

3,5-Di-*tert*-butylphenyl (D^tBuP) Group as a Protecting Group for Kinetic Stabilization. Preparation and Characterization of 2,6-Naphthoquinone Skeleton

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A potential use of a 3,5-di-*tert*-butylphenyl group for kinetically stabilization and the isolation of a stabilized 2,6-naphthoquinone derivative are discussed.

Isolation and characterization of highly reactive and instable organic molecules have been a challenge for organic chemists to understand their basic properties. One of the most effective strategy to isolate such instable molecules is to use kinetic stabilization, where bulky substituents are introduced to block the reactive sites of these compounds. This strategy has been successfully applied to compounds with highly strained chemical bonds,¹ or with multiple bonds between heteroatoms (e.g. diphosphenes² and disilenes³), or with open shell structure (e.g. neutral radicals⁴). The use of bulky alkyl substituents such as *tert*-butyl or adamantyl groups as a protecting group has been well established.⁵ A recent developed bulky substituent, 2,4,6-tris[bis(trimethylsilyl)methyl]phenyl, is a powerful protecting group of aryl type, while the difficulty in synthesis and high reactivity at α -silyl position prevent the application.^{3,6} In this paper, we wish to describe another promising aryl substituent, a 3,5-di-*tert*-butylphenyl (D^tBuP) group,^{7,8} as a kinetically stabilizing protecting group. We chose 2,6-naphthoquinone (2,6-NQ) **1a** to be protected which was first reported by Willstätter in 1907 and has not been fully characterized.⁹ This molecule is theoretically known to have highest reactivity^{10,11} and highest electron affinity¹⁰⁻¹² among isomeric naphthoquinones (1,2-, 1,4-, 1,5-, 1,7-, 2,3-, and 2,6-isomers).¹³ Because of the instability, only few property of 2,6-NQ is known. We introduced two D^tBuP groups at reactive 1- and 5-positions^{9,11} of **1a** and the resulted **1b** was structurally characterized.

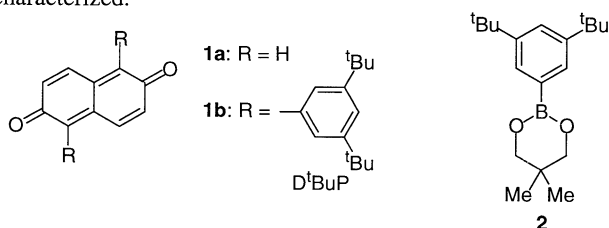
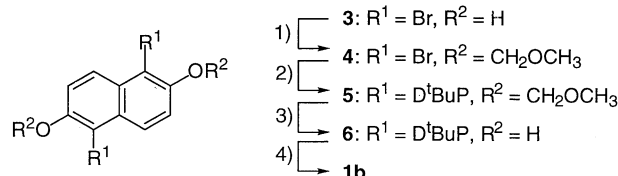


Figure 1.

The synthetic route of **1b** is shown in Scheme 1. Introduction of D^tBuP into **4** which was derived from **3**¹⁴ was achieved by an improved Suzuki coupling reaction using boric acid ester **2**⁸ to give **5** in acceptable yield (60%). After deprotection of methoxymethyl groups in **5**, **6** was oxidized with commercially available PbO₂ to give **1b** as reddish-orange solid.¹⁵ In marked contrast to the instability of **1a** having half life time of only about 30 min, **1b** is quite stable toward SiO₂ chromatography, oxygen, light, and heat and can be kept for more than several months without any decomposition under ambient conditions. It should be noted that **1b** does not react even with boiling water, although **1a** is known to be "the great

instability toward water".¹⁰



Reagents and conditions: 1) CH₃OCH₂Cl, K₂CO₃, acetone, 2) **2**, Pd(PPh₃)₄, K₂CO₃, DMF-H₂O, 3) TsOH, MeOH, 4) PbO₂, PhMe.

Scheme 1.

UV-vis. absorption of 2,6-NQ has not been reported as far as our best knowledge is concerned. As shown in Figure 2, the intensities and solvent effects of **1b**¹⁶ indicate that the characteristic two bands, *Band-I* and *Band-II*, are attributable to the π - π^* transition. A large bathochromic shift of the transitions comparing with that of *p*-benzoquinone (BQ)¹⁶ can be ascribed to the expansion of the π -system. The reduction potential of **1b** was determined to be -0.33 V (vs. Ag/AgCl in PhCN). The value is shifted to positive direction by 0.18 V compared with the corresponding value of BQ indicating also the expanded π -system of **1b**.

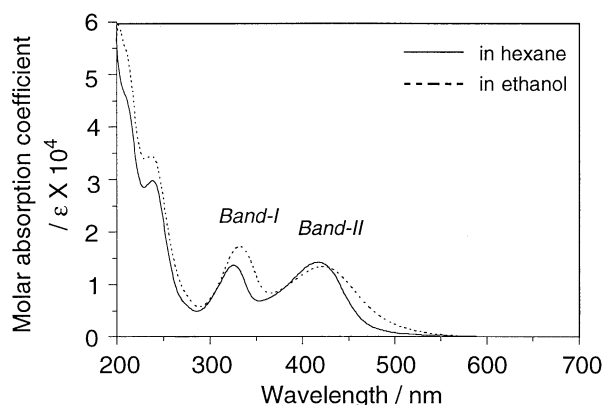


Figure 2. Absorption spectra of **1b** in hexane (solid line) and ethanol (dotted line).

A few crystal structures of the charge transfer complexes of 2,6-NQ are reported,^{13,17} while those of neutral state remained unknown. The X-ray analysis of neutral species **1b** was carried out together with the reference compound **5**.¹⁸ During X-ray irradiation, no detectable decomposition of **1b** was observed. The final results are shown in Figure 3. The intramolecular bond distances of **1b** showed marked bond alternation which is expected for a π -expanded quinonoid structure, in contrast to **5** having nearly the same bond distances for a naphthalene ring.¹⁹ Bonds *a* and *c* are significantly

shorter, while both *b* and *d* are longer comparing those for **5**. On the other hand, the observed carbonyl C=O bond distances (1.220(3) Å) is comparable to that of BQ, 1.222(3) Å,²⁰ although $\nu_{\text{C=O}}$ absorption of **1b** (1631 cm⁻¹) is shifted to lower frequency by 35 cm⁻¹ compared with that of BQ. The 2,6-NQ moiety is almost flat within ± 0.12 Å from the least squares plane. The dihedral angle between quinone plane and D^tBuP is 64.43(2)°, which is indicating small electronic perturbation between them and the stability of **1b** is mainly achieved by the bulkiness of D^tBuP.

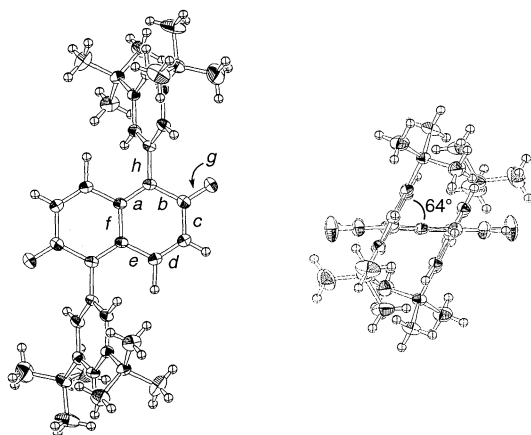


Figure 3. The ORTEP drawing of **1b**: top view (left) and side view (right). Thermal ellipsoids are at the 50% probability level. Important bond distances are the followings: *a*: 1.364(3), *b*: 1.485(3), *c*: 1.463(3), *d*: 1.331(3), *e*: 1.457(3), *f*: 1.472(3), *g*: 1.220(3), and *h*: 1.489(3) Å.

In summary, instable 2,6-NQ was kinetically stabilized by the introduction of bulky D^tBuP groups at highly reactive 1- and 5-positions.^{9,11} This made us to the isolation and full characterization of the neutral 2,6-NQ quinonoid skeleton for the first time after 92 years from the first synthetic approach. Introduction of D^tBuP group is easily accessible and will be widely applicable as a kinetically stabilizing group using Suzuki, Stille, and Negishi coupling reactions. Moreover, the solubility is much more improved by the introduction of the substituents.

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