Radical-Mediated Synthesis of Substituted Quinones with Organotellurium Compounds

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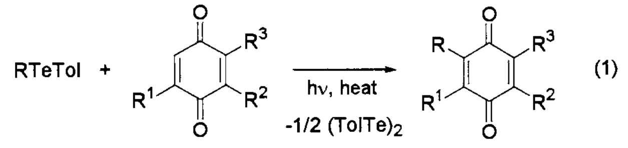
Carbon-centered radicals generated from the corresponding organotellurium compounds react with a variety of quinones under photo–thermal conditions to give the monoaddition product in good to excellent yield. The reaction can be used for the synthesis of polyprenyl quinoid natural products.

A great deal of attention has been focused on the synthesis of substituted quinones because of their unique and diverse biological functions.[1] Since a variety of quinones are available, the attachment of the carbon chain to the preexistent quinone skeleton is one of the most attractive and straightforward synthetic approaches.[2] Indeed, enormous effort has been devoted to the realization of this process by organometallic-mediated reactions and by cycloaddition.[3] While radical-mediated synthesis seems to be a desirable alternative, only a few examples have been reported so far,[4] and its synthetic scope has been limited. This is probably because the most conventional reaction system using alkyl halide and tin hydride could not be applied due to the high reactivity of the tin hydride toward quinones.[5] We have already reported that carbon-centered radicals are reversibly generated from organotellurium compounds.[6,7] Therefore, we envisaged that the radicals thus generated would be useful for the functionalization of quinones.[8] We report herein a new synthesis of substituted quinones by the radical-mediated reaction of organotellurium compounds with various quinones. The reaction proceeds under photo–thermal conditions, and affords a monoaddition product in good to excellent yield (eq 1). Since organotelluriums are readily available,[9] the current method provides a new approach for the radical-mediated synthesis of substituted quinones.



1 **2** **3**

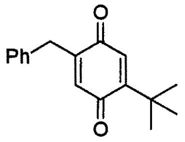
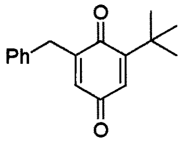
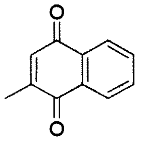
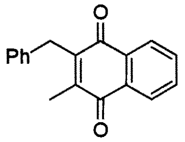
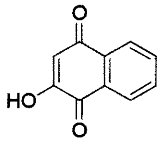
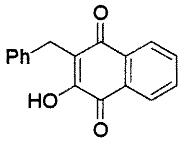
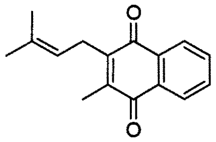
a: R = Bn
b: R = $CH_2CH=C(CH_3)_2$
c: R = *i*-Pr

A: $R^1 = R^2 = R^3 = H$
B: $R^1 = R^2 = Cl$, $R^3 = H$
C: $R^1 = Me$, $R^2 = R^3 = OMe$
D: $R^1 = Ph$, $R^2 = R^3 = H$
E: $R^1 = t\text{-}Bu$, $R^2 = R^3 = H$

The reaction conditions have been examined in detail by using benzyl tolyl telluride (**1a**)[10] and 1,4-benzoquinone (**2A**). Thus, **1a** was heated with **2A** (2.0 equiv) in C_6D_6 at 100 °C under irradiation with a 250-W high pressure Hg lamp in a Pyrex tube,[7a] and the 2-benzyl-1,4-benzoquinone (**3aA**) was formed in 57% yield. The tellurium moiety was recovered quantitatively as ditolyl ditellulide, and about 40% of the quinhydrone was also isolated. The reaction in the dark was slow, but eventually gave the same product after heating at 100 °C for 7 h (57%). The effect of the solvent is marginal, and the reaction in polar solvents, such as acetonitrile and ethanol, produced virtually identical results. The insensitivity to the solvent is consistent with the involvement of neutral radical species rather than polar intermediates, such as radical ion species.

The synthetic scope of the current reaction was examined, and the results are shown in Table 1.[11] A variety of substituted quinones react with organotellurium compounds to give the monoaddition product in good to excellent yield (entries 2–9).

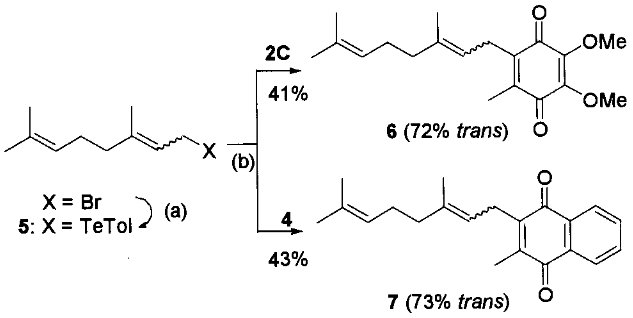
Table 1. Synthesis of substituted quinones[a]

Entry	RTeAr	Quinone	Time/h	Product	Yield/%
1	**1a**	**2A**	1	**3aA**	57
2		**2B**	1	**3aB**	71
3		**2C**	2	**3aC**	53
4		**2D**	2.5	**3aD**	57
5		**2E**	1	 Ph	55
				 Ph	23
6		 **4**	1	 Ph	87
7		 HO	1.5	 Ph HO	64
8	**1b**	**2C**	2	**3bC**	41
9		**4**	2		61
10	**1c**	**2A**	3	**3cA**	44

[a]See Ref. 11 for the experimental procedures. Two equivalents of quinone were used in all cases.

In the reaction of prenyl phenyl telluride, the prenyl moiety selectively coupled with quinones at the less hindered α-position, and the corresponding γ-coupling products could not be detected (entries 8 and 9). Not only benzyl and prenyl radicals, but also alkyl radicals, e.g., isopropyl radical, could be used for the functionalization of quinones (entry 10). The regioselectivity of the reaction deserves comment; the reaction of the phenyl-substituted quinone **2D** occurred at the C-3 position, which is conjugated with the phenyl group, to give the 2,3-disubstituted quinone **3aD** (entry 4). However, in the reaction of the *t*-butyl-substituted quinone **2E**, the selectivity was controlled by steric factors, and the reaction afforded a 7:3 mixture of the 2,6- and 2,5-disubstituted quinones in a good combined yield (entry 5). Since the reaction proceeds via radical intermediates, the free hydroxy groups were compatible under the reaction conditions (entry 7).

The current method can be applied to the synthesis of polyprenyl quinonoids as shown in Scheme 1. Thus, geranyl tolyl telluride **5** (a 73:23 mixture of the *trans* and *cis* isomers), which was prepared by SmI_2-mediated coupling of geranyl bromide and ditolyl ditelluride,[12] was allowed to react with **2C** and **4** to obtain the corresponding geranyl-substituted quinones **6** and **7**, respectively, in moderate yields. Analysis of the stereochemistry revealed that a 7:3 mixture of the *trans* and *cis* isomers was formed in both cases.[13]



Scheme 1. (a) SmI_2, HMPA/THF, r.t., 2 h, 41% (73% *trans*), (b) hv (250W Hg lamp), C_6D_6, 100 °C, 1 h.

As the radical-mediated carbotelluration reaction to alkynes and alkenes is well known,[6b–d,8b] the formation of **3** may be explained by the initial carbotelluration to quinones followed by the elimination of aryltellurol. Aryltellurols thus formed reduce quinones to hydroquinones with the generation of corresponding diarylditelluride.[14] However, several attempts to observe the reaction intermediate are unsuccessful at the present time. Experiments to ascertain the precise mechanism are now being conducted, and further synthetic explorations are currently under investigation.

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11 Typical experimental procedures (entry 6); a solution of **1a** (111 mg, 0.36 mmol) and **4** (125 mg, 0.72 mmol) in benzene (0.6 mL) in a Pyrex tube was irradiated with a 250-W high pressure Hg lamp at 100 °C for 1 h. After removal of the solvent under reduced pressure, the desired product was isolated by silica gel column chromatography in 87% yield (81.7 mg). IR (KBr) 1663 (s), 1619 (w), 1592 (m), 1333 (s), 1293 (s), 716 (s); ^{1}H NMR (300 MHz, $CDCl_3$) 2.25 (s, 3 H), 4.04 (s, 2 H), 7.16–7.30 (m, 5 H), 7.67–7.73 (m,2 H), 8.06–8.12 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) 13.22 (CH_3), 32.40 (CH_2), 126.42 (CH_3), 126.57 (CH), 126.63 (CH), 128.74 (CH, 2 C), 128.80 (CH, 2 C), 132.19 (C), 132.28 (C), 133.61 (CH), 133.64 (CH), 138.23 (C), 144.59 (C), 145.52 (C), 184.90 (C=O), 185.64 (C=O); HRMS (EI) *m/z* Found: M^+, 262.0994. Calcd for $C_{18}H_{14}O_2$: 262.0994. Anal. Calcd for $C_{18}H_{14}O_2$,: C, 82.42; H, 5.38%. Found: C, 82.26; H, 5.52%.

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