

PHOTOCHEMICAL ACTIVATION OF TRIMETHYLSILYLMETHYL ALLYLIC SULFONES FOR INTRAMOLECULAR 4+3 CYCLOADDITION

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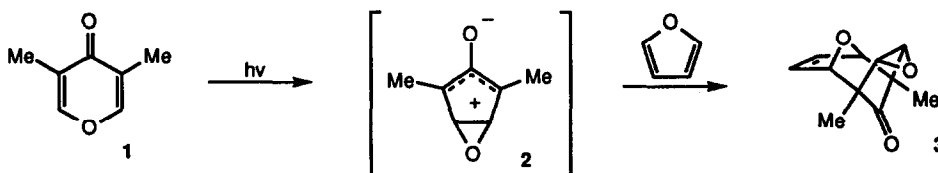
Summary: Irradiation of allylic sulfones 4-7 results in the formation of 4+3 cycloadducts 8-11. Although the yields are poor, this represents the first apparent photochemical generation of acyclic allylic cations for 4+3 cycloadditions. Mechanistically, this process is interpreted as an electron transfer process to form an internal radical cation/radical anion reactive intermediate. This eliminates p-tolylsulfinate anion to form an allylic cation which undergoes an intramolecular 4+3 cycloaddition.

The intermolecular 4+3 cycloaddition of allylic cations or their synthetic equivalents with dienes is well established.¹ Considerable but not exhaustive use has been made of this reaction in the synthesis of natural and unnatural products.^{1b}

Much less work has been done on the intramolecular version of this reaction.² Unlike the electronically related intramolecular Diels-Alder reaction,³ the intramolecular 4+3 cycloaddition reaction has been little studied from a fundamental viewpoint and seldom applied to total synthesis.

As part of a comprehensive program designed to establish the intramolecular 4+3 cycloaddition reaction as a viable tool in organic synthesis, we have been investigating development of new methodology for this reaction and studying mechanistic issues, particularly those involving stereochemistry.⁴

The generation of allylic cations used in 4+3 cycloadditions has traditionally centered on chemically-induced heterolysis of allylic carbon-heteroatom bonds. Oxyallylic zwitterions useful for 4+3 cycloadditions have been generated photochemically, but this typically involves electrocyclic ring closure of cross-conjugated dienones and results in the generation of polycyclic and often highly functionalized oxyallyls. For example,

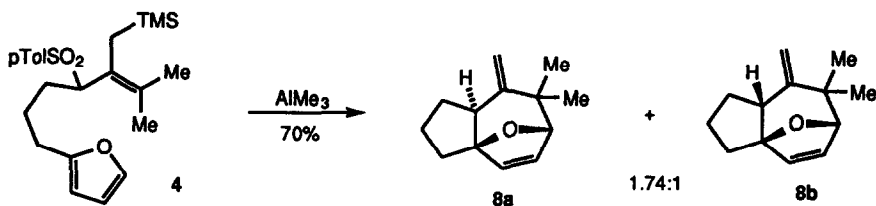


Equation 1

some time ago Barltrop reported that photolysis of pyranone 1 in the presence of furan gave the 4+3 cycloadduct

3 in low yield.⁵ Investigations of the intramolecular version of this process by West's group are proving fruitful.⁶

Recently, we reported that treatment of trimethylsilylmethyl allylic sulfones with Lewis acids results in the formation of 4+3 cycloadducts in reasonable yield (Equation 2).^{4f} Inspired by the seminal contributions of



Equation 2

Mariano in the area of photochemically mediated electron transfer processes,⁷ we reasoned that a compound such as 4 might be a suitable substrate for such a process and proceeded to test this idea.

The results of this study are shown in Table 1. While the yields are not very high, this is the first example of

Table 1. Photochemical Conversion of 4 to 8a and 8b: Optimization Studies.

Entry	Light (nm) ^a	Time (hr)	T ^o C ^d	Conc. [M]	Solvent	Yield(%) ^e	Ratio (8a:8b) ^h
1	254/Vycor ^b	2.5	35	0.5	MeCN	13(24)	1:6.5
2	254	17.3	52	0.2	MeCN	34	1:8.1
3	254	2.2	52	0.1	MeCN	20(34)	1:8.7
4	254/Vycor	2.4	52	0.05	MeCN	30	1:8.4
5	254/Vycor	3.5	52	0.02	MeCN	27	1:9 ^g
6	254/Vycor	5	52	0.01	MeCN	22	0:1 ^g
7	254/Vycor	2.5	35	0.005	MeCN	0	f
8	254/Vycor	3.5	43	0.05	Acetone	26	1:5.2
9	254/Vycor	2.5	45	0.05	Benzene	f	1:3.8
10	254/Vycor	9.5	47	0.05	MeOH	30	1:7.8
11	254/Vycor	2.5	35	0.05	CH ₂ Cl ₂	20(32)	1:1.5
12	254/Vycor	2.5	43	0.05	Ether (1 eq. LiClO ₄)	8	1:7.7
13	254/Vycor	2.5	34	0.05	Ether (5 eq. LiClO ₄)	24(28)	1:8.8
14	254/Vycor	2.5	34	0.05	Ether (1 M LiClO ₄)	8(11)	1:7.1
15	254/Vycor	2.5	32	0.05	Ether (5 M LiClO ₄)	12(14)	f
16	254	2.5	10	0.05	MeCN	19(27)	1:5.6
17	254/Vycor	2.5	35	0.05	MeCN	35(56)	1:7.8
18	254 ^c	2.5	35	0.05	MeCN	23(27)	1:7.5

^aRayonet reactor, quartz reaction vessel. ^bVycor tube surrounding reaction vessel. ^cChemical filter: 5g dihydropyran in 1L isooctane. ^dAir temperature within reactor. ^eYields in parentheses based on recovered starting material. ^fNot determined. ^gUnidentified product also formed. ^hRatios were determined by capillary GC analysis of crude reaction mixtures.

the photogeneration of an allylic cation used in a 4+3 cycloaddition reaction. Variations in concentration do not

have dramatic effects on the outcome of the reaction (Table 1 entries 1-6). The fact that no product was isolated at a concentration of 0.005M suggests that a bimolecular process may be important in the cycloaddition process, but this has yet to be rigorously established (Table 1, entry 7). Variations in solvent are also not very significant (Table 1, entries 8-15). Further, it should be noted that when naphthalene, 1,3-cyclohexadiene or benzophenone was added to the reaction, no change in the rate or outcome of the reaction was observed. Though not rigorously controlled within the reaction vessel, temperature effects appear to be minimal. The optimal reaction conditions for the process are given in entry 17 of Table 1.

In these reactions, it appeared that the ratio of **8a** to **8b** was constant over the course of the photolysis, though both were subject to photodegradation. The structures of the cycloadducts were established by ^1H and ^{13}C NMR. Stereochemical assignments were made on the basis of a shift reagent study. Thus, in the presence of 25 mol% $\text{Eu}(\text{fod})_3$, the angular proton of **8b** moved downfield by 1.69 ppm while that of **8a** shifted only 0.15 ppm.

In a preliminary attempt to examine the scope of the reaction, several other substrates were subjected to photolysis under optimal reactions conditions. These results are shown in Table 2.

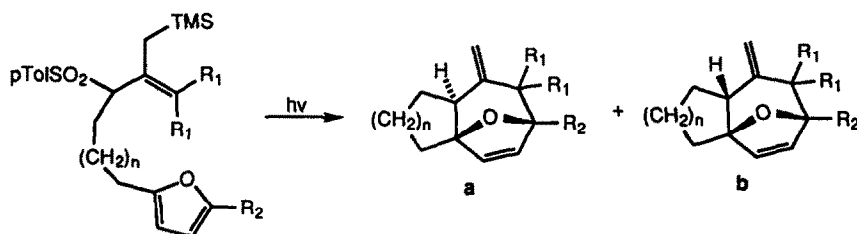


Table 2. Photochemical 4+3 Cycloadditions of Trimethylsilylmethyl Allylic Sulfones.

Entry	Substrate	R ₁	R ₂	n	Cycloadduct	Yield ^a	Ratio (a:b) ^b
1	4	Me	H	1	8	35(56)	1:7.8
2	5	-(CH ₂) ₅ -	H	1	9	11(18)	2.7:1
3	6	Me	H	2	10	16(21)	1:7.1
4	7	-(CH ₂) ₅ -	H	2	11	22(24)	1:8

^aYields in parentheses are based on recovered starting materials. ^bRatios were determined by capillary GC analysis of crude reaction mixtures.

In general, yields are poor but internal asymmetric induction is rather good.⁸ Further, the stereocontrol observed is significantly better than that seen in the corresponding Lewis acid mediated process.^{4f} The origin of the switch in stereochemistry in the 4+3 cycloaddition of substrate **6** is not yet clear. Surprisingly, little difference in yield is seen in the preparation of 5,7 and 6,7 fused ring cycloadducts. Finally, it should be noted that photolysis of alkoxyallylic sulfones does not result in the formation of 4+3 cycloadducts.⁹

At present, the mechanism of this reaction can be interpreted according to concepts introduced by Mariano.⁷ Thus, using **4** as an example, photoexcitation and subsequent electron transfer should produce intermediate **12**. Expulsion of the *p*-tolylsulfinate anion leads to the allylic cation **13** which undergoes intramolecular 4+3 cycloaddition (Scheme 1). This reasonable mechanism serves as a working hypothesis for further investigations.

In summary, we have documented the first examples of a photochemically-mediated 4+3 cycloaddition

