

Irradiation of an aryl group with a silyl tethered alkene yields a tetracyclic 2-siloxane with high regioselectivity. The multicyclic structure has been further modified to give an unstable tricyclic diol. Photocycloaddition between cyclopentene and phenylcyclopropane gave a single major cycloadduct without cyclopropyl ring opening, indicating that the putative radical intermediate involved in cycloaddition apparently has a very short lifetime if it exists at all.

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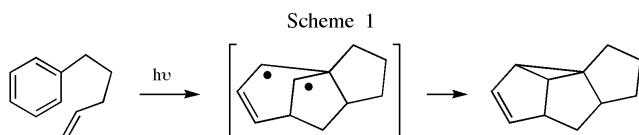
Introduction.

We have been interested in photochemical reactions involving tethered systems for the development of synthetic methodology that can be exploited in the synthesis of complex molecules [1]. Recent literature is replete with examples of using light-induced reactions for the ultimate synthesis of unnatural and natural compounds [2]. There is great potential for using controlled photochemical cycloadditions in synthesis of complex compounds because the cycloadditions typically introduce numerous carbon-carbon bonds in a single step.

Analysis of photocycloadditions that are concerted shows that control of the conformation and proximity of the tethered chromophore and its addend can allow for significant enhancement in the formation of a single product. Even photoadditions that are stepwise (*e.g.*, triplet photochemical reactions) can be controlled by tethering. In this case, the design of the reaction suggests that if formation of the first bond is controlled then the subsequent bonds can be predicted based on steric factors.

One of the most synthetically useful photochemical reactions has been the 1,3 photocycloaddition (the arene-olefin or *meta* photocycloaddition). This reaction has been investigated by many groups [3]. The use of tethering has contributed to the value of this reaction, for example, it is known that the three-atom tether is preferred in the 1,3-cycloaddition and the yields for these intramolecular reactions are typically in the 80% range. This is presumably due to the efficient overlap between the chromophore and the alkene which facilitates formation of a necessary exciplex. A tether that is removable after the reaction has been carried out would be a significant advance in the synthetic methodology of this photocycloaddition.

The mechanism of this reaction is presumed to involve a diradical intermediate that results from initial addition of the alkene across the aromatic ring in a 1,3 (or 2,6 depending on the substituents on the ring) fashion as shown in Scheme 1.



There is evidence that this intermediate is dipolar in nature. Evidence of the diradical intermediate would be a significant advance in our understanding of this reaction.

Results.

In this paper we describe the use of silicon as a temporary tether in intramolecular 1,3 photocycloaddition which allows for the synthesis of the 2-siloxane ring system. We also report our attempt to observe the diradical intermediate of this type of cycloaddition.

Our studies in the area of silicon tethered 2+2 photocycloadditions led us to an attempt of the Paterno-Büchi photocycloaddition between a tethered alkene and *o*-hydroxyacetophenone. We observed that a minor product from this reaction was a heterocyclic compound that appeared to be the result of an intramolecular 1,3-photocycloaddition between the alkene and the aromatic ring. This prompted us to examine the photochemistry of just phenol tethered to an alkene since the carbonyl portion of *o*-hydroxyacetophenone undoubtedly results in formation of the triplet excited state and the standard 1,3-photocycloaddition is a singlet process [3]. Indeed, we found that a good yield of a 1,3-photocycloadduct is obtained from irradiation of allylphenoxydimethylsilane (**1**).

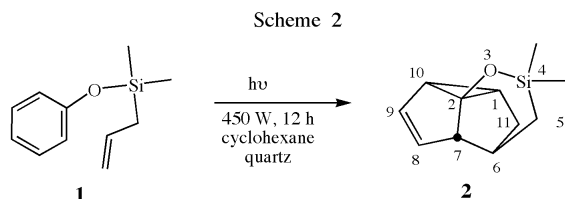
Synthesis of the silyl compound **1** was accomplished in one step by silylation of phenol with allyl-dimethylchlorosilane under standard conditions. Irradiation of this compound resulted in a 52% conversion to a major product, the tetracyclic 2-siloxane **2** (see Scheme 2). The relative stereochemistry of the heterocyclic product was verified by 500 MHz 2-D nmr analysis including COSY and HETCOR experiments. Comparison with previously reported 1,3-photocycloadducts was very helpful in the assignment of this structure [4].

There are several potential cycloaddition products but each of the alternative structures has characteristic nmr signals which are not consistent with the observed compound. For example, we initially thought that the alkene addition occurred across the 1,3 position of the aromatic ring which would produce the linear tetracyclic product similar to that shown in Scheme 1. This structure was ruled out by the signal for one of the C-11 hydrogens (see Scheme 2) that is coupled to both cyclopropyl hydrogens;

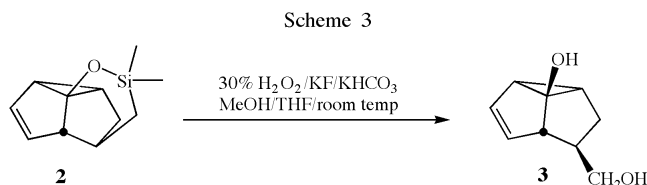
one by W-coupling and the other by vicinal coupling. The linear molecule would not have shown coupling between the methylene and the cyclopropyl hydrogens.

It is also interesting to note that the photocyclization appears to occur *via* an alkoxy stabilized radical or zwitterionic intermediate. The regiochemistry of the observed product is consistent with a stepwise-like (nonsynchronous) mechanism which has been proposed for this photocycloaddition and favors oxygen substitution at the low electron density center [5]. In addition, Gilbert has recently reported 1,3-photocycloaddition on an organosilane with regioselectivity that presumably arises from silicon stabilization of a β positive charge in the transition state [4,6]. Thus, both the oxygen and the silicon groups would favor the intermediate being zwitterionic with the positive center at the *ipso* carbon.

This example with silicon-oxygen attachment demonstrates the regioselectivity that can be obtained, it is also the first example of using a silicon tether as a removable group following the cycloaddition. This is a powerful tool in synthetic applications because there are five contiguous stereocenters that are formed with regio- and stereocontrol in one step. These centers are maintained following removal of the tethering group.



There are a number of potential manipulations that can be considered for this complex tetracyclic silane. For example, Tamao-Fleming oxidation [7] with hydrogen peroxide allowed conversion to the diol **3** (see Scheme 3).

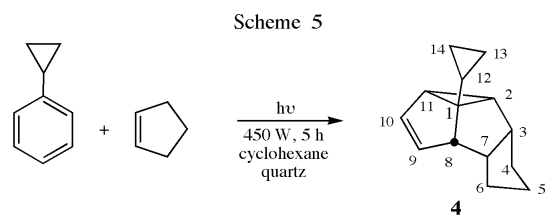


This relatively unstable compound has five contiguous stereocenters, an alkene for further modification, a primary alcohol, and a tertiary alcohol.

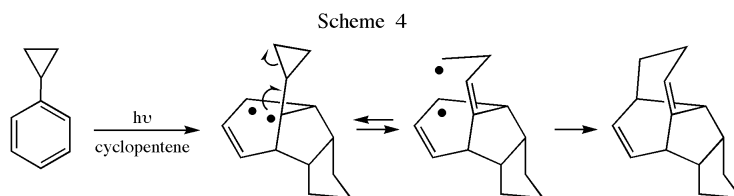
Based on the results of this siloxy tethered cycloaddition, we questioned if there is any diradical nature in the intermediate of the 1,3-photocyclization [8]. A long-lived diradical should be sensitive to *ipso* cyclopropyl substitution. So we reasoned that irradiation of phenylcyclopropane in the presence of an alkene would result in cyclopropyl ring-opened products if the diradical intermediate is involved in the reaction as shown in Scheme 4.

We have explored the photocycloaddition in excess cyclopentene as our test for ring opened photoproducts which one would predict as a result of a radical intermediate having a lifetime on the order of 10^{-8} s or more [9]. In this system, closure of the ring-opened diradical would give a bridgehead alkene with a *trans* substituted eight member ring [10] and, significantly, no cyclopropyl rings [10] and, significantly, no cyclopropyl rings (see Scheme 4). Although the ring opened photoproduct may be relatively unstable due to the bridgehead alkene, we predicted that we would be able to observe it or an alkene shifted by-product if the cyclopropyl ring opened.

Irradiation of phenylcyclopropane in the presence of a 10-fold excess of cyclopentene in photograde cyclohexane was performed using an Ace Glass Thin-Film Reactor. The estimated conversion for these conditions is 25%. One major product (>80% of tractable material) was obtained and identified as the non ring-opened photoproduct **4** (see Scheme 5). Spectral analysis of this compound is consistent with previously reported toluene + cyclopentene photoadducts [11].



The results do not completely rule out the reversible ring opening process shown in Scheme 4. However, a plausible explanation based on our observation is that the 1,3-photocycloaddition is dipolar in nature rather than radicaloid. This is consistent with previous mechanistic analysis of this cycloaddition [12]. The alkoxy substituent, in particular,



is ideally suited for stabilizing a partial positive charge at the *ipso* position that is presumably generated upon excitation. We have previously reported the results of MOPAC calculations that support such an intermediate for the irradiation of anisole [13]. More recently, Pincock has convincing evidence for an analogous species from excitation of substituted benzonitriles [14]. For the nitrile substituted aryl group, the polarization favors a partial negative charge at the *ipso* position.

The dipolar reactive intermediate explains the high regioselectivity observed in the silyl tethered phenoxy cyclization and the lack of cyclopropyl ring-opened product. We are continuing our investigation in this area.

EXPERIMENTAL

General.

All solvents used were reagent grade and used as purchased except for tetrahydrofuran (THF) and cyclohexane. THF was distilled over Na metal and benzophenone. Reagent grade cyclohexane (1.5 L) was washed with an equal volume of concentrated H₂SO₄ and HNO₃ three times (200 mL each time). Then the cyclohexane was washed with 200 mL of dilute aqueous KMnO₄ and then 200 mL of water. The cyclohexane was dried over CaCl₂ before being passed through an activated basic alumina column and then distilled over CaCl₂ to obtain photograde cyclohexane.

All reactions were run under nitrogen. Chromatography was performed using Silica Gel 60 (230-400 mesh) on a gravity column or a chromatotron made by Harrison Research. The chromatotron is a rotating chromatography disk that allows detection and separation of 25-200 mg quantities.

Nuclear magnetic resonance (nmr) spectra were obtained either on a Varian Gemini 200 MHz, a Varian Inova 300 MHz, or a Varian Unity 500 MHz spectrometer. Chemical shifts reported are ppm downfield from tetramethylsilane (TMS). High resolution mass spectra (hrms) were determined on a JEOL-SX102A mass spectrometer using direct probe sample introduction.

Irradiations were performed using a Hanovia 450 W medium pressure mercury lamp in a water-cooled quartz well. All irradiations were deoxygenated by bubbling purified nitrogen gas through the reaction solution for 10 minutes before irradiation and continuing through the time of the reaction. The nitrogen was purified by passing it through an Ace-Burlitch inert atmosphere system containing a column packed with a BASF R3-11 catalyst followed by another column packed with Aquasorb® drying agent.

Allyldimethylphenoxysilane (1).

The reaction of allylchlorodimethylsilane with phenol under standard conditions (NET₃, CH₂Cl₂, -78 °C to room temperature, 8 hours) gave an 80% yield of allyldimethylphenoxysilane following distillation, b.p. 60 °C/1.0 Torr (Kugelrohr). ¹H nmr (200 MHz, deuteriochloroform): δ 6.8-7.4 (m, 5H, aromatic H), 5.80 (m, 1H, vinylic H), 4.95 (m, 2 H, vinylic H), 1.80 (d, J = 8 Hz, 2H, allylic H), 0.30 (s, 6H, 2 x Si-CH₃); ¹³C nmr (50 MHz, CDCl₃) 154, 133, 129, 121, 120, 120, 115, 114, 24, -2; ir (neat) 2960, 1630, 1596, 1491, 1253, 1164, 1070 cm⁻¹; hrms m/z calc. 192.0970, obs. 192.0966.

Anal. Calcd. for C₁₁H₁₆OSi: C, 68.69; H, 8.39. Found: C, 68.50; H, 8.29.

3-Oxa-4-sila-4,4-dimethyltetracyclo[4.4.1.0^{2,7}.0^{2,10}]dec-8-ene (2).

Irradiation of allyldimethylphenoxysilane (107 mg) in 120 mL cyclohexane (4.6 x 10⁻³ M) for 12 hours was followed by concentration. Chromatography (pentane:EtOAc 25:1) of the photomixture gave 55.7 mg of tetracyclic siloxane **2**, b.p. 60 °C/1.0 Torr (Kugelrohr). ¹H nmr (200 MHz, deuteriochloroform): δ 5.59 (dd, 1H, H-9), 5.52 (ddd, 1H, H-8), 2.77 (bd, 1H, H-10), 2.63 (m, 1H, H-7), 2.61 (m, 1H, H-6), 1.66 (m, 1H, H-11), 1.57 (dd, 1H, H-11'), 1.44 (ddt, 1H, H-1), 1.09 (ddd, 1H, H-5), 0.68 (dd, 1H, 1 H, H-5'), 0.30 (s, 3H, Si-CH₃), 0.25 (s, 3H, Si-CH₃); ¹³C nmr (50 MHz, deuteriochloroform) 129, 127, 88, 70, 62, 50, 41, 29, 21, -1. COSY and HETCOR at 500 MHz confirm these assignments. hrms m/z calc. 192.0970, obs. 192.0978.

Anal. Calcd. for C₁₁H₁₆OSi: C, 68.69; H, 8.39. Found: C, 68.46; H, 8.50.

6-Hydroxymethyltricyclo[3.3.0.0^{2,8}]oct-3-en-1-ol (3).

In 11.6 mL of 1:1 THF and methanol was dissolved 280 mg (1.45 mmol) of 2-siloxane. To this was added 0.12 g of potassium bicarbonate, 0.296 mL of hydrogen peroxide, and 0.51 g of potassium fluoride. The reaction stirred at room temperature for 18 hours then was extracted with chloroform. The organic layer was concentrated and the crude material was analyzed by nmr. Chromatographic purification gave a poor yield (<5%) of the unstable diol. ¹H nmr (200 MHz, deuteriochloroform): δ 5.55 (bs, 2H, H-9), 3.95 (m, 2H, CH₂O), 3.2 (bs, 2H, -OH), 2.1 (m, 1H), 1.9 (m, 5H).

1-Cyclopropyltetracyclo[6.3.0.0^{2,11}.0^{3,7}]undec-9-ene (4).

Phenylcyclopropane and cyclopentene (1:10 molar equivalent) were added to 200 mL of cyclohexane (0.1 M phenylcyclopropane in cyclohexane) and circulated through a Thin-Film Reactor. After 5 hours of irradiation with a 450 W Hg lamp, the mixture was evaporated and chromatographed. The percent conversion based on unreacted phenylcyclopropane was typically 25%. The only product that is obtained in sufficient quantity to be identified is the cyclic compound **4** which is formed in >80% based on the converted phenylcyclopropane.

The data for **4** are: ¹H nmr (500 MHz, deuteriochloroform): δ 5.70 (d, 1H, H-10), 5.63 (d, 1H, H-9), 3.20 (m, 1H, H-7), 2.86 (dt, 1H, H-3), 2.81 (d, 1H, H-8), 1.82 (m, 1H, H-6), 1.65 (m, 2H, H-4, H-6'), 1.52 (d, 1H, H-11), 1.43 (m, 2H, H-2, H-4'), 1.40 (t, 2H, H-5), 1.21 (dt, 1H, H-12), 0.40 (m, 2H, H-13, H-14), 0.10 (m, 2 H, H-13', H-14'); ¹³C nmr (50 MHz, deuteriochloroform) 135.5, 130.6, 62.1, 58.4, 57.6, 49.5, 35.8, 34.8, 30.5, 29.8, 26.2, 12.0, 2.7, 2.3. COSY, HETCOR, and NOESY on a 500 MHz confirm the assignments.

Anal. Calcd. for C₁₄H₁₈: C, 90.26; H, 9.74. Found: C, 90.12; H, 9.40.

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