2,6-Di-*tert*-butyl-4-diarylmethylene-2,5-cyclohexadiene-1-thiones. First Isolable Unannelated Thioquinone Methides

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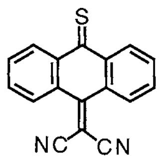
Unannelated thioquinone methides were first synthesized as labile but isolable substances with aid of steric protection; they exhibit higher dipolar properties and stronger electron affinity than the corresponding quinone methides.

Although *p*-quinone methides have been fairly extensively studied,[1] little is known about *p*-thioquinone methides probably due to the synthetic difficulty associated with their instability. Only dibenzo compound **1** has been known as an isolable thioquinone methide.[2] We here report the synthesis and properties of 7,7-diarylthioquinone methides, **2a** and **2b** (2,6-di-*tert*-butyl-4-diarylmethylene-2,5-cyclohexadiene-1-thiones) that are the first unannelated thioquinone methides to be isolated.



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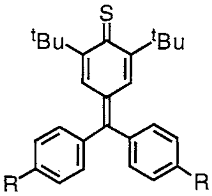
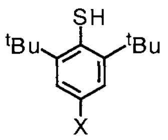


2a: R = CH_3
2b: R = $N(CH_3)_2$

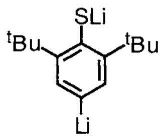
Thioketones and thioquinones are generally less stable than ketones and hence were comparatively rare.[3] There are two methodologies conceivable for the stabilization of such unstable π bonds. One is stabilization by electronic effect of substituents, particularly by conjugative effect. The other is stabilization by steric protection with bulky alkyl or aryl groups.[4] In view of high lability of known thioquinonoid compounds,[5] electronic effect alone appears not strong enough for their stabilization and hence steric protection would be necessary for more effective stabilization. For this aim, we envisioned potential utility of lithium 2,6-di-*tert*-butyl-4-lithiothiophenolate **4** as a building block for sterically protected thioquinonoid compounds.

We previously reported that bromine-lithium exchange of 4-bromo-2,6-di-*tert*-butylphenol smoothly takes place by *t*-BuLi but not completely with *n*-BuLi and the resulting 2,6-di-*tert*-butyl-4-lithiophenoxide, a dianion, has higher nucleophilicity than the corresponding *O*-protected aryllithium owing to intramolecular electronic repulsion in the dianion.[6] Reluctant bromine-lithium exchange with *n*-BuLi and smoother exchange with *t*-BuLi has also been described for 4-bromothiophenol.[7]

The precursor for **4**, namely 4-bromo-2,6-di-*tert*-butylthiophenol **3**, was prepared as a potential synthon by a modification of the reported procedure for 4-substituted 2,6-di-*tert*-butylthiophenol.[8] Treatment of **3** with *t*-BuLi (3.0 equiv.) in THF at -50–0 °C followed by addition of dimethylformamide afforded formyl compound **5**[9] in 80% yield, indicating fairly clean generation of dianion **4**. Thus, the reaction of **4** with 4,4'-dimethylbenzophenone and subsequent chromatography on alumina gave mercaptophenylcarbinol **6a** as a labile substance in 84% yield. Although the corresponding hydroxyphenylcarbinol **7** can be dehydrated cleanly to quinone methide **8a** by acid treatment, **6a** failed to give the expected thioquinone methide **2a** under acidic conditions yielding complex mixtures containing **8a** as sole identifiable product. Successful dehydration was attained, however, by the use of anhydrous $CuSO_4$ in benzene at room temperature, furnishing **2a** as deep red solid by filtering off $CuSO_4$ and concentration under deaerated condition.[10] Thioquinone methide **2a** is stable in dry deaerated benzene, but decomposed under air and moisture partly giving **8a**. Differing from the substantial lability of **2a**, bisdimethylamino compound **2b** is more stable: upon adsorption on alumina, the crude carbinol **6b**, which was obtained from the reaction of **4** with Michler's ketone, was spontaneously dehydrated to give **2b** as dark blue, fairly stable solid in 72% yield. The higher stability of **2b** over **2a** may be ascribed to higher single bond character of its thiocarbonyl group, a consequence of more dipolar property of **2b** owing to the presence of electron-donationg *p*-dimethylamino groups.



3: X = Br
5: X = CHO



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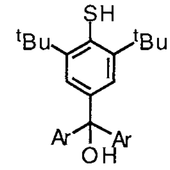
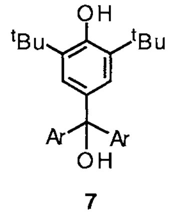


6a: Ar = *p*-tol
6b: Ar = 4-(Me_2N)C_6H_4



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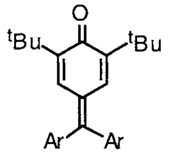

8a: Ar = *p*-tol
8b: Ar = 4-(Me_2N)C_6H_4

Thioquinone methides **2a** and **2b** exhibit intense absorptions in the visible region with large bathochromic shift compared to the corresponding quinone methides **8a** and **8b** (Table 1). Like other 7,7-diarylquinone methides,[11] **2b** as well as **8b** show bathochromic shift in dipolar solvents (positive solvatochromism). Their longest-wavelength absorptions (in wave number) are found to be in linear relationship with the solvent polarity (E_T parameter[12]) except for the hypsochromic shift of **2b** in ethanol (Figure 1). Slightly steeper line-slope of **2b** than **8b** indicates its larger degree of solvatochromism. The reason for the exceptional hypsochromic shift of **2b** in ethanol is not yet certain but may be associated with easier hydrogen-bonding between the sulfur atom and solvent.

Table 1. Selected physical data of **2a**, **2b**, **8a**, and **8b**

	^{1}H-NMR /δ ppm[a]	^{13}C-NMR /δ ppm[b]			UV-Vis	Reduction potentials/V[d]	
		C1	C4	C7	λ_{max} /nm (log ε)[c]	E_{red}^1	E_{red}^2
2a	7.63 (s, 2H), 7.17 (AA'BB', 4H), 6.93 (AA'BB', 4H), 2.07 (s, 6H), 1.64 (s, 18H)	216.76	134.80	156.23	475 (ca. 4.5)	-0.99	-1.77[e]
2b	7.82 (s, 2H), 7.43 (AA'BB', 4H), 6.43 (AA'BB', 4H), 2.35 (s, 12H), 1.83 (s, 18H)	209.88	132.63	161.18	595 (4.57), 466 (4.40), 415 (3.88), 328 (4.11)	-1.16	
8a	7.50 (s, 2H), 7.09 (AA'BB', 4H), 6.91 (AA'BB', 4H), 2.05 (s, 6H), 1.48(s, 18H)	186.21	130.03	156.17	384 (4.47)	-1.40	-1.96[e]
8b	7.74 (s, 2H), 7.37 (AA'BB', 4H), 6.46 (AA'BB', 4H), 2.40 (s, 12H), 1.63 (s, 18H)	185.86	128.75	159.22	479 (4.55), 419 (4.45)	-1.54	

[a] In C_6D_6 at 30 °C (**2**; 600 MHz, **8**; 270 MHz). [b] In C_6D_6 at 30 °C (**2**; 150 MHz, **8**; 67.9 MHz). [c] In toluene. [d] V vs Ag/Ag^+ in 0.1 M *n*-Bu_4NClO_4/CH_3CN (Fc/Fc^+ = +0.26 V), sweep rate 100 mV. [e] Peak potential.

In the ^{13}C-NMR spectra, diarylmethylene carbon (C-7) of **2a** (δ 156.23) and **2b** (δ 161.18), in particular of the latter, are observed at lower field than those of **8a** (δ 156.17) and **8b** (δ 159.22), suggesting higher dipolar property of thioquinone methides than quinone methide in consonance with the solvent effects on the absorption spectra.[13]

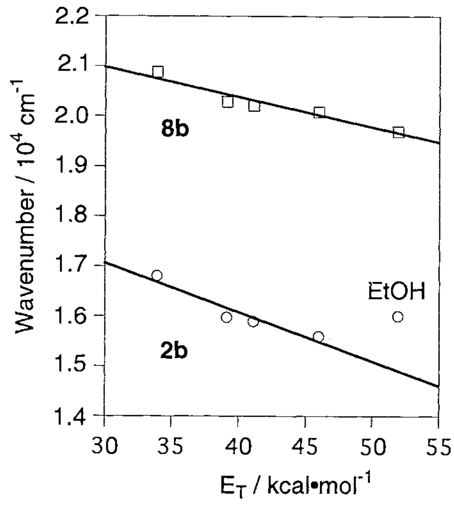

Figure 1. Relationship between the wave number of the longest absorptions of **2b** and **8b** and the solvent polarity [Toluene (E_T = 33.9 kcal•mol^{-1}), $CHCl_3$ (39.1), CH_2Cl_2 (41.1), CH_3CN (46.0), EtOH (51.9)].

Upon cyclic voltammetry, thioquinone methide **2a** shows two reduction waves, the first one being reversible at -0.99 V and the second one irreversible at -1.77 V (peak potential, Table 1). These values are 0.2–0.4 V smaller than those of quinone methide **8a**. Similar trend is also observed for **2b** and **8b**. Thus, thioquinone methides are stronger electron acceptors than quinone methides which themselves have considerable electron affinity.

In conclusion, lithium 2,6-di-*tert*-butyl-4-lithiothiophenolate **4** was proved to be a useful synthon for thioquinone methides, although steric protection by the *t*-butyl groups appears not sufficient enough,[14] and thioquinone methides thus obtained are slightly more dipolar and stronger electron acceptors than the corresponding quinone methides. In addtion to the steric protection, this dipolar property (electronic effect) seems also to contribute to the stabilization of **2** particularly for **2b**. Further applications of **4** in the synthesis of thioquinonoid compounds are in progress.

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