obtained for these multicomponent fits based on theoretical functions alone (i.e., these results are model independent). As reported elsewhere,[11] the Fe EXAFS of **3** and **4** together approximate all the major features observed in, and hence are good models for, the Fe EXAFS of the FeMo cofactor.

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Registry No. 1, 83214-35-1; **2**, 83214-36-2; **3**, 83214-37-3; **4**, 83214-38-4; nitrogenase iron molybdenum cofactor, 72994-52-6.

Supplementary Material Available: Positional and thermal parameters for **3** and **4**, EXAFS data collection and data reduction methodology and Figures A–D showing the raw X-ray absorption data (F/I_0 vs. E, eV) and the Fourier filtered EXAFS, $k^3\chi(k)$ vs. k, spectra with the sum of the fitted waves (10 pages). Ordering information is given on any current masthead page.

Total Synthesis of Gibberellic Acid. A Simple Synthesis of a Key Intermediate

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The total synthesis of gibberellic acid (GA_3, **1**, Scheme I) was first achieved via the key intermediate **2** by a route that was unambiguous with regard to structure and stereochemistry.[1,2] In addition to the original synthesis of **2** from the Diels–Alder adduct **3**, a second process was developed via the tricyclic ketone **4**.[3] Both routes to **2** are fairly lengthy, and although the individual steps are efficient, a simpler and more direct synthesis was clearly desirable. In this note we describe a novel 9-step synthesis of **4** that allows access to **2** in just 16 steps (vs. 25 steps in the original route).

Reaction of lithium cyclopentadienide in ether with 0.83 equiv of 2,3-dibromopropene at 23 °C for 48 h resulted in a mixture of monoalkylated cyclopentadienes, which was equilibrated in situ by stirring with 1,5-diazabicyclo [5.4.0]undec-5-ene (DBU) (0.02 equiv) at 23 °C for 2 h to a mixture of 2- and 1-(2-bromoallyl)cyclopentadienes (ratio ca. 2:1), readily isolated by distillation (bp 26–28 °C (0.08 torr)) in 87% yield.[4] This mixture was treated with methyl 2-acetylacrylate (1.35 equiv)[5] and boron trifluoride

Scheme I

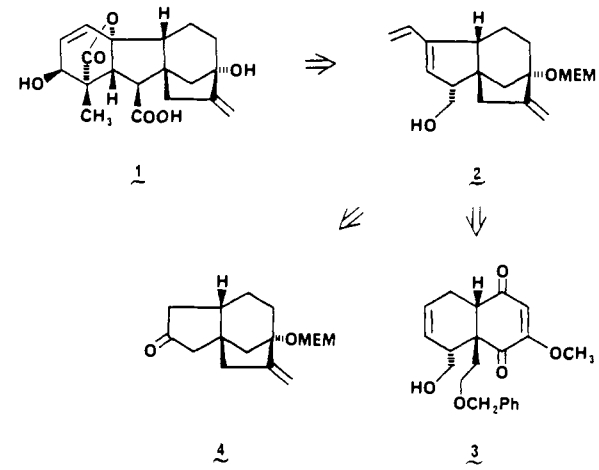
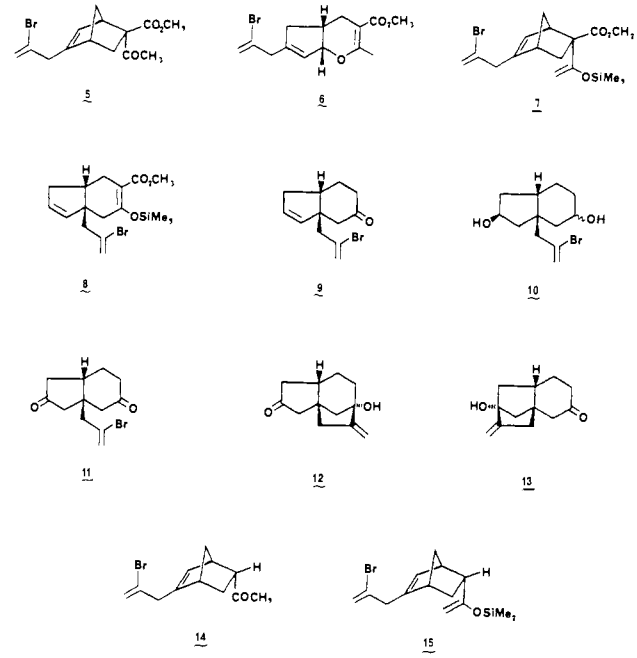


Chart I



etherate (1.1 equiv in methylene chloride at −78 °C for 30 min to afford after chromatography the desired Diels–Alder adduct, *endo*-2-acetyl-*exo*-2-carbomethoxy-5-(2-bromoallyl)-5-norbornene (**5**, Chart I) in 53% yield. ^{1}H NMR analysis indicated a >30:1 ratio of *endo*-/*exo*-acetyl substituents in accord with expectations that Lewis acid catalysis would result not only in high position-selectivity but also in enhancement of the propensity of acetyl to adopt the endo orientation.[6a] The only other compound that could be isolated from the Diels–Alder reaction was the bicyclic dihydropyran **6** (20% yield), the product of an unusual Diels–Alder reaction of 1-(2-bromoallyl)cyclopentadiene as a dienophile component with methyl 2-acetylacrylate as a diene component.[6b]

Treatment of adduct **5** with trimethylsilyl triflate[7] (2.0 equiv) and triethylamine (4.0 equiv) in methylene chloride at 23 °C for

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(2) Corey, E. J.; Danheiser, R. L.; Chandrasekaran, S.; Keck, G. E.; Gopalan, B; Larsen, S. D.; Siret, P.; Gras, J.-L. *J. Am. Chem. Soc.* **1978**, *100*, 8034.
(3) Corey, E. J.; Smith, J. G. *J. Am. Chem. Soc.* **1979**, *101*, 1038.
(4) Supplementary material for this publication contains proton magnetic resonance, infrared, and mass spectral data, as well as detailed experimental procedures. The supplementary material is reproduced from the Ph.D. dissertation of John E. Munroe, Harvard University, 1982. All reactions involving air-sensitive reactants or products were performed under an inert atmosphere (argon).
(5) We found the method of preparation of methyl 2-acetylacrylate reported previously [Masuno, M.; Asahara, T. Japanese Patent 2219 (1953); *Chem. Abstr.* **1955**, *49*, 1780g] to be unsatisfactory. An effective preparation of this reactive dienophile was accomplished by the following sequence: (1) reaction of methyl α-methylacetoacetate with phenylsulfenyl chloride (methylene chloride, 0 °C, 100% yield); (2) oxidation of sulfide to sulfoxide (*m*-chloroperbenzoic acid, methylene chloride, −40 °C, 100% yield); (3) phenylsulfenic acid elimination (distillation in vacuo from sulfolane at 60 °C with collection of methyl 2-acetylacrylate in a receiver at −78 °C, 47% yield).
(6) (a) Harrison, I. T.; Grayshan, R.; Williams, T.; Semenovski, A.; Fried, J. H. *Tetrahedron Lett.* **1972**, 5151. (b) Snider, B. B. *Ibid.* **1980**, *21*, 1133.
(7) Review: Simchen, G.; et al. *Synthesis* **1982**, 1.

0002-7863/82/1504-6129$01.25/0

1 h provided enol ether **7** in 99% yield. Heating of a solution of **7** in toluene (0.05 M) containing 30 equiv of propylene oxide (to prevent acid-catalyzed decomposition) at 160 °C for 22 h effected Cope rearrangement, leading to the *cis*-hydrindene **8**, which without purification was heated at reflux with wet Me_2SO (7.5 M water) containing 3 equiv of sodium chloride[8] for 4 h to give ketone **9** in 71% overall yield from **7**.

Treatment of **9** with 9-borabicyclo[3.3.1]nonane (9-BBN, 2.15 equiv) in THF at 23 °C for 19 h followed by oxidation with alkaline hydrogen peroxide (2 equiv, 23 °C, 30 min) gave the two epimeric bicyclic diols **10** contaminated with 1,5-cyclooctanediol. Since chromatographic separation of **10** from the latter was not easy, the mixture of alcohols was oxidized by using 2.5 equiv of pyridinium dichromate (PDC) and powdered Linde 3-Å molecular sieves[9] (1 g/mmol of PDC) in methylene chloride at 23 °C for 2.5 h to afford after chromatography diketone **11**, mp 39-40 °C (76% overall from **9**); none of the position-isomeric diketone could be detected in the reaction mixture. Highly selective hydroboration of the cyclopentene olefinic linkage in the diene **9** is to be expected in view of the known deactivating effect of vinylic bromine in hydroboration.[10]

Construction of the bridged ring utilized methodology previously developed in these laboratories specifically for the preparation of the D ring of gibberellic acid.[11] Treatment of **11** with lithium di-*n*-butylcuprate (11 equiv) in 33% hexane-diethyl ether at −78 °C for 2.5 h followed by inverse quenching with pH 8 ammonia-ammonium chloride buffer afforded tricyclic ketone **12**,[12] mp 112-113 °C, in 67% yield; only 4% of **13**, the result of cyclization involving the five-ring keto function, was isolated by chromatography.[13] This high degree of selectivity was predicted based upon the greater degree of strain in **13** with respect to **12**.[14] Protection of the hydroxy function of **12** using excess methoxyethoxymethyl (MEM) chloride and diisopropylethylamine in methylene chloride at 23 °C for 24 h provided in 96% yield the tricyclic ketone **4**, which was identical with a sample of **4** prepared by an alternate sequence[3] on the basis of ^1H NMR, infrared, and mass spectral and thin-layer chromatographic comparison. The establishment of this new route to **4** provides another synthetic pathway to gibberellic acid that is both direct and stereocontrolled.

Prior to the synthesis of **5**, the simpler norbornene **14** was prepared[15] and converted to the corresponding trimethylsilyl enol ether **15**.[16] Attempted Cope rearrangement of **15** in various solvents (benzene, toluene, xylene) at temperatures ranging from 90 to 150 °C yielded only silylated aldol dimers of **14**. In addition, thermolysis of **15** in the gas phase by passage at ca 0.1 torr through a tube heated to 425 °C afforded 2-(trimethylsiloxy)-1,3-butadiene and a mixture of 2- and 1-(2-bromoallyl)cyclopentadienes, fragments derived from a retro-Diels-Alder reaction of **15**. Evidently, a delicate balance exists between Cope rearrangement and retro-Diels-Alder pathways in this system. The utilization of substrate **7**, which contains an additional carbomethoxy group relative to **15**, was expected to favor rearrangement over fragmentation because electron delocalization from the trimethylsiloxy donor group to the withdrawing carbomethoxy group of **8** should provide driving force for the Cope but not the retro-Diels-Alder pathway.

The synthesis of **4** reported herein is conceptually quite different than previous routes. Additionally, modification of this sequence should allow for entry into a general class of *cis*-hydrindenes otherwise not readily available.[17]

Supplementary Material Available: ^1H NMR, infrared, and mass spectral data and detailed experimental procedures (35 pages). Ordering information is given on any current masthead page.

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(12) During the course of these studies, other syntheses of **12** have been reported; see: Stork, G.; Boeckmann, R. K., Jr.; Taber, D. F.; Still, W. C.; Singh, J. *J. Am. Chem. Soc.* **1979**, *101*, 7107.

(13) Tricyclic ketone **12** was readily separated from **13** and the other byproducts of the reaction (which stem from replacement of bromine in **11** by *n*-butyl (15%) and hydrogen (6%)) by column chromatography on silica gel. The R_f values obtained by using 50% ether-toluene were 0.21, 0.25, 0.51, and 0.40, respectively, for **12**, **13**, and the butyl and hydrogen halogen replacement products.

(14) MM2 conformational calculations (performed by Jay W. Ponder in these laboratories) indicated that **13** is strained by 2.5 kcal/mol relative to **12**.

(15) Treatment of the mixture of 2- and 1-(2-bromoallyl)cyclopentadienes and methyl vinyl ketone with boron trifluoride etherate (in methylene chloride at −78 °C) afforded **14** in 51% yield.

(16) Addition of a THF solution of **14** to lithium diisopropylamide in THF at −78 °C followed by quenching with a 1:1 (v/v) solution of trimethylsilyl chloride and triethylamine, previously centrifuged to settle triethylamine hydrochloride, provided **15** in 96% yield.

(17) This research was assisted financially by a grant from the National Science Foundation.

Oxygen-18 Labeling Evidence against a Hexacoordinate Phosphorus Intermediate in the Alkaline Hydrolysis of Ethyl Ethylene Phosphate

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The role of the hexacoordinate phosphorus intermediate in the reactions of phosphate esters has been the subject of much speculation but little experiment. Westheimer and co-workers[1] observed that the fraction of exocyclic cleavage for methyl ethylene phosphate increases linearly with hydroxide ion concentration from ~0% at pH 11-13 to about 15% cleavage in 10 M alkali. They suggest this result is consistent with the required pseudorotation of a dianionic pentaoxyphosphorane intermediate. They further indicate that an explanation involving a hexacoordinate phosphorus intermediate, although unsupported, cannot be eliminated.

Ramirez[2] and Gillespie et al.[3] indicate that the hydrolysis of methyl ethylene phosphate is second order in hydroxide (as suggested by Kluger et al.'s observation of an increase in exocyclic cleavage with strong base[1]) and argue for formation of a hexacoordinate intermediate in strong alkali as shown in Scheme I. This hypothesis has gained widespread recognition and has even been presented in a text[4] as a quite reasonable mechanistic possibility. The more recent preparation of stable hexacoordinated phosphorus anions, $(PhO)_6P^-$,[5] and $(CH_3O)_6P^-$,[6] and the kinetic data supporting a hexacoordinate intermediate in the hydrolysis of $(ArO)_5P$[7] suggest that the earlier hypothesis for the involvement of a hexacovalent intermediate in the strong alkali (hydrolysis of methyl ethylene phosphate is certainly quite reasonable. However, we now present ^{18}O labeling results that argue against the formation of such a species in the hydrolysis of a related five-membered ring phosphate ester, ethyl ethylene phosphate.

A 50-μL sample of 0.155 M ethyl ethylene phosphate in dry dioxane was added to 0.49 mL of 5.0 M NaOH (72% $H_2{}^{18}O$/22%

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