CHEMISTRY LETTERS, pp. 1693-1696, 1990.

Ene Reaction of Allenyl Sulfides with Aldehydes and Schiff's Bases Catalyzed by Lewis Acids

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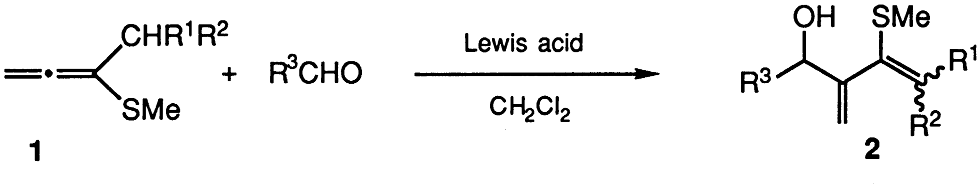
Ene reaction proceeds between α-alkylallenyl sulfides and enophiles such as aldehydes and Schiff's bases in the presence of Lewis acid to afford various 1,3-dienes.

In recent years, development of synthetic reactions by the use of allene derivatives[1)] has been investigated with much interest because of their unique structure. For instance, many kinds of allenyl metals have been devised for the introduction of allenyl or propargyl groups.[2)] Allene itself is, however, not so reactive that the introduction of suitable substituents is generally required to increase its reactivity. That is, allenyl ether,[3)] allenyl silane,[4)] and allenyl ferrocene[5)] are used in [4+2] and [3+2] cycloaddition reactions.

We have recently found that the Lewis acid-promoted [2+2] cycloaddition reaction exceptionally proceeded by employing alkenyl and alkynyl sulfides.[6)] Introduction of an alkylthio group into allene derivatives, therefore, would be expected to increase their reactivity. According to this assumption, 1-benzyl-1-methylthio-1,2-propadiene (**1a**) was prepared[7)] and the reaction with aldehydes was examined in the presence of Lewis acid. When a mixture of **1a** and benzaldehyde was treated with Et_2AlCl at -78 °C in dichloromethane, ene reaction[8)] proceeded to give 2-methylidene-3-methylthio-1,4-diphenyl-3-buten-1-ol (**2a**) in 50% yield. The yield of the ene product **2a** depended on the Lewis acid used, and the reaction with $BF_3 \cdot OEt_2$ at -78 °C afforded **2a** in 83% yield.



Since a synthetically important 1,3-diene derivative was prepared by the above reaction, the ene reactions of allenyl sulfides **1** and various aldehydes were examined under the above reaction conditions. As shown in Table 1, wide generality is observed in this ene reaction with respect to aldehydes and allenyl sulfides; aldehydes including aliphatic, aromatic, and α,β-unsaturated ones are able to be employed as enophiles. Tetra- and trisubstituted 1,3-butadiene derivatives **2** are prepared in high yields from allenyl sulfides **1a**,**b**. In spite of the instability of the dienes bearing no substituent on the terminal positions,[9)] the reactions of **1c** also give the corresponding disubstituted dienes in good yields.

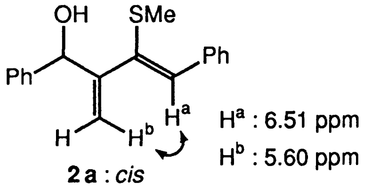
The reactivity of allenyl sulfides **1** as ene components is expectedly so high that the ene reaction proceeds even at low temperature (-78 °C).[10)] This high reactivity of **1** is attributable to the alkylthio substituent, because the ene reaction did not proceed between the alkoxy analogue of **1a**, 1-benzyl-1-methoxy-1,2-propadiene, and benzaldehyde in the presence of $BF_3{\bullet}OEt_2$.

The representative experimental procedure is as follows: To a dichloromethane (5 ml) solution of benzaldehyde (0.40 mmol) and **1a** (0.60 mmol) was added a dichloromethane (2 ml) solution of $BF_3{\bullet}OEt_2$ (0.48 mmol) dropwise at -78 °C. The mixture was stirred at that temperature for 12 h, and the reaction was quenched with 2 ml of triethylamine and then with pH 7 phosphate buffer. The crude product was purified by thin layer chromatography (silica gel) to afford the ene product **2a** (0.33 mmol, 83%).

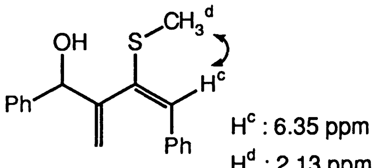
Table 1. The reaction of aldehydes with allenes **1**

Ene (R^1, R^2) Aldehyde (R^3)	Ph, H (**1a**)	Me, Me (**1b**)	H, H (**1c**)
	Yield of the ene product **2** / %, (*cis* : *trans*)		
Ph-	83 (>99:1) (**2a**)[a,b)]	75	80
$PhCH_2CH_2$-	73 (10:1)[b,c)]	88	55
$(CH_3)_2CH$-	62 (6:1)[c,d)]	83	57
cyclo-C_6H_{11}-	67 (6:1)[c,d)]	68	61
$CH_3(CH_2)_2CH{=}CH$-	—	64	—

a) Relative stereochemistry was determined by the observation of NOEs between H^a and H^b, H^c, and H^d of each isomer.



2a : *cis*



2a : *trans*

b) *cis* : *trans* Isomer ratio was determined after separation.

c) Relative stereochemistry was determined by the comparison of the chemical shifts and coupling patterns of each isomer with those of each isomer of **2a**.

d) *cis* : *trans* Isomer ratio was determined by 500 MHz ^{1}H-NMR.

Although Schiff's bases are the nitrogen analogues of aldehydes, application of them as enophiles has been restricted either to the reactions employing reactive N-sulfonylimines derived from glyoxylate or chloral,[11)] or to the intramocular reaction.[12)] But the high reactivity of allenyl sulfides **1** as ene components suggested the possibility of ene reaction with simple Schiff's bases.

Treatment of a mixture of N-isopropylidenebenzylamine (**3a**) and **1a** with $BF_3 \cdot OEt_2$, in fact, afforded the corresponding ene product **4a** in ca. 20% yield. After screening of Lewis acids, $AlCl_3$ was found to give the best result. That is, $AlCl_3$ (0.52 mmol) was added portionwise at ambient temperature to a toluene (5 ml) solution of **3a** (0.4 mmol) and **1a** (0.64 mmol), then the mixture was stirred for 12 h. The same work-up as in the case of aldehydes gave the ene product **4a** in 81% yield.

Various Schiff's bases react with allenyl sulfides **1a-c** in the presence of $AlCl_3$ (Table 2). Not only an aromatic Schiff's base but also aliphatic ones are found to be employed as enophiles. Ene reaction proceeds even in the case of the Schiff's base **3c** of a primary aldehyde, which is unstable in the coexistence of Lewis acid.

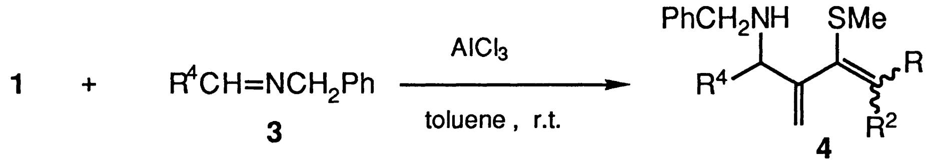


Table 2. The reaction of Schiff's bases **3** with allenes **1**

Ene (R^1, R^2) / Schiff's base (R^4)	Ph, H (**1a**)	Me, Me (**1b**)	H, H (**1c**)
	Yield of the ene product **4** / %, (*cis* : *trans*)		
$(CH_3)_2CH$- (**3a**)	81 (3:1) (**4a**)[a)]	80	—
C_6H_5- (**3b**)	83 (2.5:1)[b)]	88	53
$CH_3(CH_2)_3$- (**3c**)	28 (2:1)[b)]	43	—

a) *cis*:*trans* Isomer ratio was determined after separation. Relative stereochemistry of each isomer was determined by the observation of NOEs, analogously to **2a**.

b) Relative stereochemistry was determined by the comparison of the chemical shifts and coupling patterns of each isomer with those of isomers of **4a**.

There are a few examples in which allene derivatives have been used as ene components,[8e,f,g] and most of them are intramolecular reactions.[8e,f] The present study reveals the utility of allenes activated by an alkylthio substituent as ene components, and the ene reaction of the allenyl sulfides **1** with aldehydes and Schiff's bases affords the synthetically useful 1,3-diene derivatives.[13]

References

1) Reviews; a) D. J. Pasto, *Tetrahedron*, **40**, 2805 (1984); b) W. Smadja, *Chem. Rev.*, **83**, 263 (1988); c) "The Chemistry of Ketenes, Allenes and Related Compounds," Part 1 and 2, ed by S. Patai,

John Wiley & Sons, Chichester (1980).

2) The chapter 10 of Ref. 1c; E. J. Corey, C.-M. Yu, and D.-H. Lee, *J. Am. Chem. Soc.*, **112**, 878 (1990); M. Suzuki, Y. Morita, and R. Noyori, *J. Org. Chem.*, **55**, 441 (1990); M. Ishiguro, N. Ikeda, and H. Yamamoto *ibid.*, **47**, 2225 (1982); M. Karila, M. L. Capmau, and W. Chodkiewiez, *Bull. Soc. Chim. Fr.*, **1973**, 3371; J.-L. Moreau, *ibid.*, **1975**, 1248; D. G.-Dron, M. L. Capmau, and W. Chodkiewiez, *Tetrahedron Lett.*, **1972**, 37; E. Favre and M. Gaudemar, *J. Organomet. Chem.*, **92**, 17 (1975).

3) K. Hayakawa, K. Aso, M. Shiro, and K. Kanematsu, *J. Am. Chem. Soc.*, **111**, 5312 (1989) and references cited therein.

4) R. L. Danheiser, D. J. Carini, and A. Basak, *J. Am. Chem. Soc.*, **103**, 1604 (1981); R. L. Danheiser, D. J. Carini, M.Fink, and A. Basak, *Tetrahedron*, **39**, 935 (1983); R. L. Danheiser, C. A. Kwasigroch, and Y.-M. Tsai, *J. Am. Chem. Soc.*, **107**, 7233 (1985).

5) J. C. Watkins and M. Rosenblum, *Tetrahedron Lett.*, **26** 3531 (1985).

6) Y. Hayashi and K. Narasaka, *Chem. Lett.*, **1989**, 793; **1990**, 1295.

7) Metallation[14] of 1-methylthio-1-propyne by lithium diisopropylamide, followed by benzyl bromide, afforded **1a** in 80% yield after distillation.

8) Reviews; a) H. M. R. Hoffmann, *Angew. Chem., Int. Ed. Engl.*, **8**, 556 (1969); b) W. Oppolzer and V. Snieckus, *ibid.*, **17**, 476 (1978); c) B. B. Snider, *Acc. Chem. Res.*, **13**, 426 (1980); d) J. Dubac and A. Laporterie, *Chem. Rev.*, **87**, 319 (1987): Ene reaction using allene derivatives; e) M. Bertrand, B. Cavallin, M. L. Roumestant, and P. S.-Panthet, *Israel J. Chem.*, **26**, 95 (1985) and references cited therein; f) M. I. Johnston, J. A. Kwass, R. B. Beal, and B. B. Snider, *J. Org. Chem.*, **52**, 5419 (1987); g) C. B. Lee, R. J. Newman, and D. R. Taylor, *J. Chem. Soc., Perkin Trans. 1*, **1978**, 1161 and references cited therein: Ene reaction using vinyl sulfides; h) K. Maruoka, Y. Hoshino, T. Shirasaka, and H. Yamamoto, *Tetrahedron Lett.*, **29**, 3967 (1988); i) K. Tanino, T. Nakamura, and I. Kuwajima, *ibid.*, **31**, 2165 (1990); j) T. A. Blumenkopf, M. Bratz, A. Castaneda, G. C. Look, L. E. Overman, D. Rodriguez, and A. S. Thompson, *J. Am. Chem. Soc.*, **112**, 4386 (1990).

9) When the ene products from **1c** stood overnight at room temperature after purification, severe decomposition was observed to afford many undefined products.

10) There are rare examples in which the ene reaction proceeds at low temperature, except for the cases using the reactive enophiles like glyoxylates; K. Mikami, M. Terada, and T. Nakai, *J. Am. Chem. Soc.*, **112**, 3949 (1990); J. K. Whitesell, A. Bhattacharya, C. M. Buchanan, H. H. Chen, D. Deyo, D. James, C.-L. Liu, and M. A. Minton, *Tetrahedron*, **42**, 2993 (1986) and references cited therein.

11) O. Achmatowicz and M. Pietraszkiewicz, *J. Chem. Soc., Perkin Trans. 1*, **1981**, 2680; D. M. Tschaen, E. Turos, and S. M. Weinreb, *J. Org. Chem.*, **49**, 5058 (1984); H. Braxmeier and G. Kresze, *Synthesis*, **1985**, 683.

12) G. Demailly and G. Solladie, *J. Org. Chem.*, **46**, 3102 (1981); M. J. Melnick, A. J. Freyer, and S. M. Weinreb, *Tetrahedron Lett.*, **29**, 3891 (1988).

13) B. M. Trost, W. C. Vladuchick, and A. J. Bridges, *J. Am. Chem. Soc.*, **102**, 3554 (1980).

14) W. H. Pearson, K.-C. Lin, and Y.-F. Poon, *J. Org. Chem.*, **54**, 5814 (1989); J. Tanaka, S. Kanemasa, and O. Tsuge, *Bull. Chem. Soc. Jpn.*, **63**, 51 (1990).

(Received June 28, 1990)