DIENE-TRANSMISSIVE DIELS-ALDER REACTION OF 2-*VINYL*-1-*OXABUTADIENE SYSTEM*

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Abstract - The first example for the diene-transmissive Diels-Alder reaction of 2-vinyl-1-oxabutadiene system is presented by the reactions of 1,5-diphenyl- and 1,5-di(2-thienyl)-1,4-pentadien-3-ones with electron-rich enamines as the first dienophiles and then with electron-deficient dienophiles as the second.

It has been reported that the diene-transmissive Diels-Alder reaction of cross-conjugated trienes offers a versatile synthetic route to hydronaphthalene skeletons.[1,2] This strategy using cross-conjugated heterotrienes has been applied to a lesser extent in synthesis despite its apparent potential. To the best of our knowledge, two examples have been reported up to the present. One is the reaction of 1,5-di(p-tolyl)-1,4-pentadiene-3-thione, generated in situ by the treatment of the corresponding ketone with P_4S_{10}, with electron-deficient dienophiles at both the first and second steps, providing a useful synthetic route to sulfur-containing polycyclic compounds[3] and the other the reaction of cyclic formyl-diene whose structure corresponded to a 3-vinyl-1-oxabutadiene system, leading to the formation of tetracyclic quassinoid framework.[4]

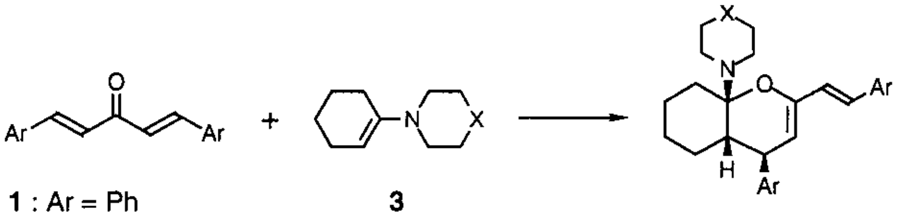
1,5-Diaryl-1,4-pentadien-3-one corresponded to a 2-vinyl-1-oxabutadiene system is generally stable and readily available in contrast to the corresponding thioketone. Thus, we planned to investigate whether 1,5-diphenyl- (**1**)[5] and 1,5-di(2-thienyl)-1,4-pentadien-3-ones (**2**)[6] as the typical 2-vinyl-1-oxabutadiene system are feasible for such a sequential Diels-Alder reaction or not.

Although pentadienones (**1**) and (**2**) were unreactive to electron-deficient dienophiles in contrast to the corresponding thioketone,[3] they reacted with electron-rich alkenes such as vinyl ethers and enamines to give the corresponding Diels-Alder adducts. It thus indicates that pentadienones (**1**) and (**2**), as well as simple α,β-unsaturated carbonyl compounds,[7] participate preferentially in inverse electron demand Diels-Alder reactions with electron-rich dienophiles. In this paper we wish to report the diene-transmissive Diels-Alder reaction of pentadienones (**1**) and (**2**) using enamines (**3**) derived from cyclohexanone at the first stage and then electron-deficient dienophiles at the second. This is the first example for the diene-transmissive Diels-Alder reaction of 2-

vinyl-1-oxabutadiene system.

Since the reactivity of **1** to **3a** (X=O) was not high, the hetero Diels-Alder reaction was investigated in the presence of a weak Lewis acid: Remarkable rate enhancement was achieved by use of Lewis acid, especially $ZnCl_2$. Rate accelaration was insufficient in the presence of a catalytic amount of $ZnCl_2$, but the cycloadduct (**4a**) (Ar=Ph, X=O), mp 154-155 °C (decomp.), was obtained as a single product in a good yield when a little less than one equivalent of $ZnCl_2$ was used. The reactivity of enamine (**3b**) ($X=CH_2$) to **1** was somewhat higher than that of **3a**, and the $ZnCl_2$-catalyzed reaction of **1** with **3b** gave again the single cycloadduct (**4b**) (Ar=Ph, $X=CH_2$), mp 122-123 °C (decomp.), in a good yield. Similar reaction of **2** with **3a** in the presence of $ZnCl_2$ gave the corresponding cycloadduct (**5a**) (Ar=2-thienyl, X=O), mp 147-148 °C (decomp.), as a single product in a moderate yield (Table 1).

Table 1. Diels-Alder reactions of pentadienones with enamines[a)]



1 : Ar = Ph
2 : Ar = 2-thienyl

3

4 : Ar = Ph
5 : Ar = 2-thienyl

Pentadienone	Enamine			Catalyst	Reaction	Cycloadduct			
		X	(equiv)	(equiv)	Time, h		Ar	X	Yield, %
1	**3a**	O	(1.5)	None	10	**4a**	Ph	O	trace
1	**3a**	O	(1.1)	$ZnCl_2$ (0.1)	6	**4a**	Ph	O	48
1	**3a**	O	(1.1)	$ZnCl_2$ (0.5)	6	**4a**	Ph	O	77
1	**3a**	O	(1.1)	$ZnCl_2$ (0.9)	6	**4a**	Ph	O	88
1	**3a**	O	(1.1)	$FeCl_3$ (0.9)	6	**4a**	Ph	O	68
1	**3b**	CH_2	(1.5)	None	6	**4b**	Ph	CH_2	63
1	**3b**	CH_2	(1.1)	$ZnCl_2$ (0.9)	1	**4b**	Ph	CH_2	89
2	**3a**	O	(1.1)	$ZnCl_2$ (0.9)	6	**5a**	Thi[b)]	O	60

a) All the reactions were carried out in dry benzene at 20 °C. b) Thi : 2-thienyl

On the basis of ^1H nmr spectra the configuration between 4-H and 4a-H in all the cycloadducts (**4a**, **4b** and **5a**) was assigned as trans.[8] Finally, the *cis*-fused structure of **4b** was determined by X-ray crystallographic analysis. ORTEP drawing of **4b** is shown in Figure 1.[9] It may be thus concluded that at least the hetero Diels-Alder reaction of **1** with **3b**, and presumably the other two reactions proceed in an endo-addition manner with high regioselectivity. The adducts (**4a**) and (**5a**) were deduced to have the same stereochemistry as **4b**.

The sequential Diels-Alder reaction of the newly formed diene moiety in the initial adducts (**4** and **5a**) was next investigated: The reaction was found to only occur with strong electron-deficient dienophiles. The adducts (**4**) and (**5a**) reacted with tetracyanoethylene (TCNE) under mild conditions to give excellent yields of the corresponding Diels-Alder adducts (**6a**) (Ar=Ph, X=O), mp 162-163 °C (decomp.), (**6b**) (Ar=Ph, X=CH_2), mp 126-128 °C (decomp.), and (**7a**) (Ar=2-thienyl, X=O), mp 141-142 °C (decomp.), respectively. 4-Methyl-1,2,4-triazoline-3,5-dione (MTAD) was somewhat sluggish, but the corresponding cross-cycloadducts, (**8a**) (Ar=Ph, X=O), mp 185-186 °C (decomp.), (**8b**) (Ar=Ph, X=CH_2), mp 189-190 °C (decomp.), and (**9a**) (Ar=2-thienyl,

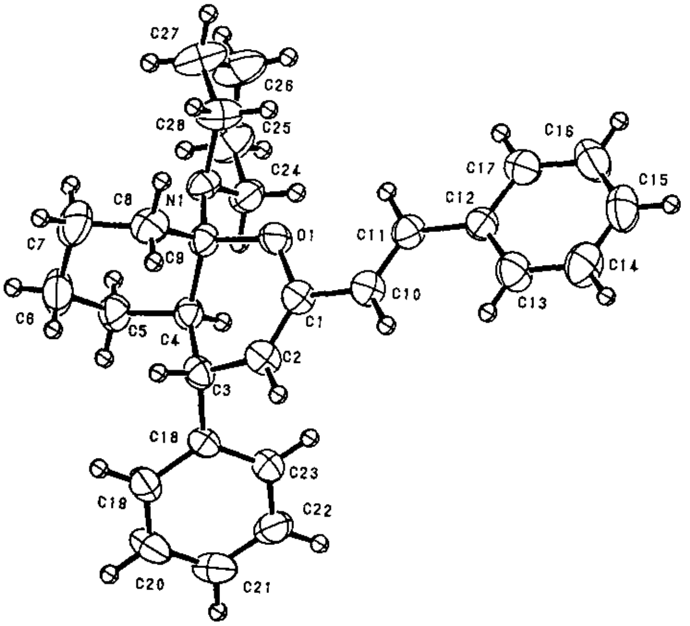
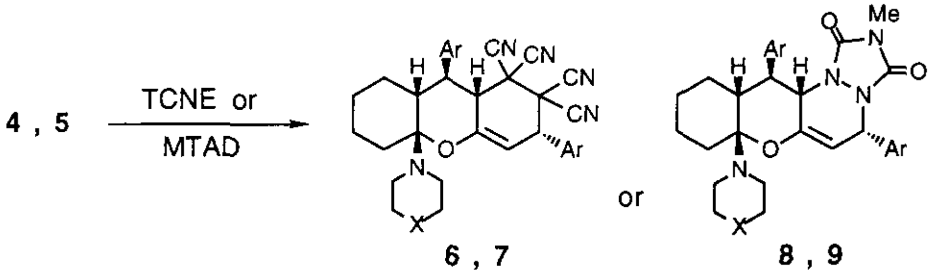


Figure 1. ORTEP drawing of **4b**

Table 2. Diels-Alder reactions of initial adducts leading to cross bis-cycloadducts[a)]



Initial adduct	Dienophile (equiv)	Reaction Conditions		Bis-cycloadduct			
		Solvent	Time, h		Ar	X	Yield, %
4a	TCNE (1.0)	Benzene	1.5	**6a**	Ph	O	91
4b	TCNE (1.0)	THF	0.5	**6b**	Ph	CH_2	93
5a	TCNE (1.1)	THF	1	**7a**	Thi[b)]	O	92
4a	MTAD (1.5)	THF	3	**8a**	Ph	O	36
4b	MTAD (1.5)	THF	3	**8b**	Ph	CH_2	44
5a	MTAD (2.0)	THF	3	**9a**	Thi[b)]	O	45

a) All the reactions were carried out at 20 °C. b) Thi : 2-thienyl

X=O), mp 166-167 °C (decomp.), were obtained in a moderate yield together with unidentified compounds, respectively (Table 2). Stereochemistry of bis-cycloadducts (**6**-**9**) was determined on the basis of ^{1}H nmr spectra.[10]

As mentioned above, the pentadienones (**1**) and (**2**) exclusively participate in inverse electron demand Diels-Alder reaction but the mono-adducts in normal electron demand one. Consequently, cross type of diene-transmissive hetero Diels-Alder reaction of the pentadienone was carried out easily and the results have wide application for the synthesis of various oxygen-containing polycyclic compounds.

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6. The pentadienone (**2**) as yellow plates [mp 121-122 °C] was prepared in 84% yield by the condensation of 2-thiophenecarboxaldehyde with acetone in the presence of NaOH in aqueous ethanol in a similar manner as **1**. All the new compounds in this paper gave satisfactory elementary analyses.
7. D. L. Boger and S. M. Weinreb, Hetero Diels-Alder Methodology in Organic Synthesis, Academic Press, New York, 1987, p.167.
8. Cycloadducts (**4a**, **4b** and **5a**) are colorless prisms. The spectral data of **4b** are shown. ^{1}H Nmr ($CDCl_3$) δ=1.0-2.0 (14H, m), 2.10-2.41 (1H, m, 4a-**H**), 3.60 (1H, dd, J=8.7, 2.9 Hz, 4-**H**, changed to a doublet on irradiation at δ=4.83), 4.83 (1H, d, J=2.9 Hz, 3-**H**), 6.46, 6.90 (each 1H, d, J=15.8 Hz), 7.02-7.77 (10H, m); ^{13}C nmr ($CDCl_3$) δ=22.79, 25.14, 26.63, 26.93, 41.38, 45.01, 92.89, 105.05, 124.98, 126.23, 126.50, 127.20, 128.20, 128.48, 137.35, 145.48, 148.98; ms m/z 399 (M^+).
9. X-Ray crystallographic analysis of **4b** was carried out on a Rigaku AFC5S diffractometer. The diffraction data were collected with the use of MoKα radiation and 5179 independent reflections were used the structures by the TEXSAN program (TEXSAN TEXRAY, Structure Analysis Package, Molecular Structure Corporation). Crystal data: $C_{28}H_{33}NO$, F.W.=399.57, triclinic, space group P1, a=10.406 (9) Å, b=12.253 (6) Å, c=10.112 (7) Å, α=100.03 (5)°, β=115.00 (6)°, γ=75.99 (5)°, v=1130(1) Å^3, Z=2, Dcalcd=1.174 g/cm^3, R (Rw)=0.050 (0.054).
10. All the cross bis-cycloadducts (**6**-**9**) are colorless crystals. The ^{1}H nmr ($CDCl_3$) data of **8b** are shown: δ=0.60-2.32 (14H, m), 2.40-3.35 (6H, m), 3.12 (3H, s), 5.01 (1H, d, J=9.3 Hz, 12a-**H**), 6.03 (1H, d, J=15.9 Hz, 5-**H**, changed to a singlet on irradiation at δ=7.30), 7.05-7.70 (11H, m).

Received, 5th October, 1994