β-Silyl Arenes in the Arene–Olefin Photocyclization Reaction

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This correspondence is dedicated to Professor Paul Wender on the occasion of his 60th birthday. Professor Wender’s pioneering total syntheses using arene–olefin photochemistry remain to this day as premier examples of the power of this transformation.

Abstract: The ‘β-silyl effect’ of ground-state chemistry has been found to be operative in excited-state systems as well, where it exerts just as remarkable of an effect on the yields and selectivity of the intermolecular arene–olefin photocyclization reaction. Benzyltrimethylsilane has been found to undergo intermolecular arene–olefin photocyclization with alicyclic hydrocarbon alkenes to provide 2,6-meta-adducts with yields of 65–90% in a regio- and stereoselective manner. Particularly encouraging are the reactions with cyclohexene and with cis-cyclooctene, as both of these substrates give anomalous results with many arenes, but fall perfectly in line when coupling with benzyltrimethylsilane. These data auger well for the use of β-silyl directing groups in more complex photocyclization reactions. The ability of a C–Si sp3 bond to stabilize an incipient positive charge in the β-position by hyperconjugation apparently also allows it to stabilize a transiently electron-deficient excited state, in the same way that an electron-donating group (e.g., a methyl or a methoxy group) has been observed to direct the regiochemistry of the arene–olefin photocyclization reaction. To fully characterize the photoadducts, they have been elaborated via radical addition of substituted thiophenols to crystalline compounds and X-ray crystal structures obtained.

Key words: photochemistry, cycloadditions, neighboring group effects, hyperconjugations, radical reactions

Scheme 1 Published arene–olefin photochemistry results

Benzyltrimethylsilane has been irradiated several times, but never under arene–olefin conditions. When irradiated in the presence of hydrogen bromide/bromine, it undergoes a slow, bromine-dependent desilation to give the parent toluene. When irradiated in the presence of titanium(IV) oxide, it undergoes a transition-metal-catalyzed dimerization to the dihydrostilbene skeleton. We investigated its photochemical behavior as part of our program to broaden the scope of the arene–olefin intermolecular photocyclization reaction, and Table 1 presents some results of our studies. We have found that placement of the β-silicon group on an arene allows for the smooth formation of single products in high yield with the series of cycloalkenes from C5 to C8.

We theorize that the placement of a silicon atom in the β-position relative to the aryl ring allows the polarizable C(sp3)–Si(sp3) bond to overlap with the excited-state electron-deficient aromatic system thus facilitating the electronic and geometric changes that occur as the aromaticity is broken. During this process, the carbon containing the directing group bends out-of-plane, as does its electron cloud, creating a transient, isolated p-orbital before recombining with the incipient allyl radical on the other end.

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of the arene skeleton as the [5+2] addition completes, giving the vinylcyclopropane skeleton of the product (Scheme 2). Since an isolated p-orbital is neutral as well as electron-deficient, there need not be invoked an ‘incipient positive charge’ the stabilization of which directs the course of the reaction, as proposed by Srinivassian to explain the then-remarkable directing effects of the methoxy group. The argument for the existence of transient cation or a charge-separated intermediate has been controversial since the arene–olefin reaction has no significant solvent effect, as might be expected if there were a charge-separated intermediate. Further, Sheridan has shown that dinitrogen expulsion to give the diradical equivalent of a putative diradical transition state of an arene–olefin reaction, gives product ratios identical to the photolytic ones. However the Yamamura group at Keio University has also shown that they can induce an arene–olefin-like cyclization of phenols via an oxidation of phenol, presumably going through a radical cation. Further, Büchi and Chu, in their total synthesis of gymnominol, found that Lewis acids could initiate a 2,6-meta-addition of a disubstituted cyclopentene with a quinone. Thus the stabilization of an electron-deficient, but not necessarily cationic, intermediate is supported by the discovery that the β-silicon stabilization effect is operative in the arene–olefin photocyclization reaction.

Table 1  Product of β-Silylarene–Olefin Photolysis

<table>
<thead>
<tr>
<th>Entry</th>
<th>Arene</th>
<th>Olefin</th>
<th>Major product</th>
<th>Isolated yield (%)</th>
<th>Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image1.png" alt="Arene 1" /></td>
<td><img src="image2.png" alt="Olefin 1" /></td>
<td><img src="image3.png" alt="Product 1" /></td>
<td>80</td>
<td>endo/exo/minor</td>
</tr>
<tr>
<td>2</td>
<td><img src="image4.png" alt="Arene 2" /></td>
<td><img src="image5.png" alt="Olefin 2" /></td>
<td><img src="image6.png" alt="Product 2" /></td>
<td>78</td>
<td>endo/exo/minor</td>
</tr>
<tr>
<td>3</td>
<td><img src="image7.png" alt="Arene 3" /></td>
<td><img src="image8.png" alt="Olefin 3" /></td>
<td><img src="image9.png" alt="Product 3" /></td>
<td>81</td>
<td>endo/exo/minor</td>
</tr>
<tr>
<td>4</td>
<td><img src="image10.png" alt="Arene 4" /></td>
<td><img src="image11.png" alt="Olefin 4" /></td>
<td><img src="image12.png" alt="Product 4" /></td>
<td>93</td>
<td>endo/exo/minor</td>
</tr>
<tr>
<td>5</td>
<td><img src="image13.png" alt="Arene 5" /></td>
<td><img src="image14.png" alt="Olefin 5" /></td>
<td><img src="image15.png" alt="Product 5" /></td>
<td>65</td>
<td>endo/exo/minor</td>
</tr>
<tr>
<td>6</td>
<td><img src="image16.png" alt="Arene 6" /></td>
<td><img src="image17.png" alt="Olefin 6" /></td>
<td><img src="image18.png" alt="Product 6" /></td>
<td>89</td>
<td>endo/exo/minor</td>
</tr>
</tbody>
</table>
The presence of a β-silicon group has a powerful stabilization effect on the products of the photochemistry as well, allowing the reactions to be run to complete consumption of the starting arene without significant polymer formation. In contrast, the yields of many of the arene–olefin reactions that have been investigated decrease dramatically upon prolonged irradiation as intractable polymeric are formed.

Scheme 2 Reaction progress results in the formation of an isolated p-orbital

Understanding the reaction pattern of cyclohexene itself is difficult, e.g., it gives eight distinct products when irradiated with benzene and a 2,6-meta-adduct in merely 20% yield with anisole. In the β-silicon case, however, the reaction of cyclohexene gives a single product 2a in high yield (Table 1, entry 2). cis-Cyclooctene gave the corresponding product 4a in high yield as well, despite the fact that with tert-butylbenzene (Scheme 1) the major product is the 3,5-adduct. However, cis-cyclooctene did yield a 4:1 ratio of the expected endo-product and the exo-addition product, as the larger ring is apparently less subject to the steric restrictions that preclude an exo approach for the smaller rings. This loss of absolute endo selectivity with the larger cycloalkenes has been observed in their additions to anisole and toluene as well. Interestingly, cyclooctadiene (Table 1, entry 6) gives exclusively the endo-isomer 6a in excellent yield. This finding, combined with the ease of creating a photoadduct of cyclohexadiene (Table 1, entry 5), demonstrates that the functionality needed for further elaboration of these hydrocarbons can be easily introduced in the third, or ‘C’ ring. Attempts to introduce functionality into the central, or ‘B’ ring, however, have thus far resulted in the rearrangement of the photoadducts to exocyclic methylene-bicyclo[3.2.1]octene systems as shown in Scheme 3, the details of which will be published separately.

Placement of the silicon in the α-position (Table 1, entry 7) has quite the opposite effect, as multiple products were formed and no attempt was made to isolate them, although a pattern in the NMR which was consistent with the arene–olefin cycloadduct was discernable amidst the peaks. Placement of the silicon in the γ-position (Table 1, entries 8, 9) while less effective than the β-placement, still stabilizes the reaction sufficiently to allow for reasonable yields.

From the above data, the silicon-stabilization effect appears to be a reasonably general phenomenon when carbon is the adjacent atom, however, a β-silicon is also found in the photochemical substrate, (trimethylsilylarene–Olefin Photolysis (continued))

<table>
<thead>
<tr>
<th>Entry</th>
<th>Arene</th>
<th>Olefin</th>
<th>Major product</th>
<th>Isolated yielda (%)</th>
<th>Ratio b</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>8</td>
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<td>9</td>
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</tr>
</tbody>
</table>

a Yields of isolated material after one round of flash chromatography. Yields are considered in the context that the C5 and C6 adducts are volatile and all compounds are subject to polymerization and are inseparable at this point from trace (1–2% by NMR) isomers.

b By NMR.

c Tentative assignment.
d Not determined.
e Multiple inseparable products.
loxy)benzene, which was investigated by Mattay, and in that case the yields and the selectivities reported were poor even with cyclopentene. No other \( \beta \)-silyl compounds have been described to date. From a synthetic standpoint, a silyl group is an easily manipulated functional group. It may be replaced by a proton, alkyl groups, or oxygen. When treated with a source of fluoride, it may create a nucleophile that can react in high yield with proton sources, alkyl iodides and triflates, aldehydes, and ketones, as well as acylating groups such as acid chlorides and carbon dioxide.

The unstable photoadducts were elaborated to more stable compounds in order to properly characterize them and, in particular, to verify the \( \text{cis-syn-cis} \)-relationship of the rings that should arise as a result of the \( \text{endo} \) selectivity (Scheme 4). The regio- and stereospecific addition of free radicals to the top face of the vinyl cyclopropanes formed in the reaction was used to add substituted thiophenols to the \( \text{exo} \) face of the vinylcyclopropane, at first following a protocol in refluxing acetonitrile with benzoyl peroxide, then in a ‘green’ fashion of solventless reaction in air at

**Table 2** Formation of Stabilized Products for X-ray Crystallography

<table>
<thead>
<tr>
<th>Entry</th>
<th>Photoadduct</th>
<th>Thiol</th>
<th>Product</th>
<th>Crystal structure</th>
</tr>
</thead>
<tbody>
<tr>
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<td><img src="image1.png" alt="Image" /></td>
<td>1a</td>
<td><img src="image2.png" alt="Image" /></td>
<td>1b</td>
</tr>
<tr>
<td>2</td>
<td><img src="image3.png" alt="Image" /></td>
<td>2a</td>
<td><img src="image4.png" alt="Image" /></td>
<td>2b</td>
</tr>
<tr>
<td>3</td>
<td><img src="image5.png" alt="Image" /></td>
<td>3a</td>
<td><img src="image6.png" alt="Image" /></td>
<td>3b</td>
</tr>
<tr>
<td>4</td>
<td><img src="image7.png" alt="Image" /></td>
<td>4a</td>
<td><img src="image8.png" alt="Image" /></td>
<td>4b</td>
</tr>
</tbody>
</table>
room temperature with 1–2.2 equivalents of the neat thiophenol. These reactions gave adducts which, either as the sulfide, or as the sulfone derivative, were crystalline solids which were suitable for X-ray crystallographic analysis. The products (Table 2) could thus be easily purified and are stable. Extensive NMR analysis (for numbering, see Figure 1), coupled with the crystallography confirmed the initial assignments of endo-selective addition products leading to a cis-syn-cis geometry (Table 2).

In summary, the arene–olefin photochemical cycloaddition reaction has a new substrate, benzyltrimethylsilane. It reacts with cycloalkenes in a consistent manner, giving good yields and predominantly single products, even with problematical cyclohexene and cis-cyclooctene. These yields dispel the thought that the anomalous reactivity of cyclohexene in meta photocycloaddition, attributable to sterically unfavored ‘chair’ conformations of the cycloalkene, is unavoidable. The improvement is attributed to the effect of the silicon atom at the β-position of the system, stabilizing an electron-deficient early transition state. The scope of this stabilization and its implications for natural product synthesis and medicinal chemistry are currently under further investigation.

Benzyltrimethylsilane (BTMS) and the cycloalkenes are all commercially available (Aldrich) and were used with no further purification. Flash chromatography refers to low-pressure column chromatography.

X-ray data for 1b, 2b, 3b, 4b were collected using a Bruker Smart Apex CCD area detector diffractometer and molybdenum radiation. The crystal was cooled to 120K during data collection using a Oxford Cryosystem. Data handling was done using: SMART (data collection), initial cell refinement, SAINT (data reduction), SADABS (absorption correction), and the SHELXTL programs (structure solution, refinement and molecular graphics preparation).

**Scheme 4** Elaboration to stable products

**Figure 1** Standard numbering for 1a, 2a, and systematic numbering of 1b

**Photolysis of Benzyltrimethylsilane and an Alkene; General Procedure A**

For small-scale reactions, BTMS (328 mg, 2.0 mmol) and the cyclic alkene (25 mL) were added to a sealable, base-washed, oven-dried quartz tube. The soln was purged with a gentle stream of either argon or N2 gas for 30 min and sealed. The flask was irradiated by a 450-W medium pressure Hanovia lamp through a Vycor filter. Irradiation times varied from 8 h to 37 h; the solns became pale yellow to dark yellow. The mixtures were filtered, concentrated under reduced pressure (133 mbar), and purified by flash chromatography (100% hexanes) to produce the isolated materials as given in the associated table. The products were pale yellow oils.

**Photolysis of Benzyltrimethylsilane and an Alkene; General Procedure B**

For large-scale reactions, BTMS (1.64 or 3.28 g) and the alkene (220 mL) were added to the quartz chamber. Otherwise the procedure was as for General Procedure A.

3-[(Trimethylsilyl)methyl]-cis-syn-cis-tetra-cyclo(6.3.0.02,4.03,7)undec-5-ene (1a)

Using General Procedure A with cyclopentene as the alkene, irradiation for 8 h gave a slightly yellow soln that was filtered, carefully concentrated (133 mbar; then 8 h at 1.33 mbar), and then purified by flash chromatography (Flash40 apparatus, Biotage AB, Uppsala, Sweden; hexanes) to give 1a as a pale yellow oil (370 mg, 80%).

1H NMR (300 MHz): δ = 5.67 (dd, J = 2.0, 5.6 Hz, 1 H, H5), 5.55, (dd, J = 2.4, 5.4 Hz, 1 H, H6), 3.27 (m, 1 H, H8), 2.98 (m, 1 H, H1), 2.6 (ddd, J = 2.5, 3.6, 6.6 Hz, 1 H, H7), 1.8 (m, 1 H), 1.2–1.6 (m, 7 H), 0.95 (s, 2 H), –0.50 (s, 9 H).

13C NMR (75 MHz): δ = 135.20 (C6), 131.26 (C5), 61.82 (C7), 58.36 (C8), 53.68 (C3), 49.83 (C1), 39.10 (C2), 38.28 (C4), 30.92 (C11), 30.08 (C10), 26.70 (C9), 22.53 (C12), –0.275 [Si(CH3)3].

3-[(Trimethylsilyl)methyl]-cis-syn-cis-tetra-cyclo(6.4.0.02,4.03,7)todec-5-ene (2a)

Following General Procedure A with cyclohexene as the alkene, 2a was obtained after chromatography as a volatile yellow oil (380 mg, 78%).

1H NMR (300 MHz): δ = 5.62 (s, 2 H, H5, H6), 2.59 (m, 2 H, H7, H8), 2.42 (m, 1 H, H1), 1.2–2.0 (m, 10 H), 0.99 (AB, J = 4.62, 3 H, 2 H), 0.03 [s, 9 H, Si(CH3)3].

13C NMR (75 MHz): δ = 135.01, 130.98, 60.77, 49.50, 49.20, 40.47, 39.75, 35.67, 28.85, 26.61, 24.89, 22.92, 22.34, –0.56.

3-(Trimethylsilylmethyl)-cis-syn-cis-tetra-cyclo(6.5.0.02,4.03)tridec-5-ene (3a)

Following General Procedure B with cycloheptene as the alkene and BTMS (3.28 g, 0.02 mol), 3a was obtained after chromatography as a pale yellow, volatile oil (4.23 g, 81%).

FT-IR: 2914, 2850, 1246 (s, Me-Si), 834, 801, 755, 688 cm–1.

1H NMR (500 MHz): δ = 5.68 (dd, J = 2.4, 5.7 Hz, 1 H, H5), 5.58 (dd, J = 5.7, 3.8, 2.0 Hz, 1 H, H6), 2.67 (m, 1 H, H8), 2.53 (m, 1
H, H7), 2.46 (m, 1 H, H11), 1.75 (m, 2 H, H11), 1.72 (m, 1 H, H1(α), 1.68 (m, 1 H, H12b), 1.55 (m, 1 H, H9a), 1.52 (complex t, 1 H, H2), 1.42 (dd, J = 5.0, 6.0 Hz, 1 H, H12a), 1.39 (dd, J = 2.5, 7.5 Hz, 1 H, H4), 1.15 (m, 1 H, H9b), 1.04 (m, 3 H, H13, H10b), 0.99 (AB, J = 15, 27.2 Hz, H2, H12), 0.05 [s, 9 H, Si(CH3)3].

13C NMR: δ = 133.91 (C6), 131.60 (C5), 59.30 (C7), 56.08 (C8), 54.66, 53.98, 36.58, 32.64, 30.97, 29.75, 29.60, 25.22, 24.46, 21.74, –0.57.

3-[3-(Trimethylsilyl)phenyl][3-cis-syn-cis-tetra-cyclo(6.6.0.02,6)tetradec-5-ene (5a)]

Following General Procedure A with cis-cyclooctene (Aldrich, 90%, remainder cyclooctene) as the alkene, the alkene was obtained after chromatography as a volatile, yellow oil (510 mg, 93%) as a 4:1 mixture.

1H NMR (500 MHz): δ = 5.75 (dd, 1 H, H5), 5.55 (dd, 1 H, H6), 2.62 (m, 1 H), 2.50 (m, 2 H), 2.2–1.2 (m, 14 H), 0.98 (AB, 2 H), 0.07 (s, 9 H).

13C NMR (125 MHz): δ = 132.13, 132.04, 65.55, 61.75, 56.47, 46.64, 45.88, 45.04, 36.38, 32.64, 30.97, 29.75, 29.60, 25.22, 24.46, 21.74, –0.57.

3-[3-(Trimethylsilyl)phenyl][3-cis-syn-cis-tetra-cyclo(6.4.0.02,4)tetradec-5-ene (5a)]

Following General Procedure A with cyclooctadiene, irradiation for 60 h led to 5a, which was obtained after chromatography as a volatile, yellow oil (320 mg, 65%).

FT-IR: 3018.7, 2896.9, 1679.6, 1435.5, 1246.5 (Me-Si), 995.8, 835.4, 755.7, 690.0 cm⁻¹.

1H NMR (300 MHz): δ = 5.68, (s, 1 H, H10), 5.61, (m, 2 H, H5, H11), 5.45, (d, 1 H, H6), 2.78 (m, 1 H, H8), 2.69 (m, 1 H, H7), 2.42 (m, 1 H, H1), 2.24 (m, 1 H, H12a), 2.20 (m, 1 H, H9a), 2.00 (m, 1 H, H9b), 1.93 (m, 1 H, H12b), 1.62 (m, 1 H, H2), 1.50 (d, 1 H, H4), 1.10, 0.93 (ABd, 2 H, H13), 0.03 (s, 9 H).

13C NMR (75 MHz): δ = 132.98 (C6), 131.59 (C5), 127.39 (C10), 125.03 (C11), 60.94 (C7), 48.71 (C8), 48.16 (C3), 41.85 (C2), 36.75 (C4), 34.14 (C1), 30.87 (C9), 25.68 (C12), 22.46 (C13), –0.21 [Si(CH3)3].

3-[3-(Trimethylsilyl)phenyl][3-cis-syn-cis-tetra-cyclo(6.6.0.02,6)tetradec-5-11-diene (6a)]

Following General Procedure A with cyclooctadiene (Aldrich) as the alkene, the alkene was obtained after chromatography as a pale yellow oil (480 mg, 89%).

1H NMR (500 MHz): δ = 5.69 (s, 1 H, H11), 5.63 (s, 1 H, H5), 5.58 (s, 1 H, H12), 5.47 (s, 1 H, H6), 2.78 (m, 1 H, H1), 2.60 (m, 1 H, H13a), 2.40 (d, J = 7.0 Hz, 1 H, H7), 2.37 (d, J = 1.0 Hz, 1 H), 2.17 (m, 1 H, H8), 2.10 (m, 2 H, H9a, H10b), 2.00 (m, 1 H, H14a), 1.82 (m, 1 H, H3b), 1.60 (m, 2 H, H2, H14b), 1.44 (m, 1 H, H4), 1.36 (m, 1 H, H9), 0.91, 1.06 (AB, J = 15.0 Hz, H15), 0.03 [s, 9 H, Si(CH3)3].

13C NMR (125 MHz): δ = 136.61 (C12), 132.49 (C11), 130.90 (C5), 129.43 (C6), 61.67 (C7), 57.39 (C8), 47.56 (C3), 42.17 (C2), 41.63 (C1), 36.96 (C4), 31.32 (C14), 29.86 (C10), 29.26 (C9), 26.06 (C13), 22.24 (C15), –0.182 [Si(CH3)3].

3-[2-(Trimethylsilyl)ethyl][3-cis-syn-cis-tetra-cyclo(6.3.0.02,6)undec-5-ene (8a)]

Following General Procedure A with trimethyl(propenyl)silane (2.0 mmol) as the silane, 8a was obtained after chromatography as a yellow oil (300 mg, 61%).

FT-IR: 2950, 1352, 1247, 1188, 1021, 861, 836, 758, 691 cm⁻¹.

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separatory funnel, where an additional portion of EtOAc–hexanes (95:5, 25 mL) was added. The soln was washed with 10% K2CO3 (3 × 100 mL), and brine (1 × 100 mL), and the combined aqueous layers back-extracted with EtOAc (1 × 25 mL). The combined organic layers were filtered (MgSO4), and concentrated. The crude isolate was dissolved in CH2Cl2 (50 mL) and MCPBA (65% pure peracid used as received, 2.1 equiv) were added. The material was subjected to flash column chromatography (glass column, 5% EtOAc–hexanes), and yielded product that was 95% pure (H NMR). This material was recrystallized (hexanes with a small amount of Et2O), giving material that was suitable for X-ray crystallographic analysis.

FT-IR: 2924, 2859, 1711, 1467, 1440, 1313, 1292, 1248 (Me-Si), 1149, 1115, 1083, 1015, 950, 842, 789, 766, 730, 694 cm–1.

MS: m/z (%) = 453.2 [M + Na]+ (100), 275.4 [M – MePhSO2]+ (30), 242.2, 201.4, 139.2.


Anal. Calcld for C23H33O2SSi: C, 68.89; H, 8.58.

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