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A novel dendrimer-type *m*-terphenyl substituent for the kinetic stabilization of highly reactive species

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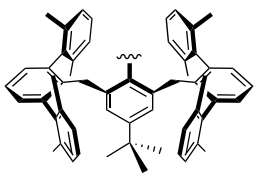
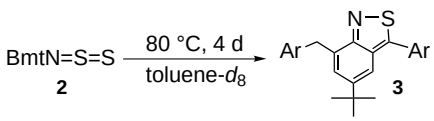
Abstract—A novel *m*-terphenyl-based steric protection group (Bpq group) bearing a dendrimer-type framework was designed and successfully applied to the stabilization of the corresponding *N*-thiosulfinylaniline and arenesulfenyl iodide. The Bpq group was found to provide a very inert environment for the reactive functionality embedded in its cleft.

In the kinetic stabilization of reactive species, it is of great importance to design a reaction environment suitable for the stabilization of the target species. Recently, we have developed a novel bowl-type steric protection group **1** (denoted as Bmt hereafter), where the central functionality is surrounded by two *m*-terphenyl units, and reported that it is very effective in preventing reactive species from undergoing dimerization or self-condensation.[1] The use of the Bmt group has enabled us to successfully synthesize and isolate the reactive species such as an arenesulfenic acid (ArSOH)[1b] and an arenesulfenyl iodide (ArSI)[1d] as stable crystals; these species have not been synthesized even by using a bulky substituent such as the 2,4,6-tri-*tert*-butylphenyl (Mes*) group. In some special cases, however, the methylene groups at *ortho*-positions of a Bmt group are involved in the reaction with a functional group in the cavity. For example, heating of *N*-thiosulfinylaniline **2** for a prolonged time resulted in intramolecular cyclization to afford 2,1-benzisothiozole **3** (Scheme 1).[1e] Such kind of intramolecular reaction involving the *ortho*-alkyl group is one of the major problems associated with an aromatic steric protection group, and similar cyclization reactions were also reported for *N*-thiosulfinylanilines **4**[2] and **5**.[3] Recently, *m*-terphenyl-2′-yl groups represented by the general formula **6** have been widely utilized as excellent steric protection groups which are not liable to undergo such intramolecular reactions.[4] Even in **6**, however, the alkyl groups at 2,2″,6,6″-positions are considerably close to the central functionality and sometimes involved in its reaction.[5] We report here the design of a novel *m*-terphenyl-based dendrimer-type substituent **7** (denoted as Bpq hereafter)[6] as a more inert and effective steric protection group and its appli-



1 ≡ **Bmt**



(Ar = 2,2",6,6"-tetramethyl-*m*-terphenyl-2'-yl)

Scheme 1.

Keywords: steric protection; *m*-terphenyl; *N*-thiosulfinylaniline; arenesulfenyl iodide.

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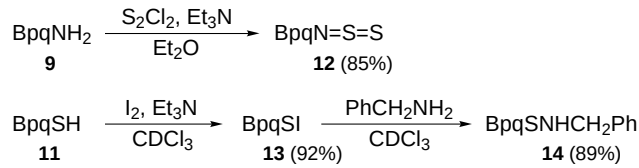
cation to the synthesis of a stable *N*-thiosulfinylaniline and an arenesulfenyl iodide.

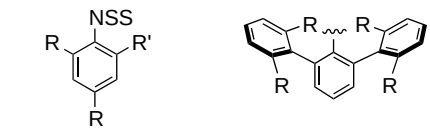
In BpqX, the *m*-terphenyl framework extends like a dendrimer to form a large molecular cleft. The CPK model examination indicates that the two biaryl bonds at the *ortho*-positions of X can rotate rather freely. However, in any conformation of the molecule, the central functionality X is always embedded in the cleft and its dimerization is expected to be very difficult. Furthermore, because the skeleton of BpqX consists of solely rigid biaryl units, the peripheral isopropyl groups cannot be close to the central functionality X, thus providing an inert environment without alkyl groups around X. The framework of BpqX can be readily constructed by repetition of the Hart's method for the *m*-terphenyl synthesis[7] via bromide **8** as shown in Scheme 2. Quenching the second reaction with trimethylsilylmethyl azide or iodine afforded amine **9** or iodide **10**, respectively. Iodide **10** was further converted to thiol **11** via lithiation.[8] The signal pattern of the ^{1}H NMR spectra indicated that, in compounds **9**, **10**, and **11**, two biaryl bonds at the *ortho*-positions of the central functionality rotate rapidly on the NMR time-scale as expected.

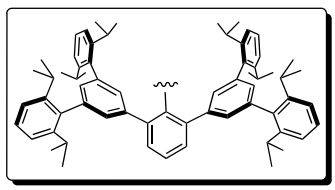
The reaction of aniline **9** with disulfur dichloride in the presence of triethylamine afforded *N*-thiosulfinylaniline **12**, which was isolated by silica-gel chromatography as red crystalline solids in 85% yield (Scheme 3).[9] *N*-Thiosulfinylaniline **12** showed remarkable thermal stability in comparison with compound **2** bearing a Bmt group. While **2** underwent intramolecular cyclization reaction to **3** upon heating in toluene-d_8 at 80°C for 4 days in a sealed tube,[1e] no decomposition of **12** was observed after heating in benzene-d_6 at 80°C for 11 days and even after subsequent heating at 100°C for 7 days in a sealed tube. Compound **12** is much more stable than compound **5**,[3] which has so far been known as the most stable *N*-thiosulfinylaniline; **5** was reported to decompose to the corresponding benzisothiazole after 1 week upon heating at 80°C in benzene. These results clearly demonstrate that the Bpq group is not only effective for prevention of the bimolecular decomposition of the reactive species such as an *N*-thiosulfinylaniline but also provides very inert reaction environment to the species as expected.

As another reactive species to be stabilized by a Bpq group, we synthesized a sulfenyl iodide, which has been known to be very unstable because of the ready disproportionation reaction ($2RSI \rightarrow RSSR+I_2$).[10] Oxidation of thiol **11** with an equimolar amount of iodine in the presence of triethylamine afforded sulfenyl iodide **13** in 92% yield after chromatographic purification (Scheme 3).[11] The structure of **13** was established by X-ray crystallographic analysis (Fig. 1).[12] The shortest intermolecular S···I distance is 8.69 Å, indicating that sulfenyl iodide **13** is monomeric in the crystalline state. The S–I functionality is incorporated in the molecular cleft formed by the rigid dendrimer-type framework and surrounded by the isopropyl groups from a distance.

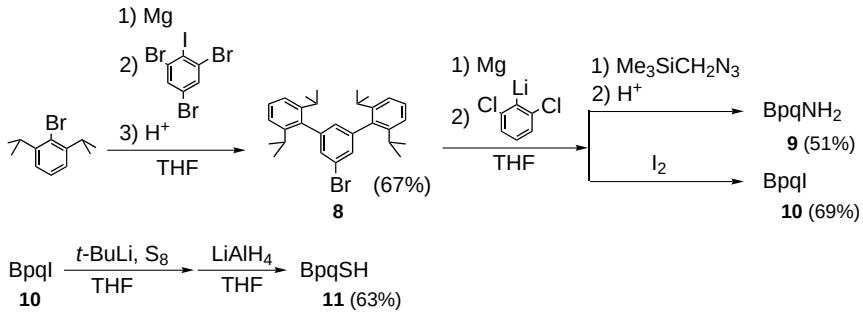


Scheme 3.





7 ≡ **Bpq**



Scheme 2.

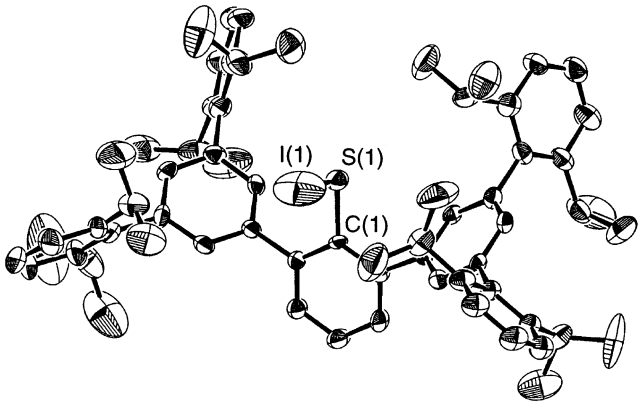


Figure 1. ORTEP drawing of **13** (30% probability). Selected bond lengths (Å) and angles (°): S(1)–I(1), 2.316(4); S(1)–C(1), 1.777(9); I(1)–S(1)–C(1), 103.8(4).

Thus its disproportionation process is considered to be extremely difficult. In fact, compound **13** was found to be stable both in the crystalline state and in solution, similarly to the sulfenyl iodide bearing a Bmt group.[1d] Heating of **13** at 80°C for 12 h in toluene-d_8 resulted in no decomposition, indicating the effectiveness of the Bpq group again. Treatment of **13** with benzylamine afforded sulfenamide **14**, which demonstrates that there is a space around the S–I functionality large enough for its reaction with a relatively small reagent such as benzylamine. The ^{1}H NMR spectra of *N*-thiosulfinylaniline **12** and sulfenyl iodide **13** showed the same signal pattern as that of **9**, **10**, and **11**, indicating that the C–N bond of **12** and the C–S bond of **13** as well as the biaryl bonds at the *ortho*-positions of the central functionalities of both compounds rotate rapidly on the NMR time-scale. These results also demonstrate that there is a large space around the central functionality to allow free rotation of these bonds.

The application of this novel steric protection group to the synthesis of other reactive species as well as the development of further extended dendrimer-type substituents are currently in progress.

Acknowledgements

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6. Bpq denotes 5′,5‴-bis(2,6-diisopropylphenyl)-2,6,2‴,6‴-tetraisopropyl-*m*-quinquephenyl-2″-yl.
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8. Thiol **11** was also obtained by quenching the second reaction of the *m*-terphenyl synthesis with elemental sulfur followed by reduction with $LiAlH_4$. However, the products were much more complex than the reaction starting from iodide **10**, and purification of **11** was difficult.
9. Spectral and analytical data for **12**: mp 264–266°C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.05 (d, $J=6.7$ Hz, 24H), 1.13 (d, $J=6.7$ Hz, 24H), 2.72 (m, 8H), 6.94 (t, $J=1.5$ Hz, 2H), 7.16 (d, $J=1.5$ Hz, 4H), 7.17 (d, $J=7.6$ Hz, 8H), 7.31 (t, $J=7.6$ Hz, 4H), 7.48–7.54 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.1 (q), 24.2 (q), 30.5 (d), 122.4 (d), 127.9 (d), 128.0 (d), 128.3 (d), 130.0 (d), 130.1 (d), 132.0 (s), 138.5 (s), 138.9 (s), 140.3 (s), 145.7 (s), 146.7 (s). UV–vis (hexane) λ_{max} 345 (ε 2830), 468 (640, sh), 557 (160, sh) nm. Found: C, 83.28; H, 8.17; N, 1.47; S, 6.50%. Calcd for $C_{66}H_{77}NS_2$: C, 83.58; H, 8.18; N, 1.48; S, 6.76%. HRMS (FAB): Found m/z 948.5558. Calcd for $C_{66}H_{78}NS_2$: $[M+H]^+$ 948.5576.
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11. Selected spectral data for **13**: mp 235–237°C (dec.). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.09 (d, $J=6.9$ Hz, 24H), 1.14 (d, $J=6.9$ Hz, 24H), 2.94 (m, 8H), 7.06 (t, $J=1.5$ Hz, 2H), 7.18–7.22 (m, 8H), 7.31–7.36 (m, 8H), 7.41–7.50 (m, 3H). UV–vis ($CHCl_3$) λ_{max} 330 (ε 4700), 509 (250) nm.
12. Crystal data for **13**: $C_{66}H_{77}SI\cdot C_6H_{14}$, FW = 1115.48, triclinic, space group $P\bar{1}$, $a=16.024(5)$, $b=19.251(7)$, $c=11.743(3)$ Å, $\alpha=105.70(2)$, $\beta=100.22(3)$, $\gamma=99.43(3)°$, $V=3345(1)$ Å^3, $Z=2$, $D_{calcd}=1.107$ g/cm^3, $\mu=5.47$ cm^{-1}, R (R_w) = 0.074 (0.074).