rate constants at the same basicities. The order of anion E2 rate constants with c-$C_6H_{11}Br$ thus revealed, $ArS^- >$ 2-$NpO^- > Cb^- >$ 9-$MeFl^-$, contrasts sharply with the order of the anion S_N2 rate constants with $PhCH_2Cl$, $ArS^- >$ 9-$MeFl^- >$ 2-$NpO^- > Cb^-$.[9,11] The E2 rate constants of oxanions and nitranions reacting with c-$C_6H_{11}Br$ are much greater than their S_N2 rate constants, causing essentially complete elimination to occur. On the other hand, the S_N2 rate constants of carbanions reacting with c-$C_6H_{11}Br$ are much greater than their E2 rate constants, causing essentially complete substitution.[10] We conclude that the apparent correlation between anion E2 and S_N2 rate constants observed earlier was fortuitous and that there is no reason to believe that in some E2 transition states the anion is bonded to carbon as well as to hydrogen.

Acknowledgment. This work was supported by the National Science Foundation. We are grateful to a reviewer for helpful comments.

Registry No. 9-$MeFl^-$, 31468-21-0; 2-Br-9-$MeFl^-$, 81255-42-7; 2,7-Br_2-9-$MeFl^-$, 73872-46-5; Cb^-, 23560-25-0; 3-$ClCb^-$, 80010-03-3; 3,6-Br_2Cb^-, 79990-92-4; 2-NpO^-, 15147-55-4; 6-Br-2-NpO^-, 78232-03-8; 4-$MeOC_6H_4S^-$, 26971-83-5; 3-$CF_3C_6H_4S^-$, 78232-02-7; 2,4,5-$Cl_3C_6H_2S^-$, 78232-01-6; cyclohexyl bromide, 108-85-0.

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(11) S_N2 rate constant orders for these anions have been found to be somewhat substrate dependent,[9] but there is no evidence for a correlation with anion E2 rate constants.

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A Novel Entry into the Bicyclo[5.4.0]undecane Ring System

Summary: A four-step cycloaddition–oxyanion Cope rearrangement sequence starting from 2,4,6-cycloheptatrien-1-one leads to a cis-fused 11-substituted bicyclo[5.4.0]undec-8-en-4-one species.

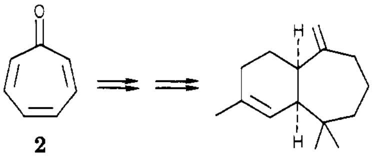
Sir: In recent years considerable effort has been expended in developing stereoselective syntheses of natural products that possess seven-membered carbocycles.[1] The bulk of these studies have been directed toward compounds possessing the hydroazulene moiety. Comparatively little work has been reported on the construction of other related ring systems. A particularly intriguing structural array from a synthetic point of view is the bicyclo[5.4.0]undecane series which is characteristic of several classes of sesquiterpenes, including the himachalenes (e.g., α-himachalene (**1**)).[2] Several approaches to this general ring system have been disclosed in recent years,[3,4] but at present the ability to control the critical ring fusion stereochemistry in a general fashion remains a synthetic challenge. We herein report a potentially general strategy for the construction of cis-fused bicyclo[5.4.0]undecanes with complete control of the ring fusion stereochemistry.

Table I. C-9 Substituted Cycloadducts of Tropone[a]

cycloadduct[12]	rctn condtns	% yield	ratio of epimers[b] at C-9
3a, X = *n*-BuO	95 °C, 24 h	63[c]	1:1[d]
3b, X = *n*-BuS	130 °C, 4 h	68	5:1[d]
3c, X = SPh	130 °C, 4 h	64	1.5:1[d]
3d, X = OAc	140 °C, 24 h	50[e,f]	1:1[g]

[a] The identity of the regioisomer was determined by 300-MHz ^1H NMR decoupling experiments on the corresponding saturated ketones **5**. [b] No effort was made to assign epimer structures. [c] Based on recovered starting material. [d] Ratio of epimers based on weight of each component after careful chromatography. [e] Accompanied by considerable decomposition products. [f] Prepared in a sealed tube experiment. [g] Determined by ^1H NMR integration on **3d**.

Tropone (2,4,6-cycloheptatrien-1-one (**2**))[5] is a very attractive starting material for the synthesis of complex natural products because it possesses considerable functionality in a relatively small molecule and exhibits rather unique reactivity that is particularly amenable for exploitation in carbon–carbon bond-forming reactions.[6,7]



2

1

In the present work, an alkoxide accelerated Cope rearrangement[8] is employed as the key step for formation of the requisite cis ring fusion. The overall brevity of our process results from the ease with which the bicyclo[3.2.2]non-6-en-2-one precursor is prepared from tropone (**2**).

Several examples of [4 + 2] cycloaddition reactions of troponoids with a variety of dienophiles have been reported.[9] However, most of these examples have involved electron-poor olefin partners such as acrylonitrile and usually resulted in the formation of mixtures of the regioisomers **3** and **4** (X = CN) in which **3** was the major adduct.[9a] In view of the well-established electrophilicity of tropone and through consideration of the reactant frontier orbital coefficients,[10] it was anticipated that reversing the electronic sense of the dienophile would result

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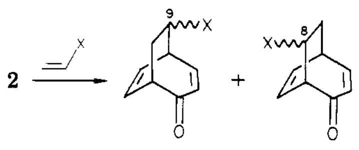
in greater regioselectivity in the reaction.

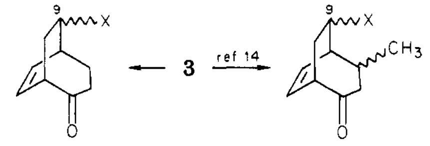


3 4

Tropone underwent smooth cycloaddition with a variety of electron-rich dienophiles that were used as solvent at temperatures between 95 and 140 °C (see Table I).

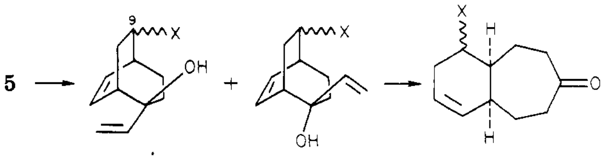
Typically, the various isomer ratios were ascertained by examination of the products obtained after selective reduction of the α,β-unsaturated ketone double bond. The structural analysis was performed on the reduced cycloadducts because separation of the components was not possible from the initial cycloadduct mixtures. In each case examined, we have been able to isolate only one of the two possible regioisomeric cycloadducts. This has been shown to be the expected C-9 substituted compound.[11] On the other hand, a mixture of exo and endo epimers at the C-9 position was routinely observed. These results agree qualitatively with a previous study of the cycloaddition of styrene with tropone.[9b]

The selective reductions were achieved by using lithium/liquid ammonia in examples **3a** → **5a** and **3b** → **5b** in total yields of 81% and 77%, respectively.[12] Attempted selective reduction of the phenylthio-substituted compound **3c** resulted in considerable reduction of the phenyl group as well as the enone system when dissolving metal conditions were employed. However, selective reduction of the enone functionality in **3c** was realized in excellent yield with lithium trimethoxyaluminum hydride–copper(I) bromide.[13]



5

Addition of vinylmagnesium bromide to compounds **5a–c** at 0 °C gave in each case a quantitative yield of a crude mixture of two allylic alcohols.[15,16] Typically, the resulting allylic alcohol mixtures were treated with 1.2 equiv of potassium hydride (oil free) in refluxing THF containing 2 equiv of 18-crown-6 for a period of 1.5–2 h.[17] The major adducts of ketones **5a** (upper epimer) and **5b** (major epimer) rearranged smoothly under these conditions to give 70–75%[18] and 59–61% yields of the respective 11-substituted bicyclo[5.4.0]undec-8-en-4-ones **6a** and **6b**.[12,19] In each case, only the major alcohol isomer underwent rearrangement and the unreacted isomer was recovered unchanged. In contrast to these results, the vinyl adducts of the phenylthio-substituted ketone **5c** failed to rearrange smoothly in refluxing THF. The small amounts of products produced in this reaction have not been identified.



major minor 6

The very efficient four-step approach to the *cis*-bicyclo[5.4.0]undecane ring system outlined in this communication offers considerable potential for application to synthesis. The strategic placement of latent functionality in the bicyclo[5.4.0]undecene species obtained through the methodology reported herein makes these intermediates potentially very versatile points of departure for the synthesis of a wide variety of naturally occurring substances. We are currently examining its utility for the total synthesis of the himachalene sesquiterpenes.

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[11] The possibility that the C-8 substituted regioisomer was selectively destroyed in the reduction cannot be rigorously excluded, but the material balance was extremely high in all three examples.

[12] The structures assigned to these compounds are in accordance with their spectral and analytical properties (^{1}H NMR, IR, ^{13}C NMR, MS, combustion analysis). The 60-MHz ^{1}H NMR and IR data are given below. **3a**: ^{1}H NMR (CCl$_4$) δ 1.0 (m, 3 H), 1.2–2.5 (m, 8 H), 3.3 (m, 2 H), 3.9 (m, 1 H), 5.6–7.0 (m, 4 H); IR (CCl$_4$) 1680 cm^{-1}. **3b**: ^{1}H NMR (CCl$_4$) δ 0.98 (m, 3 H), 1.2–1.8 (m, 5 H), 2.2–2.8 (m, 3 H), 3.0–3.5 (m, 3 H), 5.5–7.0 (m, 4 H); IR (CCl$_4$) 1680 cm^{-1}. **3c**: ^{1}H NMR (CCl$_4$) δ 2.0 (m, 1 H), 2.5 (m, 1 H), 3.4 (m, 2 H), 3.7 (m, 1 H), 5.8–7.0 (m, 4 H), 7.4 (s, 5 H); IR (CCl$_4$) 1670 cm^{-1}. **3d**: ^{1}H NMR (CCl$_4$) δ 1.8 (m, 1 H), 2.0 (2 s, 1.5 H and 1.5 H), 2.5 (m, 1 H), 3.4 (m, 2 H), 5.0 (m, 1 H); 5.5–7.0 (m, 4 H); IR (CCl$_4$) 1745, 1675 cm^{-1}. **5a**: (upper epimer) ^{1}H NMR (CCl$_4$) δ 0.98 (m, 3 H), 1.2–3.0 (m, 12 H), 3.4 (m, 2 H), 3.8 (m, 1 H), 6.1 (m, 2 H), IR (CCl$_4$) 1705 cm^{-1}. **5a**: (lower epimer) ^{1}H NMR (CCl$_4$) δ 0.9 (m, 3 H); 1.0–2.9 (m, 12 H), 3.2 (m, 2 H), 3.6 (m, 1 H), 5.8 (m, 2 H); IR (CCl$_4$) 1710, 1100 cm^{-1}. **5b**: (major epimer) ^{1}H NMR (CCl$_4$) δ 1.0 (m, 3 H), 1.3–2.0 (m, 8 H), 2.1–3.2 (m, 5 H), 6.0–6.6 (m, 2 H); IR (CCl$_4$) 1705 cm^{-1}. **5c**: ^{1}H NMR (CCl$_4$) δ 1.6–2.0 (m, 3 H), 2.4–3.2 (m, 5 H), 3.7 (m, 1 H), 6.0–6.5 (m, 2 H), 7.3 (m, 5 H); IR (CCl$_4$) 1700 cm^{-1}. **6a**: (from **5a** upper epimer) ^{1}H NMR (CCl$_4$) δ 1.0 (m, 3 H), 1.2–3.0 (m, 16 H), 3.4 (m, 3 H), 5.5–6.0 (m, 2 H); IR (CCl$_4$) 1700 cm^{-1}. **6a**: (from **5a** lower epimer) ^{1}H NMR (CCl$_4$) δ 0.98 (m, 3 H), 1.2–2.9 (m, 16 H), 3.4 (m, 3 H), 5.8 (m, 2 H); IR (CCl$_4$) 1700 cm^{-1}. **6b**: ^{1}H NMR (CCl$_4$) δ 1.0 (m, 3 H), 1.2–3.0 (m, 19 H), 5.4–6.0 (m, 2 H); IR (CCl$_4$) 1705 cm^{-1}.

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[14] Adduct **3a** undergoes clean 1,4-addition with lithium dimethylcuprate to give a mixture of 4-methylated ketones in 79% yield.

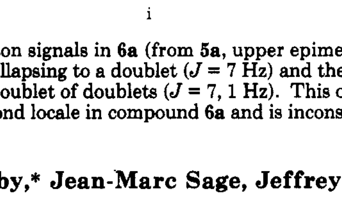
[15] The two C-9 epimers of ketone **5a** (referred to as upper epimer and lower epimer on the basis of TLC mobility) were reacted separately with vinylmagnesium bromide. Only the major isomer of compound **5b** was subjected to the Cope rearrangement sequence.

[16] Careful column chromatography on the alcohol mixture resulted in isolation of the isomeric alcohols in a 2:1 ratio for **5a** (upper epimer) and in a 3:1 ratio for **5b** (major epimer). The alcohols from ketone **5a** (lower epimer) were inseparable. On preparative scale runs the isomers were not separated before rearrangement.

[17] No reaction was detected in the absence of 18-crown-6 after 2 days in refluxing THF.

[18] Rearrangement of the alcohols derived from the other C-9 epimer of compound **5a** gave only 16% actual yield of the corresponding ketone **6a** and 68% of the starting alcohol was recovered.

[19] No signal attributable to an allylic ether proton as would be found in structure i was observed. This supports the structural assignments for cycloadduct **3a**, since the regioisomeric adduct **4a** would have lead to ketone i on rearrangment. Sequential irradiation at 300 MHz on each of the two vinylic proton signals in **6a** (from **5a**, upper epimer) resulted in the upfield signal collapsing to a doublet (J = 7 Hz) and the downfield signal collapsing to a doublet of doublets (J = 7, 1 Hz). This observation confirms the double bond locale in compound **6a** and is inconsistent with structure i.



i