Facile Cyclization of Terphenyl to Triphenylene: A New Chemodosimeter for Fluoride Ions
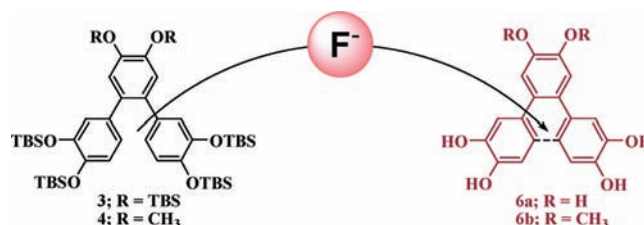
Vandana Bhalla,* Hardev Singh, and Manoj Kumar*

Department of Chemistry, UGC Sponsored-Centre for Advance Studies-I, Guru Nanak Dev University, Amritsar-143005, Punjab, India

vanmanan@yahoo.co.in; mksharmaa@yahoo.co.in

ABSTRACT

Terphenyl derivatives 3 and 4 having OTBS groups have been synthesized via a Suzuki−Miyura coupling reaction. These compounds undergo unprecedented irreversible cyclization to symmetrically/unsymmetrically substituted triphenylenes while carrying out the deprotection of OTBS groups using tetrabutylammonium fluoride. Terphenyl 3 also serves as a new chemodosimeter for fluoride ions.

Terphenyls have attracted a lot of attention due to a wide range of significant biological activities, for example, potent immunosuppressant, neuroprotective, antithrombotic, anticoagulant, specific 5-lipoxygenase inhibitory, and cytotoxic activities.[1] Besides, terphenyls can also be converted to triphenylenes, which have great potential in supramolecular and material chemistry owing to their role as liquid crystalline materials,[2] molecular scale devices,[3−5] and molecular receptors.[6−8] They are potential components for organic and optoelectronic devices.[9] Particularly appealing are hexas-

ubstituted derivatives as peripheral substitution on triphenylene core has a large effect[10] on the thermal behavior of liquid crystalline materials. However, the only existing rational routes for the synthesis of symmetrically/unsymmetrically hexasubstituted triphenylene involve the iodine promoted photocyclisation[11] or iron(III) chloride[12] promoted cyclization of *ortho*-terphenyl which are prepared by Ullman coupling reaction or by palladium catalyzed cross coupling reactions involving aryl boronic acids. Iron(III) chloride and

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MoCl$_5$[13] have been shown to promote the cyclotrimerization of 1,2-dialkoxybenzene derivatives and also to allow a selective coupling of a 3,3′,4,4′-tetraalkoxybiphenyl and a 1,2-dialkoxybenzene.[14] All of these reagents, iron(III) chloride, and molybdenum chloride are insoluble in common organic solvents, and therefore, the synthesis of triphenylenes from terphenyls on a large scale using conventional oxidizing agents is inconvenient. Keeping in view the importance of triphenylenes, the development of new methods which allow the preparation of triphenylenes on large scale without using conventional oxidizing reagents will be very beneficial.

Our research work on molecular recognition and sensing is focused on the development of novel artificial receptors for the selective sensing of soft metal ions[15] and inorganic anions of clinical interest.[16] We recently reported "Turn On" fluorescent sensors for mercury ion based on terphenyls appended with pyrene and quinoline moieties which exhibit high binding affinity for mercury.[17]

Scheme 1
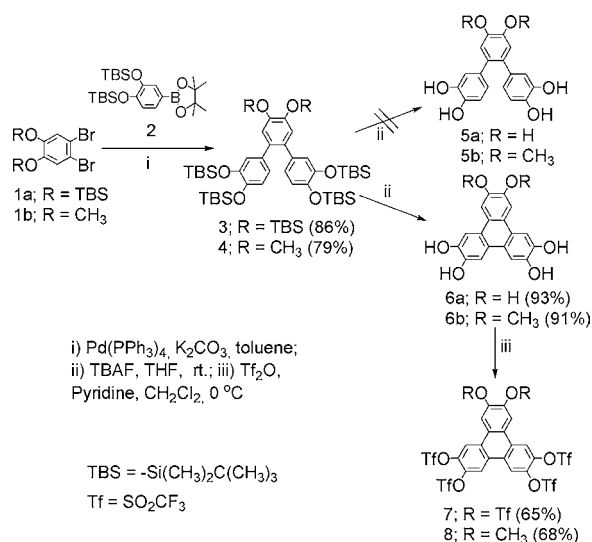
As part of our ongoing research on terphenyl-based materials, we were interested in synthesis of symmetrically/unsymmetrically hexasubstituted terphenyls. For this multistep synthesis, we employed hydroxyl group protection/deprotection strategy for selective reaction on a particular site. However, while carrying out unmasking of silyl ether with tetrabutylammonium fluoride (TBAF) in tetrahydrofu-ran, we observed an unprecedented irreversible cyclization of intermediate terphenyls **3** and **4** to triphenylenes **6a** and **6b** along with significant color changes. Thus, in the present manuscript, we report terphenyls having OTBS groups which are easily converted to hexasubstituted triphenylenes during the deprotection of terphenyl using TBAF. We also investigated the sensing behavior of terphenyl **3** toward fluoride ions using UV−vis and fluorescence spectroscopy. To the best of our knowledge, this is the first report where cyclization of terphenyl to triphenylene has been carried out in absence of any oxidizing reagent.

Palladium catalyzed Suzuki−Miyura cross coupling of boronic ester **2** with dibromide **1a** and **1b** furnished terphenyls **3** and **4** in 86 and 79% yields, respectively (S4 and S7 Supporting Information). The structures of compounds **3** and **4** were confirmed from their spectroscopic and analytical data (Scheme 1).

The ^{1}H NMR spectrum of compound **3** showed six singlets (18H, 12H) for TBS group, two singlets and two doublets (2H each) for aromatic protons of terphenyl moiety. The FAB mass spectrum showed a parent ion peak at 1011 (M$^+$) corresponding to coupled product **3**. These spectroscopic data corroborates the structure **3** for this compound. Now that the terphenyl **3** was in hand in substantial quantities, its deprotection to corresponding hexahydroxy terphenyl **5a** was examined using tetrabutylammonium fluoride. Interestingly, the treatment of terphenyl **3** with tetrabutylammonium fluoride furnished hexahydroxy triphenylene **6a** along with drastic color changes. The reaction, which was complete in five minutes, probably involves two steps. The first step is cleavage of Si−O bond in the presence of F$^-$ ion follwed by cyclization and both steps are very fast and irreversible. The structure of compound **6a** was confirmed from its spectroscopic data. The ^{1}H NMR spectrum of compound **6a** showed one singlet (6H) for protons of triphenylene core and one broad signal for OH groups. Similarly, deprotection of **4** with TBAF yielded compound **6b**. ^{1}H NMR of **6b** in THF showed one singlet (6H) due to methoxy protons, three singlets (2H, each) due to aromatic protons and two singlets (2H, each) for OH groups. Compound **6a** and **6b** were further confirmed by their conversion to their triflate derivatives **7** and **8** (S5 and S8 Supporting Information).

To gain deeper insight into mechanism of the reaction *viz a viz* number of OTBS moieties, its topology, we also prepared terphenyl derivatives **9a** (S10 Supporting Information) **9b**−**9c** (S13 Supporting Information) and carried out their deprotection using TBAF. However, no aryl−aryl bond formation was observed in **9a**−**9c** derivatives (Scheme 2).

Although we were not surprised that **9a** having two OTBS groups on the central aryl ring and **9b** having OTBS groups meta to the ring closing site did not undergo cyclization, we were amazed that **9c** having OTBS groups para to ring closing site did not lead to the formation of triphenylene either, during deprotection reaction. On the basis of these results, we may conclude that increased negative charge on phenolate oxygens after deprotection of OTBS groups in terphenyls **3** and **4** provide an optimal amount of directing ability and electron density to complete cyclization. The

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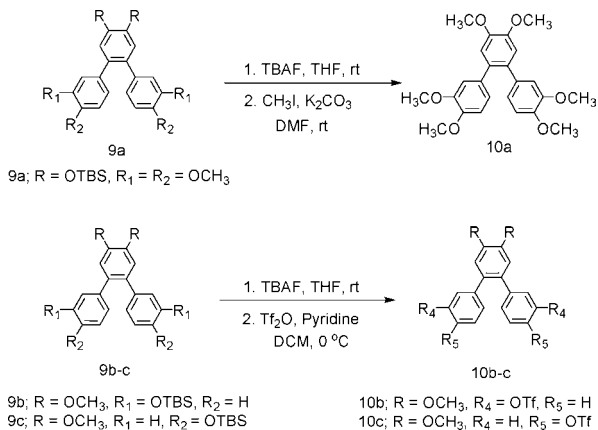(14) Boden, N.; Bushby, R. J.; Cammidge, A. N. *J. Chem. Soc., Chem. Commun.* **1994**, 465.
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Scheme 2

9a; R = OTBS, R₁ = R₂ = OCH₃

9b; R = OCH₃, R₁ = OTBS, R₂ = H
9c; R = OCH₃, R₁ = H, R₂ = OTBS

10b; R = OCH₃, R₄ = OTf, R₅ = H
10c; R = OCH₃, R₄ = H, R₅ = OTf

cyclization is also enthalpically favored by the greater conjugation of planar triphenylene relative to terphenyl. A feasible mechanism for this cyclization involves a common phenolate anion intermediate obtained via fluoride-mediated desilylation, followed by cyclization to triphenylene through oxidative dehydrogenation as shown in Scheme 3.

**Scheme 3.** Proposed Mechanism for Cyclization of Terphenyl **3** and **4** to Triphenylene
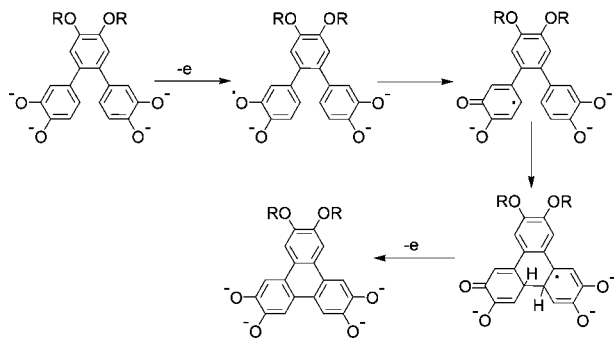
Since the cyclization of terphenyl **3** in the presence of fluoride ions was accompanied by drastic color changes, we examined the behavior of terphenyl **3** toward different anions by UV−vis and fluorescence spectroscopy as the selective recognition and sensing of anions by artificial optical receptors has emerged as a key research theme within the host guest chemistry.[18] Among the biologically important anions, fluoride is of particular interest owing to its role in preventing dental caries[19] and in the treatment for osteoporo-

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sis.[20] Furthermore, F⁻ ions are also associated with anesthetics, hypnotics, psychiatric drugs, nerve gases, in the analysis of drinking water, and in the refinement of uranium used in nuclear weapon manufacture.[21] Thus, due to diversity of its functions, the development of optical sensors for naked eye detection of fluoride ion becomes important.

The UV−vis experiments were carried out in THF at 5.0 × 10⁻⁵ M concentration of dosimeter **3**. In the absence of anions, the absorption spectrum of receptor **3** is characterized by the presence of one absorption maximum peak at 295 nm (Figure 1). It was found that the UV−vis absorption band
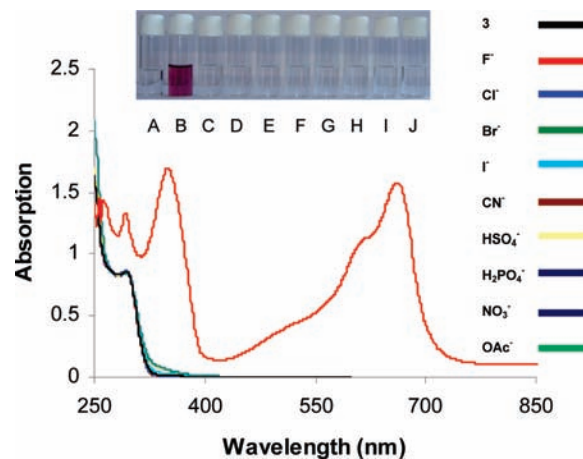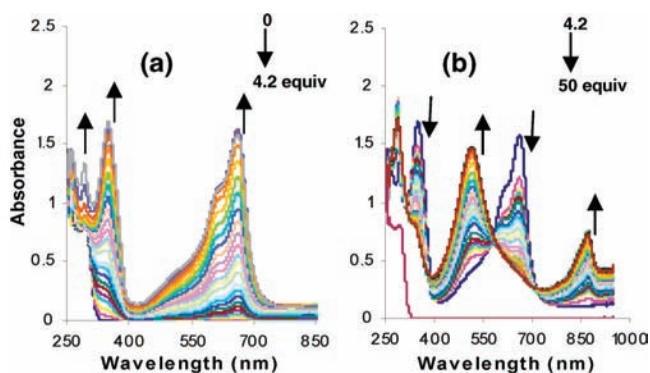

Figure 1. UV−vis spectrum of **3** (5×10^{-5} M) in the presence of different anions (210 μM) in THF. A = Free ligand, B = F⁻, C = Cl⁻, D = Br⁻, E = I⁻, F = CN⁻, G = HSO₄⁻, H = H₂PO₄⁻, I = NO₃⁻, J = OAc⁻.

of receptor **3** is red-shifted to 342 nm ($\Delta\lambda$ 47 nm) and at 663 nm ($\Delta\lambda$ 368 nm) as fluoride ions come in contact with solution of receptor **3** and most importantly, at such a low concentration these changes were clearly visible to the naked eye where the solution changes from colorless to violet (Figure 1, inset). However, there was absolutely no change in the absorption spectrum of receptor **3** or color of the solution in the presence of chloride, bromide, iodide, nitrate, acetate, cyanide, hydrogen phosphate and hydrogen sulfate ions, as their tetrabutylammonium salts, respectively at this particular concentration (Figure 1, inset).

Thus, upon the addition of 0.0−4.2 equiv of F⁻, the UV−vis absorption band centered at 294 disappeared completely and new bands centered at 342 and 663 nm appeared (Figure 2a). On further addition of fluoride ions, the band at 663 nm decreased and three new bands centered at 879, 526, and 287 nm appeared with isosbestic points at 716, 582, and 315 nm, respectively (Figure 2b) and the color of solution turned violet (Figure 3). The band at 287 nm is characteristic band for the triphenylene moiety. Thus, we

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Figure 2. UV−vis spectrum of **3** (5×10^{-5} M) in the presence of TBAF in THF.

propose that the spectral changes in Figure 2 are due to the formation of triphenylene moiety. To test the practical applicability of compound **3** as F⁻ selective sensor, competitive experiments were carried out in the presence of F⁻ at 210 μM mixed with Cl⁻, Br⁻, I⁻, OAc⁻, HSO₄⁻, NO₃⁻, H₂PO₄⁻, CN⁻ at 500 μM, no significant variation in


Figure 3. Change in color intensity of **3** (5×10^{-5} M) upon the addition of F⁻ ion (from left to right, free ligand, 1, 2, and 6 equiv) in THF.

absorption behavior was observed by comparison with or without the other anions besides F⁻. This means that compound **3** has high selectivity for F⁻ ion over other anions studied (S41 Supporting Information).

We also used fluorescence spectroscopy to investigate the behavior of terphenyl **3** in the presence of fluoride ions. Hexasubstituted terphenyl **3** exhibited a fluorescence emission at 393 nm when excited at λ_{max} 294 nm. Upon addition of F⁻ ions, a red-shifted band appeared at 425 nm (a shift of 32 nm) with 32% enhancement of fluorescence emission (Figure 4A). The presence of fluoride ions results in cleavage of Si−O bond which increases negative charge on the phenolate oxygen followed by cyclization to triphenylene as a result of which the conjugation is extended. This

extended conjugation leads to the red shift and enhancement of fluorescence emission. On further addition of F⁻ ions, fluorescene emission intensity was decreased (Figure 4B). This decrease in emission intensity may be ascribed to an electron transfer from phenolate oxygen to triphenylene moiety. It was found that **3** has a detection limit of 2×10^{-6}
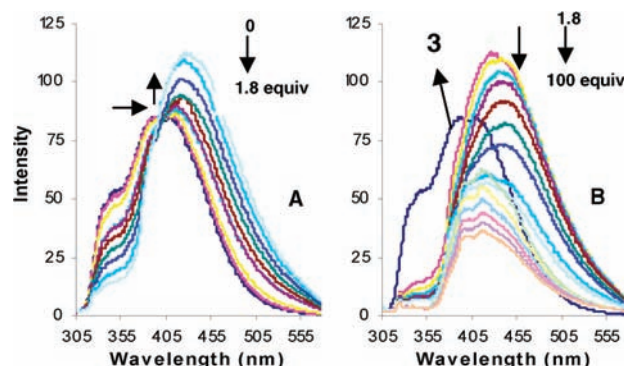
Figure 4. Fluorescence spectrum of **3** (5×10^{-6} M) in the presence of TBAF in THF.

mol L⁻¹ for F⁻ which is sufficiently low for the detection of submillimolar concentration range of F⁻ ions found in many chemical systems. The other anions (Cl⁻, Br⁻, I⁻, HSO₄⁻, OAc⁻, H₂PO₄⁻, NO₃⁻, and CN⁻) did not cause any change in fluorescence spectra (S42−S45 Supporting Information).

Thus, these UV−vis and fluorescence changes indicate that protected terphenyl **3** can also be exploited for the development of fluoride sensor. In conclusion, we synthesized terphenyl based derivatives **3** and **4** responsible for the fluoride ion induced cyclization to symmetrically/unsymmetrically substituted triphenylenes in absence of any oxidizing reagent. Terphenyl derivative **3** is also found to be highly selective for fluoride ions over the other anions tested.

Supporting Information Available: Experimental procedure, characterization data including mp, ¹H, ¹³C and mass spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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