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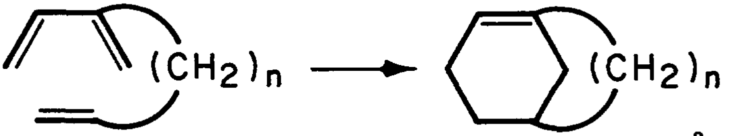
INTRAMOLECULAR DIELS-ALDER CYCLOADDITIONS. SYNTHESIS OF SUBSTITUTED DERIVATIVES OF BICYCLO[3.n.1]BRIDGEHEAD ALKENES.

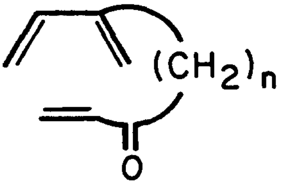
Kenneth J. Shea* and Sean Wise
Department of Chemistry, University of California, Irvine, California 92717

We recently reported the first examples of an intramolecular Diels-Alder cycloaddition that results in formation of bicyclo[3.n.1]bridgehead alkenes, eq. 1.[1] We now report that we have been successful in determining an equilibrium constant for one of these reactions, the cycloaddition of 3-methylene-1,7-octadiene to bicyclo[3.3.1]non-1-ene (eq 1, n = 3),

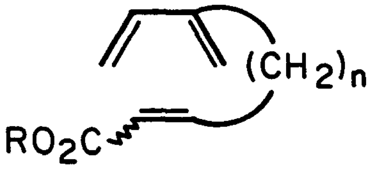


(1)

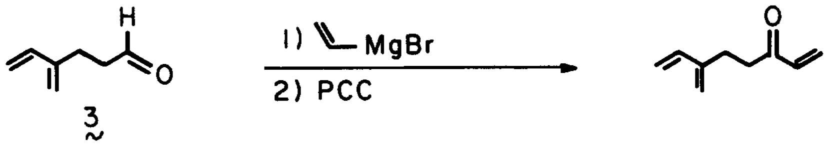
$K_{427\ {}^{\circ}C} = 0.28$.[2] This value, together with available thermodynamic data[3] permit evaluation of the pertinent energetic relationships between product and reactant. Surprisingly, the reaction is quite exothermic (ΔH^0_{Rxn} - 18.3 Kcal/mole); however, at the temperature necessary to bring about cycloaddition the unfavorable reaction entropy (ΔS^0 - 29 eu) precludes a high product yield. With a goal towards improving the synthetic potential of these cycloadditions, we have examined the possibility of enhancing Diels-Alder reactivity by substitution of electron withdrawing groups on the dienophile. In intramolecular cycloadditions of this type the activating group(s) can be incorporated either within the bridge joining the diene and dienophile (1) or external to it (2). In this communication we report the synthesis of triene representatives of 1 and 2 and document their high yield conversion to bicyclo[3.n.1]bridgehead alkenes.



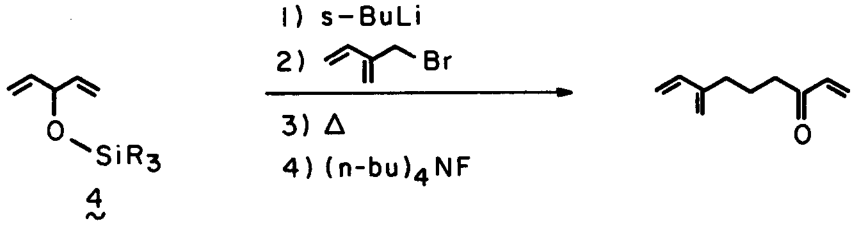
1
a: n=3
b: n=4



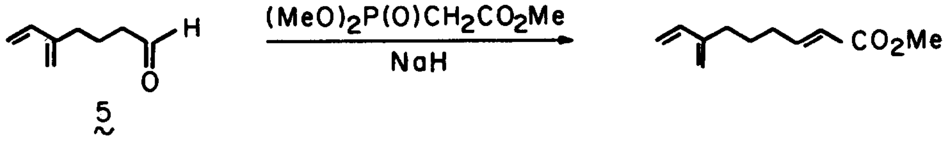
2
a: n=3, trans
b: n=4, trans
c: n=4, cis



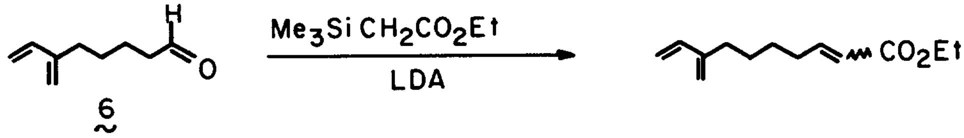
(2)



(3)



(4)



(5)

Chart 1

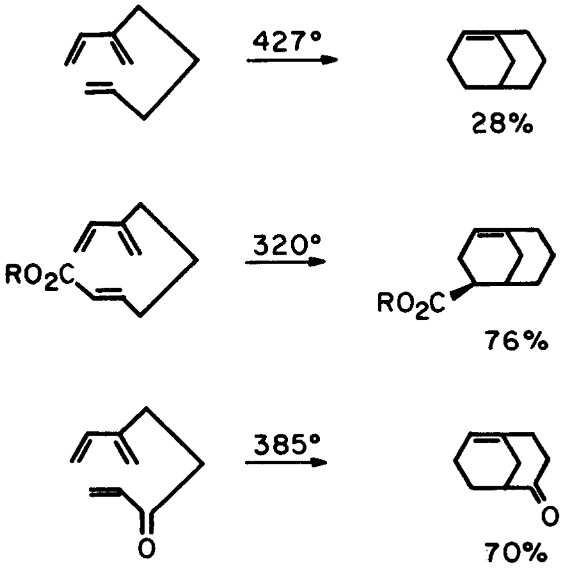
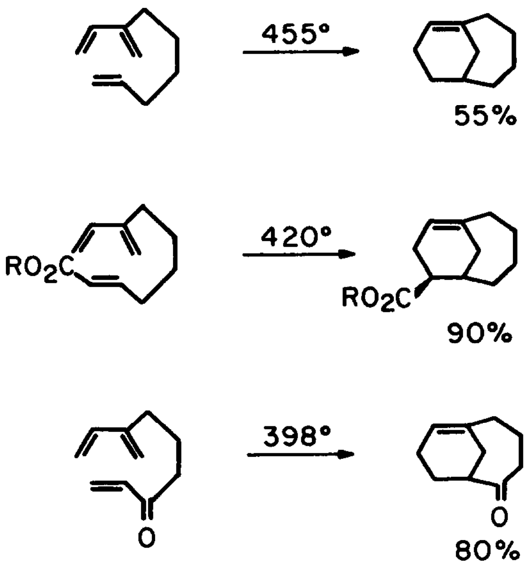


Chart 2



Internally activated trieneones **1a**,**b** have been obtained by the methods outlined in eq 2,3. Vinylation of dienal **3**[4] (50%) followed by PCC oxidation[5] (86%) gives trieneone **1a**.[6] Treatment of the anion derived from 3-siloxy-1,4-pentadiene[7] (4) with 2-bromomethylbutadiene[8] gives a mixture (1 : 4) of α- and γ-alkylation products. Thermal rearrangement to the more stable γ-alkylation product (150° - 1 hr) followed by deprotection[9] affords trieneone **1b** in 63% overall yield. The externally activated triene esters have been obtained by olefination of the appropriate dieneals, eq 4,5. Thus, Wadsworth-Emmons olefination of dieneal **5** yields *trans*-**2a** (54%), while treatment of homolog **6** with lithium trimethylsilylacetate[10] gives a mixture (3 : 2) of *trans*-**2b** and *cis*-**2c** in 65% yield. This mixture could be readily separated by column chromatography.

The thermal behavior of trienes **1a**,**b** and **2a-b** were studied in a flow pyrolysis apparatus at atmospheric pressure under N_2. In all cases thermolysis results in intramolecular cycloaddition to produce bridgehead alkenes (Charts 1 and 2).[11] The bridgehead alkenes were contaminated with unreacted starting material and could be readily isolated by preparative VPC. Comparison of reactivities with unactivated hydrocarbon trienes is instructive. In all cases examined, activated triene esters and ketones undergo cycloaddition under milder conditions and in higher yield than unactivated hydrocarbons. These results restablished that substitution of electron withdrawing substituents, either in the bridge joining the diene and dienophile (**1**) or external to it (**2**), results in enhanced activity of the dienophile.

Finally, we have extended our study of these cycloadditions to the condensed phase; trienes **1b**, **2b**, and **2c**, which give rise to bicyclo[4.3.1]decenes, undergo high yield cycloaddition in solution. For example, a 0.06 M xylene solution (sealed tube) of triene **1b** undergoes 82% conversion in 15 min at 200 °C. Under similar conditions *cis*-**2c** gives exclusively the endo-cycloadduct in 65% yield after 4 hr at 232 °C; while *trans*-**2b** gives only exo-cycloadduct (80%) after 1 hr at 206 °C. The preceding examples establish the reaction is stereospecific at the dienophile.

These findings support our earlier results[1] which establish the regiochemistry of the cycloaddition (meta with respect to the bridge joining the diene and dienophile). Further examples of this type of cycloaddition and investigations of the chemistry of bicyclo[3,n.1]-bridgehead alkenes will be the subject of future reports.

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References and Notes

1. K. J. Shea and S. Wise, *J. Am. Chem. Soc.*, (1978), **100**, 6519.
2. The equilibrium value was obtained in a flow pyrolysis apparatus that has been previously described.[1] Pyrolysis of triene or bridgehead alkene gives identical product distributions at 427 °C at contact times of 5 s or greater.
3. The heat of formation of bicyclo[3.3.1]non-1-ene ($\Delta H^{0}_{f_{298}}$ = 10.25) and the enthalpy and entropy of formation of 3-methylene-1,7-octadiene ($\Delta H^{0}_{f_{298}}$ = 28.56, $\Delta S^{0}_{f_{298}}$ = 111.6 eu) were estimated from group equivalents; S. W. Benson, F. R. Cruickshank, D. M. Golden, G. R. Hargen, H. E. O'Neal, A. S. Rodgers, R. S. Haw, and R. W. Walsh, *Chem. Rev.*, (1969) **69**, 279; and literature values for the heat of hydrogenation of bicyclo-[3.3.1]non-1-ene (12 kcal/mole, P. M. Lesko and R. B. Turner, *J. Am. Chem. Soc.*, (1968), **90**, 6888) and strain energy of bicyclo[3.3.1]nonane (10.3 kcal/mole, N. L. Allinger, M. T. Tribble, M. A. Miller, and D. W. Wertz, *J. Am. Chem. Soc.*, (1971), **93**, 1637).
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11. Numbers given are % conversions and were measured by VPC. Contact times were varied (5 - 15 sec) to optimize product yield at the indicated temperature.

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