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INTRAMOLECULAR DIELS-ALDER REACTIONS OF 1,3,8-NONATRIENE AND 1,3,9-DECATRIENE

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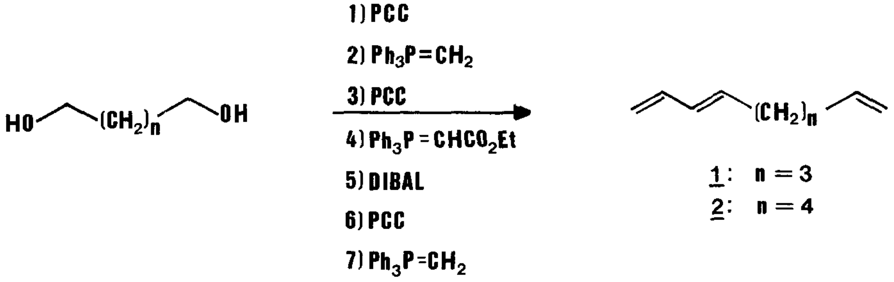
Abstract: The stereoselectivities of the title reactions have been investigated from 140-340°C, and relative activation parameters for cis and trans product formation have been determined.

Now a two-decade-old concept,[1] the formation of the hydrindane or decalin skeletons by intramolecular Diels-Alder reactions is a useful technique for natural product synthesis,[2] as reflected by the recent flood of major reviews.[3] Most 1,3,8-nonatrienes and 1,3,9-decatrienes for which intramolecular Diels-Alder reactions have been observed are substituted by activating electron-withdrawing substituents on the dienophile terminus (C_9 or C_{10}, respectively). These reactions give predominantly trans-fused hydrindane systems with moderate selectivities and trans-fused decalin systems with very low stereoselectivities.[2,3] Various rationalizations of these tendencies have been offered, usually focussing on interactions of the connecting-chain with the forming cyclohexene ring.[2-5] In connection with our development of computational models of intramolecular cycloadditions,[6] we were interested in the stereochemistries of the reactions of the parent hydrocarbons. Surprisingly, these have never been reported.[7] We now report the stereoselectivities of these reactions over a large temperature range. In a subsequent communication,[6a] we will provide a unified concept to rationalize the effects of substituents on intramolecular cycloaddition stereoselectivity.

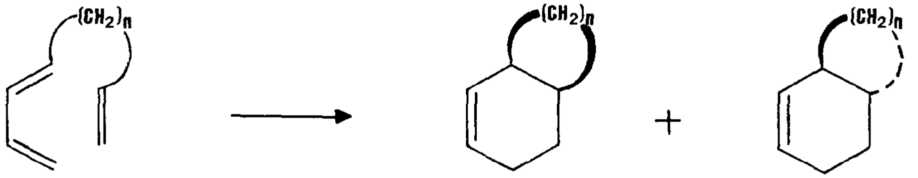
The parent systems, 1 and 2, were synthesized by the standard techniques shown below.[8]



Preparative cycloadditions were carried out at 200°C in sealed tubes in cyclohexane solvent. Products were separated by preparative glc.[9a] The separated products were reduced with diimide[10,11] to give the pure cis- or trans-hydrindanes or decalins. Structures of the reduced products were proven by comparisons of 300 MHz nmr spectra with those obtained for authentic samples.[12] Whereas both cis-hydrindane and cis-decalin have all nmr resonances between 1.3-1.8δ, the spectra of both trans-hydrindane and trans-decalin have separate six-proton multiplets at 0.9δ, so that the isomers are easily distinguished by nmr.[13,14]

In order to determine the influence of temperature on product ratios, the cycloadditions were investigated over the temperature range from 140°C to 340°C in degassed cyclohexane, with or without added BHT. The product ratios obtained at different temperatures were determined by glc,[9b] and are listed in Table I.

Table I: Product ratios at different temperatures.



		1,3,8-Nonatriene		1,3,9-Decatriene	
T(°C)	Time (hrs)	Conversion	[cis]/trans] Ratio	Conversion	[cis]/[trans] Ratio
140 ± 1	240	no rxn.		no rxn.	
162 ± 1	90	45%	76.4/23.6	46%	53.9/46.1
190 ± 1	35	85%	75.4/24.6	87%	52.9/47.1
220 ± 1	7	90%	74.0/26.0	92%	52.1/47.9
252 ± 2	1.5	95%	72.6/27.4	95%	51.8/48.2
300 ± 2	1	95%	71.3/28.7	95%	51.7/48.3
340 ± 2	0.5	99%	69.8/30.2	95%	51.5/48.5

Control experiments established that the products do not interconvert under the reaction conditions: sampling at various reaction times at a given temperature gave constant product ratios, and the separated products are stable under the reaction conditions. The relative activation parameters, listed in Table II, were determined from Arrhenius or Eyring plots of the data. For both reactions, the enthalpies of activation favor the cis-isomers, while the differences in the entropies of activation are essentially zero.

Nonatriene cyclizes to form preferentially the cis isomer, in contrast to the results favored with most substituted derivatives.[2-6a] The 1 kcal/mol preference for formation of the cis product is of the same magnitude as the preference for the trans isomer in the 9-ester derivative.[5] Decatriene gives a miniscule preference for the cis adduct, whereas the 10-ester gives a similarly small preference for the trans adduct.[5]

Table II: Relative Activation Parameters [ΔX = X(cis)-X(trans)][a]

	$\Delta\Delta H^{\ddagger}$	$\Delta\Delta S^{\ddagger}$	ΔE_{act}	Δ log A
1,3,8-Nonatriene	-1.00±0.03	0.0±0.1	-1.00±0.03	0.0±0.1
1,3,9-Decatriene	-0.27±0.06	-0.3±0.1	-0.27±0.06	-0.1±0.1

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[a] $\Delta\Delta H^{\ddagger}$ and E_{act} in kcal/mol;$\Delta\Delta S^{\ddagger}$ in e.u.

There is a qualitative correspondence between rates of formation of stereoisomeric products and the stabilities of these products for the nonatriene case, but not for the decatriene case. Allinger's MM2 force-field[15] predicts that cis-bicyclo[4.3.0]non-2-ene is 1.2 kcal/mol more stable than trans, in close agreement with the difference in $\Delta H^{\ddagger}$ for formation of these products. However, trans-bicyclo[4.4.0]-dec-2-ene is predicted[15] to be 2.0 kcal/mol more stable than cis, but the activation energy for formation of the trans product is 0.3 kcal/mol higher than for formation of cis.[16,17] Thus, product stabilities are not of general value in understanding product ratios.

The dramatic changes upon substitution which occur in the nonatriene series, but not the decatriene series, will be rationalized in a subsequent communication.[6a]

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(7) The reaction of 1,3,8-nonatriene has been reported, but the product stereochemistry was not determined: Sagredos, A.N., Liebigs Ann. Chem., 1974, 176. The simplest related compounds for which stereochemistries have been reported are 5-trimethylsiloxy-trans,trans-1,3,8-decatriene (Oppolzer, W.; Fehr, C.; Warneke, J., Helv. Chim. Acta, 1977, 60, 48.), which forms a 2:1 ratio of cis:trans products at 245°C, and 6-hydroxy-1,3,9-decatriene (Wilson, S.R.; Mao, D.T., unpublished results reported in Wilson, S.R.; Huffmann, J.C., J. Org. Chem., 1980, 45, 560.), which gives a 55:45 cis:trans ratio.

(8) (a) All new compounds were analyzed by 300 MHz nmr spectroscopy and high resolution mass spectrometry. (b) The Wittig reaction in step 4), carried out in CH_2Cl_2 at room temperature, gave a mixture of trans and cis alkenes in a ratio of 9:1, which were separated by column chromatography.

(9) (a) 20% SE-30 on Chromosorb W column; (b) 10′ x 1/8″ 3% OV-17 on Chromosorb W column.

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(11) Catalytic hydrogenation with Pd/C gave both cis and trans products starting from pure cis adducts, but only trans products from trans adducts.

(12) (a) Authentic samples of cis and trans decalin were obtained from the Aldrich Chemical Co. (b) The nmr spectrum of cis-hydrindane was obtained from the Aldrich nmr catalog.

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(14) The nmr spectra of cis- and trans-bicyclo[4.3.0]non-2-ene, and cis- and trans-bicyclo[4.4.0]dec-2-ene, are also distinctive in the same way.

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(16) For comparison, the trans isomers of both hydrindane and decalin are more stable. Allinger's force-field[15] predicts 1.2 and 2.7 kcal/mol, respectively, while experimental heats of formation favor the trans isomers by 1.0 and 3.1 kcal/mol, respectively.[17]

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