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STEREOSELECTIVITY OF DIENE-TRANSMISSIVE DIELS-ALDER REACTION; CYCLOADDITION REACTION OF CROSS-CONJUGATED TRIENE SYSTEM TO OLEFINIC DIENOPHILES

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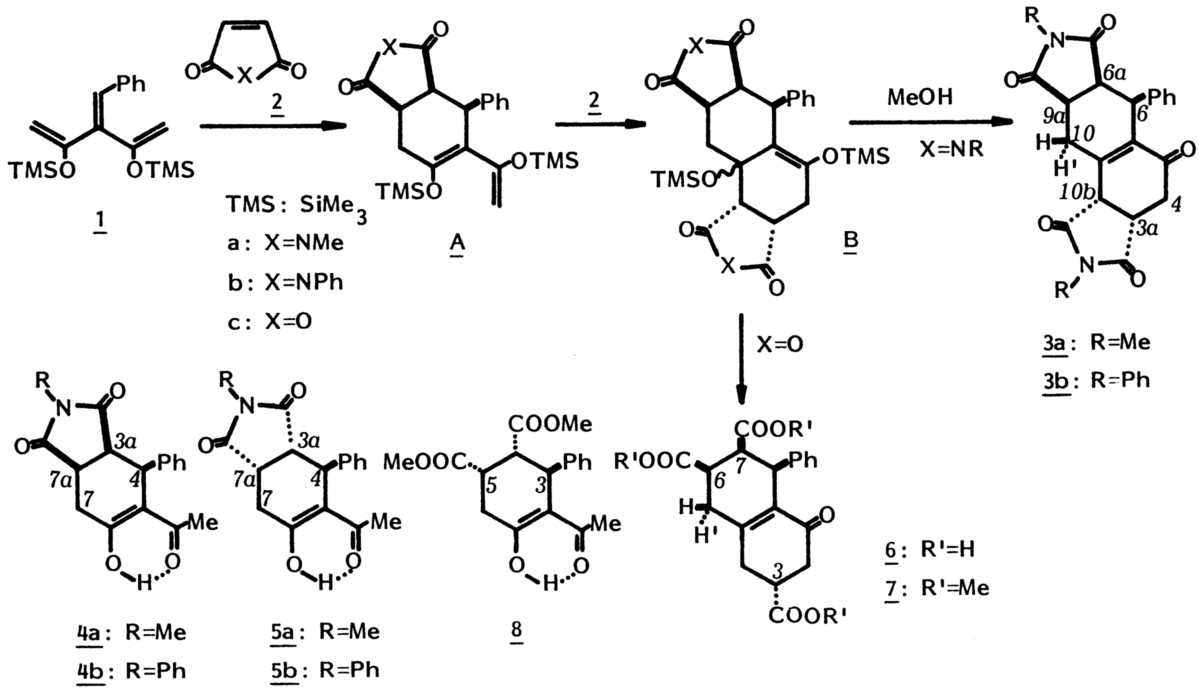
The stereoselectivity of diene-transmissive Diels-Alder reaction of a cross-conjugated triene, 3-benzylidene-2,4-bis(trimethylsilyloxy)-1,4-pentadiene, with a variety of olefinic dienophiles was investigated. Cyclic dienophiles gave the stereoselective bis-adducts via the endo mono-cycloadducts, whereas the exo mono-adducts were obtained as major products in the reaction with acyclic dienophiles. The steric regulation of diene-transmissive Diels-Alder reaction was discussed.

The preceding communication has described that a cross-conjugated triene system, 3-benzylidene-2,4-bis(trimethylsilyloxy)-1,4-pentadiene, reacts with acetylenic dienophiles in a new manner of double Diels-Alder reaction that was referred to as "diene-transmissive Diels-Alder reaction".[1] The initial cycloaddition reaction across a diene part of the triene forms a ring and an endocyclic double bond which then takes part in the second cycloaddition reaction as a part of newly formed diene conjugation. In this reaction, the silyloxy moieties have played a prominent role both in the activation of dienes and the regioselectivity of reactions. The newly formed diene was found more highly activated than the diene participated in the initial cycloaddition reaction, the regioselective bis-adducts being obtained as major products.

As to the stereochemical characteristics of diene-transmissive Diels-Alder reaction, we have been investigating the cycloaddition reaction of the triene with olefinic dienophiles. In the present communication, are discussed the stereoselectivity for the initial cycloaddition reaction and the steric regulation for the second cycloaddition reaction. Cyclic dienophiles gave the stereoselective bis-adducts via the endo mono-cycloadducts, whereas the exo mono-adducts were obtained as major products in the reaction with acyclic dienophiles.

The reaction of 3-benzylidene-2,4-bis(trimethylsilyloxy)-1,4-pentadiene 1 with three equivalents of N-methylmaleimide 2a in dry benzene under reflux for 72 h under nitrogen and the work up with methanol afforded a bis-adduct 3a in 60% yield together with low yields of two isomeric mono-adducts 4a (2%) and 5a (3%) (Scheme 1). The minor products 4a and 5a were assigned as the endo and exo mono-adducts, respectively, on the basis of the spectral data, especially of the chemical shifts of 2-Me and the coupling constants between 3a-H and 4-H.[2,3] The inspection of ^{1}H-NMR spectrum as well as the comparison with the spectra of 4a and 5a determined the structure of major product 3a as shown in Scheme 1 (Table 1). As the configuration at the 3a- and 10b-positions has not been confirmed by only the spectral data, their stereochemistry was tentatively assigned on the basis of the reaction pathway that will be mentioned later.

Similarly the reaction of 1 with three equivalents of N-phenylmaleimide 2b under reflux in benzene for 48 h gave a bis-adduct 3b in 80% yield together with minor mono-adducts 4b and 5b (in 3 and 6% yields, respectively).



Scheme 1.

Maleic anhydride 2c was found much more reactive than the maleimides. The reaction of 1 with two equivalents of 2c at room temperature for 72 h precipitated the silylated bis-cycloadduct B (X=O) whose purification was unsuccessful because of its instability. The work up of the reaction mixture with methanol afforded the decarboxylated bis-adduct 7 in 80% yield together with the exo mono-adduct 8 (7%), while no trace of the endo mono-adduct was obtained. The decarboxylation apparently occurred during the course of hydrolytic desilylation at the 10b-position of B since the hydrolysis of

Table 1. Stereoselective Bis-adducts 3a, 3b, and 7.

	Mp [°C]	$\nu_{C=O}$ [cm^{-1}]	M^+ [m/e]	^{1}H-NMR [δ ppm, Hz]							
				6-H	10-H	10'-H	10b-H	J_{6-6a}	J_{10-9a}	$J_{10'-9a}$	Others
3a	213-215	1760, 1675	392	$4.70^{br.d}$	2.53^{dd}	2.95^{dd}	3.92^{d}	6.0	9.0	4.5	a)
3b	232-234	1770, 1700	516	4.86^{d}	2.63^{dd}	3.05^{dd}	3.96^{d}	6.5	9.0	5.5	
7	141-143	1720, 1650	400	$4.14^{br.d}$	2.40^{dd}			7.5	12.4		b)
				(8-H	5-H)			(J_{8-7}	J_{5-6})		

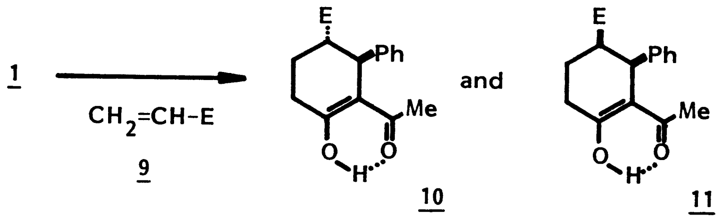
a) 8-Me: 2.33^{s}; 2-Me: 3.04^{s}.

b) 7-OMe: 3.10^{s}; 3- and 6-OMe: 3.63^{s} and 3.70^{s}.

8 into 6 followed by the esterification in the presence of p-toluenesulfonic acid afforded 7 in a good yield. The elimination at the 3a-position should have yielded another bis-adduct that shows methylene multiplets in higher field than 2 ppm. The low yield formation of an isomer of 8 that has the other stereochemistry at the 3a- and 10b-positions was observed in the crude reaction mixture, but the corresponding isomer of 7 was not isolated.

Thus, the cyclic dienophiles 2 react with 1 leading to the stereoselective bis-cycloadducts 8 as major products. No formation of bis-cycloadducts via the exo mono-cycloadducts indicates that the endo mono-cycloadducts have a more favored geometry for the second cycloaddition reaction. All the attempts to obtain the mono-adducts as major products ended in failure.

Contrary to the cyclic dienophiles, acyclic ones afforded a mixture of the exo and endo mono-adducts in the reaction with 1. The reaction of 1 with a large excess of methyl vinyl ketone 9a in benzene under reflux for 6 d and the work up with methanol gave the regioselective exo 10a and endo mono-adduct 11a in 48 and 20% yields, respectively (Scheme 2). The structures of mono-adducts were determined on the basis of the spectral data, especially of the chemical shifts of 4-MeCO and the coupling constants between 3-H and 4-H as shown in Table 2.



a: E=COMe
b: E=COOMe
c: E=CN

Scheme 2.

Similar results were obtained in the reaction of 1 with methyl acrylate 9b (with a large excess of 9b under reflux in benzene for 5 d) or acrylonitrile 9c (the nitrile was used as a solvent under reflux for 58 h): the exo mono-adducts 10b (70%) and 10c (54%), and endo ones 11b (22%) and 11c (18%) were isolated.

It is noteworthy that the reaction with acyclic dienophiles gives the mono-adducts even when excess

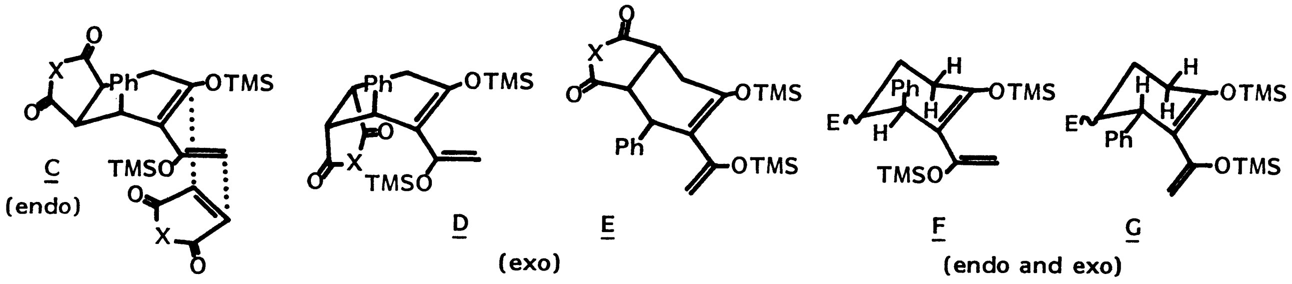
Table 2. Mono-adducts 10 and 11 to Acyclic Olefinic Dienophiles 9.

	Mp [°C]	IR [cm^{-1}]			M^+ [m/e]	^1H-NMR [δ ppm, Hz]					
		ν_{OH}	$\nu_{C=O}$	ν_{CN}		3-H	4-H	2-Ac	4-E	J_{3-4}	J_{4-5}
10a	31-32	3400	1700, 1590		258	4.31^d	2.74^{dt}	1.85^s	2.15^s	4.0	5.2
10b	liquid[a)]	3400	1725, 1590		274	4.40^d	2.76^{dt}	1.88^s	3.71^s	3.4	4.5
10c	153-155	3380	1590	2250	241	4.20^d	3.00^{dt}	1.88^s	-	2.7	4.1
11a	81-82	3400	1720, 1590		258	4.26^d	2.83^{ddd}	1.85^s or	1.88^s	4.9	4.0, 12.1
11b	75-80	3390	1700, 1600		274	4.29^d	2.92^m	1.89^s	3.56^s	5.0	b)
11c	144-146	3380	1600	2215	241	4.09^d	3.11^m	1.86^s	-	4.9	b)

a) Bp 110 °C/1 mmHg. b) Coupling constants were not given due to the complex splitting of signals for 4-H and 5-CH_2.

of the dienophiles are used under the conditions comparable to those employed in the reaction with cyclic dienophiles, and that an exo selectivity was preferred for the initial cycloaddition reaction.

The difference of stereoselectivity in the initial cycloaddition reaction between cyclic and acyclic dienophiles is not surprising since it is well known that a high endo selectivity has been often observed in the Diels-Alder reaction with cyclic dienophiles such as 2 while acyclic dienophiles such as 9 show a rather low stereoselectivity.[4] The steric repulsion among substituents during an endo approach may be inevitable in the Diels-Alder reaction of 1 which bears three bulky substituents on the diene skeleton (phenyl, 1-(trimethylsilyloxy)ethenyl, and trimethylsilyloxy groups).



Scheme 3.

As shown in Scheme 3, a possible conformer C for the endo mono-cycloadduct A to cyclic dienophiles has a favorable stereochemistry for the second cycloaddition reaction, the dienophiles being able to approach from the lower side without any critical hindrance. However, neither of the conformers D and E for the exo mono-cycloadduct allow the ready cycloaddition. The both sides of diene moiety are considerably hindered from an endo approach of the dienophiles (D) or the diene moiety may hardly take a s-cis conformation (E).

The cyclohexene ring of mono-cycloadduct to acyclic dienophiles is rather flexible compared with that to the cyclic dienophiles. Both the exo and endo mono-cycloadducts may take half-chair conformations (F and G). The conformer G carries a s-trans diene moiety due to the repulsion between the phenyl and silyloxy groups. In the other one F that has a s-cis diene moiety, the axial substituents at the 3- and 6-positions obstruct an endo approach of the dienophiles.

Such remarkable difference for the second cycloaddition reaction seems to depend upon not only the steric demand of mono-cycloadducts but also the reactivity of the second dienophiles. Although no bis-adducts were obtained in the reaction with rather inactive acyclic dienophiles, it would be still possible to get cross bis-adducts by using more reactive dienophiles as the second ones. Studies along this line are in progress.

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References

1) O. Tsuge, E. Wada, and S. Kanemasa, Chem. Lett., 1983, 239.
2) The words, endo and exo, are used for the approach of dienophile to the trans diene of 1. It is known that a trans diene undergoes the Diels-Alder reaction much faster than a cis diene (J. Sauer, Angew. Chem., Int. Ed. Engl., 6, 16 (1967) and references cited therein).
3) All the isolated products gave satisfactory elemental analyses.
4) As reviews, a) J. G. Martin and R. K. Hill, Chem. Rev., 61, 537 (1961); b) The reference in Ref. 2; c) J. Sauer and R. Sustmann, Angew. Chem., Int. Ed. Engl., 19, 779 (1980). See also references cited therein.

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