drastically different from that of the ground state, with near concerted participation by the benzoyl group in the Chamberlin–Hehre sense. Our data do not provide the means to distinguish between these views.

Acknowledgment. This work was supported by PHS Grant AI 16943. Crystallographic measurements and computations were carried out on facilities supported by the Yale Chemical Instrumentation Center. We thank Professor A. R. Chamberlin of the University of California at Irvine for a stimulating communication (see ref 4).

Supplementary Material Available: ORTEP drawings of compounds 1 and 6 and tables containing fractional coordinates, temperature factors, bond distances, torsional angles, and anisotropic temperature factors for 1 and 6 (15 pages). Ordering information is given on any current masthead page.

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Received March 26, 1987

A New Approach to the Cedrane Ring System via Intramolecular [4 + 2] Tropone-Olefin Cycloaddition. Total Synthesis of (±)-α- and (±)-β-Pipitzol

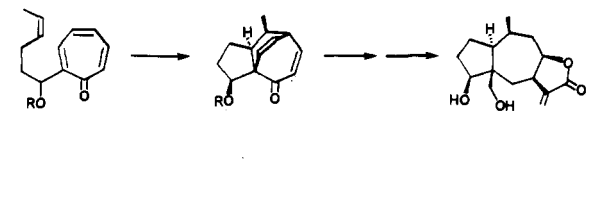
Summary: A new strategy for the preparation of polycarbocyclic natural products is demonstrated by a concise transformation of an intramolecular tropone–olefin cycloadduct (**3**) to the cedrane ring system of the pipitzols (**1a,b**).

Sir: We have recently demonstrated that intramolecular [6 + 4] and [4 + 2] tropone–olefin cycloadditions proceed smoothly and with high stereoselectivity.[1] The [4 + 2] cycloaddition reactions typically afford endo cycloadducts that possess both bicyclo[5.3.0]decane and bicyclo[3.2.2]nonane substructures as depicted in Scheme I. Thus, these cycloadducts can be conceivably transformed into various naturally occurring ring systems. For example, removal of the olefinic two-carbon bridge would leave the perhydroazulene ring system of the pseudoguaianolides (Scheme I). Alternatively, excision of one carbon of the olefinic two-carbon bridge would provide the bicyclo[3.2.1]octane subunit of the cedrane class of compounds (Scheme I). Herein, we verify that the latter ring transmutation is indeed viable and report on the total syntheses of β- and α-pipitzol (**1a,b**),[2] two highly oxygenated members of the cedrane family.

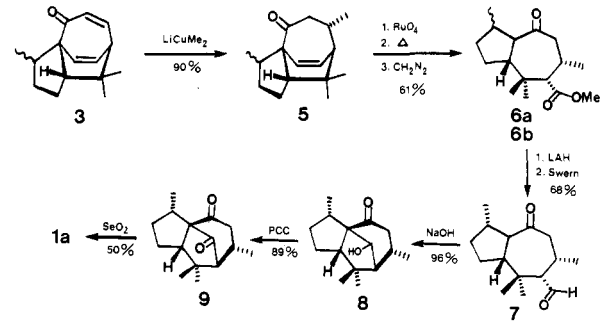
It was recognized that the 5:1 (αMe:βMe) diastereomeric mixture of enones **3**, obtained from the thermal (240 °C, 72 h; 85%) or catalyzed (0.1 equiv of Et_2AlCl, 110 °C, 36 h; 88%) [4 + 2] cycloaddition reaction of tropone **2**,[3] contained sufficient functionality for further elaboration into pipitzol. As alluded to previously, the major operation dictated by this synthetic strategy is the transformation of the bicyclo[3.2.2]nonane substructure present in **3** to the bicyclo[3.2.1]octane subunit present in the pipitzols (**1a,b**). In addition, a fourth methyl substituent must be introduced. To this end, conjugate addition of lithium dimethylcuprate to the enones **3** proceeded with high stereoselectivity (>20:1) to afford ketones **5** in 90% yield. (Scheme II). The stereochemical assignment shown in **5** is tentative but is the expected consequence of addition from the less hindered α-face. Oxidative cleavage of the double bond of **5** according to the Sharpless methodology[4] ($RuCl_3$, H_2O, CH_3CN, CCl_4, HIO_4) and subsequent decarboxylation effected removal of the extraneous bridging carbon. Esterification (CH_2N_2) of the resulting mixture of keto acids furnished two keto esters **6** in 61% overall yield from **5**. The mixture of keto esters **6** could be separated by chromatography on silica gel. The synthesis was first completed with the major diastereomer **6a** (αMe, mp 89–90 °C). Subjection of **6a** to a reduction (LAH)–reoxidation (Swern[5]) sequence provided a single keto aldehyde (**7**) in 68% overall yield.

The crucial reconstruction of the bridged bicyclic system was smoothly realized upon treatment of **7** with 2% aqueous NaOH in refluxing MeOH, affording a single stereoisomer of the aldol product **8** (mp 138–140 °C) in 96% yield.[6] Oxidation of **8** (PCC) gave the crystalline

Scheme I



Scheme II



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(6) Although construction of the bicyclo[3.2.1]octane ring systems via intramolecular aldol reactions of substituted cyclohexanones[7a-c] and cyclopentanones[7d-f] is a frequently employed strategy in natural product synthesis; the analogous closure of a substituted cycloheptanone appears to be quite rare.[8]

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dione **9** (mp 97–98 °C) in 89% yield. Further oxidation of **9** with SeO_2 (dioxane/H_2O 10/1, 70 °C, 6 h) furnished (±)-β-pipitzol (**1a**) (mp 125–126 °C) in 50% yield, which was identical (TLC, IR, 360-MHz ^1H NMR) with an authentic sample kindly provided by Professor P. Joseph-Nathan, Instituto Politecnico Nacional, Mexico. Subjection of the minor diastereomer **6b** to the same sequence of reactions afforded (±)-α-pipitzol (**1b**), also identical with an authentic sample.

In conclusion, we have demonstrated that the intramolecular [4 + 2] tropone–olefin cycloadducts are useful intermediates for the construction of complex ring systems, in this case the cedranoid ring system of (±)-β- and (±)-α-pipitzol (**1a,b**). Extension of this strategy to the syntheses of other ring systems embodied in natural products is under active investigation in our laboratories.

Acknowledgment. We thank the National Science Foundation (CHE-8205144), Eli Lilly and Company, and the Alfred P. Sloan Foundation for financial and material support. High-field (360 MHz) ^1H and ^{13}C NMR spectra were obtained on a spectrometer purchased with funds provided, in part, by the National Science Foundation (CHE80-24328); mass spectra were obtained through the National Science Foundation Regional Mass Spectroscopy Center at the University of Nebraska (CHE-82-11164).

Registry No. (±)-**1a**, 100761-39-5; (±)-**1b**, 108647-46-7; (±)-**3** (isomer 1), 108647-47-8; (±)-**3** (isomer 2), 108647-48-9; (±)-**5** (isomer 1), 108592-55-8; (±)-**5** (isomer 2), 108647-49-0; (±)-**6a**, 108592-56-9; (±)-**6b**, 108592-57-0; (±)-**7**, 108592-58-1; (±)-**8**, 108592-59-2; (±)-**9**, 108592-60-5.

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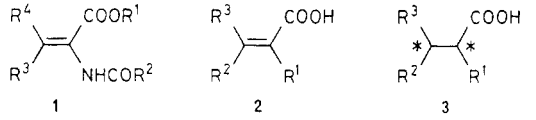
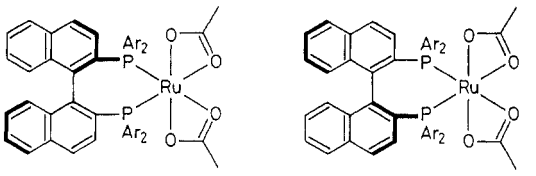
Asymmetric Hydrogenation of Unsaturated Carboxylic Acids Catalyzed by BINAP-Ruthenium(II) Complexes

Summary: Homogeneous hydrogenation of α,β- or β,γ-unsaturated carboxylic acids in the presence of a catalytic amount of Ru[(*R*)- or (*S*)-2,2′-bis(diarylphosphino)-1,1′-binaphthyl](OCOCH$_3$)$_2$ affords the corresponding saturated products in high enantiomeric excesses and in quantitative yields. The new hydrogenation has been applied to the asymmetric synthesis of (*S*)-naproxen, a 1β-methylcarbapenem precursor, and some methylated γ- and δ-lactones.

Sir: Rhodium(I) complexes bearing certain chiral phosphine ligands catalyze the highly enantioselective hydrogenation of unsaturated carboxylic acids or esters of type 1.[1] The extensive, systematic study led to the conclusion that the double-bond geometry and the presence of the α-acylamino group are obligatorily important for the efficiency. Without the amide or related groups, any of the catalyst systems designed so far were unable to give high enantiomeric excesses.[1c] To our knowledge the only exceptional substrate is itaconic acid, an unsaturated dicarboxylic acid being reduced in up to 97.7/2.3 enantioselectivity.[2] We have found that the *ruthenium(II) complexes*[3,4] possessing the BINAP[5] ligand serve as catalyst precursors for the highly stereoselective hydrogenation of a range of substituted acrylic acids lacking the acylamino moiety. With many substrates, the highest enantioselectivities have been recorded.





a, Ar = C_6H_5
b, Ar = p-$CH_3C_6H_4$
c, Ar = p-$CH_3OC_6H_4$

We examined hydrogenation of the olefinic substrates of type **2**, giving **3**, catalyzed by the chiral diphosphine–Ru complexes under varying reaction conditions. All the BINAP–Ru dicarboxylate complexes, **4a–c**, proved to be equally efficient catalysts for the enantioselective transformation. The cationic catalyst system prepared in situ by addition of 2 equiv of fluoroboric acid to the dicarboxylate complex was also effective. A series of experiments using tiglic acid (**2a**) revealed that methanol is the solvent of choice. The optically active dihydro compounds were obtained in nearly quantitative yields by using substrate to catalyst mole ratios (S/C) of 100 to 600. Addition of tertiary amines to the reaction system had little or no effect on the stereoselectivity. The degree of enantioselection is highly affected by hydrogen pressure but the effect depends on the substrates and is not straightforward. The reaction of **2a** preferred low pressure; hydrogenation in methanol using (*S*)-**4a** as catalyst at initial hydrogen pressures of 4 and 101 atm gave the product, (*S*)- **3a**, in 91% and 50% ee, respectively. However, the opposite trend was observed in the reaction of atropic acid

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