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# Photochemical Rearrangement of Calix[4]arene-Derived Bis(spirodienones): Formation of a New Macrocycle

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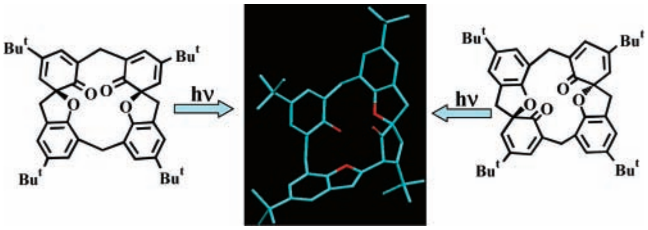
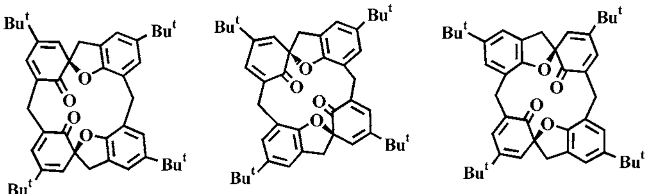
*Received October 27, 2006*



Bis(spirodienones) of calix[4]arene undergo a facile photochemical rearrangement leading to a new macrocycle having a spirocyclic cyclopentenone−THF unit, a trisubstituted phenol, and a benzofuran moiety. The macrocyclic ring system has a 14-membered irregular cavity and resembles a partial bowl in the solid state.

Calixarenes[1] constitute an important class of macrocycles in the realm of host−guest chemistry. They have a unique electron-rich, cavity-shaped architecture, and their ability to be functionalized by anchoring reactive groups either at their lower or upper rim has generated considerable interest in the design of selective receptors. As significant changes in the chemical and physical properties can be brought to calixarenes by functionalizing them, they have been widely used as three-dimensional building blocks for the design of selective receptors for anions, cations, and even neutral molecules.[2,3] An interesting molecular skeleton based on calixarene was obtained by the mild oxidative cyclization of adjacent phenolic hydroxyls by Biali et al.[4−9] These molecules **1a**−**c** (Figure 1) are bestowed with carbonyl and ether linkages in an alternant/nonalternant fashion as part of a 14-membered cavity making them potential candidates as ionophores or as precursors for designing modified calixarenes. The two cyclohexadienone rings attached to a five-membered cyclic ether ring through a spirocenter in these molecules can be valuable routes for functionalization of the calixarene skeleton and design of new macrostructures. Our results have shown that they are excellent substrates for Diels−Alder cycloaddition and show different trends in reactivity profile behaving as 4$\pi$ component with acetylenes[10] and double-bonded systems and as 2$\pi$ components with 1,2-benzoquinones.[11]



**1a** **1b** **1c**

**FIGURE 1.** Oxidative cyclization products of *p-tert*-butylcalix[4]arene.

The participation of bis(spirodienone) **1b** as a 2$\pi$ component in cycloaddition reactions prompted the investigation of its cycloaddition under photochemical conditions. Accordingly, we irradiated solutions of **1a** and **1b** with dimethyl acetylenedicarboxylate (DMAD) in dry acetonitrile at $\lambda$ 300 nm in separate experiments. Both reactions afforded the same product **2** in 45% and 50% yields, respectively. Cycloaddition did not take place under the experimental conditions and the DMAD was recovered quantitatively from the reaction mixture. The investigations on the structural elucidation of the product revealed the formation of an interesting macrocycle in good yield through a photoinduced radical rearrangement of **1a**/**1b**. The results are being discussed in detail in this note.

The bis(spirodienones) **1a** and **1b** were prepared as reported in the literature.[4] Degassed solutions of **1a** and **1b** in acetonitrile were irradiated at 300 nm separately in a photochemical reactor (Scheme 1). During the course of 3 h, the original yellow solutions gradually turned colorless. After workup and column chromatography, a single product was isolated from each reaction mixture and assigned the structure **2** by detailed spectral analysis.

The compound **2** exhibited a well-defined $^1$H NMR spectrum in full agreement with the molecular structure. Protons of one of the methylene groups resonated as a broad singlet at $\delta$ 3.21.

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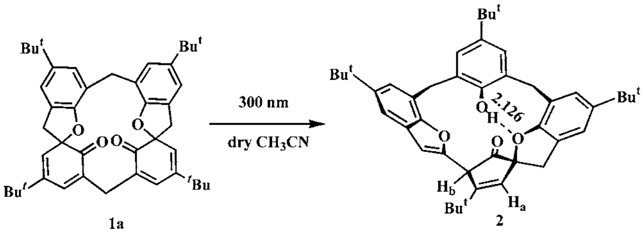
10.1021/jo062231f CCC: $37.00

**SCHEME 1. Photochemical Rearrangement of 1a**



Each set of protons of the other two methylene groups exhibited diastereotopicity and appeared as AB systems at $\delta$ 4.98 and 3.44 ($J = 13.5$ Hz) and at $\delta$ 4.26 and 3.44 ($J = 14.4$ Hz). The presence of the three methylene carbons was further confirmed by DEPT experiments. The proton $H_a$ resonated at $\delta$ 6.18 as a close doublet ($J = 1.8$ Hz) and showed allylic coupling with $H_b$ which resonated at $\delta$ 4.19 ($J = 1.8$ Hz). The singlet at $\delta$ 6.58 which readily underwent deuterium exchange was assigned to the phenolic hydroxyl group. In the IR spectrum, the cyclopentenone carbonyl was discernible at 1766 cm$^{-1}$. The $^{13}$C NMR spectrum displayed the characteristic signal for the carbonyl carbon at $\delta$ 206.0 and the spiro carbon at $\delta$ 89.9. The FAB mass spectrum exhibited the (M + 1) peak at $m/z$ 645, the same as that of the parent compound.

**X-ray Structure Analysis.** Single crystals of suitable quality were obtained by slow evaporation of an ethyl acetate solution of **2**, and final confirmation of the structure was obtained by X-ray analysis (Figure 2, a).[12] The molecule in the solid state assumes a cup-shaped architecture due to strong hydrogen bonding between the phenolic hydroxyl and the tetrahydrofuranoyl oxygen (09) (O---H = 2.126 Å). The crystal packing exhibited "stacked bowl" like arrangement in a linear direction with an ethyl acetate molecule juxtaposed between two bowls (Figure 2, b).

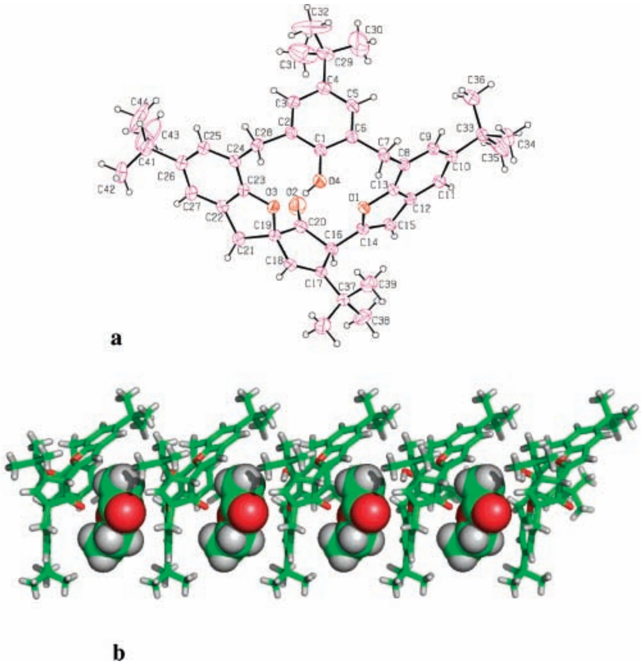


**FIGURE 2.** (a) ORTEP diagram of **2**. (b) Packing diagram of **2** resembling a stacked bowl architecture entrapping ethyl acetate molecules in between.

In the normal course, linearly conjugated cyclohexadienones on photolysis undergo ring-opening, giving rise to an unsaturated ketene which can be trapped by a good nucleophile like an amine.[13] In the absence of such a nucleophile, the ketene either reverts back to the original cyclohexa-2,4-dienone or undergoes cyclization to yield bicyclo[3.1.0]hex-3-en-2-one. But in this case, we were not able to detect the formation of a ketene intermediate spectroscopically. In order to obtain information on the reaction mechanism of the photochemical rearrangement of **1a** containing two such cyclohexa-2, 4-dienone units, irradiation experiments were carried out at $\lambda$ 300 nm in the NMR tube. A solution of **1a** in CDCl$_3$ was irradiated at intervals of 1, 2, 3, 4, 5, 10, 15, 20, 25, 30, and 35 min, and after each irradiation, the $^1$H NMR spectrum was recorded (Figure 3). The methylene protons of **1b** began to appear soon after the first irradiation and the isomerization to **1b** progressed after successive irradiations, indicating that the rearrangement is taking place through the intermediacy of **1b**. After 15 min, the spectrum appeared very complicated.

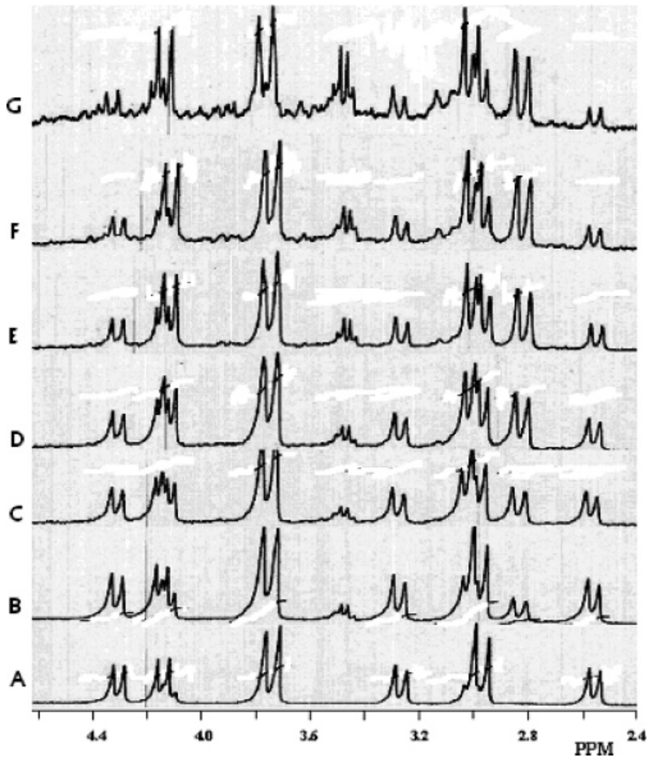
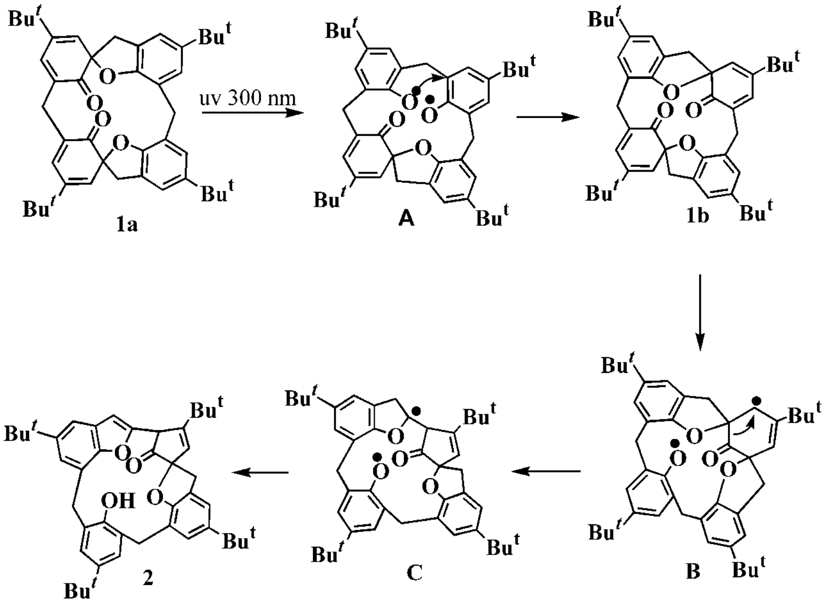


**FIGURE 3.** (A) $^1$H NMR spectrum of the methylene region of **1a**: (B) after 1 min of UV irradiation; (C) after 3 min; (D) after 4 min; (E) after 5 min; (F) after 10 min; (G) 15 min; in CDCl$_3$. The doublets at $\delta$ 4.12, 3.75, 3.00, 2.82 correspond to the isomer **1b** and are formed by the slow isomerization of **1a**.

Keeping with this finding, a possible mechanism has been proposed for the photochemical rearrangement (Scheme 2). The molecule absorbs a photon, and the spirocarbon C(sp3)−O bond undergoes photochemical cleavage in the initial step leading to the formation of two phenoxy radicals, the driving force for this cleavage being the aromatization of the ring and the ensuing stability of the radical. Regeneration of the C−O bond occurs with reversal of the directionality of the spirodienone moiety leading to the formation of the most stable isomer **1b**. Further rearrangement and ring contraction leads to the formation of a cyclopentenone ring (C), followed by hydrogen abstraction forms the final product **2**. $^1$H NMR studies showed that even though the isomerization of **1a** to **1b** is almost quantitative, further radical cleavage and rearrangement leading to the product

**SCHEME 2. Proposed Mechanism for the Photochemical Rearrangement of 1a to 2 via 1b**



is not taking place in a quantitative manner. It is also noted that **2** is the only isolable product in the rearrangement. In order to look into the mechanistic details, we have carried out the reaction in the presence of oxygen and a radical scavenger, tri-*n*-butyltin hydride. In the presence of oxygen, the reaction did not take place and more than 80% of the starting material (**1a** and **1b**) was recovered. This suggested that the transformation from **1a** to **A** most probably involved a triplet intermediate which is quenched by oxygen. In the presence of tri-*n*-butyltin hydride, 23% of the product and 15% of **1a** were isolated, the remaining being intractable material. This suggested that radicals are definitely involved in the reaction. Further experiments will be carried out to look into the detailed mechanistic aspects.

In conclusion, we have unravelled a photochemical rearrangement by which the calix[4]arene-derived bis(spirodienones) of *p*-*tert*-butylcalix[4]arene can be converted to a highly functionalized new macrocycle having a spirocyclic cyclopentenone−THF unit, a trisubstituted phenol, and a benzofuran moiety.

## Experimental Section

A solution of calix[4]bis(spirodienone) **1a** (50 mg, 0.0778 mmol) in dry acetonitrile (5 mL), after purging with dry $N_2$ gas, was irradiated in a photochemical reactor at $\lambda$ 300 nm. The initial yellow solution gradually turned colorless, and the reaction was stopped after 3 h when TLC (10% ethyl acetate−hexanes) indicated the complete absence of **1a**. The reaction mixture was concentrated in vacuo, and the crude product was purified by column chromatography on silica gel (5% ethyl acetate−hexane) to get a colorless solid (50% yield): mp dec above 160 °C; IR (KBr) $\nu_{max}$ 3440, 2956, 1766, 1597, 1480, 1359, 1186 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$, rt) $\delta$ 7.31 (d, $J = 6.1$ Hz, 2H), 7.11 (s, 1H), 7.04 (s, 1H), 6.89 (d, $J = 9.7$ Hz, 2H), 6.58 (s, 1H), 6.37 (s, 1H), 6.18 (d, $J = 1.8$ Hz, 1H), 4.98 (d, $J = 13.5$ Hz, 1H), 4.26 (d, $J = 14.4$ Hz, 1H), 4.19 (d, $J = 1.8$ Hz, 1H), 3.44 (uneven t, $J_1 = 14.4$ Hz, $J_2 = 13.5$ Hz, 2H), 3.27 (bs, 2H), 1.41 (s, 9H), 1.33 (s, 9H), 1.11 (s, 18H); $^{13}$C NMR ($CDCl_3$) $\delta$ 206.8, 159.4, 153.2, 152.1, 151.9, 148.6, 145.7, 144.8, 143.7, 129.4, 127.4, 126.5, 125.8, 125.5, 125.2, 125.0, 122.9, 122.5, 119.8, 114.7, 106.8, 89.9, 51.0, 36.6, 34.5, 31.9, 31.8, 31.4, 28.7; FAB MS *m*/*z* calcd for $C_{44}H_{52}O_4$ 644, found 645 (M + 1).[12]

**Acknowledgment.** V.B.G. acknowledges the Council of Scientific and Industrial Research (CSIR), New Delhi for a research fellowship. We thank Professor M. V. George and Dr. K. R. Gopidas, Photosciences and Photonics Group, RRL, for valuable discussions. We also thank Ms. Soumini Mathew and Ms. S. Viji for recording NMR and mass spectra respectively.

**Supporting Information Available:** Experimental procedures proving radical hypothesis and all spectral data (UV−vis, $^1$H NMR, $^{13}$C NMR, DEPT 135, and DEPT 90) of **2**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(12) The crystal structure for compound **2** has been deposited at the Cambridge Crystallographic Data Centre and allocated the reference no. CCDC 291367.

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