

Diels-Alder Reactions of Dienophiles and Cyclopentadiene Using a Sealed Tube Protocol

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Abstract: The Diels-Alder reaction of various reactive dienophiles with cyclopentadiene is reported. Rather than cracking dicyclopentadiene in a separate step, the reagents were mixed in a sealed tube and the reactions carried out at 185C. Conversion to the adducts is dependent on the nature of the dienophile and the reaction time. In those cases where stereochemistry is relevant, the endo/exo ratios are reported and compared to those reported at lower temperatures.

Introduction:

The Diels-Alder reaction is one of the most powerful tools for the construction of complex structures in few steps with control of stereochemistry and regiochemistry.¹ The array of diene-dienophile couplings is well-understood. Within the range of materials available to the synthetic chemist, 1,3-cyclopentadiene is one of the most reactive dienes. The diene is only available as its dimer, the product of the [4 +2] cycloaddition with itself.²

The traditional method for utilizing cyclopentadiene in a reaction involves thermal cracking of the dimer at extremely high temperature, trapping the distilled monomer at a low temperature and using it in a reaction before it reverts back to the dimer³. The dimer is in a slow equilibrium with the monomer so that reactions of cyclopentadiene are reported using the diene and allowing reaction of the monomer to drive the equilibrium to the product.⁴ There are reports of conducting this reaction in the dimer as solvent at its reflux temperature with some success.⁵

We report a herein a related strategy wherein we place the two reactants in a sealed tube and raise the temperature to above 180C. Using a sealed tube allows volatile dienophiles to be used at these temperatures and seems to reduce decomposition reactions. Analysis using GC/MS and NMR shows that the stereochemical (exo/endo) ratio of products is often more mixed than the reaction at lower temperature.⁶

Experimental:

General Procedure. All reactions were conducted in a Q-tube™, available from Q Labtech LLC. This device allows a pressure release if the internal pressure exceeds a setpoint (in our case 200 psi). At no point did the pressure release occur in any of these reactions. The tube was charged with a magnetic stirbar, dicyclopentadiene (1.1eq) and the dienophile in the amounts listed in the table. All the dienophiles were added without removing the free radical inhibitor (to prevent polymerization). The tube was heated to 185C and stirred at that temperature for the listed time, then cooled via a stream of compressed air. The reaction was dissolved in ethyl acetate and analyzed via GC/MS. The product was purified by column chromatography where necessary and the products further characterized by IR and HNMR (500MHz). All products have been previously reported in the literature. See Table I for results.

Results and Discussion – See Table I

Cycloadditions with Alkyne dienophiles.

The Diels-Alder reaction with alkynes has no stereochemical implications. The cycloaddition with dimethylacetylene dicarboxylate (entry 2) proceeded smoothly to give the norbornadiene in serviceable yield.^{7,8} The reaction with phenylacetylene (entry 4) was much less effective, with only a trace of the Diels-Alder product observed by GC/MS. The Diels-Alder reaction between phenylacetylene and cyclopentadiene has not been reported. The normal method to obtain these products is through the cycloaddition of cyclopentadiene and a phenyl acetylene sulfone derivative, followed by reductive desulfonylation.⁹

Cycloadditions with alkene dienophiles.

The endo rule generally governs the stereoselectivity of the Diels-Alder reaction.¹⁰ Such selectivity is generally formulated as a kinetic effect and is discussed in terms of the competing transition states. The endo/exo ratios vary as a function of steric effects, temperature and solvent. Most of these effects at moderate temperatures can be related to changes in the rate constants, but at the elevated temperatures in this study reversibility of the reaction leading to a thermodynamic mixture of products must be considered.

Table I. Diels-Alder Reactions of Dicyclopentadiene and Dienophiles at 185°C. Sealed Tube

Dienophile	Mass dienophile Time	Product	Endo/Exo	Yield
	3.5g 60min		NA	75%
	2.55g 90min		NA	trace
	4.96g 60min		4/1	46%
	3.25g 3.5h		1.85/1	90
	2.55g 3.5h		0.64/1	80%
	2.14g 60min		2.56/1	10%

Reaction with maleic anhydride (entry 1) afforded a solid product. GC/MS analysis of the product mixture indicated a ratio of adducts in a ratio of 4/1. Purification by recrystallization and NMR analysis confirmed that the major product was that of endo addition. Reactions at room temperature are reported to give the endo product almost exclusively.⁶ Reactions in refluxing dicyclopentadiene are reported to lead to increasing amounts of the exo isomer with time,⁵ suggesting equilibration at elevated temperature.

Reaction with butyl acrylate afforded the adducts in good yield with exo/endo ratio of 1.85/1. The ratio at room temperature for methyl acrylate is about 3/1⁶ with the ratio declining only modestly as the reaction temperature is raised to 100C. In a reaction strategy quite similar to ours, the heating of dicyclopentadiene with both methyl acrylate and butyl acrylate in a sealed vessel was investigated at temperatures from 160-300C.¹¹ At temperatures above 180C a ratio of nearly 1/1 is achieved after eight hours. Presumably this represents an equilibrium value.

Reaction with methyl methacrylate (entry 5) likewise affords the Diels-Alder products in good yield. The exo product predominates by 1.5/1, a ratio that is consistent with reports of this reaction at a wide range of temperatures.⁷

It was difficult to separate the products of the reaction of methyl vinyl ketone (entry 6) from recovered dicyclopentadiene, such separation requiring multiple chromatography steps. The exo/endo ratio of 2.6/1 is similar to those obtained at lower temperature.⁷

Conclusion

The strategy of in-situ preparation of 1,3-cyclopentadiene in a sealed tube with other reactants is an effective method for obtaining the Diels-Alder adducts without prior formation of the diene. Further work is planned to optimize yields, determine the stability of the products to the reaction conditions (equilibration) and to extend the protocol for other reactions using cyclopentadiene as a starting material.

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