

INTRAMOLECULAR DIELS-ALDER REACTIONS OF DIENAMINES WITH ACRYLATES:
TRENDS IN STEREOSELECTIVITY UPON SUBSTITUTION.

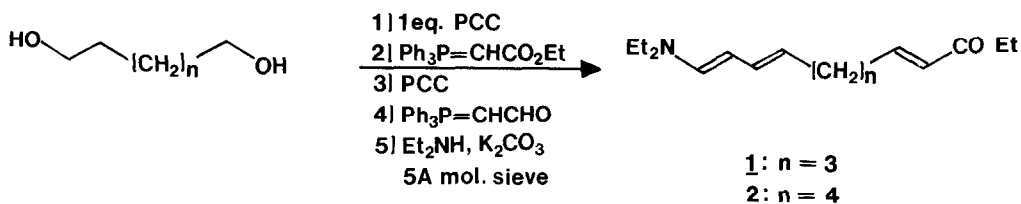
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Abstract: Intramolecular Diels-Alder reactions of all-trans ethyl 10-diethylamino-2,7,9-decatrienoate and 11-diethylamino-2,8,10-trienoate occur readily to produce trans and cis-fused products in ratios of 85:15 and 55:45, respectively.

Intramolecular Diels-Alder cycloadditions of 1,3,8-nonatriene and 1,3,9-decatriene give predominantly cis products (trans:cis = 25:75 and 47:53, respectively),¹ whereas the 9- or 10-ethoxycarbonyl derivatives give the trans products preferentially (trans:cis = 60:40² and 51:49,³ respectively). We have studied the cycloadditions of more highly activated derivatives, containing an electron-donating diethylamino substituent on the diene and an electron-withdrawing ethoxycarbonyl substituent on the dienophile. These compounds undergo cycloadditions near room temperature, and show increased stereoselectivity as compared to less activated analogs.

The dienaminoalkylacrylates, 1 and 2, were prepared starting from the diols, as shown below.⁴

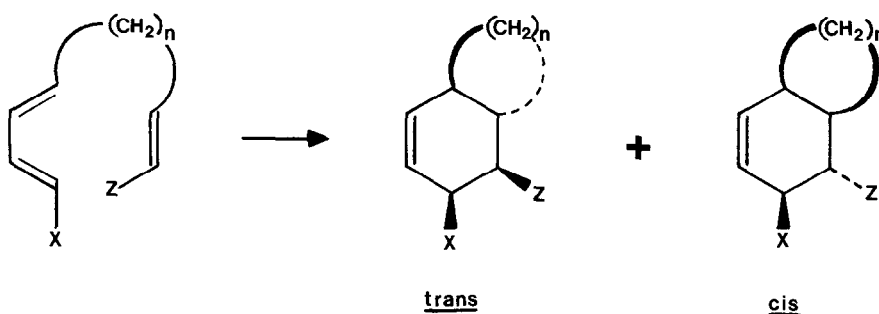


The dienamines readily undergo intramolecular cycloadditions at 40–60° in benzene solution. Adducts from 1 and 2 were obtained in 62% and 35% yield (based upon the aldehyde precursors), and stereochemistries of the products were established by nmr spectroscopic studies of the separated adducts.⁵ The ratios of adducts were established independently by isolation, and by integration of the resonances due to the proton

α to the amino group in the nmr spectra of reaction mixtures. Elimination of diethylamine from the adducts was achieved by refluxing the separated adducts in KOH/EtOH solution. The nmr spectra of the resulting dienes confirmed the cis or trans assignments.^{5b}

As shown in Table I, the diethylamino group has a relatively large effect on stereoselectivity in the nonatriene series, causing a 0.8 kcal/mol lowering of the energy of the trans transition state relative to the cis, while the effect in the decatriene case is a nearly negligible 0.1 kcal/mol. Table I includes additional results, from which several trends can be established.

Table I. Stereoselectivities of Intramolecular Diels-Alder Cycloadditions of Nonatrienes and Decatrienes.



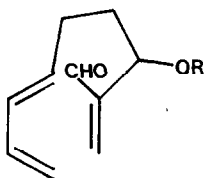
Substituents		Nonatrienes(n=3)			Decatrienes(n=4)		
X	Z	T(°C)	trans:cis	$\Delta\Delta G^\ddagger$ ^a	T(°C)	trans:cis	$\Delta\Delta G^\ddagger$ ^a
H	H	190	25:75 ^b	-1.0	190	47:53 ^b	-0.1
H	CO ₂ Et	150	60:40 ^c	0.3	155	51:49 ^d	0.0
i-Pr	CO ₂ Et	150	72:28 ^c	0.8	155	50:50 ^e	0.0
Et ₂ N	CO ₂ Et	60	85:15 ^f	1.1	40	55:45 ^f	0.1
i-Pr	CO ₂ Et·AlCl ₂ Et	25	>98:2 ^c	>2.3	22	88:12 ^e	1.2

^a $\Delta\Delta G^\ddagger = \Delta G^\ddagger(\text{cis}) - \Delta G^\ddagger(\text{trans})$, in kcal/mol. ^b Reference 1. ^c Reference 2. ^d Reference 3. ^e Roush, W.R.; Gillis, H.R., *J. Org. Chem.*, **1982**, *47*, 4825. ^f This work.

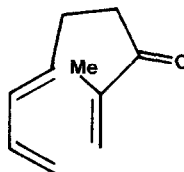
These trends are as follows. (1) While 1,3,8-nonatriene forms the cis product preferentially, donors at C-1 or acceptors at C-9 promote trans stereoselectivity. The single dienophile ester substituent causes a

1.3 kcal/mol shift from a cis preference toward a trans preference. In the series shown in Table I, there is a more than 3.3 kcal/mol variation in selectivity. (2) The same trends are found in the 1,3,9-decatriene series, but stereoselectivity is always low and is influenced to only a small extent by substituents. In the whole series in Table I, substituents have only a 1.3 kcal/mol influence on stereoselectivity.

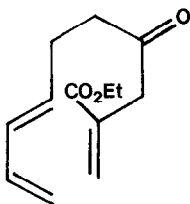
Other studies indicate that acceptors at the internal position of the alkene promote cis-stereoselectivity. For example, the molecules shown below give the trans/cis ratios shown in brackets under each compound structure.⁶



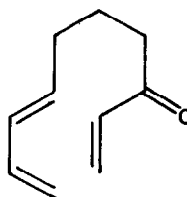
i [22:72]



ii [30:70]



iii [25:75]



iv [5:95]

These examples suggest that an acceptor at the internal position has a smaller influence upon stereoselectivity in the nonatriene series than in the decatriene series.

The stereoselectivities of intramolecular cycloadditions have been discussed by various authors in terms of asynchronous transition states for these reactions.⁷ However, the differences in trends for nonatrienes and decatrienes have not previously been noted, and are not simply explained in terms of product stabilities. In the following communication, we describe model calculations which provide more detailed insights into the origins of these trends.⁷

Acknowledgement. We are grateful to the National Institutes of Health and the National Science Foundation for financial support of this research, and to Professors Kathryn Parker and Michael Jung for helpful discussions.

References and Notes

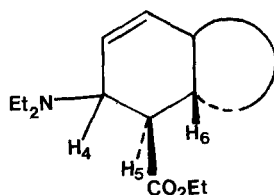
(1) Lin, Y.-T.; Houk, K.N., *Tetrahedron Lett.*, in press.

(2) Roush, W.R.; Gillis, H.R.; Ko, A.I., *J. Am. Chem. Soc.*, **1982**, *104*, 2269.

(3) Roush, W.R.; Hall, S.E., *J. Am. Chem. Soc.*, **1981**, *103*, 5200.

(4) All new compounds were characterized by nmr, ir, and by high resolution mass spectra.

(5) (a) Although 300 MHz nmr spectra in CDCl_3 and C_6D_6 did not result in resolution of the bridgehead proton couplings, the following coupling constants (in Hz) are indicative of structure. 1: cis-adduct ($J_{45}=11.5$, $J_{56}=10.7$), trans-adduct ($J_{45}=8.5$, $J_{56}=12.0$); 2: cis-adduct ($J_{45}=10.5$, $J_{56}=11.7$), trans-adduct ($J_{45}=8.5$, $J_{56}=12.5$). Both cis adducts have H_4 , H_5 , and H_6 all axial, while H_4 is equatorial in the trans adducts. The coupling constants agree with those found for cyclostachnine A and B, which have analogous stereochemistries and substitution patterns (Joshi, B.S.; Viswanathan, N.; Gawad, D.H.; Balakrishnan, V.; von Philipsborn, W., *Helv. Chimica Acta*, **1975**, *58*, 2295).



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(b) The bridgehead hydrogens are coupled by 7.5 Hz in the cis-dienes and 19.0 Hz in the trans-dienes.

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(7) Brown, F.K.; Houk, K.N., *Tetrahedron Lett.*, following communication.

(Received in USA 24 January 1985)