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STEREOSELECTIVE SYNTHESIS OF 2-SUBSTITUTED 1-METHOXY-1,3-DIENES BY 1,4-ELIMINATION WITH TRIBUTYLSTANNYLLITHIUM

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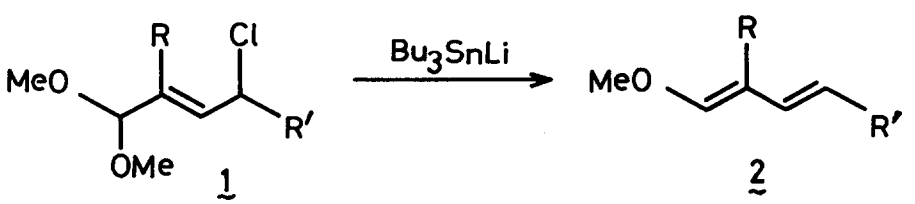
Summary: Highly stereoselective synthesis of 2-substituted 1-methoxy-1,3-dienes was developed by 1,4-elimination of 2-substituted 4-chlorocrotonaldehyde dimethylacetal derivatives with tributylstannyllithium.

1-Oxygenated 1,3-dienes have played a major role in the development of Diels-Alder reaction and have been applied for the synthesis of various natural products.[1] Although some stereocontrolled syntheses of these dienes have been reported recently,[2] development of new methods which are stereoselective and applicable to various systems have been still required.

In the synthetic study of phospholipase A_2 inhibitor, manoalide,[3] we encountered unexpected 1,4-elimination reaction. Treatment of 4-chloro-1,1-dimethoxy-2-butene derivative 1 with tributylstannyllithium afforded 1-methoxy-1,3-diene derivative 2 quantitatively. Generally trialkylstannyllithium affords allylic stannanes by a reaction with allylic halides.[4] Elimination reaction of alkoxy halides with trialkylstannylmetal has been studied only in a vicinal system, and it has been reported that elimination reaction of vicinal alkoxy halides is highly affected by the used solvent and results in competition with substitution.[5] Herein we wish to report on a new synthetic method of 1-methoxy-1,3-dienes by 1,4-elimination of 4-chloro-1,1-dimethoxy-2-butene derivatives with tributylstannyllithium.



1 2

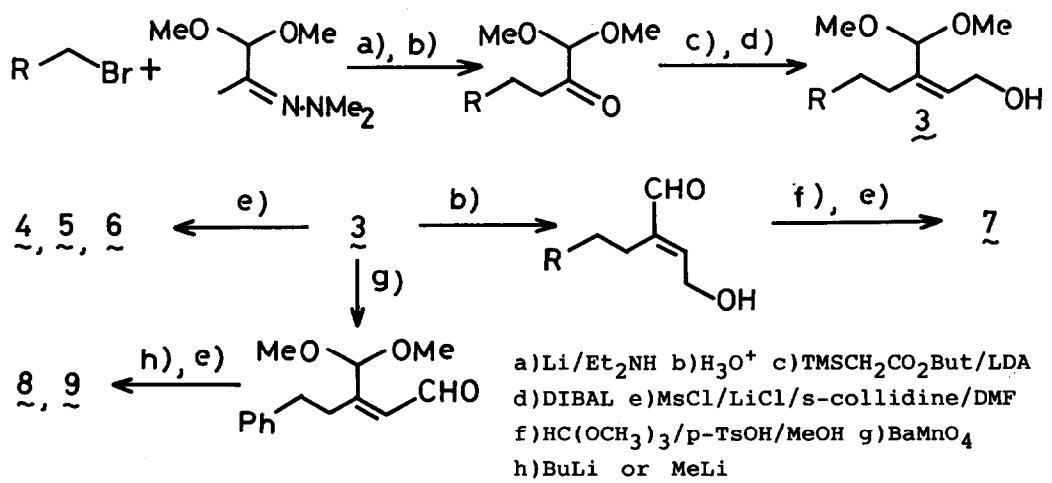
Dimethoxy allylic chlorides 4 - 9 in the Table were prepared from the corresponding bromide and N,N-dimethylhydrazone of pyruvaldehyde dimethylacetal as shown in Scheme 1.[3] E-isomer 7 was obtained from alcohol 3 by

acid treatment followed by acetalization and then chlorination. Secondary allylic chlorides 8 and 9 were prepared by alkylation of the aldehyde derived from alcohol 3 with the corresponding alkyllithium, and then chlorination.

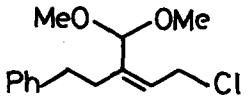
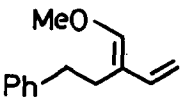
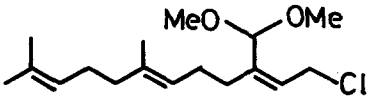
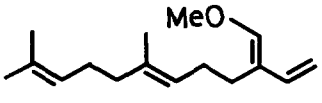
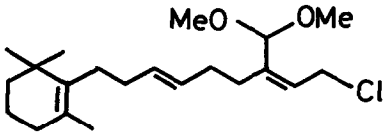
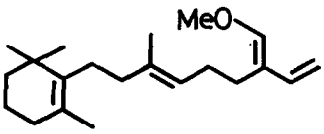
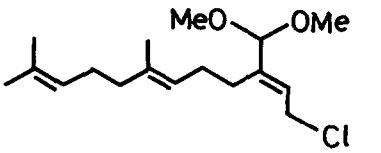
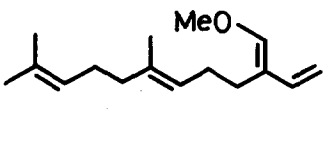
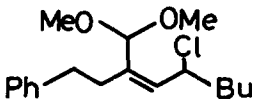
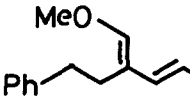
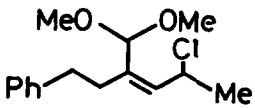
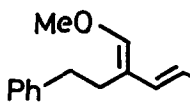
A typical procedure for 1,4-elimination is as follows. Dimethoxy allylic chloride 4 (1.4 mmol) was treated with tributylstannyllithium prepared at 0°C from lithium diisopropylamide (2.8 mmol) and tributylstannane (3.5 mmol)[6] in THF at -78°C for 20 minutes. The reaction mixture was worked up as usual manner to give pure alkoxy-1,3-diene 10 after column chromatography. The results are summarized in the Table. The stereochemistry of the product 10 was confirmed in comparison with the authentic compound which was synthesized together with its stereoisomer 15 by an alternative route.[7] It is noteworthy that this elimination reaction afforded E-diene with excellent stereoselectivity, for example, both E- and Z-isomer of the primary chloride, 5 and 7, gave the same E-diene 11 in excellent yield. In the case of the secondary chloride 8 or 9, E,E-isomer 13 or 14 was obtained respectively[9] although excess of tributylstannyllithium was required.

The excellent stereoselectivity may be understood based on the allylic strain concept.[10] As shown in Scheme 2, 1,4-elimination reaction of the primary Z-chlorides must proceed from the favorable conformer A in which allylic hydrogen, Ha is located in the same plane as one of the double bond, and gives E-methoxy-1,3-diene. The similar consideration may be applicable to the case of the primary E-chloride and the secondary chlorides shown in Scheme 2. For the process of this elimination reaction,

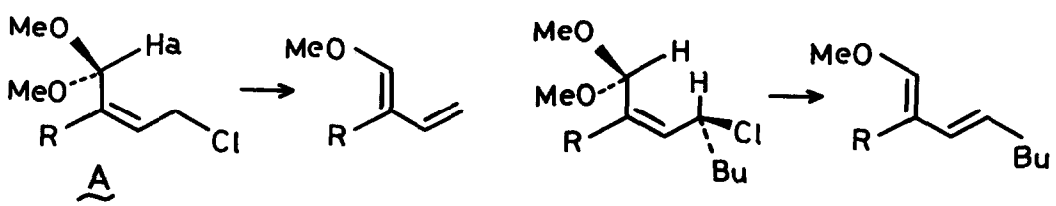
Scheme 1



either mechanism of electron transfer from tributylstannyllithium to allylic chloride or ionic mechanism which involves the generation of an allyl anion from allylic chloride, may be postulated as the case of 1,2-alkoxy halide reported by Kuivila.[5,11] Unfortunately we have obtained no

substrate	product	(yield %)
 4	 10	(98.3%)
 5	 11	(94 %)
 6	 12	(quant.)
 7	 11	(84%)
 8	 13	(99%)
 9	 14	(64%)

Scheme 2

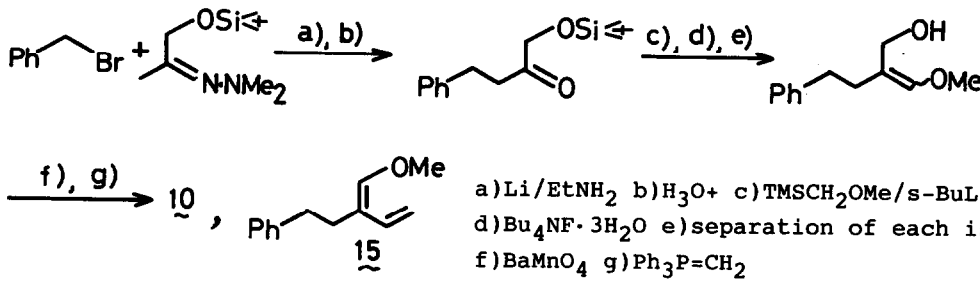


conclusive informations for the mechanism of the present 1,4-elimination reaction, although several efforts have been made.[12]

References and Notes

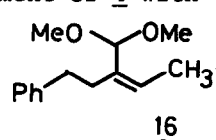
† Present address; Faculty of Science, Kwansei Gakuin University, Uegahara 1-1-155, Nishinomiya, Hyogo 662, Japan.

1. M.Petrzilka, Synthesis, **1981**, 753. One of the recent example is S.Hashimoto, S.Sakata, M.Sonegawa, S.Ikegami, J. Am. Chem. Soc., **1988**, 110, 3670.
2. a) J.I.Luengo, M.Koreeda, Tetrahedron Lett., **1984**, 25, 4881. b) P.G. McDougal, J.G.Rico, J. Org. Chem., **1987**, 21, 4817. c) C.J.Kowalsky, G.S. Lal, Tetrahedron Lett., **1987**, 28, 2463.
3. S.Katsumura, S.Fujiwara, S.Isoe, Tetrahedron Lett., **1985**, 26, 5827; S.Katsumura, S.Fujiwara, S.Isoe, Tetrahedron Lett., **1988**, 29, 1173.
4. a) Naruta, K.Maruyama, Chem. Lett., **1979**, 881. b) Quintard, A.Rahm, "Tin in Organic Synthesis", Butterworths Pub., London (1987).
5. H.G.Kuivila, Y.M.Choi, J. Org. Chem., **1979**, 44, 4774.
6. W.C.Still, J. Am. Chem. Soc., **1978**, 100, 1481.
7. The authentic compound of 10 was synthesized by the following sequences.



a)Li/EtNH$_2$ b)H$_3$O+ c)TMSCH$_2$OMe/s-BuLi/KH[8] d)Bu$_4$NF·3H$_2$O e)separation of each isomer f)BaMnO$_4$ g)Ph$_3$P=CH$_2$

8. C.Burford, F.Cooke, P.Magnus, Tetrahedron Lett., **1983**, 39, 867.
9. The stereochemistry of 13, 14 and 17[12] was determined by the comparison of their nmr spectra with each other (J=13-15 Hz), and with 10 and its stereoisomer 15.
10. F.Johnson, Chem. Rev., **1969**, 68, 375.
11. We thank to Professor Shinji Murai(Osaka University) for giving us useful informations about the reaction mechanism.
12. Treatment of compound 4 with tributylstannane in the presence of AIBN only afforded 16. Treatment of 4 with LDA afforded chloro-1,3-diene 17[9] in good yield.



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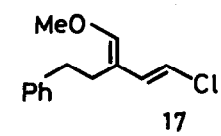

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