Gleixner et al. also found some substitution on the quinone nucleus. Similarly, Golubev et al. used ESR to determine by spin trapping that 2-cyanopropyl radicals react five times as fast on oxygen as on the nucleus.[12] The unreasonable products[13] supposedly arising from the ketenimine resonance structure of 2-cyanopropyl radicals were thus shown to be in error.



Rembaum and Szwarc examined the reaction of methyl radicals from acetyl peroxide with 18 quinones, leading to a scale of relative reactivities termed methyl affinities.[14] BQ was among the most reactive compounds and it was suggested that methyl radicals initially attack the quinone nucleus. The possibility was raised in this work that the final isolated product might arise by intramolecular rearrangement of the initial radical–BQ adduct. Most relevant to the present report, Breitenbach et al.[15] determined the reaction products of BQ with 1-phenethyl radicals (**3**), which were taken as a model for propagating styrene chains. Using azo-α-phenylethane in benzene at 80 °C as a radical source, they found products analogous to those of AIBN, namely mono- and diethers **4** and **5**. A third compound present in the GC trace was insoluble in aq hydroxide, which was taken as evidence against a ring substituted phenol, as exemplified by **6**. Using the free radical clock technique, Citterio et al. determined the rate constant for addition of 5-hexenyl radicals to BQ as 2.0×10^7 M^{-1} s^{-1} at 69 °C.[16]

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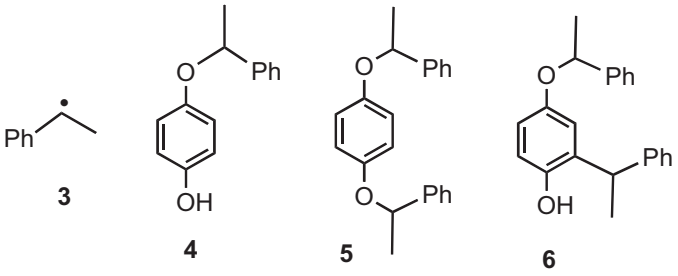
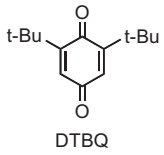
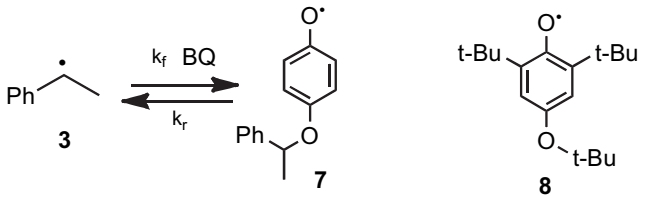


The much more hindered 2,6-di-*tert*-butylbenzoquinone (DTBQ) has received less attention in the literature than BQ. Roginskii and Belyakov[17] reported that DTBQ is a useful trap for alkyl radicals, and they recorded the ESR spectra of several of the resulting hindered phenoxy radicals. Using kinetic ESR, Maeda and Ingold[18] determined the rate constant for DTBQ trapping of 6-hepten-2-yl radicals as $9.3\times10^4\ M^{-1}\ s^{-1}$ at 40 °C while Shlyapnikova et al. reported that the trapping rate constant for *sec*-decyl radicals was $8\times10^5\ M^{-1}\ s^{-1}$ at 50 °C.[19] Simandi and Tudos obtained a value of 61 for the trapping to propagation rate ratio of styrene polymerization at 50 °C.[20] Velikov et al. employed micro-calorimetry to study the effectiveness of various quinone inhibitors on the autoxidation of cumene and polymerization of styrene. DTBQ showed no induction period in the autoxidation, indicating poor radical scavenging ability.[21] Similarly, Fujisawa et al.[22] found that 1 mol of DTBQ only scavenged 0.003 moles of radicals in the AIBN initiated polymerization of methyl methacrylate. Finally, Hageman reported the astonishing result that DTBQ trapped two 2-cyanopropyl radicals, one on each oxygen, to form a hydroquinone diether[23] (see below).



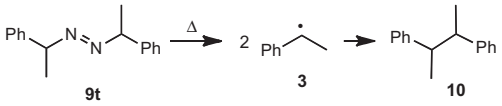
One factor governing the inhibition efficiency of quinones is the degree to which the initial trapping step is reversible, illustrated below for α-phenethyl radicals **3**. This topic has received little attention in the literature, the most relevant example being the work of Roginskii et al.[24] on hindered phenoxy radical **8**. It has also been shown that phenoxymethylation of BQ on carbon[25] and radical carboxylation of naphthoquinone on carbon[26] are reversible. The reversibility question was of great concern to us in this investigation; consequently, we sought to study BQ and DTBQ at relatively low temperatures. Not only was reversibility expected to be minimized, but low temperatures should diminish the redox processes often seen with quinones.[27] Moreover, radical trapping rate constants are not valid unless the trapping reaction is irreversible under the measurement conditions.



Since much of the early work on quinone radical chemistry suffered from a lack of modern separation and identification methods, we have delved into the reactions of two quinones with **3** in some detail. As mentioned above, **3** is structurally similar to propagating styrene chains. Our goals were as follows: to confirm and extend the BQ product studies of Breitenbach et al.,[15] to analyze the radical trapping products of DTBQ, to establish the extent of reversibility, and to determine the rate of BQ radical trapping.

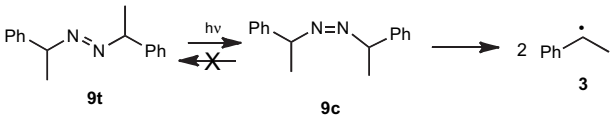
2. An azoalkane precursor of 3

Although radical **3** can be generated by a variety of methods,[28] we preferred to avoid two component redox systems for our competition study and focused instead on unimolecular initiators. The fact that azoalkanes are widely used to generate radicals of a specific structure[29] makes Breitenbach's azo-α-phenylethane (**9t**)[30] a logical source of **3** (cf. Scheme 1). However, this compound undergoes thermolysis only at rather high temperatures (>100 °C)[29,31] and we feared that attack of **3** on our inhibitors would be reversible. Although **9t** is a useful initiator at higher temperatures, we also sought low temperature sources of **3**.



Scheme 1. Thermolysis of **9t**.

An appealing alternative is still based on **9t** but would replace thermolysis with ambient temperature photolysis in the presence of quinones. Unfortunately, the nitrogen quantum yield of **9t** at 366 nm in isooctane is only 0.035, the quinones are UV light absorbers, and excited quinones are photoreactive.[32,33] We imagined that it might be possible to first photoisomerize **9t** to the cis isomer **9c**, which should be considerably more labile than the trans isomer[34] (cf. Scheme 2). Although some acyclic *cis* azoalkanes revert thermally to *trans*,[35] our experience suggested that **9c** would lose nitrogen.[34] After photoisomerization, the quinone would be added and the mixture heated mildly to generate **3**. Our concern that **9c** would be more prone to the tautomerization sometimes seen[36,37] in **9t** proved to be unfounded. In fact, we never observed tautomerization of either isomer of **9**, even though the hydrazone is more stable thermodynamically than the azo form.[38,39]



Scheme 2. Formation and thermolysis of **9c**.

Irradiation of 0.02 M **9t** with a 500 W mercury lamp and monochromator at 313 nm and −50 °C for 2.5 h led to formation of **9c** in 47.4% conversion (cf. Table 1), with the only by-products being *meso* and *dl*-2,3-diphenylbutane **10**, as seen by ^{1}H NMR. Irradiation at 366 nm was less effective and gave only 20% **9c** at the photostationary state, most likely because **9c** absorbs light at longer wavelength than does **9t**.[34,40] We also tried both irradiation through a potassium chromate filter and 254 nm irradiation with

Table 1
Relative methine ^{1}H NMR peak areas for 313 nm monochromator irradiation of 0.02 M **9t** at −50 °C in toluene-d_8

Time, h	**9t**	**9c**	Total **9**	% **9c**	% **9** remaining
0	1.52	0	1.52	0	(100)
1.0	0.954	0.534	1.49	35.9	97.8
2.5	0.819	0.603	1.27	47.4	83.6

added naphthalene and pyrene as singlet sensitizers.[41] Although too much diphenylbutane (**10**) was formed, we learned in these experiments that 0 °C was cold enough to produce and store **9c**. Use of a fresh sample proved critical to achieve a photo-stationary state rich in **9c**, probably because α-phenethyl radicals recombine to a small extent at the *ortho* position and produce a light-absorbing triene.[42] Indeed, the UV spectrum of **9c** after warming in isooctane showed a 306 nm band that would certainly interfere with 313 nm irradiation. The UV spectrum of **9c** exhibited a broad absorption with λ_{max} ~376 nm, which is ~10 nm longer than that of **9t**.[34,40] Thermolysis of **9c**, which was monitored by ^{1}H NMR (cf. Table 2), proceeded smoothly at temperatures slightly above ambient, with activation parameters $\Delta H^{\ddagger}$=28.3 kcal/mol, $\Delta S^{\ddagger}$=15.6 eu, and $\Delta G^{\ddagger}$ (40 °C)=23.4 kcal/mol. No regeneration of **9t** was observed, but instead the products were the usual dimers **10**. The thermolysis rate of **9c** was not accelerated by inclusion of BQ or DTBQ, thus showing the expected[43] absence of quinone-induced decomposition. Compound **9c** was also thermolyzed in acetonitrile, giving a roughly 3-fold slower decomposition rate, in accord with earlier reports concerning *cis* azoalkanes in polar solvents.[44]

Table 2
Decomposition rate of **9c** in toluene-d_8[a]

Temp, °C	10^4 k, s^{-1}	Half life, h
30.2	0.708	2.72
37.8	2.12	0.908
46.2	7.81	0.246

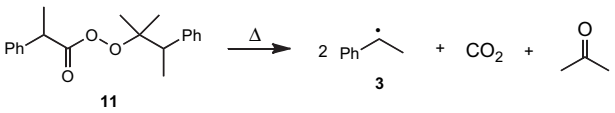
[a] Concentration of **9c** was 0.011–0.022 M.

One problem with using **9c** as the source of **3** is that its preparation is always accompanied by unreacted **9t**. Compound **9t** will then decompose on the GC injector to generate **3** at a far higher temperature than the original experiment and introduce uncertainty into quantification of quinones and their products. However, this problem disappears if analysis is conducted by HPLC or NMR, as was done in much of this work. With these analytical methods, **9c** proved to be a good low temperature source of **3**. It was later found possible to separate **9c** and **9t** by TLC, HPLC, and column chromatography; hence, GC analysis could be used with pure **9c** as the radical precursor if no other thermally labile compounds were involved.

Not all α-phenethyl radicals from thermolysis of **9c** are available for reaction on account of the cage effect. Quantitatively, the cage effect is the percent of radicals formed that recombine before diffusing into the bulk solution. Because this phenomenon has been studied exhaustively,[45,46] we did not measure the cage effect for **9c**; nevertheless, a good estimate can be derived from the 29–32% value for **9t** at 105 °C.[47,48] Since both *cis* and *trans* azoalkanes exhibit the same cage effect at a given temperature,[49,50] we extrapolated these figures to our typical temperature of 43 °C using the activation energy of 1.3 kcal/mol for the diffusion to recombination ratio of cumyl radicals.[51] The result is a 38% cage effect, corresponding to a radical efficiency of 62% for **9c** at 43 °C. The unavoidable formation of **10** is a disadvantage of **9c** but this product is relatively inert and gives an easily recognized NMR and GC signature (1:1 mixture of diastereomers).

3. A perester precursor of 3

Another mild source of **3** was found in the new perester **11**, which was used in a few of the studies reported here but ultimately proved less desirable than **9c**. The perester undergoes homolysis of the O–O bond followed by loss of CO_2 and acetone to afford two radicals **3** (cf. Scheme 3).[52,53] The activation parameters for thermolysis of **11** were determined as $\Delta H^{\ddagger}$=25.1 kcal mol^{-1}, $\Delta S^{\ddagger}$=0.90 eu, and $\Delta G^{\ddagger}$ (40 °C)= 24.8 kcal/mol based on four kinetic runs. Three of these runs were



11 3

Scheme 3. Formation of **3** by thermolysis of **11**.

conducted in the presence of BQ and another inhibitor 2,6-di-*tert*-butyl-4-benzylidenecyclohexa-2,5-dienone (QM)[54] while the fourth run included no added inhibitor (cf. Table 3). The observation that all points fell on the same Eyring plot mitigates against self induced decomposition of **11** and decomposition induced by the inhibitors.[14,55,56] The activation parameters show that **11** is somewhat more stable than **9c** but far more labile than **9t**. However, storage of neat **11** at −25 °C for several months resulted in much decomposition. Extrapolation of the activation parameters for **11** leads to a predicted half life of many years at this temperature, indicating that self induced decomposition becomes important in neat samples.

Table 3
Thermolysis rate constants of 0.02 M **11** in C_6D_6[a]

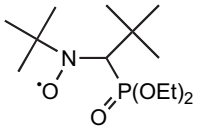
Temp,°C	10^5 k, s^{-1}
39.2	2.81[b]
44.2	5.85[c]
49.9	12.1[b]
60.4	40.0[b]

[a] Monitored by ^{1}H NMR with TMSOTMS as internal standard.
[b] With 0.02 M BQ and 0.02 M QM.
[c] Compound **11** alone.

The thermolysis products of **11** were analyzed by GC to ensure that this perester was a viable source of **3**. The dominant product was dimer **10**, accompanied by styrene, ethylbenzene, and styrene oligomers. The other products contained oxygen or were of unknown structure (10–15% of total GC peak area). No detailed discussion of the products is presented here because they are similar to those of bis-1-phenethylacyl peroxide.[57] Although the complexity of the product mixture from thermolyzed **11** alone was a disadvantage in analysis of the BQ products, both **9c** and **11** generate **3** in substantial yield, allowing us to study the reaction of **3** with quinones.

4. The trapping rate constant of 3 with BQ

In the competition kinetics method, a trapping reaction of unknown rate is allowed to compete against one whose rate is not only known but, which falls in the same range as the one to be determined.[58] TEMPO (2,2,6,6-tetramethylpiperidine-1-oxyl) is a common bimolecular trap[59–61] but we soon found that it combines with **3** much faster than does BQ. We therefore used the stable nitroxyl radical SG1, whose reaction rate with **3** is a conveniently slow 4.0×10^6 M^{-1} s^{-1} at 60 °C.[61] BQ and SG1 were simply allowed to compete for **3** generated by thermolysis of **9c**. Provided that no unwanted reactions occur, the ratio of starting materials reacted yields the rate ratio.



SG1

The advantage of this method is that the products can be ignored; on the other hand, quantifying starting material disappearance is subject to greater error than product appearance.

Initial control experiments showed that SG1 in benzene was stable at 60 °C. A solution of SG1 and BQ in benzene heated at 60 °C for 3 h showed no change in the reactant ratio and no new HPLC

peaks. For the competition experiment, a toluene solution of 0.37 M SG1, 0.035 M BQ, 0.27 M **9c** was divided into five ampoules, which were degassed and sealed. Compound **9c** had been prepared by irradiating **9t** for 5 h at −10 °C. These ampoules were heated at 43 °C for various times, removed from the bath, and analyzed several times by HPLC without workup to determine the amount of SG1 and BQ reacted (cf. Table 4). The wavelength was set to 450 nm to avoid light absorption by any other compounds besides BQ and SG1, which are colored.

Table 4
Relative trapping rate constant of **3** in PhMe by SG1 and BQ

Time, min[a]	SG1[b]	BQ[b]	k_{SG1}/k_{BQ}[c]
0	1431	1330	
15	1366	1258	0.85
30	1221	1050	0.67
45	1125	980	0.79
60	1054	946	0.90

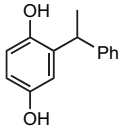
[a] Thermolysis time.
[b] HPLC peak area at 450 nm, average of 5–6 injections.
[c] Relative trapping rate by SG1 versus BQ calculated from parallel second order reaction kinetics.[58]

The average value of k_{SG1}/k_{BQ}=0.80 was converted to an absolute value of $k_{BQ}=4.4\times10^6$ M^{-1} s^{-1} using the calculated absolute rate $k_{SG1}=3.5\times10^6$ M^{-1} s^{-1} at 43 °C taken from Sobek et al.[61] We conclude that BQ is a relatively rapid scavenger of α-phenethyl radicals.

5. BQ product analysis

Because the literature on BQ contains a wide variation in product structures depending upon the attacking radical and the mode of radical generation, we carried out a careful product study of BQ reacting with **3**. First, a degassed solution of **9t** in CD_3CN was thermolyzed at 120 °C to obtain the ^1H and ^{13}C NMR spectra of the two diastereomeric phenethyl dimers **10**. Then a CD_3CN solution of **9t** was irradiated at 10 °C until about half of the trans isomer had been converted to cis. This solution exhibited small ^1H NMR peaks due to **10** plus smaller ones due to acetophenone, formed presumably by reaction of **3** with residual oxygen. Thermolysis of the **9c**, **9t** mixture at 30 °C caused disappearance of **9c**, a large increase in **10**, and a few tiny new peaks possibly due to α,*o* and α,*p* dimers,[42] whose position was noted to avoid confusing them with BQ products in the next experiment.

When BQ was reacted with pure **9c** (isolated by preparative TLC) in CD_3CN at 30 °C, the ^1H and ^{13}C NMR spectra clearly showed **4**.[62] Also apparent were 1-phenethyl alcohol, acetophenone, and a few small, unidentified ^{13}C NMR and ^1H peaks. No tautomerization of **9c** to the corresponding hydrazone was detected nor was the product distribution affected by changing the solvent to benzene-d_6. Notably absent were any unexplained carbonyl signals and peaks due to ring substitution product **12**.[62]



12

Further product analysis was carried by GC/MS. Heating BQ with **11** at 50 °C yielded only one major product peak whose MS showed it to be **4**, in accord with Breitenbach et al.[15] As expected,[63] a characteristic fragmentation of the aryl ethers in this series was loss of neutral styrene. When **3** was generated at 120 °C using **9t** as the radical source, **4** was still the major product but two new peaks of later retention time were also apparent. We assigned the first of these to diether **5** because its mass spectrum (*m*/*z*=318, 214, 110, 105) matched that of Breitenbach.[15] The latest GC peak was assigned as **6** in part because it was obviously an isomer of **5**. Loss of styrene from the molecular ion affords the base peak at *m*/*z*=214, which fragments further with loss of methyl. Both **4** and **5** exhibited a hydroquinone ion at *m*/*z*=110 but **6** showed no such peak. Although the earlier workers had concluded on the basis of its insolubility in aq KOH that **6** was not a phenol, this test is unreliable for a large phenol.

Further support for structures **4**, **5**, and **6** was obtained by treating a BQ+**9t** thermolysis mixture with diazomethane. The GC peak due to **4** disappeared and was replaced by one of shorter retention time whose MS showed a shift of $M^{+\cdot}$ and *m*/*z*=110 to higher mass by 14 units, indicative of a methyl ether. As expected, the peak assigned to **5** remained unchanged while that due to **6** moved to shorter retention time. The MS of this new peak showed the same mass shift as **4**, consistent with the methyl ether of **6**. A number of other minor GC product peaks were noticed, some with long retention times, but they were not investigated further. We conclude that under mild conditions **4** is the major product of BQ+**3**. NMR showed a minor, unidentified, labile product along with some minor thermally stable compounds. Under no conditions did we see **12** nor any cyclohexadienones.

Taking advantage of our three unimolecular sources of **3**, we determined the relative amount of the three GC products over a wide temperature range, leading to the results in Table 5. These data show an obvious increase in diadducts **5** and **6** at higher temperatures. Although the GC trace of the 132 °C reaction showed some minor peaks besides ethylbenzene, styrene, and styrene oligomers, TLC revealed no spot at the origin, suggesting a relatively clean reaction. In contrast, Breitenbach[15] obtained 42% of 'nonvolatile, high molecular weight material' in benzene at 80 °C. We observed no hydroquinone by GC at either low or high temperature, unlike some earlier work with BQ and primary alkyl and phenyl radicals.[27,64–66]

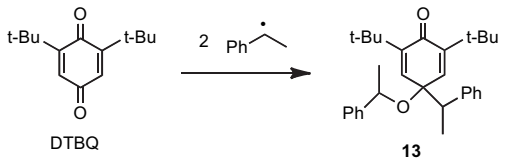
Table 5
Products of BQ with **3**

Precursor	[Precursor], M	[BQ], M	Temp, °C	**4**[a]	**5**[a]	**6**[a]
9c	0.02	0.01	30	1.0	—	—
11	0.04	0.02	35	1.0	—	—
11	0.4	0.10	60	1.0	—	—
11	0.04	0.02	75	1.0	0.081	0.12
9t	0.04	0.02	85	1.0	0.070	0.11
9t	0.15	0.10	85	1.0	0.056	0.14
9t	0.15	0.10	120	1.0	0.26	0.23
9t	0.03	0.02	132	1.0	0.44	0.17

[a] Relative GC peak areas.

6. DTBQ product analysis

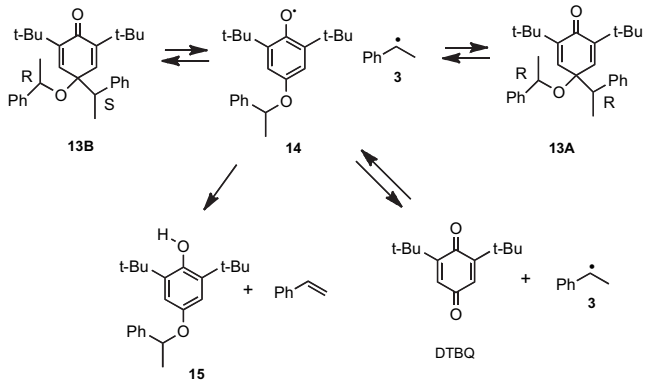
The products of **3** and DTBQ were investigated initially under mild conditions using atom transfer radical addition (ATRA).[67,68] A mixture of DTBQ, 1-phenethyl bromide, CuBr, and PMDETA in toluene was degassed and stirred at room temperature for 2 h. GC analysis demonstrated consumption of phenethyl bromide and formation of dimer **10**. Interestingly, while the UV spectrum revealed no absorption for DTBQ, the GC trace exhibited a peak for this quinone. Flash chromatography allowed isolation of an oil whose ^1H NMR spectrum was consistent with a mixture of two diastereomers of **13** (cf. Scheme 4). Diastereomer **13A** exhibited cyclohexadienone peaks at 5.99 and 6.56 ppm while **13B** showed these peaks at 6.16 and 6.42 ppm. The ^{13}C NMR spectrum of **13B** showed a characteristic cyclohexa-2,5-dienone carbonyl peak[69–71]



Scheme 4. Trapping of **3** by DTBQ.

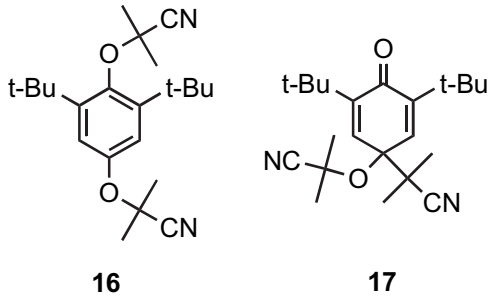
at 185.6 ppm while close examination of the spectrum revealed smaller peaks at 205.3 and 206.1 ppm, indicative of *ortho* recombination of **3** and **14**.[69,72]

The diastereomers were separated by HPLC and a solution of **13B** in toluene-d_8 was degassed, sealed in an NMR tube, and heated at 120 °C. Compound **13B** gradually disappeared while **13A** built up and then eventually disappeared also (cf. Scheme 5).



Scheme 5. Generation and fragmentation of phenoxyl radical **14**.

This kinetic behavior suggested homolysis of **13B** to **14**, followed by recombination of the formed radicals **14** and **3** to **13A** in competition with disproportionation of the radicals to **15**+styrene. The designations *R* and *S* are arbitrary since we do not know the absolute configuration of the diastereomers. In view of the relatively high temperature needed for thermolysis of **13**, we conclude that these cyclohexadienone products are stable at 25 °C where our ATRA study was carried out. Formation of **13** is not surprising in view of the dominant disproportionation of **3** and **7**, coupled with the large steric hindrance to this process in **14**. In this regard, a report[23] on AIBN reacting with DTBQ stated that the exclusive product formed in 90% yield was diether **16**. While such a structure (**5**) is observed with BQ and **3** at elevated temperature and with BQ and 2-cyanopropyl radicals (**2**),[9] recombination of 2-cyanopropyl at the hindered phenoxy radical from DTBQ is most unlikely. The only evidence for structure **16** was ^{1}H NMR, which exhibited an 'aromatic' singlet at 6.80 ppm. Our experience with **13** and **15** suggested that this peak could just as well arise from the β-cyclohexadienone protons of **17**. To test this possibility, a sealed, degassed NMR tube of DTBQ and AIBN in a 1.0:1.5 mole ratio in C_6D_6 was heated at 80 °C for 8 h. ^{1}H NMR revealed nearly complete disappearance of AIBN and appearance of Hageman's 6.80 singlet at 6.77 ppm.



However, ^{13}C NMR showed a prominent quaternary carbon at 185.1 ppm, characteristic of the cyclohexa-2,5-dienone system.[69–71] It follows that moderately hindered radicals such as **3** and 2-cyanopropyl attack DTBQ at the less hindered oxygen and then at the aromatic ring 4-position. The resulting cyclohexadienones are thermally labile at elevated temperatures because a structure such as **17** lacks the aromatic stabilization that its isomer **16** possesses. This ground state destabilization is also found in 3-methylene-1,4-cyclohexadienes, which dissociate much more easily than their aromatic tautomers because the energy required to reach the radicals is lower when starting from the non-aromatic compound.[73]

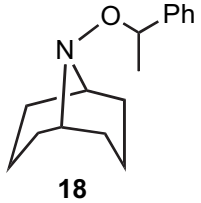
The disappearance of the diastereomeric mixture **13A**,**B** followed first order kinetics with $k_d=1.39\times10^{-4}$ s^{-1} at 120 °C ($t_{½}$=1.39 h), which is the dissociation rate of **13A**,**B** assuming that the rates are the same. The product mixture was analyzed by NMR and GC, revealing **15** and DTBQ in a 1:8 ratio, along with styrene. The presence of DTBQ is interesting because it indicates that even the first addition of **3** to DTBQ is reversible (cf. Scheme 5). Since **13** was formed in the original phenethyl bromide reaction, the disappearance of DTBQ by UV but not by GC is readily explained as thermolysis of **13** on the GC injector. In fact a GC trace of **13** exhibited not only sharp peaks for DTBQ, **10**, and **15** but also a very broad peak at ~25 min indicative of a thermally labile compound.

An independent experiment with DTBQ and **9t** gave similar results. A solution of 0.01 M DTBQ and 0.03 M **9t** in benzene was degassed, sealed in a UV cell, and heated at 120 °C for 3 h. According to UV, DTBQ was gone but GC again showed the characteristic peak for this quinone. We also saw phenol **15** and the broad 25 min GC peak mentioned above. NMR showed a small amount of **15** plus the diastereomers of **13**, indicating that they had partially survived the reaction.

In order to secure an authentic sample of **15**, a solution of 1 M **13** and 300 mg thiophenol in 0.5 mL toluene-d_8 was degassed, sealed in an NMR tube, and heated at 120 °C for 2 days. ^{1}H NMR showed no DTBQ but a large amount of **15**, which could be isolated by preparative reverse phase HPLC and identified by NMR. Obviously, thiophenol effectively scavenged **14** before it could fragment.

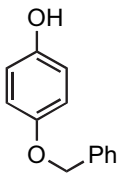
7. Reversibility of BQ scavenging α-phenethyl radicals

Our planned approach to test for reversibility in the reaction of BQ with **3** was to expose phenol **4** to a nitroxyl radical, hoping to form **7**, which would then cleave and lead to the trialkylhydroxylamine from **3**. However, the required phenol **4** proved to be a difficult synthetic target and it was unstable to normal phase HPLC on silica gel. Although isolated **4** was unknown at the time of our work, the recent literature contains one reference to this phenol, which was made from an alkylcatecholborane and was isolated by reverse phase HPLC.[62] (See later discussion of **4**.) When a small sample of **4** was exposed to the bicyclic nitroxyl ABNO at 25 °C, the solution rapidly formed a deep red solid. GC analysis showed many unknown peaks but not the expected trapping product **18**, even when the reaction was repeated at 120 °C.



To circumvent the scarcity of **4**, we carried out further experiments with the commercially available 4-benzyloxyphenol **19**, reasoning that fragmentation of **20** would require the same process in **7**. Furthermore, we used TEMPO in place of the much less

accessible ABNO, which behaved poorly with **4** (see above). The high reactivity of ABNO relative to TEMPO is readily explained by its 6.6 kcal/mol higher OH bond strength.[74] Another advantage of **19** over **4** is that radical trapping product **21** is more stable thermally than it's α-phenethyl analog and can therefore be analyzed by GC.[67,75–78]



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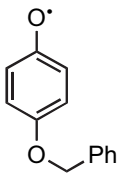

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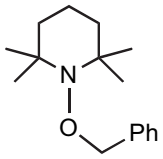

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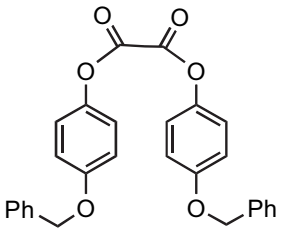

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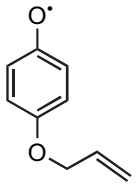


23

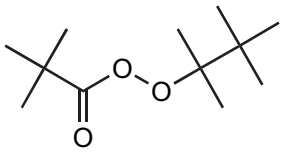
We found that TEMPO did not react with **19** thermally nor upon irradiation, which is known to enhance hydrogen atom transfer to TEMPO.[76,79] Even visible light and 313 nm irradiation of a mixture of **19** and TEMPO at 100 °C revealed no obvious disappearance of starting materials and no formation of **21**, as proven by GC comparison with an authentic sample. In a second approach, a mixture of **19** and TEMPO was shaken at 100 °C for 15 h with active lead dioxide,[80] which is expected to oxidize **19** to **20**.[24,81] Again there was no sign of **21**, though **19** was gone and TEMPO remained. Control experiments proved that lead dioxide did not attack TEMPO and although it destroyed **19**, no products were recognizable by GC. These results argue against fragmentation of **20**. Finally, an attempt was made to generate **20** at elevated temperatures by irradiation of oxalate **22**. It is known that diaryl oxalates decarbonylate upon 254 nm irradiation to generate phenoxy radicals.[82] If **20** were to fragment, we would expect to see BQ, bibenzyl, hydroquinone dibenzyl ether, or toluene formed by hydrogen abstraction from solvent. Samples of **22** were irradiated at 254 nm and 100 °C in THF, *t*-BuOH, CH_3CN, and as a neat solid. None of these products were formed; instead, we saw only **19**. If **20** does not fragment at 100 °C, is it possible that the α-methyl group of **7** allows fragmentation during our competition kinetics measurement, which was run at 43 °C (Table 4)?

The fragmentation rate of **7** at 43 °C can be roughly evaluated from a theoretical calculation on the 4-allyloxyphenoxy radical **23**. Homolysis of **23** to BQ plus allyl is calculated at the B3LYP level to be endothermic by 12.9 kcal/mol.[83] Since the benzyl radical is ~2 kcal/mol less stable than allyl,[84] we estimate that cleavage of **20** is endothermic by 14.9 kcal/mol. Subtracting the 2.7 kcal/mol stabilization energy of **3** versus benzyl, derived from azoalkane thermolysis rates,[29] indicates that fragmentation of **7** is uphill by 12.2 kcal/mol. The activation energy for this process is certainly not zero but should be at least 3 kcal/mol while the *A* factor will be taken as 10^{13}, by comparison with similar reactions. Using E_a=15.2 kcal/mol and log *A*=13 in the Arrhenius equation leads to a fragmentation rate constant at 43 °C of 310 s^{-1}, which is 500 times slower than the pseudo first order trapping rate constant (0.035 M×4.4×10^6 M^{-1} s^{-1}) for **3**+BQ. A far smaller fragmentation rate for **7** has been calculated by Denizov,[85] who obtained E_a=28.2 kcal/mol and used log *A*=10^{14}. These values lead to a fragmentation rate constant of only 3.2×10^{-6} s^{-1}, which is 5×10^{10} slower than trapping. We conclude that the reaction of BQ with **3** is irreversible at 43 °C, thus validating our measured trapping rate. Furthermore, the concentration of SG1 in the competition kinetics experiment was 10.6 times higher than that of BQ. Any α-phenethyl radicals arising from fragmentation of **7** are therefore unlikely to recombine with BQ.

8. Discussion

We employed **11** and **9c** as simple, unimolecular, low temperature sources of free radicals in our competition kinetics experiment to avoid possible complications from metal induced redox reactions. ATRA chemistry was used in one product study and led to no unexpected behavior that could not be readily attributed to reaction temperature differences. Other phenethyl radical sources have been employed in the past[16,27,28] but few are likely to compete with **9c** for chemical simplicity.

Our kinetic study of perester **11** ($t_{1/2}$=29 min at 60 °C) showed it to be somewhat more labile than the analogous **24** ($t_{1/2}$=2.16 h at 60 °C)[52] as expected from the greater stability of α-phenethyl radicals than *tert*-butyl radicals.[86] The yield of free **3** is not quantitative, as evidenced by the formation of oxygenated products.



24

Azoalkanes **9t** and **9c** are much cleaner phenethyl radical precursors than **11**. While **9t** is only useful above 85 °C, **9c** decomposes at temperatures slightly above ambient. Thus the same radicals can be generated over a large temperature range. Not only does **9c** exhibit no induced decomposition nor tautomerization under our conditions, but it can even be isolated pure. The behavior of **9c** and **9t** is in accord with the sizeable body of knowledge about thermolysis of *cis* and *trans* azoalkanes.[29,34,40]

Table 6 summarizes the present and previously published rate constants for trapping of radicals by BQ. The figures span a range of nearly 10^5 and depend on the structure of the attacking radical. Our value of 4.4×10^6 M^{-1} s^{-1} for **3** should be similar to the one for propagating styrene chains, but it is actually about 50 times faster. This difference could be due to slower diffusion in the polystyrene solution or to the fact that the propagation rate of styrene is a poor clock because the many literature reports of its rate are widely

Table 6
Radical trapping rate constants of BQ

Entry	Radical	Temp, °C	Rate constant, M^{-1} s^{-1} A	Ref.
1	Me_2CCN	35	6×10^2	12
2	Me_3C	26	4.1×10^7	12
3	RCHPh[a]	50	8.8×10^4[b]	20
4	$RCH_2^{\cdot}$	69	2.0×10^7	16
5	PhCHMe	43	4.4×10^6	This work
6	CH_3	65	5.2×10^6	90

[a] Polystyryl radical.
[b] Calculated from the known propagation rate of styrene (170 M^{-1} s^{-1} at 50 °C)[91] and the reported ratio of the inhibition rate constant to the propagation rate constant.

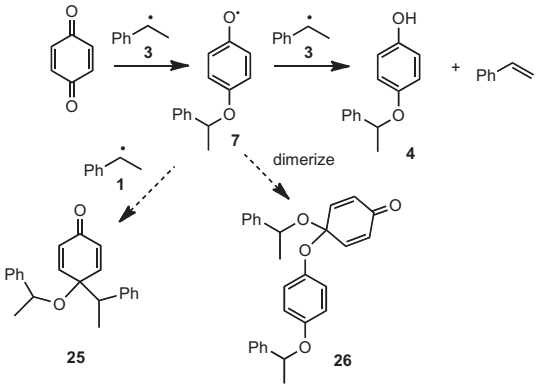
scattered.[87] The 9-fold faster addition rate of *tert*-butyl (entry 2) than methyl radicals (entry 6) is surprising but the much faster rate of **3** compared to 2-cyanopropyl (entry 1) is probably due to the polar effect in radical addition reactions.[88,89]

8.1. BQ product studies

The reaction of BQ with free radicals often leads to ring substitution products analogous to **12**.[12,13,16,27,92–98] Many of these studies were carried out using metal ions or strong oxidizers, which could affect the nature of the products, and others did not employ modern methods of structure determination. In the case of phenethyl radicals, the products we found (**4**–**6**) arise by attack at quinone oxygen. Breitenbach et al. reported **4** and **5** in roughly a 6:1 ratio starting with BQ and **9t** in chlorobenzene while Kumli et al.[62] found **4** and **12** in a 7:1 ratio using a borane precursor. The effect of temperature on the BQ product distribution has not been observed previously but was easily studied here because three sources of **3** were available. When comparing products of quinones with various radicals, it is now necessary to consider the possible effect of reaction temperature. In view of our findings, the claim[8] that propagating polystyrene chains substitute BQ on the ring becomes doubtful.

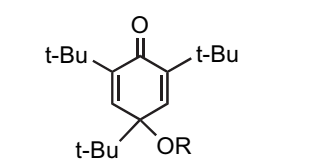
A possible explanation for the formation of **12** in the work of Kumli et al.[62] versus its absence in our study is that **12** might be a hydrolysis product of **6**. Although **4** is unstable to silica gel, we found by GC that subjecting a mixture of **4**, **5**, and **6** to the published workup (washing with saturated NH_4Cl and drying with $MgSO_4$)[62] led to no perceptible loss of these products relative to dimers **10**. Even if **12** were a hydrolysis product of **6**, our analysis did not reveal **6** at ambient temperature by ^1H NMR. We suggest that our product distribution differs from that of Kumli et al.[62] because a non-radical pathway intervenes in the borane chemistry.[99]

Some of the plausible reactions (dashed arrows) and the main observed reactions (solid arrows) of **3**+BQ are shown in Scheme 6. The absence of possible product **25** is not due to its homolytic dissociation under these mild conditions because analogs **13** and **27**[24,100] are readily isolable. Instead, the failure of **7** to produce **25**



Scheme 6. Reaction of BQ with **3**.

leads to the interesting conclusion that disproportionation to **4** and styrene is a faster reaction than *para* recombination and suggests that the bulky *tert*-butyl groups slow down disproportionation of the phenoxy and phenethyl radicals that actually lead, especially at lower temperatures, to **13** (i.e., *tert*-butyl groups slow down the reaction **7**+**3**→**4**). Based on our observation of **6**, it is likely that **25** forms at high temperatures, but this compound would not survive the GC injector. Because these product studies were carried out with a clean, unimolecular source of **3** without workup, we believe that they reflect the inherent reactivity of BQ with **3**.



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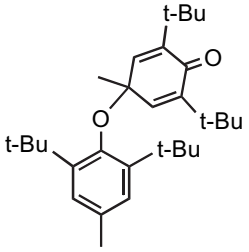

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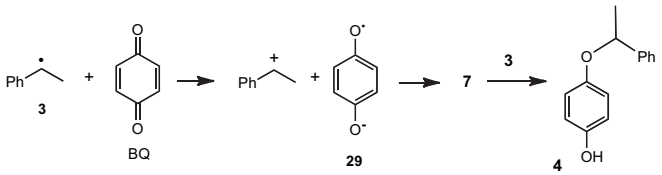
Dimer **26** resembles **28**, which can be isolated but dissociates rapidly in solution.[101–103] Although **26** does not suffer the front strain present in **28**, radical **7** is substantially stabilized by the additional oxygen at the *para* position.[104,105] Thus **26** may form but dissociate rapidly even at 30 °C in our NMR experiments. Simple phenoxyl radicals also dimerize carbon to carbon[106,107] but again, we did not see any unexplained cyclohexadienone protons nor carbonyls in our 30 °C NMR experiment.

Our surprisingly high yield of **4** may arise because electron-rich radicals such as **3** reduce BQ to the radical anion **29** (cf. Scheme 7). Recombination then takes place on oxygen because it has more negative charge than the ring carbons.[16,20,93,108] After **3** attacks BQ to form phenoxy radical **7**, the subsequent reaction at lower temperatures is disproportionation to **4** rather than recombination to **5**. Recombination of **3** and **7** must have a higher activation energy than disproportionation since **5** and **6** appear only at elevated temperatures. The dominance of disproportionation (**3**+**7**→**4**, not **5**) is noteworthy because the delocalized radicals **3** exhibit roughly nine times more self recombination than disproportionation.[109] On the other hand, alkoxy radicals exhibit far more disproportionation than recombination, both in self reaction and in cross reaction with alkyl radicals.[109] Apparently, the **3**+**7** pair takes on much of the character of the alkoxy pairs, possibly due to involvement of anionic phenoxide structures.[110]



Scheme 7. Electron transfer from **3** to BQ.

The exclusive formation of **4** rather than **5** at low temperatures stands in contrast to the behavior of 2-cyanopropyl radicals from AIBN, which lead to both mono- and diether (**1** and **2**)[9,11] plus some attack on the quinone ring.[11,12] In view of the lack of modern analytical techniques employed by some of the earlier workers, it would be interesting to re-examine the AIBN+BQ products and to determine whether the temperature effect on product distribution found here extends to other radicals.

8.2. Reversibility

We have demonstrated that α-phenethyl radical trapping by DTBQ on oxygen is reversible. In a rarely cited paper, Roginskii et al.[24] showed in 1981 that phenoxy radical **8** undergoes fragmentation with a half life of 14 min at 94 °C, which is directly analogous to the fragmentation of **14**. In contrast to **14** at 120 °C, the same process in **7** is slow at 43 °C. Besides the expected large effect of temperature, **14** is a persistent phenoxy radical;[81] hence, it survives long enough to undergo a slow reaction like fragmentation while **7** quickly follows other reaction paths like disproportionation.

We find that phenoxy radical **14** recombines in part with a second α-phenethyl radical to afford cyclohexa-2,5-dienone **13**. This

type of reaction was suspected earlier in the reaction of DTBQ with *sec*-decyl radicals, but the only evidence was an UV absorption band at 240 nm.[19] Since we now know that 2-cyanopropyl radicals behave the same way, it is likely that addition of two radicals is common during hindered quinone inhibited polymerization of monomers. The cyclohexadienones are thermally labile, complicating the radical scavenging process at elevated temperatures.

9. Summary

We have developed methods for generating α-phenethyl radicals **3** by mild thermolysis of precursors **9c** and **11**. *cis* Azoalkane **9c** was employed in a competition study to determine the rate constant of trapping **3** with BQ. While previous reports claimed oxygen and ring attack on BQ, we established that the initial attack of **3** is on oxygen but that the product distribution is temperature-dependent. Surprisingly, **3** and **7** disproportionate rather than recombine at lower temperatures. 2,6-Di-*tert*-butylbenzoquinone (DTBQ) scavenges two radicals **3** to afford thermally labile cyclohexa-2,5-dienone **13**. The trapping reaction of DTBQ is found to be reversible, most likely diminishing its inhibition efficiency at elevated temperatures.

10. Experimental section

10.1. Materials

All reagents and NMR solvents (Cambridge Isotope Laboratories) were used as supplied unless otherwise noted. HPLC solvents were HPLC grade and were sonicated before use. Aqueous solutions were made with laboratory deionized water.

10.2. General methods

Melting points (uncorrected) were obtained on a Mel-Temp apparatus. NMR spectra were recorded on a Bruker 250, 400 MHz or 500 MHz spectrometer. Chemical shifts (δ, ppm) are based on TMS, hexamethyldisilane (TMSTMS) or solvent signal ($C_6D_5CD_3$, CD_3CN) as reference. UV/visible spectra were run on a Hewlett Packard 8452A diode array spectrometer. HPLC analyses and purifications were conducted with a Thermo Separation Products Spectra System P2000 HPLC system equipped with a Hewlett Packard 1050A UV detector interfaced to a PC. The normal phase CN and reversed phase C18 columns (5 μm, 250 mm×4.6 mm) were purchased from Alltech. The solvents were either H_2O/CH_3CN or 2-propanol/hexane. The flow rate was 0.7 mL/min and the UV/visible absorbance was monitored simultaneously at 266, 313, 330, 360 and 450 nm. GC analyses were carried on a Hewlett Packard 5890 instrument with FID detectors and a J & W scientific DB-5 capillary column (0.25 μm, 30 m×0.25 mm). This GC was interfaced to a PC running HP Chemstation software. The usual GC conditions were: injector 230 °C, detector 250 °C, initial column temperature 35 °C for 5 min, program at 10 °C/min to 250 °C and hold for 10 min.

Samples for thermolysis or photolysis were prepared in 7 mm×3″ Pyrex tubes or 5 mm medium wall NMR tubes and were freeze/thaw degassed three times at −78 °C and sealed on a high vacuum line. The tubes were immersed completely in a DC-200 silicone oil bath contained in a 1.5 gallon Dewar flask with mechanical stirrer. The temperature was regulated precisely by a Bayley Model 123 temperature controller and was measured with a Hewlett Packard Model 3456A digital voltmeter and a platinum thermometer. An Oriel 500 W high pressure mercury lamp fitted with a Bausch and Lomb high intensity grating monochromator was employed in photolysis work.

10.3. *trans* Azo-α-phenylethane 9t

This *trans* azoalkane was prepared from acetophenone in 40% yield according to a published procedure.[30] ^{1}H NMR (CD_3CN) δ 7.35 (m, 10H), 4.63 (q, 2H), 1.48 (d, 6H). ^{13}C NMR (CD_3CN) δ 142.5, 129.7 128.5, 128.4, 77.3, 20.6.

10.4. Photoisomerization of 9t

A 40 mg sample of **9t** was dissolved in 0.3 mL CD_3CN or $C_6D_5CD_3$ in a medium wall NMR tube. To avoid thermolysis of **9c**, the tube was placed in a copper cooling coil that kept the temperature at −20 to −10 °C. The cold solution was irradiated for 5–6 h at 313 nm and the conversion to **9c** was monitored by the methine proton of **9c** at 4.83 ppm and **9t** at 4.63 ppm (C_7D_8). Compound **9c**: ^{1}H NMR (CD_3CN) δ 7.20–7.29 (m, 10H), 5.32 (q, J=6.4 Hz, 2H), 1.67 (d, J=6.4 Hz, 6H). ^{13}C NMR (CD_3CN) δ 143.2, 130.0, 130.0, 128.7, 68.4, 22.4. TLC on silica gel eluting with 20% EtOAc in hexane: R_f: **9t** 0.67, **9c** 0.39.

10.5. Thermolysis of 9c

Toluene-d_8 solutions of **9c** were degassed, sealed into NMR tubes, and thermolyzed at 30.2 °C (0.022 M **9c**), 37.8 °C (0.02 M **2c**), and 46.2 °C (0.0114 M **9c**). The disappearance of **9c** was monitored by ^{1}H NMR of its methine protons using TMSTMS as internal standard. The rate constants are shown in Table 2.

10.6. Purification and analysis of 9c

The cis isomer was purified by HPLC using a C18 column with 30% H_2O+70% CH_3CN and a flow rate of 0.7 mL/min. Retention times: **9c** 5.15 min, **9t** 8.84 min.

10.7. *N,N*-(1,1-Dimethylethyl-1)-(1-diethylphosphono-2,2-dimethylpropyl-1)-nitroxyl (SG1)

SG1 was prepared as a red oil in 35% yield according to the literature.[111] The ^{1}H NMR spectrum of SG1 was obtained on SG1-H by adding a few drops of phenylhydrazine. ^{1}H NMR δ ($CDCl_3$) 4.02 (m, 4H), 3.16 (d, J=20.0 Hz, 1H), 1.23 (m, 6H), 1.09 (s, 9H), 1.03 (s, 9H).

10.8. 2-Methyl-3-phenyl-but-2-yl hydroperoxide[112]

To a solution of 100 mL 50% hydrogen peroxide and 10 mL 85% H_3PO_4 was carefully added 2.5 g 2-methyl-3-phenyl-butan-2-ol.[113] The mixture was stirred at 55 °C for 24 h. When the starting material disappeared according to NMR, hexane was added. The organic layer was separated and washed with 10% $NaHCO_3$, then with water. NaOH (40%) was added to the solution to precipitate the hydroperoxide as its sodium salt. The precipitate was filtered off and acidified with dilute HCl. After extraction into CH_2Cl_2, the hydroperoxide was isolated by evaporating the solvent under vacuum. ^{1}H NMR δ 7.8 (s, 1H), 7.05 (s, 5H), 3.13 (q, J=7.0 Hz, 1H), 1.28 (d, J=7.0 Hz, 3H), 1.13 (s, 3H), 1.12 (s, 3H).

10.9. 2-Methyl-3-phenyl-2-butyl per(2-phenylpropionate) 11

2-Methyl-3-phenyl-but-2-yl hydroperoxide (0.18 g, 1 mmol) was dissolved in 1 mL pentane. KOH (40%, 1 equiv) was added dropwise and the mixture was stirred for 30 min. Most of the pentane was carefully aspirated away from the precipitate and the residual solid was evacuated to dryness. The solid was dissolved in 1 mL CH_2Cl_2 and the solution was cooled to −2 °C. After dropwise addition of 0.15 mL 2-phenyl-propionyl chloride, the solution was stirred at −2 °C for 3 h. The CH_2Cl_2 solution was separated from the

white solid, washed three times with cold 10% aq NaOH, and dried over $MgSO_4$. Evaporation of the solvent gave an oil whose NMR spectrum showed that it contained unreacted hydroperoxide, 2-phenyl-propionyl chloride, and perester **11**. The starting materials were removed by dissolving the oil in 2 mL cold pentane and cooling in an ice bath. An excess of freshly pentane-washed NaH was added and the mixture was shaken for 5 min. The solid was removed by filtration and the solvent was evaporated under vacuum to leave the diastereomers of **11** (125.3 mg, 40%). Obtaining a completely pure sample of **11** was impossible because of its thermal lability, the fact that $CDCl_3$ induces its decomposition, and because it is a mixture of diastereomers. ^{1}H NMR δ 7.1–7.4 (m, 10H), 3.82 (q, J=7.2 Hz, 2H), 2.94–3.07 (two q, J=7.2 Hz, 1H), 1.62 (t, J=7.0 Hz, 6H), 1.36 (d, J=7.0 Hz, 3H), 1.29 (d, J=7.0 Hz, 3H), 1.17 (s, 6H), 1.10 (s, 3H), 1.05 (s, 3H).

10.10. Competition kinetics experiments with BQ, SG1, and α-phenethyl radicals

A toluene solution containing 0.035 M BQ, 0.37 M SG1, and 0.27 M **9c** was degassed three times, sealed in four 7 mm Pyrex tubes, and heated at 43 °C. The disappearance of BQ and SG1 was monitored at 450 nm by HPLC using a silica gel column (2-propanol/hexane=5:95) after every 15 min of thermolysis.

10.11. The reaction of DTBQ with 9t

A solution of 0.01 M DTBQ and 0.03 M **9t** in benzene was degassed, sealed in an UV cell and heated at 120 °C for 3 h. UV showed no DTBQ absorbance but GC revealed DTBQ, attributed to thermolysis of an intermediate on the GC injector. After separation by column chromatography (silica gel, 1% EtOAc in hexane), a mixture of two diastereomers **13A**,**B** was isolated. ^{1}H NMR (C_7D_8): diastereomer 1: δ 6.90–7.50 (m, 5H), 6.56 (d, J=3.0 Hz, 1H), 5.99 (d, J=3.0 Hz, 1H), 4.35 (q, J=6.6 Hz, 1H), 3.08 (q, J=7.2 Hz, 1H), 1.39 (s, 9H), 1.38 (d, J=6.6 Hz, 3H), 1.30 (d, J=7.2 Hz, 3H), 0.969 (s, 9H); diastereomer 2: δ 7.02–7.60 (m, 5H), 6.42 (d, J=3.0 Hz, 1H), 6.16 (d, J=3.0 Hz, 1H), 4.35 (q, J=6.6 Hz, 1H), 3.05 (q, J=7.0 Hz, 1H), 1.39 (d, J=6.6 Hz, 3H), 1.34 (d, J=7.0 Hz, 3H), 1.27 (s, 9H), 1.06 (s, 9H). ^{13}C NMR (C_7D_8) diastereomer 2: δ 185.6, 149.9, 147.9, 147.3, 141.8, 141.8, 129.7, 128.8, 128.3, 128.1, 127.9, 127.5, 127.3, 126.4, 78.5, 74.2, 50.4, 35.3, 35.1, 29.8, 29.2, 29.2, 26.5, 15.9. HRMS calcd for ($C_{30}H_{39}O_2$+H): 431.29505, found 431.29377.

10.12. Thermolysis of 13

A 0.023 M solution of diastereomer **13B** (δ 6.15) in toluene-d_8 containing TMSTMS as internal standard was degassed, sealed in an NMR tube, and heated at 120 °C. NMR showed the disappearance of this diastereomer and formation of the other diastereomer **13A** (δ 6.00). The final product also contained DTBQ and 2,6-di-*tert*-butyl-4-[1-phenylethoxy] phenol **15**.

10.13. 2,6-Di-*tert*-butyl-4-[1-phenethoxy] phenol 15

A solution of 0.5 mmol **13** and 300 mg thiophenol in 0.5 mL toluene-d_8 was degassed, sealed in an NMR tube, and heated at 120 °C for 2 days. NMR was used to monitor the reaction products. The solution was washed with saturated aq $NaHCO_3$ and water. The solvent was evaporated and the residue was separated by reverse phase HPLC (C18, CH_3CN/water=90:10) to isolate pure **15**. This phenol was very easily oxidized by air and should be kept in a sealed tube. ^{1}H NMR (C_6D_6) δ 7.2 (m, 5H), 7.12 (s, 2H), 5.18 (q, J=7.0 Hz, 1H), 4.59 (s, 1H), 1.56 (d, J=7.0 Hz, 3H), 1.42 (s, 18H). ^{13}C NMR (C_6D_6) δ 152.1, 148.2, 144.8, 137.3, 129.0, 127.6, 126.2, 113.4, 76.9, 34.8, 30.5, 25.1.

10.14. *N*-(1-Phenethyloxy)-9-azabicyclo[3.3.1]nonane 18

An authentic sample of nitroxyl trapping product **18** was prepared by heating a benzene solution of 0.122 M **9t** and 0.0714 M 9-azabicyclo[3.3.1]nonane-*N*-oxyl (ABNO) at 120 °C for 3 h in a sealed tube. GC analysis of the resulting mixture showed dimers **10** and a peak at 23.6 min, whose GC/MS/CI spectrum exhibited m/z=246 (base) and fragments at 142, 124, and 105. Preparative TLC on silica gel with 5% Et_2O/hexane afforded 3.5 mg (20%) of **18** (R_f 0.33). ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.23–7.39 (m, 5H), 4.71 (q, J=6.5 Hz, 1H), 3.21 (br s, 1H), 2.97 (br s, 1H), 2.33 (m, 2H), 1.80 (m, 8H), 1.44 (d, J=6.5 Hz, 3H), 1.26 (2H m). ^{13}C NMR (62.5 MHz $CDCl_3$) δ 144.8, 127.9, 126.9, 126.5, 78.7, 54.8, 54.2, 23.2, 22.0, 20.0, 19.9. HRMS calcd for ($C_{16}H_{24}NO$+H): 246.1858, found 246.1868.

10.15. Bis(4-benzyloxyphenyl)oxalate 22

The oxalate ester was made by treating 4-benzyloxyphenol with oxalyl chloride according to the procedure of Lahti et al.[82] The white, solid product was recrystallized from CH_3CN. Mp 159–160 °C. ^{1}H NMR ($CDCl_3$) δ 7.33 (m, 10H), 7.11 (d, J=9.2 Hz, 4H), 6.95 (d, J=9.2 Hz, 4H), 5.01 (s, 4H). ^{13}C NMR δ 157.4, 156.3, 143.8, 136.8, 128.9, 128.4, 127.7, 122.0, 115.9, 70.7. The exact mass of **22** was determined on a Thermo Electron Corp. LTQ Orbitrap mass spectrometer. $NaHCO_3$ used in the workup left Na in the sample. Calcd for $C_{28}H_{22}O_6Na$: 477.13141, found 477.13092.

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