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HIGH EXOSELECTIVITY IN DIELS-ALDER ADDITIONS OF α-VINYLIDENE AND α-METHYLENE-γ-BUTYROLACTONES TO CYCLOPENTADIENE.

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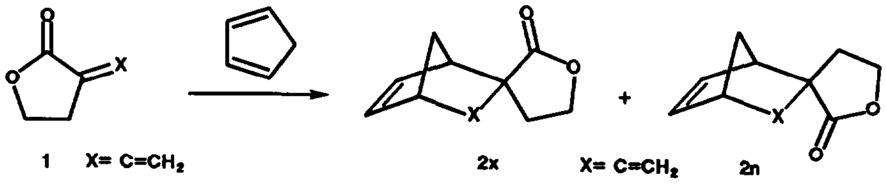
Abstract : Regardless of the conditions, catalytic or thermal, lactones **1** and **8** undergo kinetically controlled Diels-Alder cycloadditions to cyclopentadiene with pronounced exoselectivity. The activation parameters are reported for both reactions. It is suggested that such exoselectivity is a general property of conformationally rigid cyclic cisoid dienophiles.

Literature offers many examples of substrates which violate the prevalent Alder-Stein principle[1], giving predominantly the corresponding *exo* stereomers in kinetically controlled Diels-Alder reactions[2]. Hoffmann and Ismail[3] have shown that the stereoselectivity in the addition of α-alkylated allenic esters to cyclopentadiene depends essentially on the experimental conditions. Thus, formation of the *exo* adduct is preferred under thermal conditions (*endo/exo* ratio 40:60), whereas usual endoselectivity is observed when a Lewis acid is used (*endo/exo* ratio 76:24)[4].

In contrast, we describe for the first time catalyzed Diels-Alder reactions which exhibit the same exoselectivity as does the thermal process.



1 X= C=CH$_2$ 2x X= C=CH$_2$ 2n
8 X= CH$_2$ 9x X= CH$_2$ 9n

We have investigated here the addition of α-vinylidene-γ-butyrolactone **1** with cyclopentadiene[5] under different, however typical, conditions, varying solvent and catalyst. Results are summarized in Table I.

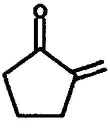
Table I : 2a/2x Ratios for Diels-Alder Reactions of Allenic Lactone 1 to Cyclopentadiene

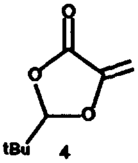
entry	catalyst	solvent	temperature	*endo*/*exo* ratio[a]	yield %[b]
1	-	toluene	reflux	12:88	97
2	-	CH_2Cl_2	reflux	13:87	98
3	-	water[c]	r.t.	21:79	99
4	$ZnCl_2$[d]	CH_2Cl_2	r.t.	22:78	97
5	$AlCl_3$[d]	CH_2Cl_2	-30°C	13:87	74
6	$TiCl_4$[d]	CH_2Cl_2	-30°C	10:90	40
7	$Eu(fod)_3$[d,e]	toluene	0°C	11:89	36

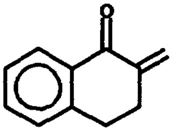
a) Determined by capillary GC on a CP-WAX 51 column; exo adduct 2x having the shorter retention time. b) Determined by capillary GC of the reaction mixture. c) The reactants being hydrophobic, the reaction is performed under vigourous stirring in biphasic medium[6]. d) Lewis acid catalyst (0.1 molar equiv. with respect to 2) was stirred 20 mn with the lactone solution before cyclopentadiene (2 equiv.) was added. e) Europium(III) tris(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octadionate) was reported to be an efficient catalyst in Diels-Alder addition of cyclopentadiene to allenic esters[7].

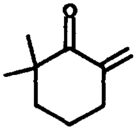
Clearly, all the reactions exhibit remarkable exoselectivity, regardless of the conditions.

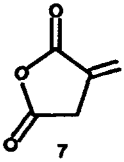
Several exocyclic methylene dienophiles, such as α-methylenecyclopentanone 3^{8a}, 2-(tert-butyl)-5-methylene-1,3-dioxolan-4-one 4^{8b}, α-methylene tetralone 5^{8c}, 2,2-dimethyl-6-methylene cyclohexanone 6^{8c} and itaconic anhydride 7^{8d} have been reported earlier to give predominantly the corresponding *exo* adducts with cyclopentadiene, either under catalytic or thermal reactions conditions.











Dienophiles	3	4	5	6	7
endo/exo **ratios of cyclopentadiene adducts**	9 : 91	4 : 96	3 : 97	11 : 89	0 : 100

These examples seem to illustrate a more general phenomenon. Indeed, a tight *relationship* appears between the rigid cisoid conformation of the conjugated double bond of the cyclic dienophiles and exoselectivity. However, with these substrates, this peculiar exoselectivity remains to be tested under different conditions.

In order to confirm our assumption, we investigated in a similar way the addition of cyclopentadiene to α-methylene-γ-butyrolactone 8, the ethylenic equivalent of 1. In fact, the *exo* stereomer $9x^{9}$ was obtained predominantly (92-98%), whatever the experimental conditions. 8 Behaves very like 1 toward cyclopentadiene, with enhanced exoselectivity (Table II).

Table II : 9n/9x Ratios for Diels-Alder Reactions of Methylene Lactone 8 to Cyclopentadiene

entry	catalyst	solvent	temperature	*endo/exo* ratio[a]	yield %[b]
1[c]	$AlCl_2OR^*$	toluene	-78°C	2:98	-
2	-	toluene	reflux	8:92	96
3	-	CH_2Cl_2	reflux	8:92	95
4	$ZnCl_2$[d]	CH_2Cl_2	r.t.	7:93	96
5	$AlCl_3$[d]	CH_2Cl_2	-15°C	6:94	72
6	$TiCl_4$[d]	CH_2Cl_2	-15°C	4:96	51

a,b,d: see footnotes a,b,d, respectively, in Table I. c) This reaction have been reported in the presence of (-)-menthoxyaluminum dichloride catalyst[8c] (results concerning asymmetric induction will be reported elsewhere).

Moreover, the observed *endo/exo* ratios of adducts 2 and 9 do not result from an equilibrium process to give the supposed thermodynamically more stable *exo* stereomers[10], but are determined by the energy gap between the transition states leading to the *endo* and *exo* isomers respectively, through a kinetically controlled process.

In fact, kinetic measurements were performed in toluene at different temperatures for reactions of both dienophiles with a large excess of cyclopentadiene. We noticed that the stereomers proportions remained constant throughout the course of each reaction, indicating that neither isomerization of cycloadducts nor preferential degradation of one of them occurred[11].

Allenic lactone 1 reveals high reactivity towards cyclopentadiene, undergoing cycloaddition about two times faster than its ethylenic counterpart[12]. The activation parameters determined from the temperature dependence of the rate constants, using Eyring's model, are presented in Table III.

Table III : Activation Parameters for the Formation of Cycloadducts.

adduct	$\Delta H^{\ddagger}$ kcal mol^{-1} [a]	$\Delta\Delta H^{\ddagger}_{endo-exo}$	$\Delta S^{\ddagger}$ cal $mol^{-1}K^{-1}$ [b]	$\Delta\Delta S^{\ddagger}_{endo-exo}$
2n	15.5	1.6	-33.3	0.4
2x	13.9		-33.7	
9n	15.1	1.1	-36.5	-1.9
9x	14.0		-34.6	

a,b) Average errors in determination are ± 0.5 kcal mol^{-1} and 0.6 cal $mol^{-1}K^{-1}$.

The activation parameters are in the same order of magnitude as in other Diels-Alder reactions[2b]. The values of the enthalpy and entropy gaps between the *endo* and *exo* transition states indicate that stereoselectivity is mostly enthalpic in origin. This result accords with our general knowing about Diels-Alder additions and ascertains that the reactions studied are under kinetic control.

Conclusively, exoselectivity in the reported Diels-Alder reactions of conformationally rigid cyclic cisoid dienophiles with cyclopentadiene seems to admit no exception. Exoselectivity being conspicuously related with α-substitution of the dienophile[13], one can suggest that it may result from unfavorable steric interactions of substituents with the methylene group of cyclopentadiene in the *endo* transition state of the cycloaddition. Nevertheless, numerous other factors can interfer and general studies are now in progress to evaluate the respective influences of steric, conformational, electronic or dipolar effects on the stereoselectivity of the Diels-Alder reaction.

References and Notes :

(1) Alder, K.; Stein, G. *Angew. Chem.* 1937, *50*, 510.

(2) (a) Kobuke, Y.; Fueno, T.; Furukawa, J. *J. Am. Chem. Soc.* 1970, *92*, 6548. (b) Sauer, J.; Sustmann, R. *Angew. Chem., Int. Ed. Engl.* 1980, *19*, 779 and references therein.

(3) (a)Ismail, Z. M.; Hoffmann, H. M. R. *J. Org. Chem.* 1981, *46*, 3549 and references therein. (b) Gandhi, R. P.; Ishar, M. P. S.; Wali, A. *J. Chem. Soc., Chem. Commun.* 1988, 1074. (c) Gandhi, R. P.; Ishar, M. P. S. *Indian J. Chem.* 1989, *28B*, 287.

(4) Hoffmann[3a] compared this transgression of the endo rule with those reported for methacrylic type dienophiles[2].

(5) The first Diels-Alder reactions of 1 are reported in the previous communication in the same issue.

(6) On hydrophobic acceleration of Diels-Alder reactions, see : Breslow, R.; Rideout, D. *J. Am. Chem. Soc.* 1980, *102*, 7816. Notable enhancement of *endo/exo* ratio is observed when the addition of cyclopentadiene to methyl vinyl ketone is carried out in water, and this ratio is affected by salts which change the hydrophobicity of the medium : Breslow, R.; Maitra, U. *Tetrahedron Lett.* 1984, *25*, 1239.

(7) Gandhi, R. P.; Ishar, M. P. S.; Wali, A. *J. Chem. Soc., Chem. Commun.* 1988, 1074.

(8) (a) Sauers, R. R.; Henderson, T. R. *J. Org. Chem.* 1974, *39*, 1850. (b) Mattay, J.; Mertes, J.; Maas, G. *Chem. Ber.* 1989, *122*, 327. (c) Northcott, C. J.; Valenta; Z. *Can. J. Chem.* 1987, *65*, 1917. (d) Hill, R. K.; van Auken, T. V. *J. Org. Chem.* 1958, *23*, 626.

(9) Isolation and identification of adducts 9 were carried out as for 2 [5].

(10) Lindsay Smith, J. R.; Norman, R. O. C.; Stillings, M. R. *Tetrahedron* 1965, *34*, 1381. See also [2a].

(11) Retrodienic reaction of compound 9x occur under flash vacuum thermolysis at 550°C : Haslouin, J.; Rouessac, F. *Tetrahedron Lett.* 1976, *50*, 4651. Recently, [4+2] cycloreversions of norbornene derivatives at low temperature in the presence of methylaluminum dichloride were reported : Grieco, P. A.; Abood, N. *J. Org. Chem.* 1989, *54*, 6008. Such behavior was precluded in our case : in catalytic conditions, 2n gave no traces of 2x and reciprocally.

(12) At 40°C the pseudo first-order rate constants of formation of adducts 2 and 9 were 3.56 10^{-5} and 6.87 10^{-5} s^{-1} respectively.

(13) Mark, V. *J. Org. Chem.* 1974, *39*, 3181.

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