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1-(2-Butadienyl)pyridinium Bromide, a Novel Diene in Diels−Alder Reactions

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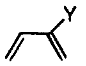
Summary: 1-(3-Sulfolenyl)pyridinium bromide (**4**) serves as the stable precursor for a novel, positively charged diene **6** which undergoes [4 + 2] cycloadditions with a number of electron-poor dienophiles.

It has been well established that 3-sulfolenes are stable precursors to synthetically useful 1,3-dienes.[1] 2-(Methoxycarbonyl)- (**1a**),[1b] 2-nitro- (**1b**),[1c] 2-(phenylsulfonyl)- (**1c**),[1d,e] and 2-cyano-1,3-butadienes (**1d**)[1f] may be generated *in situ* by thermolysis of the corresponding 3-sulfolenes **2a**−**2d** and react directly with electron-deficient dienophiles to give [4 + 2] cycloadducts.[1] In the absence of a dienophile, the electron-poor diene also reacts as a dienophile so as to produce [4 + 2] dimers. We thought that a positively-charged substituent at the 2-position would increase the electron-deficiency of a 1,3-butadiene and influence both the reactivity and the mode of cycloaddition reactions. It was anticipated that this highly reactive diene could be most conveniently generated from the corresponding 3-sulfolene **3**. We report herein the use of the readily available 1-(3-sulfolenyl)pyridinium bromide (**4**) as the stable precursor for a novel, positively charged diene and the study of its Diels−Alder reactions.



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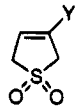

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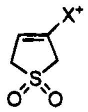

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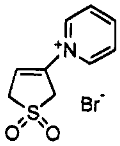

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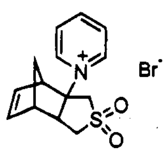
a: Y = CO_2Me
b: Y = NO_2
c: Y = SO_2Ph
d: Y = CN

Treatment of 3,4-dibromosulfolane with pyridine at ambient temperature produced compound **4** in 40% yield.[2] Because substituted vinylpyridinium salts are very reactive dienophiles[3] and since electron-poor 3-sulfolenes **2a** and **2d** react as dienophiles,[4] it was at first anticipated that **4** might react as a dienophile with electron-rich cyclopentadiene to give cycloadduct **5**. However, treatment of **4** with cyclopentadiene at 110 °C for 1 h did not produce compound **5** but instead gave a complex mixture. On the other hand, thermolysis of **4** in acetonitrile at 140 °C for 1 h caused SO_2 extrusion and gave **6** in quantitative yield. Diene **6** was stable upon storage at room temperature for over 1 month without appreciable decomposition or dimerization. This phenomenon was quite surprising because a diene bearing a strongly electron-withdrawing group was expected to dimerize or polymerize readily.



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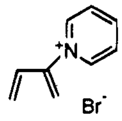

6

The reaction of isoprene with **6** at room temperature for 6 h resulted in the recovery of starting materials. No cross cycloadducts were obtained. Apparently the vinylpyridinium functionality of **6** does not react as a dienophile. However, diene **6** reacted with a number of alkenes in CH_3CN at 140 °C to give [4 + 2] cycloadducts (eq 1, Scheme 1, and Table 1). The cycloadducts were treated with aqueous $NaPF_6$ for counterion exchange so that they could be purified and characterized more easily by recrystallization. It is noteworthy that the highly electron-deficient diene **6** reacts smoothly with electron-poor dienophiles. The cycloadditions with *N*-phenylmaleimide, dimethyl fumarate, and methyl vinyl ketone (e.g., entries 1, 4, and 8 of Table 1) were complete at 140 °C in 1 h. In fact, the reactions can even be performed at lower temperatures. For example, reaction of **6** with *N*-phenylmaleimide at room temperature for 6 h or at 70 °C for 2 h produced **7a** in almost quantitative yield. In addition, it is not necessary to use CH_3CN as the solvent. The cycloaddition reaction of **6** with *N*-phenylmaleimide also took place smoothly in water.

In addition to spectral analysis, the structure of the cycloadduct **7a** was confirmed by chemical transformations. Sodium borohydride reduction[5] of the pyridinium salt followed by hydrolysis[6] converted **7a** into the substituted cyclohexanone **9** (eq 2). Therefore, compound **6** may be looked at as a water-solule version of 2-alkoxy-1,3-butadiene in aqueous Diels−Alder reactions.

Two regioisomers were obtained (*para*:*meta* = 2:1) when **6** was reacted with unsymmetric alkenes (entries 7 and 8 of Table 1). The ratios of these two isomers were determined by ^{13}C NMR spectral analyses. Counterion exchange ($NaPF_6$) and recrystallization of the mixture of **8e**/**8e′** or **8f**/**8f′** gave the major regioisomer as a white crystal of which the structure was determined to be "*para*" by 2D NMR COSY experiments.

Competitive Diels−Alder reactions were carried out by reacting **6** with mixtures of dienophiles to examine their relative dienophilicity. Reaction of **6** with a mixture of

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Scheme 1

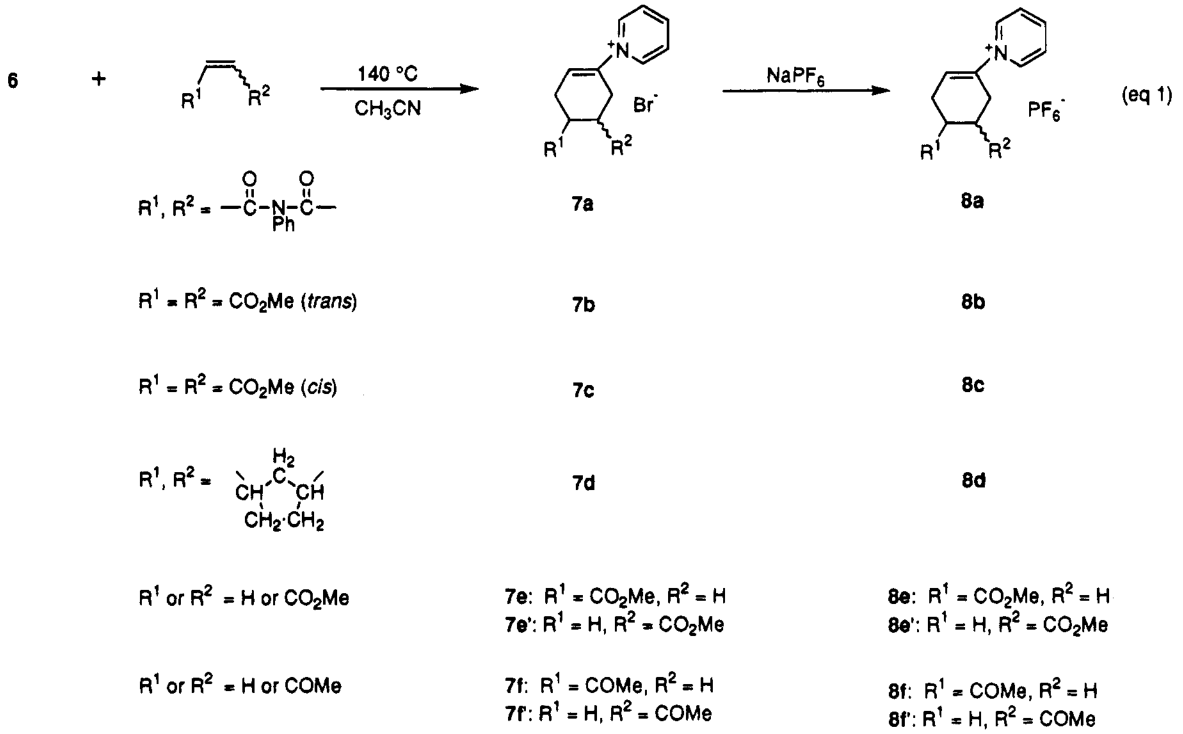
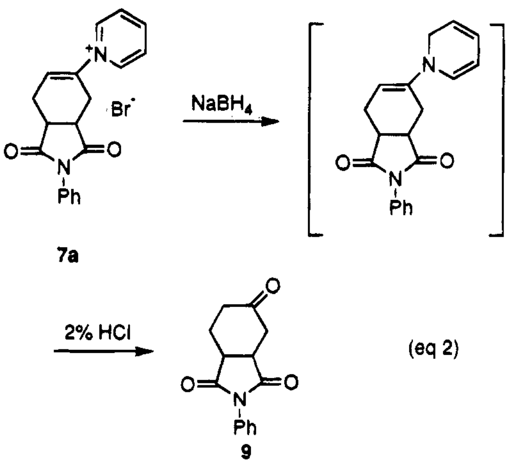


Table 1. Diels–Alder Reactions of Diene 6 in CH_3CN

entry	dienophile	condns (°C, h)	product (ratio)	PF_6 salt (yield,[a] %)
1	*N*-phenylmaleimide	140, 1	**7a**	**8a** (88)
2	*N*-phenylmaleimide	rt, 6	**7a**[b]	
3	*N*-phenylmaleimide	70, 2	**7a**[b]	
4	dimethyl fumarate	140, 1	**7b**	**8b** (86)
5	dimethyl maleate	140, 3	**7c**	**8c** (79)
6	norbornene	140, 1.5	**7d**	**8d** (92)
7	methyl acrylate	140, 1.5	**7e** + **7e′** (2:1)	**8e** + **8e′** (82, 2:1)
8	methyl vinyl ketone	140, 1	**7f** + **7f′** (2:1)	**8f** + **8f′** (85, 2:1)

[a] Isolated yields of the hexafluorophosphate salts after recrystallization. [b] Compound **7a** was obtained in nearly quantitative yield. The ^1H NMR spectrum indicated its purity to be greater than 95%.



equal molar equivalents of *N*-phenylmaleimide and norbornene in CH_3CN at 140 °C for 1 h produced **7a** as the only cycloadduct. Reaction of **6** with a mixture of equal molar equivalents of *N*-phenylmaleimide and dimethyl fumarate gave a mixture of **7a** and **7b** in a 2:1 ratio.[7] The results of these competitive studies indicate that *N*-phenylmaleimide is more dienophilic than dimethyl fumarate, and even more so than norbornene. This trend is the same as the Diels–Alder reactions of other electron-rich dienes.[8] It thus appears that **6** behaves as a normal diene despite its electron-deficient nature.

Diels–Alder reactions of **6** could be carried out by heating **4** with dienophiles directly. However, a small amount of unidentified side products formed under these conditions so that the one-pot procedure is not preferred. Whereas the cycloaddition reactions of **6** proceeded smoothly with electron-deficient dienophiles, the reactions with electron-rich dienophiles were not successful. Treatment of **6** with ethyl vinyl ether in CH_3CN at 100 °C for 3 h resulted in no reaction, whereas the reaction with ethyl vinyl ether or dihydrofuran in CH_3CN at 140 °C for 1 h gave no cycloadducts but mainly unidentified polymer. Apparently inverse electron demand Diels–Alder reactions[9] do not take place with **6**.

Treatment of an equimolar mixture of **6** and another diene (2,3-dimethyl-1,3-butadiene or isoprene) with *N*-phenylmaleimide at room temperature for 1 h led to the formation of cycloadduct **7a** as the only product with no indication of the formation of **10** or **11**. This result indicates that the dienic reactivity of **6** is apparently higher than that of 2,3-dimethyl-1,3-butadiene and isoprene.

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(7) This ratio was easily determined by ^1H NMR spectral analysis since the vinyl proton of **7a** (δ 6.42) exhibits a lower chemical shift than that of **7b** (δ 6.18).

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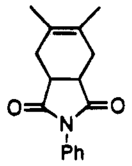

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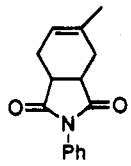

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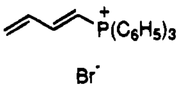
Cycloaddition reactions of 1,3-butadienes bearing a cationic substituent are virtually unknown. For example, butadienylphosphonium salts **12**[10,11] or butadienylsulfonium salts **13**[12] do not undergo cycloaddition reactions



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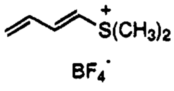

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with maleic anhydride or tetracyanoethylene. That 1-(2-butadienyl)pyridinium bromide (**6**) undergoes [4 + 2] cycloadditions with a number of electron-poor dienophiles is in sharp contrast to the chemical behavior of other cationically-substituted 1,3-butadienes. Further study on the reactions and applications of **6** is in progress.

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Supplementary Material Available: General procedure for the Diels–Alder reaction of compound **6**, characterization data for compound **6** and the cycloadducts (**8a–8f**), ^1H NMR spectra for compounds **6** and **8a–8f**, ^{13}C NMR spectrum for **8f**, and $^1H-^1H$ COSY spectra for **8e** and **8f** (18 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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