The First Example of the [4+2] Cycloaddition Reaction of Silylketenes with 1,3-Dienes: A Convenient Preparation of 2-Pyranones and Isochromenes

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Abstract: Silylketenes easily undergo the [4+2] cycloaddition reaction with electron-rich 1,3-dienes and oquinodimethanes to give the corresponding 2-pyranones and isochromenes, respectively.

The [2+2] cycloaddition reaction of silylketenes 1, a thermally stable substitute for very labile ketene, with unsaturated compounds giving 4-membered ring compounds is one of the most synthetically useful reactions of $1.^1$ To our knowledge, however, there is no report dealing with [4+2] cycloaddition reactions of 1 with all-carbon 1,3-dienes which will be another useful reaction.² We now wish to report the first example of [4+2] cycloaddition reaction of 1 with 1,3-dienes. We have found that silylketenes 1 smoothly react with electron-rich 1,3-dienes 2 under reflux in dry benzene to give 2-pyranones 3 after purification on a silica gel column.



A typical experimental procedure is as follows (entry 7 in Table): A mixture of $1c^3$ (123 mg, 0.79 mmol) and 2a (303 mg, 1.24 mmol) in dry benzene (2 ml) was stirred under reflux for 3 days. After concentration *in vacuo*, the residue was purified by column chromatography on silica gel (BW-200, Fuji Davison, hexane: AcOEt = 2:1) to give 3g (144 mg, 77%).

The results are summarized in Table. Trimethylsilylketene 1a smoothly underwent the [4+2] cycloaddition with 2a to give 2-pyranone 3a (entry 1). The reaction was completely regioselective and no regioisomer of 3a could be detected. The observed high regioselectivity of the addition will be explained by the calculated data of the atomic charges of 1a and 2a, as shown below.⁴ Analogously, 1a reacted with the other electron-rich 1,3-dienes such as 2b and 2c to afford the corresponding 3b and 3c, respectively (entries 2 and

Entry	1	2	Reaction Conditions		3 R3	R ³	Yield (%)	mp(°C)
1	1a	2a	reflux, 3 days	a	Me3	Me	51	55-56
2	1a	2 b	r. t., 5 h; reflux, 2.5 days	b	Me3	MeO	54	52-54
3	1a	2 c	r. t., 1 h; reflux, 2 days	с	Me3	HO	47	102-104
4	1b	2a	reflux, 3 days	d	Et3	Me	73	oil
5	1 b	2 b	r. t., 6 h; reflux, 2.5 days	e	Et3	McO	70	oil
6	1 b	2 c	r. t., 1 h; reflux, 2 days	f	Et3	HO	51	oil
7	1 c	2a	reflux, 3 days	g	t-BuMe2	Me	77	37-48
8	1 c	2 b	r. t., 6 h; reflux, 2.5 days	h	t-BuMe2	MeO	61	41-42
9	1 c	2 c	r. t., 1 h; reflux, 2 days	i	t-BuMe ₂	HO	46	108-110
10	1 d	2a	reflux, 3 days	j	t-BuPh2	Me	75	88-89
11	1 d	2 b	r. t., 5 h; reflux, 2.5 days	k	t-BuPh2	MeO	48	113-115
12	1 d	2 c	r. t., 2 h; reflux, 1 day	I	t-BuPh2	Ю	25	168-170

Table.^a The [4+2] Cycloaddition of Silvlketenes 1 with 1.3-Dienes 2

a) All products gave satisfactory spectral data and elemental analysis.



3).⁵ Various silylketenes 1b-d could also be used as the heterodienophiles for this cycloaddition reaction giving 3 (entries 4-12). Unexpectedly, addition of boron trifluoride etherate, zinc chloride or magnesium bromide as catalyst, known as accelerators of the [4+2] cycloaddition reaction of carbonyl dienophiles with 1,3-dienes,⁶ inhibited the reaction and no cycloadducts were obtained. Removal of the trialkylsilyl group of 3 is easily achieved by treatment with tetra-*n*-butylammonium fluoride in tetrahydrofuran in good yield.⁷

Interestingly, treatment of 1a with 2b at room temperature for 12 h afforded the cycloadduct 4 (24%) and the acyclic product 5 (23%). As shown in Table (entry 2), only the desired 2-pyranone 3b was obtained in 54% yield when the reaction was carried out under reflux for 3 days.



These experiments clearly demonstrate that the [4+2] cycloaddition of 1 and 2 proceeds by a stepwise process, not by a concerted cycloaddition process. Nucleophilic attack of 2 on the sp carbon atom of 1 will first produce the betain intermediate 6. Stopping the reaction at this stage will give the acylic ester 7

accompanied with expulsion of the trialkylsilyl group during the work-up. Prolonging the reaction time and/or raising the reaction temperature will promote the cyclization of 6 to afford the dihydropyrane intermediate 8, which is isomerized to the pyrane by heating and then hydrolyzed with water on a silica gel column to furnish 3.



o-Quinodimethanes, easily generated *in situ* by thermolysis of benzocyclobutenes, are well known to react with various dienophiles to give [4+2] cycloadducts.⁸ Silylketene 1c also reacted with benzocyclobutenes **9a** and **9b** under reflux in dry toluene for 25~46 h to give the corresponding isochromenes **10a** and **10b**, respectively. In contrast to **9**, 1-acetoxybenzocyclobutene and 1,1-dimethoxybenzocylobutene were completely inactive under similar reaction conditions. In the case of benzocyclobutenol, only the acylation of the hydroxy function occurred and no cycloadducts were obtained.



In conclusion, silylketenes can be effectively used as heterodienophiles for the [4+2] cycloaddition reaction with electron-rich 1,3-dienes or benzocyclobutenes. Furthermore, as compared with the known synthetic procedure for 2-pyranones⁹ and isochromenes,¹⁰ the method described is simple and will provide a convenient method for the preparation of 2-pyranones and isochromenes.

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References and Notes

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