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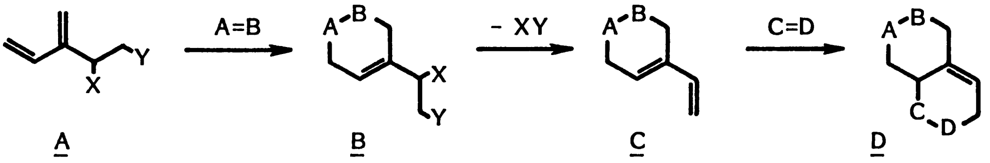
STEPWISE SEQUENCE OF DOUBLE DIELS-ALDER REACTION OF CROSS-CONJUGATED TRIENE EQUIVALENT

Otohiko TSUGE,* Eiji WADA, Shuji KANEMASA, and Hirohiko SAKOH
Research Institute of Industrial Science, and Department
of Molecular Science and Technology, Interdisciplinary
Graduate School of Engineering Sciences, Kyushu University,
Kasugakoen, Kasuga 816

Alcohols with a 2-(1,3-butadienyl) substituent are readily available from the Grignard reaction of chloroprene and are important as cross-conjugated triene equivalents. Some examples of double Diels-Alder reaction of the alcohols are first reported.

The versatility of diene-transmissive Diels-Alder reaction has been demonstrated in recent years.[1)] Although chemoselective control of this reaction was successful when an activated triene was used,[2)] its generality is still rather limited. It has been required to find a synthetic equivalent for cross-conjugated trienes in order to make the double Diels-Alder reaction of cross type a useful and general synthetic tool.[3)]

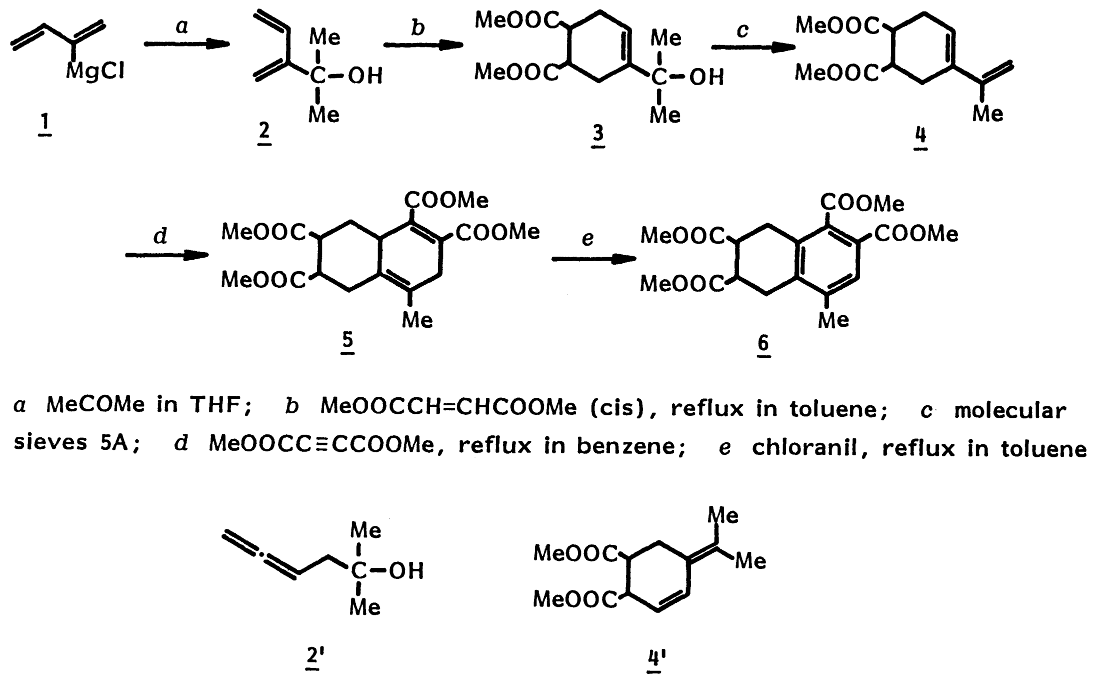
A triene equivalent of our choice is the diene A with a masked olefin moiety. Its double cycloaddition involves three stages: the first cycloaddition to A=B (A→B), the elimination of XY to reveal an additional diene functionality (B→C), and the second cycloaddition to C=D to form a bis-cycloadduct D that corresponds to a cross product (C→D).



We describe here the first demonstration of double Diels-Alder reaction of cross type by employing alcohols with a 2-(1,3-butadienyl) moiety, the equivalents of cross-conjugated trienes.

A typical example of the title reaction is outlined in Scheme 1. The Grignard reaction of 2-(1,3-butadienyl)magnesium chloride 1 that was prepared from readily available chloroprene with acetone gave a mixture of two alcohols, the 1,3-butadienyl 2 and allenyl alcohols 2' (3:1).[4)] The desired alcohol 2 was hardly separated by distillation, however this mixture was employed in the first cycloaddition without any trouble. When the mixture was heated with dimethyl maleate (an equivalent to 2), a 1:1 adduct 3 was obtained in 95% yield, the other alcohol 2' being quantitatively recovered.5) The structure of 3 was determined on the basis of the spectral data as well as elemental analysis.6)

Dehydration of 3 to reveal a diene functionality was most conveniently carried out with molecular sieves 5A.7) The mono-cycloadduct 3 was treated with molecular sieves at room temperature giving a diene 4 in 62% yield along with its isomer 4' (11%). For the second cycloaddition, the diene mixture (4 and 4') has to be separated from the dehydrating agent as 4 gradually isomerizes into 4' in the presence of molecular sieves 5A.8) However when the second dienophile is highly reactive, both the dehydration and the second cycloaddition can be achieved in a flask.9) Thus the mono-cycloadduct 3 was allowed to react with three equivalents of dimethyl acetylenedicarboxylate in the presence of molecular sieves 5A to provide the bis-cycloadduct 5 in 63% yield, the isomerized diene 4' being obtained in 12% yield. Dehydrogenation of 5 was quantitatively performed with chloranil affording a tetrahydronaphthalenetetracarboxylate 6.



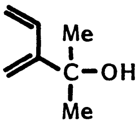
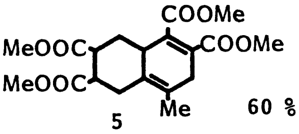
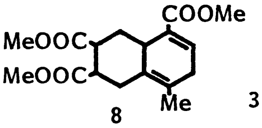
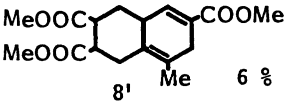
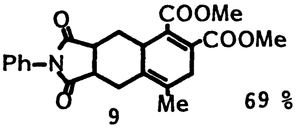
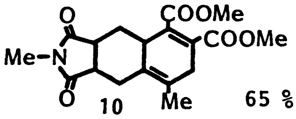
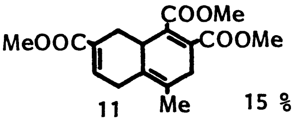
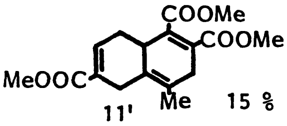
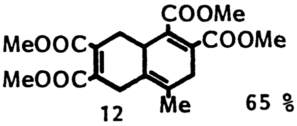
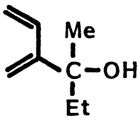
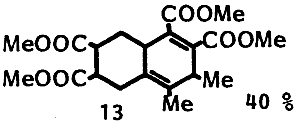
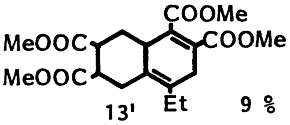
a MeCOMe in THF; *b* MeOOCCH=CHCOOMe (cis), reflux in toluene; *c* molecular sieves 5A; *d* MeOOCC≡CCOOMe, reflux in benzene; *e* chloranil, reflux in toluene

Scheme 1.

The results obtained from the reactions of 1,3-butadienyl alcohols 2 and 7 with a variety of dienophiles are summarized in Table 1. Any combination between olefinic and acetylenic dienophiles might be possible, while we used only acetylenic ones as the second in order to make the dehydrogenation of bis-cycloadducts with chloranil easy.10) When olefinic and acetylenic dienophiles were used as the first dienophiles, the tetrahydronaphthalenes (from 5, 8, 8', 9, 10, 13, and 13') or naphthalenes (from 11, 11', and 12) were yielded after dehydrogenation, respectively.

In contrast with the moderate regioselectivity for the second cycloaddition using dimethyl propiolate (8:8'=6:1), the first cycloaddition with the same dienophile was extremely nonregioselective (11:11'=1:1). Although molecular sieves are a convenient agent, its regioselectivity of dehydration was not satisfied. The dehydration of mono-cycloadduct of 7 to dimethyl maleate favored the more stable inner double bond (13:13'=4:1).

Table 1. Double Diels-Alder Reactions of Cross-conjugated Triene Equivalents

1,3-Butadienyl Alcohol	Dienophiles[a] 1st 2nd Reaction	Conditions[b]	Bis-cycloadduct[c] yield %[d]	
 2	DMM DMAD	A B*	 5 60 %	
	DMM MP	A C	 8 37 %	 8' 6 %
	N-PhMI DMAD	B B*	 9 69 %	
	N-MeMI DMAD	B B*	 10 65 %	
	MP DMAD	B B*	 11 15 %	 11' 15 %
	DMAD DMAD	B B*	 12 65 %	
 7	DMM DMAD	A D*	 13 40 %	 13' 9 %

[a] DMM: dimethyl maleate; DMAD: dimethyl acetylenedicarboxylate; MP: methyl propiolate; N-PhMI: N-phenylmaleimide; N-MeMI: N-methylmaleimide. [b] All the reactions were carried out under reflux. A: 48 h in toluene ; B: 20 h in benzene; C: 60 h in benzene; D: 45 h in benzene. The conditions with asterisk indicate the reaction was performed in the presence of molecular sieves 5A. [c] All the bis-cycloadducts were dehydrogenated with chloranil in quantitative yields. [d] Isolated yields based on the 1,3-butadienyl alcohols. In the second reaction with methyl propiolate the unchanged diene 4 was recovered in 29 % yield under the given conditions (the condition C).

The present system has such advantages as 1) a variety of triene equivalents are easily available from chloroprene and carbonyl compounds, 2) the double Diels-Alder reaction with two different dienophiles gives satisfactory yields of cross bis-cycloadducts, 3) molecular sieves work well as a convenient dehydrating agent, 4) the total procedure is very simple as the separation of desired products is not always necessary and therefore the dehydration and cycloaddition steps can be performed in the same flask.

We are grateful to the Toyo Soda Manufactural Company for a generous sample of chloroprene.

References

1) O. Tsuge, E. Wada, and S. Kanemasa, Chem. Lett., 1983, 239 and 1525.
2) O. Tsuge, S. Kanemasa, H. Sakoh, and E. Wada, Chem. Lett., 1984, 273 and 277.
3) Synthesis and some reactions of 3-methylene-5-phenylthio-1-pentene as a cross-conjugated triene equivalent was studied by Okawara and his co-workers who presented the results at the 45th annual meeting of Chemical Society of Japan (Tokyo): H. Sano, Y. Ueno, and M. Okawara, the preprint II, 973 (1982).
4) It is known that 2-(1,3-butadienyl)magnesium chloride reacts with carbonyl compounds also as 4-(1,2-butadienyl)magnesium reagent (K. Kondo, S. Dobashi, and M. Matsumoto, Chem. Lett., 1976, 1077; S. Nunomoto and Y. Yamashita, J. Org. Chem., 44, 4788 (1979)).
5) The yield is based on the maleate. The quantitative recovery of 2' shows that 2' has not participated in the cycloaddition through its isomerization.
6) All the compounds reported herein gave satisfactory elemental analyses.
7) Molecular sieves 4A could be effectively used as well. Some examples for the dehydration with molecular sieves are known (O. Makabe, Y. Murai, and S. Fukatsu, Heterocycles, 13, 239 (1979); H. Narkgraf, E. W. Greeno, M. D. Miller, and W. J. Zaks, Tetrahedron Lett., 24, 241 (1983)).
8) Although no detectable isomerization of 4 was observed when the mixture of 4 and 4' (11:1) was heated under reflux in toluene for 60 h, under reflux in benzene in the presence of molecular sieves 5A the ratio changed as follows: 4:4'=1:2 after 60 h and 1:4.5 after 100 h.
9) The one flask procedure has an advantage that the desired diene (e.g. 4) can be captured by an activated dienophile before it isomerizes into the unreactive diene (e.g. 4').
10) Only the single isomers of bis-cycloadducts were obtained in the double reactions with olefinic and then acetylenic dienophiles. These results indicate that the second cycloaddition path proceeds in a highly stereoselective manner.

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