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THE INTRAMOLECULAR [4+2]π CYCLOADDITIONS OF (3-ALKENYL)CYCLOPENTADIENES

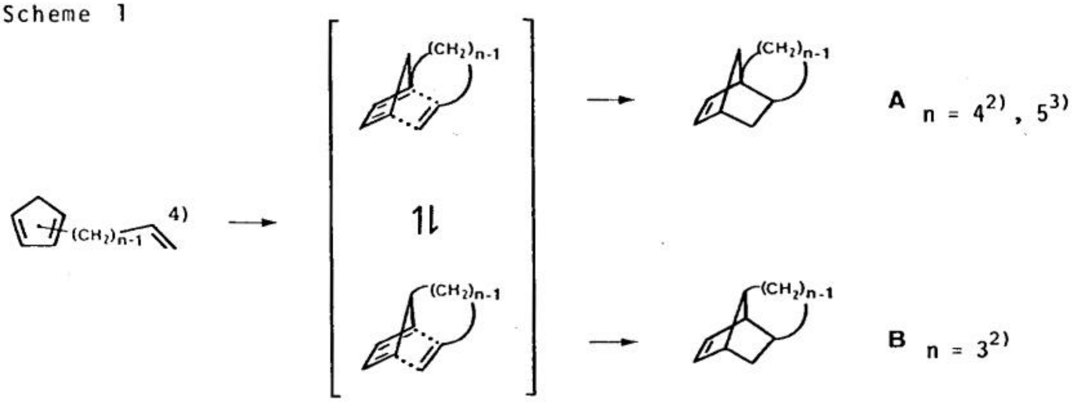
Roger L. Snowden

Firmenich SA, Research Laboratories, 1211 Geneva 8, Switzerland

Abstract: The intramolecular cycloadditions of four specifically functionalised (3-alkenyl)cyclopentadienes are studied; the observed regiochemistries are in agreement with the predictions of frontier orbital theory.

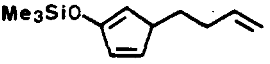
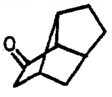
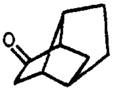
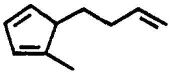
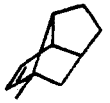
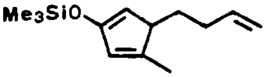
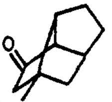
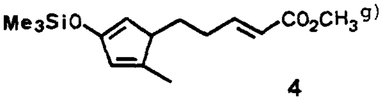
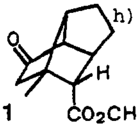
The thermal intramolecular [4+2]π cycloadditions[1] of (n-alkenyl)cyclopentadienes give, depending on the carbon chain length, two types of tricyclic cycloadducts, A or B (Scheme 1). A chain length of 5 (n = 4)[2] or 6 (n = 5)[3] leads specifically to structures of type A (*via* the 1-(n-alkenyl) isomer) whereas a chain length of 4 (n = 3)[2] gives exclusively (*via* the 5-(n-alkenyl) isomer) tricyclo[4.3.0.0^{3,7}]non-4-ene (type B). Although the former cycloaddition has been used as a key step in a synthesis of (±)-cedrene[5] no synthetic application has been found for the latter cycloaddition despite the fact that several naturally occurring sesquiterpenes such as sativene[6], longifolene[7] and sinularene[8] are structurally related to cycloadduct B (n = 3). In an attempt to synthesise regio- and stereospecifically functionalised tricyclic molecules of type B the intramolecular cycloadditions of 1-(3-butenyl)-3-trimethylsilyloxycyclopentadiene (1)[9], 1-(3-butenyl)-2-methylcyclopentadiene (2), 1-(3-butenyl)-2-methyl-4-trimethylsilyloxycyclopentadiene (3) and methyl 5-(2-methyl-4-trimethylsilyloxycyclopentadienyl)-2(*E*)-pentenoate (4) were studied, see Table.

Scheme 1



The intramolecular cycloadditions of 1, 2 and 3 were effected by thermolysis at 250°. In experiments (i) and (iii) the product mixtures were then treated with methanol to convert the labile intermediate tricyclic trimethylsilylenol ethers to the mixtures of 5, 6 and 9, 10 respectively. In experiment (iv), treatment of cyclopentenone 14 with triethylamine (2 eq), trimethylchlorosilane (2 eq) and zinc chloride (0.03 eq) in toluene at reflux during 3 days gave directly, in 94% yield, methyl 3-methyl-5-oxo-tricyclo[4.3.0.0^{3,7}]nonane-2-carboxylate (11) as a mobile oil, bp 130 - 140° (bath)/0.1 Torr. Because 11 is not formed in the absence of trimethylchlorosilane, the trimethylsilylenol ether 4 appears to be the key reaction intermediate. This may then lead to 11 by either a stepwise double Michael reaction[13,14] or a concerted intramolecular cycloaddition. Despite the non-observance of either 4 or the trimethylsilylenol ether of 11 decisive support for the latter mechanism comes from the stereospecificity[15] of the transformation (14 → 11).

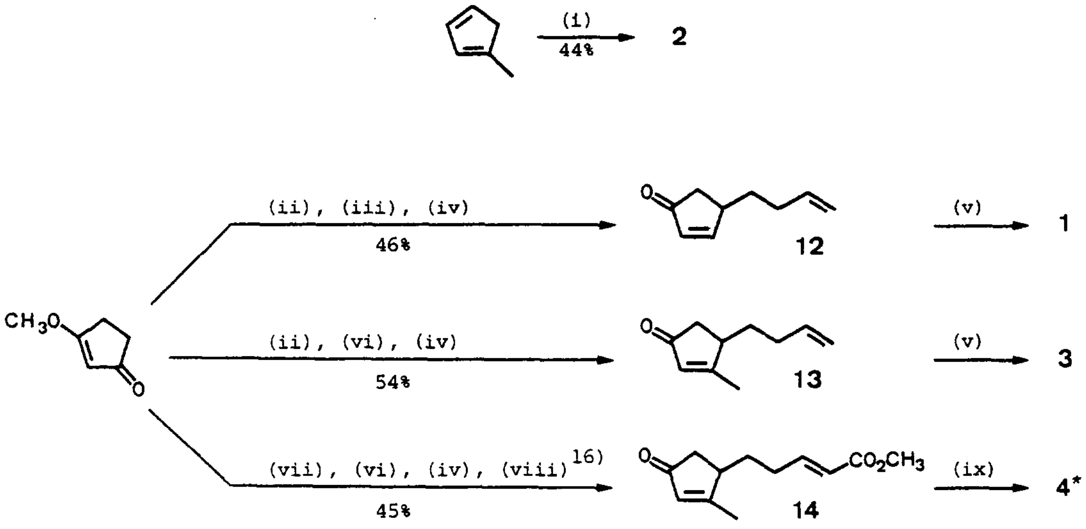
Table.

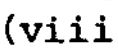
Exp.	SUBSTRATE a)	Cycloaddition Conditions b)	PRODUCTS 10) (REGIOCHEMISTRY) c)	YIELD d) %
(i)	 1	250°/24 h e)	 5 +  6 (54 : 46)	72
(ii)	 2 f)	250°/24 h	 7 +  8 (73 : 27)	30
(iii)	 3	250°/24 h e)	 9 +  10 (78 : 22)	77
(iv)	 4	110°/3 d	 11 (100 : 0)	94

a) For simplicity only the cyclopentadiene which can undergo intramolecular cycloaddition, from the five possible double bond isomers, is drawn. b) For experiments (i), (ii) and (iii) thermolysis was effected in 5% benzene solution in sealed silylated Pyrex tubes, for experiment (iv) in 5% toluene solution. c) Isomeric mixtures not separated: proportions calculated from ^{13}C-NMR and GC (capillary column). Regiochemical assignments follow from chemical correlation[11] coupled with comparison of NMR spectra and GC (capillary column) co-injection. Confirmation of these assignments is provided by the conversion of 11 to (±)-sativene[12]. d) Refers to pure (preparative GC or distillation) products. e) Thermolysis followed by treatment with methanol (20°/16 h). f) Contains *ca.* 20% of 1,3-positional isomer. g) Not isolated, see text. h) Directly isolated after thermolysis.

The syntheses of the four cycloaddition substrates (1 → 4 inclusive) are described in Scheme 2. The dialkylcyclopentadiene 2 is obtained by the mono-alkylation of the sodium salt of methylcyclopentadiene. The trimethylsilyloxycyclopentadienes 1, 3 and 4 are prepared from their analogous cyclopentenones 12, 13 and 14[16] which are themselves derived from 3-methoxy-2-cyclopentenone[17].

Scheme 2[10)]



(i) NaH/Br/-30°/THF. (ii) LDA/THF/-70° then HMPA/I/-70°/1d. (iii) DIBAH/toluene. (iv) H_3O^+. (v) $ZnCl_2$ (0.03 eq)/$(CH_3)_3SiCl$ (2 eq)/Et_3N (2 eq)/45°/16 h. (vi) CH_3Li/THF. (vii) LDA/THF/-70° then HMPA/I/-70°/1d. (viii) $(CH_3O)_2P(O)$-$CH_2CO_2CH_3$/NaH/THF/20°/2min. (ix) $ZnCl_2$ (0.03 eq)/$(CH_3)_3SiCl$ (2 eq)/Et_3N (2 eq)/110°/3d.

*Not isolated, under the conditions of its formation 4 is transformed directly into 11.

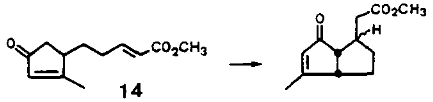
From a theoretical viewpoint the cycloaddition regiochemistries exhibited by 1, 2, 3 and 4, progressively increasing to culminate in the regio- and stereospecific formation of 11, are in full agreement with the predictions of frontier orbital theory[19]. The cycloadditions of 1, 2 and 3 are particularly significant as they provide rare examples where "meta" adducts are predicted, diradical theory making an opposite prediction[20].

For preparative purposes these intramolecular cycloaddition experiments demonstrate that functionalised tricyclo[4.3.0.0^{3,7}]nonanes may be constructed regio- and stereospecifically from suitably substituted (3-alkenyl)cyclopentadienes. As a synthetic application a stereoselective synthesis of (±)-sativene is described in the following letter.

References and Notes

1. For two recent reviews of intramolecular cycloadditions, see W. Oppolzer, Angew. Chem. Int. Ed., 16, 10 (1977); G. Brieger and J.N. Bennett, Chem. Rev., 80, 63 (1980).
2. G. Brieger and D.R. Anderson, J. Org. Chem., 36, 243 (1971); J.C.L. Tam and P. Yates, Chem. Commun., 739 (1975).
3. E.J. Corey and R.S. Glass, J. Am. Chem. Soc., 89, 2600 (1967).

4. At equilibrium the relative proportions of the 5-, 1- and 2-isomers of a monosubstituted cyclopentadiene (rapidly interconverting by 1,5-hydrogen shifts) are 1 : 44 : 55, see S. McLean and P. Haynes, Tetrahedron Lett., 2385 (1964); *idem*, Tetrahedron, 21, 2329 (1965). The intramolecular cycloaddition of the 2-(n-alkenyl) isomer (not drawn), strongly disfavoured for reasons of severe angle strain in the transition state, has never been observed.
5. E.G. Breitholle and A.G. Fallis, J. Org. Chem., 43, 1964 (1978).
6. For previous syntheses, see following paper, reference 2.
7. For a recent synthesis, see W. Oppolzer and T. Godel, J. Am. Chem. Soc., 100, 2583 (1978).
8. P.A. Collins and D. Wege, Aust. J. Chem., 32, 1819 (1979).
9. For a previous example of a trialkylsilyloxycyclopentadiene as the diene component in a Diels-Alder reaction, see G.M. Rubottom and D.S. Krueger, Tetrahedron Lett., 611 (1977).
10. All compounds give spectral data (IR, ^{1}H- and ^{13}C-NMR, and MS) in accordance with their structures; yields are not optimised.
11. The 78 : 22 mixture of 9 and 10 was converted ($TsNH{\cdot}NH_2/EtOH$ then CH_3Li/Et_2O) to an identical mixture of 7 and 8 in 64% yield; 11 was transformed into 9 ($HOCH_2CH_2OH/H^+$; $LiAlH_4/Et_2O$; H_3O^+ and $(Ph_3P)_3RhCl$/toluene/110^o) in 33% yield.
12. See following paper.
13. Treatment of 14 with LDA (1 eq) in THF at -70^o and warming to ambient temperature gives low yields of 11, presumably *via* a double Michael reaction (for a related intermolecular case, see G.A. Kraus and H. Sugimoto, Tetrahedron Lett., 3929 (1977)); the major side-products are the two isomeric bicyclo[3.3.0]octanes resulting from a single Michael reaction, see 18.
14. For the Lewis acid promoted intermolecular Michael reaction of silylenol ethers with α,β-unsaturated esters, see K. Narasaka, K. Soai, Y. Aikawa and T. Mukaiyama, Bull. Soc. Chem. Jpn., 49, 779 (1976).
15. Intramolecular cycloaddition of the (*Z*)-isomer of 14, under the same conditions, stereospecifically gives the epimer (at C-2) of 11, mp 78 - 79^o.
16. S. Danishefsky and T. Kitahara, J. Am. Chem. Soc., 96, 7807 (1974).
17. For the same strategy, for the construction of specifically substituted cyclopentenones, see M.L. Quesada, R.H. Schlessinger and W.H. Parsons, J. Org. Chem., 43, 3968 (1978); *idem*, J. Am. Chem. Soc., 102, 889 (1980).
18. A short reaction time is essential owing to the facile base-catalysed intramolecular Michael reaction:



19. I. Fleming, "Frontier Orbitals and Organic Chemical Reactions", J. Wiley and Sons, London-New York-Sydney-Toronto, 1976.
20. R.A. Firestone, J. Org. Chem., 37, 2181 (1972).

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