of Health for support of this research (CA-21840). The Varian XL-200 spectrometer used in these investigations was provided by NSF Grant 7841, and access to the 470-MHz ^{1}H NMR spectrometer was made available by the Purdue University Biological Magnetic Resonance Laboratory (NIH RR 01077).

Registry No. **5**, 7326-64-9; (*E*)-**8b**, 97654-73-4; (*Z*)-**8b**, 97654-74-5; **11**, 55795-17-0; (*E*)-**12a**, 97645-11-9; (*Z*)-**12a**, 61893-91-2; **12b**, 97654-72-3; (*E*)-**14**, 110-57-6; (*Z*)-**14**, 1476-11-5; *t*-**15a**, 85335-83-7; *e*-**15a**, 85335-84-8; *t*-**15b**, 97645-03-9; *e*-**15b**, 97645-04-0; *t*-**15c**, 97645-05-1; *e*-**15c**, 97645-06-2; (*Z*)-**16a**, 85335-85-9; (*E*)-**16a**, 85335-86-0; (*Z*)-**16b**, 97645-07-3; (*E*)-**16b**, 97645-08-4; (*Z*)-**16c**, 97645-09-5; (*E*)-**16c**, 97645-10-8; **17a**, 85336-07-8; **17b**, 97654-75-6; **17c**, 97654-76-7; **18**, 97644-82-1; (*Z*)-**19**, 97644-83-2; (*E*)-**20**, 51870-34-9; (*Z*)-**20**, 97645-12-0; **21**, 97644-84-3; **22**, 25145-58-8; **23**, 10472-24-9; **24**, 85335-96-2; **25**, 32774-63-3; **26**, 85335-98-4; **27**, 97644-85-4; **28**, 97644-86-5; **29**, 97645-14-2; **30**, 97644-87-6; **31**, 97644-88-7; **32**, 97644-89-8; **33**, 41302-34-5; **34**, 85335-94-0; **35**, 874-23-7; **36F**, 85336-00-1; **36S**, 85336-02-3; **37**, 17216-08-9; **38S**, 85336-05-6; **38F**, 85336-04-5; *cis*-**39**, 85335-97-3; *trans*-**39**, 97644-98-9; *cis*-**40**, 97644-94-5; *trans*-**40**, 85335-95-1; *cis*-**41**, 97644-96-7; *trans*-**41**, 97644-95-6; **42**, 97644-99-0; *cis*-**43**, 97645-00-6; *trans*-**43**, 97645-13-1; *cis*-**44**, 97645-01-7; *trans*-**44**, 97645-02-8; (*E*)-**45**, 85335-88-2; (*Z*)-**45**, 85335-89-3; **46**-*Z*,*E*, 85336-08-9; **46**-*Z*,*Z*, 85336-09-0; **47**-*Z*,*E*, 85335-90-6; **47**-*Z*,*Z*, 85335-91-7; **48**-*E*,*E*, 97644-90-1; **48**-*E*,*Z*, 97644-91-2; **48**-*Z*,*E*, 85335-92-8; **49**, 97644-92-3; **50**, 97644-93-4; **51**, 97644-97-8; C_6H_5SBr, 28074-23-9; CH_3SBr, 18681-52-2; $C_6H_5CH_2SBr$, 57490-10-5; C_6H_5CHO, 100-52-7; $(C_6H_5)_3PO$, 791-28-6; (*E*)-$Cl(CH_2)_2C(SCH_3)=CH_2$, 97654-77-8; (*Z*)-$Cl(CH_2)_2C(SCH_3)=CH_2$, 97654-79-0; (*E*)-$(CH_2Ph(CH_2)_2C(SCH_3)=CH_2$, 97654-78-9; (*Z*)-$CH_2Ph(CH_2)_2C(SCH_3)=CH_2$, 97654-80-3; C_6H_5SH, 108-98-5; 2-(Phenythio)-2-sulfolene, 32132-55-1.

Supplementary Material Available: Synthesis and extensive tabular spectral information available for (*E*)-**8b**, (*Z*)-**8b**, *t*-**15b**, *e*-**15b**, *t*-**15c**, *e*-**15c**, (*E*)-**16b**, (*Z*)-**16b**, (*E*)-**16c**, (*Z*)-**16c**, **18**, **24**, **12b**, **12c**, (*E*,*Z*)-**20**, **22**, and **24** (26 pages). Ordering information is given on any current masthead page.

A Silyl Enol Ether Variation of the Robinson Annulation

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The Lewis acid catalyzed reaction of regioselectively generated silyl enol ethers with vinyl ketones has been explored as an alternative to the Robinson annulation sequence. Alkylation of the trimethylsilyl enol ethers of cyclohexanone, 2-methylcyclohexanone, and 2,3-dimethylcyclohexanone with ethyl vinyl ketone, 3-penten-2-one, and methyl vinyl ketone ethylene ketal gave a series of 1,5-diketones. Cyclization of the diketones affords 2-octalones in fair to good overall yield. This procedure has been used to prepare in good yield 5,10-dimethyl-$\Delta^{1(9)}$-2-octalone, an important intermediate for sesquiterpene synthesis, with a cis/trans ratio of 3 to 1. Alkylation of the trimethylsilyl enol ether of isobutyraldehyde with 3-penten-2-one, methyl vinyl ketone, and its ethylene ketal followed by cyclization affords 4,4,5-trimethyl- and 4,4-dimethyl-2-cyclohexen-1-one. This method has been employed in the synthesis of 5-(hydroxymethyl)-2,4,4-trimethyl-2-cyclohexen-1-one, a potential synthon for ring A of the taxane diterpenes.

Since it was first developed 50 years ago[1] the Robinson annulation sequence has found extensive use in the synthesis of a variety of cyclic molecules.[2] Although this synthetic procedure is of great value, it has long been recognized that it is beset with several serious problems which limit its utility: the yields with relatively weakly acidic ketones are usually moderate at best and the vinyl ketones used as Michael acceptors tend to polymerize under the strongly basic reaction conditions. As a consequence of the sensitivity of vinyl ketones to strong base and the reversible nature of the initial Michael reaction, it is not usually possible to employ regioselectively generated enolates in traditional Robinson annulations.[2b] In order to circumvent these problems a variety of modifications have been devised which include the use of catalytic amounts of base[3] or strong acids[4] to effect the annulation. Modified vinyl ketones[5] or vinyl ketone equivalents[6] have also been used. Very recently, a procedure for carrying out the Robinson annulation with strong base under aprotic conditions has been described.[7]

In the course of a variety of projects being carried out in our laboratory, and in connection with several projected problems, we needed a mild, general alternative to the Robinson annulation which was applicable to both aldehydes and ketones, and which would permit the use of either kinetically or thermodynamically generated enolates. An attractive possibility for such an alternative annulation sequence is based on the reaction of silyl enol ethers with vinyl ketones as described several years ago by Mukaiyama's group.[8] Although the extension of this reaction to the preparation of the 1,5-diketones needed for the second step of the annulation seems obvious, at the time our work was initiated there appeared to be only one report in the literature of the use of this reaction as an alternative to the Robinson annulation.[9]

(1) Rapson, W. S.; Robinson, R. *J. Chem. Soc.* **1935**, 1285.
(2) For review of the Robinson annulation, see: (a) House, H. O. "Modern Synthetic Reactions", 2nd ed.; W. A. Benjamin; Menlo Park, CA, 1972; pp 606-611. (b) Jung, M. E. *Tetrahedron* **1976**, *32*, 3.
(3) Marshall, J. A.; Fanta, W. I. *J. Org. Chem.* **1964**, *29*, 2501.
(4) Heathcock, C. H.; Ellis, J. E.; McMurry, J. E.; Coppolino, A. *Tetrahedron Lett.* **1971**, 4995.
(5) (a) Boeckmann, R. K. *J. Am. Chem. Soc.* **1973**, *95*, 6867; **1976**, *96*, 6179. (b) Stork, G.; Ganem, B. *Ibid.* **1973**, *95*, 6152. (c) Stork, G.; Singh, J. *Ibid.* **1974**, *96*, 6181.
(6) (a) Mander, L. N.; Hamilton, R. J. *Tetrahedron Lett.* **1981**, *22*, 4115. (b) Stork, G.; Danishefsky, S.; Ohasi, M. *J. Am. Chem. Soc.* **1967**, *89*, 5459. (c) Stork, G.; McMurry, J. E. *Ibid.* **1967**, *89*, 5463, 5464. (d) See also ref 2b.
(7) Ziegler, F. E.; Hwang, K.-J. *J. Org. Chem.* **1983**, *48*, 3349.
(8) Narasuka, K.; Joai, K.; Aikawa, Y.; Mukaiyama, T. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 779.
(9) Yanami, T.; Miyashita, M.; Yoshikoshi, A. *J. Org. Chem.* **1980**, *45*, 607.

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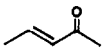
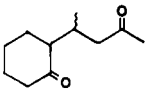
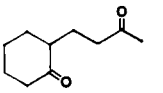
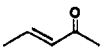
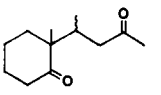
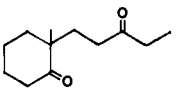
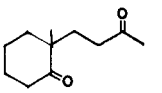
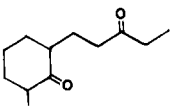
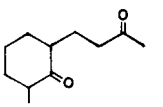
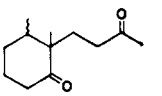
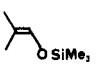
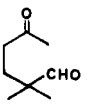
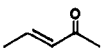
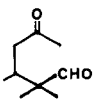
Table I. Reactions of Vinyl Ketones with Trimethylsilyl Enol Ethers

entry	enol ether	vinyl ketone	catalyst (equiv)[a]	time (min)	temperature (°C)	product, % yield
1			A (1.7)	10	−95	 72[f]
2		MVK ketal	B (1.2)	10	−95	 63[c,d]
3			A (1.7)	10	−65	 66[b]
4		MVK ketal	B[e]	10	−80	 90[c,d]
5		EVK	B[f]	5	−95	 60[c]
6		MVK ketal	B (1.5)	10	−80	 66[c,d]
7		EVK	B (1.2)	5	−95	 45[c]
8		MVK ketal	B (1.5)	60	−80	 81[c]
9		MVK ketal	B (1.5)	5	−95	 66[c]
10		MVK	B (1.5)	5	−95	69[c]
11			A (0.5)	20	−78	 51[b]

[a] A, $TiCl_4$; B, $TiCl_4$, $Ti(O\text{-}i\text{-}Pr)_4$; 1:1. [b] Isolated of distilled product, homogeneous to GLC. [c] By GLC. [d] Mixture of diketone and ketal. [e] $TiCl_4$ (1.5); $Ti(O\text{-}i\text{-}Pr)_4$ (1.0). [f] $TiCl_4$ (1.2); $Ti(O\text{-}i\text{-}Pr)_4$ (1.0).

Silyl enol ethers have been employed frequently as specific enol equivalents and are easily prepared by standard procedures.[10,11] For the purpose of optimizing the conditions of the alkylation, two ketones, cyclohexanone and 2-methylcyclohexanone, plus an aldehyde, isobutyraldehyde, were used as substrates. With 2-methylcyclohexanone both the kinetic (6-methyl-1-[(trimethylsilyl)oxy]cyclohexene) and the thermodymic (2-methyl-1-[(trimethylsilyl)oxy]cyclohexene) silyl enol ethers were used. For Michael acceptors, 3-penten-2-one, ethyl and methyl vinyl ketone (EVK and MVK) were examined. Although both the pentenone and EVK gave acceptable yields of alkylation products, MVK in most cases gave complex mixtures which contained only small amounts of the alkylation product. The major course of the reactions with MVK appeared to be polymerization; however, this problem could be circumvented with use of the ethylene ketal of MVK[12] as the Michael acceptor which affords a mixture of the 1,5-diketone and its monoketal. Brief treatment of the crude reaction mixture with aqueous acid gives the diketone.

Although the alkylations could be effected with $TiCl_4$ as the catalyst, in most cases better yields and cleaner products were obtained by using mixtures of $TiCl_4$ and $Ti(O\text{-}i\text{-}Pr)_4$.[8] In general, optimum yields are obtained with use of temperatures in the −80 °C to −90 °C range. The results of the alkylations are summarized in Table I. The diketones obtained in runs 1–7 were cyclized to the corresponding enones, all of which are known compounds. Although these enones are readily accessible by traditional procedures, they were prepared to confirm the utility of this reaction sequence as an alternative to the traditional Robinson annulation and to identify with certainty the initial alkylation products. The bicyclic enones prepared from the diketones in runs 2, 4, 5, and 6 were available in our laboratory and their identity was established by comparison with authentic samples. The octalone prepared from the alkylation product obtained in run 1 has been reported by Marshall as a mixture containing enone 1 as the major product plus an unspecified amount of a nonconjugated isomer.[13] Our procedure gave a mixture of

(10) For review of the preparation and reactions of silyl enol ethers, see: (a) Brownbridge, P. *Synthesis* **1983**, 1, 85. (b) Rasmussen, J. K. *Ibid.* **1977**, 91.

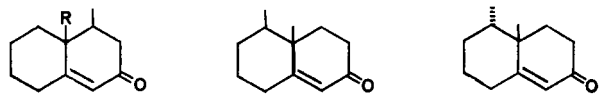
(11) (a) Stork, G.; Hudrlik, P. F. *J. Am. Chem. Soc.* **1968**, *90*, 4462, 4464. (b) House, H. O.; Czuba, L. J.; Gall, M.; Olmstead, H. D. *J. Org. Chem.* **1969**, *34*, 2324. (c) Fleming, L.; Patterson, I. *Synthesis* **1979**, 736.

(12) Hahn, E. *J. Org. Chem.* **1973**, *38*, 2092.

(13) Marshall, J. A.; Ruden, R. A. *J. Org. Chem.* **1972**, *37*, 659.

three isomers in a ratio of 82:16:2 (GC/MS). The NMR spectrum agreed with that recorded for **1**, and it is assumed that this is the major isomer. On the basis of the virtual identity of the mass spectra of the two major isomers, we tentatively assign the isomer present to the extent of 16% a structure in which the methyl group is trans to the bridgehead hydrogen. The minor isomer is assumed to be a nonconjugated enone. Cyclization of the alkylation product from run 3 gave a 2:1 mixture of stereoisomers, in which the cis isomer (**2**) is the minor product. Both the trans[14] and cis[15] isomers have been reported previously and the product distribution from the Mukaiyama-type alkylation is qualitatively similar to that obtained from more classical annulation procedures.[15]

We have employed this variation of the Robinson annulation in a synthesis of dimethyl octalone (**3**), an intermediate of considerable utility in the synthesis of eremophilane sesquiterpenes. However, the direct Robinson annulation of 2,3-dimethylcyclohexanone affords a mixture of enone **3** and the trans isomer **4** in poor yield with **3** as the minor product.[16] Although a variety of other syntheses of **3** have been described, most proceed in low yield or require several steps from commercially available materials.[5a,16a,17] Quite recently Zoretic et al. have described an acid-catalyzed annulation of 2,3-dimethylcyclohexanone which was reported to give a greater than 9:1 ratio of **3** to **4** in 33% yield.[18]



1 R=H
2 R=CH$_3$

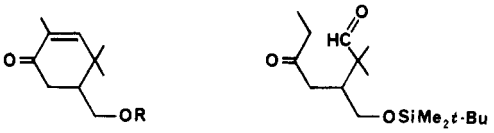
3 **4**

Assuming that the preferred conformation of the trimethylsilyl ether of the thermodynamic enol of 2,3-dimethylcyclohexanone is that in which the secondary methyl is quasi-axial due to an A$^{1(2)}$ interaction with the vinyl methyl[19] and that approach of the complexed vinyl ketone equivalent is from the least hindered face of the molecule, the major alkylation product of the silyl enol ether is predicted to be the diketone precursor of enone **3**. In practice, cyclization of the diketone mixture from run 8 gave a mixture of **3** and **4** in a ratio of 3 to 1 (capillary GLC). Although Zoretic reports a greater than 9 to 1 ratio, repetition of his annulation procedure gave a **3** to **4** ratio of 2.8:1.[20] While our procedure is slightly more complex than that described by Zoretic, the yields are superior and the sequence appears to be somewhat more stereoselective.

The traditional base-catalyzed annulation of isobutyraldehyde with MVK to give 4,4-dimethylcyclohexenone proceeds in poor yield and affords a multitide of byproducts.[21] Although a multistep sequence involving an initial Diels–Alder reaction of isobutyraldehydepyrrolidine enamine and MVK gives adequate yields of 4,4-dimethylcyclohexenone, the more common one-step enamine alkylation–cyclization reaction does not.[22] Also, the enamine of isobutyraldehyde fails to react with two vinyl ketones, 3-penten-2-one and 6-[(tetrahydropyranyl)oxy]-4-hexen-3-one (see below) which have an alkyl substituent in the β-position. The acid-catalyzed reaction of aldehydes and vinyl ketones to afford cyclohexenones proceeds in fair to good yield;[23] however this procedure is obviously unsuitable for acid-sensitive vinyl ketones.

The alkylation of the silyl enol ethers of aldehydes appeared to be a reasonable alternative approach to the diketone precursors of cyclohexenones. At the time our work was carried out no alkylations of an aldehyde silyl enol ether with a vinyl ketone had been reported, but subsequent to the completion of this phase of our work two groups reported similar reactions.[24] As indicated in runs 8–11, alkylation of the trimethylsilyl enol ether of isobutyraldehyde with MVK or its ketal and 3-penten-2-one proceed in reasonable yield. Cyclization of the derived diketones gives 4,4-dimethylcyclohexen-2-one and 4,4,5-trimethylcyclohexen-2-one, respectively.

This alkylation of the trimethylsilyl enol ether of isobutyraldehyde has also been employed in the synthesis of 2,4,4-trimethyl-5-(hydroxymethyl)cyclohex-2-en-1-one (**5**), a synthon for ring A in an abortive approach to the taxane diterpenes.[25] Enone **5** appeared to be readily available via the annulation of isobutyraldehyde with a suitable derivative of 6-hydroxy-4-hexen-3-one.



5 R = H
7 R = SiMe$_2$t-Bu

6

Initially it was envisioned that the tetrahydropyranyl ether of the hydroxyhexenone would be condensed with the enamine of isobutyraldehyde and that the hexenone would be prepared by the reaction of 1-(tributylstannyl)-3-[(tetrahydropyranyl)oxy]propene[26] with propionyl chloride by using the conditions of Milstein and Stille.[27] Although the preparation of the enone proceeded smoothly, as noted above, the enamine alkylation failed presumably for steric reasons.

Attempted alkylation of the trimethylsilyl enol ether of isobutyraldehyde with the THP ether of the hydroxyhexenone failed;[28] however, the corresponding *tert*-butyldimethyl silyl ether was a suitable substrate for alkyl-

(14) (a) Coates, R. M.; Shaw, J. E. *Chem. Commun.* **1968**, 47. (b) Hale, R. L.; Zalkow, L. H. *Ibid.* **1968**, 1249.
(15) Sims, J. J.; Selman, L. H. *Tetrahedron Lett.* **1969**, 561.
(16) (a) Piers, E.; Britton, R. W.; de Waal W. *Can. J. Chem.* **1969**, *47*, 4307. (b) Berger, C.; Franck-Neuman, M.; Ourisson, G. *Tetrahedron Lett.* **1968**, 3451.
(17) Kelley, R. B.; Zamecnik, J.; Beckett, B. A. *Can. J. Chem.* **1972**, *50*, 3455.
(18) Zoretic, P. A.; Galen, J. A.; Saltzman, M. D. *J. Org. Chem.* **1981**, *46*, 3554.
(19) Johnson, F. *Chem. Rev.* **1968**, *68*, 375.
(20) The analysis reported in ref. 18 was carried out by using ^{13}C NMR. In our hands, analysis by ^{13}C gave a **3** to **4** ratio of 2.3:1 for material prepared by Zoretic's method and 6:1 for that by the silyl enol ether procedure.
(21) Krabbenhoft, H. O. *J. Org. Chem.* **1979**, *44*, 4050.
(22) Chan, Y.; Epstein, W. W. *Org. Synth.* **1973**, *53*, 48.
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ation. 6-[(*tert*-butyldimethylsilyl)oxy]-4-hexen-3-one was prepared in a manner analogous to that of the THP ether and gave keto aldehyde **6** on reaction with the trimethylsilyl ether of isobutyraldehyde. Base-catalyzed cyclization afforded a mixture of enone **5** and its *tert*-butyldimethylsilyl ether (**2**). Although this mixture could be separated, considerable material loss resulted and in practice the crude reaction mixture was treated with tetrabutylammonium fluoride to give enone **5**.[29]

On the basis of the results presented in Table I, plus the use of this reaction to prepare enone **5**, it is clear that the silyl enol ether variation of the Robinson annulation constitutes a method of effecting this useful synthetic transformation in fair to good yield under mild conditions using regioselectively generated enolates and employing readily available Michael acceptors.

Experimental Section

Infrared spectra were obtained as neat films between salt plates, as solutions in carbon tetrachloride or chloroform, or as potassium bromide pellets using a Perkin-Elmer Model 1310 infrared spectrophotometer. ^{1}H NMR spectra were obtained on Hitachi Perkin-Elmer Model R-24 (60 MHz) or JEOL FX-90Q (90 MHz) spectrometers using deuteriochloroform as solvent. ^{13}C NMR spectra were obtained on a JEOL FX-90Q spectrometer operating at 22.5 MHz using deuteriochloroform as solvent. Both ^{13}C and ^{1}H NMR spectral data are reported in parts per million (δ) relative to Me_4Si. GLC analyses were performed on a Perkin-Elmer Sigma 3B Dual FID chromatograph with a Sigma 15 chromatography data station utilizing a flame ionization detector. Columns used included 2 ft × 0.125 in. OV-101, 6 ft × 0.125 in. 10% SE-30 on 80–100-mesh Chromosorb W, and 9 ft × 0.125 in. OV-17 on 80–100-mesh Chromosorb W. Mass spectral analyses were performed on a Hewlett-Packard 5985 gas chromatograph/mass spectrometer at 70 eV using a 2 ft × 0.125 in. 2% OV-101 column on 100–200-mesh Chromosorb WHP. 2,3-Dimethylcyclohexanone was prepared by oxidation of the corresponding alcohol, which is commercially available (Aldrich). The other cyclohexanones and isobutyraldehyde are commercial products (Aldrich) and were converted to the trimethylsilyl enol ethers without prior purification. The vinyl ketones are all commercially available (Aldrich) and were freshly distilled before use. The ethylene ketal of MVK was prepared by the method of Hahn.[12] The trimethylsilyl enol ethers of isobutyraldehyde, cyclohexanone, and those derived from the thermodynamic enols of 2-methyl- and 2,3-dimethylcyclohexanone were prepared by the triethylamine-catalyzed reaction of the corresponding carbonyl compound with Me_3SiCl in DMF.[11b,c] The silyl enol ether derived from the kinetic enolate of 2-methylcyclohexanone was prepared by the procedure of House et al.[11b]

General Procedure for Alkylations. To a stirred solution of the appropriate amount of freshly distilled $TiCl_4$ in dry CH_2Cl_2 (8 mL/mmol) under a dry nitrogen atmosphere at −78 °C was added the requisite amount of Ti(O-*i*-Pr)$_4$. The mixture was stirred for 5 min, the temperature was adjusted to that indicated in Table I, a solution of the Michael acceptor in CH_2Cl_2 (1.5 mL/mmol) was added, and the mixture was stirred for 5 min. A solution of the trimethylsilyl enol ether in CH_2Cl_2 (1.5 mL/mmol) was then added, and the reaction mixture was stirred for the time indicated in Table I. After quenching with 5% aqueous K_2CO_3 (8 mL/mmol), the product was isolated by using ether. In those reactions (runs 3 and 11) in which $TiCl_4$ was the only catalyst, the procedure was identical save for omitting the addition of Ti(O-*i*-Pr)$_4$. In runs 2, 4, 6, 8, and 9 in which MVK ketal was employed as a Michael acceptor, a mixture of diketone and ketal which contained 10% to 30% of ketal was obtained. This mixture could be converted to diketone by hydrolysis using a 1:1 mixture of 10% HCl and THF. In all reactions the product mixture was subjected to analysis by GC/MS with the results noted in Table I.

General Procedure for Cyclizations. The alkylation product was dissolved in 5% ethanolic potassium hydroxide (0.75 mL/mmol of substrate) and stirred at reflux under N_2 for 1 h. After cooling, the mixture was neutralized with 10% aqueous hydrochloric acid and extracted with ether. The ethereal extracts were washed with water and then brine, and dried, and the solvent was removed at reduced pressure to give the crude enone. The products were purified by bulb-to-bulb distillation. The enones from runs 2, 4–6, 9, and 10 were identical with samples available in our laboratory.

4-Methyl-$\Delta^{1(9)}$-2-octalone (1). This enone was obtained as a mixture of isomers, bp 95 °C (air bath, 0.5 mm), by cyclization of the product from run 1. GC/MS showed the presence of three isomers (A, B, and C) in a ratio of 2:82:16 in order of increasing retention time: mass spectra, *m/e* (relative intensity) A, 164 (76), 149 (5), 122 (100), 107 (55), 94 (18), 93 (60); B, 164 (59), 149 (11), 136 (14), 122 (100), 121 (39), 107 (24), 94 (39), 93 (17); C, 164 (47), 149 (10), 136 (13), 122 (100), 121 (36), 107 (24), 94 (36), 93 (16); NMR δ 1.05 (d, 3 H, J = 5 Hz, CH_3CH), 5.55 (br s, 1 H, HC=); IR 1665. The IR and NMR data agree with those reported for enone **1**.[13]

4,10-Dimethyl-$\Delta^{1(9)}$-2-octalone (2). Cyclization of the stereoisomeric mixture of diketones obtained in run 3 gave an inseparable mixture of enone **2** and its trans isomer (bp, 100 °C (air bath, 0.5 mm)) in a ratio of 1:2 (NMR): mass spectrum, *m/e* (relative intensity) 178 (38), 163 (9), 136 (100), 121 (58), 109 (16), 93 (20); NMR (cis) δ 0.94 (d, 3 H, J = 6 Hz, CH_3CH), 1.09 (s, 3 H, CH_3), 5.74 (m, 1 H, CH=C); trans 1.00 (d, 3 H, J = 6.7, CH_3CH), 1.29 (s, 3 H, CH_3), 5.74 (m, 1 H, CH=C); IR 1620, 1670. The spectral data agree well with those reported for the cis[15] and trans[14] isomers.

1,8-Dimethyl-$\Delta^{1(9)}$-2-octalone. Cyclization of the alkylation product obtained in run 7 gave 1,8-dimethyl-$\Delta^{1(9)}$-2-octalone, bp 110 °C (air bath, 0.7 mm): mass spectrum, *m/e* (relative intensity) 178 (100), 163 (33), 150 (11), 149 (12), 136 (33), 135 (27), 122 (50), 121 (35); NMR δ 0.99 (d, 3 H, J = 6 Hz, CH_3CH), 1.78 (d, 3 H, J = 2 Hz), CH_3C=C); IR 1663, 1607. The NMR and IR data agree with those reported.[30]

***cis*- and *trans*-5,10-Dimethyl-$\Delta^{1(9)}$-2-octalone (3 and 4).** Cyclization of the alkylation product from run 8 gave a mixture of enones **3** and **4**, bp 110 °C (air bath, 0.4 mm), which appeared to be homogeneous by conventional GLC. However, capillary GLC with use of a 50-m SE56 column indicated a **3**:**4** ratio of 3:1. Analysis by ^{13}C NMR showed a ratio of 6:1, with the expected chemical shifts for all signals.[31] The mass spectrum agreed with that reported recently.[32] The NMR and IR spectra were identical with those of a sample prepared by Zoretic's method[18] and those of enone **3** were identical with those of a pure sample generously supplied by Professor A. R. Pinder.

4,4,5-Trimethyl-2-cyclohexen-1-one. Cyclization of the alkylation product from run 11 gave the title enone, bp 60–65 °C (air bath, 0.15 mm): NMR δ 0.96 (d, 3 H, J = 6 Hz, CH_3CH), 1.02, 1.15 (s, 3 H each $(CH_3)_2C$), 5.90, 6.69 (d, 1 H each, J = 10 Hz, CH=CH); IR 1670. These spectral properties are consistent with the structure and in fair agreement with those reported by Flaugh et al.[23]

6-[(*tert*-Butyldimethylsilyl)oxy]-4-hexen-3-one. To 2.35 g of propionyl chloride in 10 mL of freshly distilled THF was added 0.077 g of benzylchlorobis(triphenylphosphine)palladium(II) and 11.7 g of 1-(tributylstannyl)-3-[(*tert*-butyldimethylsilyl)oxy]-1-propene,[33] and the mixture was heated at reflux for 9 h. After cooling, 20 mL each of ether and saturated aqueous $NaHCO_3$ were added, the aqueous layer was drawn off and extracted with three portions of ether, and the combined organic extracts were treated with 25 mL of 10% methanolic KF. The resulting turbid solution was washed with brine, and the organic layer was de-

(29) Although enone **5** is an apparently attractive synthon for ring A of the taxanes, numerous attempts to employ the derived iodide as an alkylating agent failed, apparently due to steric congestion caused by the *gem*-dimethyls. The corresponding aldehyde could not be induced to undergo aldol condensation with a ring-C synthon.

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canted from the precipitated solids. After drying, the solvent was removed at reduced pressure to give a viscous oil which on distillation afforded 4.70 g (81%) of enone, bp 85–90 °C (0.45 mm): NMR δ 0.08 (s, 6 H, $(CH_3)_2Si$), 0.91 (s, 9 H, $(CH_3)_3C$), 1–10 (t, 3 H, J = 7 Hz, CH_3CH_2), 2.15 (m, 2 H, CH_3CH_2), 4.30 (m, 2 H, $O—CH_2CH=$), 5.92 (m, 1 H, $CH_2CH=$), 6.70 (d of t, 1 H, J = 15 Hz, J = 3 Hz, $CH=CHCH_2O$); IR 1675. Anal. Calcd for $C_{12}H_{24}O_2Si$: C, 63.12; H, 10.59. Found: C, 62.88; H, 10.65.

5-(Hydroxymethyl)-2,4,4-trimethyl-2-cyclohexen-1-one (5). The reaction of 2.28 g of 6-[(*tert*-butyldimethylsilyl)oxy]-4-hexen-3-one with 1.44 g of 1-[(trimethylsilyl)oxy]-2-methylpropene was carried out by using 1.89 g of $TiCl_4$ according to the general procedure described above to give 2.65 g (88%) of crude keto aldehyde 6. In one run, a small portion of the crude product was purified by chromatography in silica gel: NMR δ 0.09 (s, 6 H, $(CH_3)_2Si$), 0.86 (s, 9 H, $(CH_3)_3C$), 1.0–2, 1.04 (s, 3 H each, $(CH_3)_2C$), 9.5 (s, 1 H, HC=O); IR 1710.

Cyclization of 2.65 g of crude keto aldehyde using the general procedure outlined above afforded 2.33 g of a mixture of enone 5 and its *tert*-butyldimethylsilyl ether (7). The crude mixture was stirred with 7.2 mL of 1 M n-Bu_4NF for 40 min and quenched with water, and the product was isolated using ether. Distillation (bp 97–105 °C, 0.35 mm) gave 1.18 g (70%) of enone 5 as a viscous oil: mass spectrum, m/e (relative intensity) 168 (50), 137 (100), 123 (49), 111 (54), 95 (39), 55 (22); NMR δ 1.02, 1.20, 1.73 (s, 3 H each, CH_3), 2.50 (m, 2 H, CH_2CO), 3.80 (br m, CH_2O), 6.33 (s, 1 H HC=); IR 3660, 1680.[34]

Chromatography of the crude reaction mixture on silica gel resulted in considerable loss of material but indicated an approximately 1:2 ratio of enone 5 and t-$BuMe_4Si$ ether (7), bp 78–82 °C (0.25 mm): NMR δ 0.09 (s, 6 H, $(CH_3)_2$ Si), 0.86 (s, 9 H, $(CH_3)_3C$), 1.05, 1.15 (s, 3 H each $(CH_3)_2C$) 1.60 (s, 3 H, $CH_3C=$), 2.25 (m, 2 H, CH_2CO), 3.60 (t, 2 H, J = 6 Hz, CH_2OSi), 6.30 (m, 1 H, HC=); IR 1680, 1085. Anal. Calcd for $C_{16}H_{30}O_2Si$: C, 68.03; H, 10.70. Found: C, 68.08; H, 10.73.

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(34) The analytical data for this compound were consistently and irreproducibly low in carbon although the material was apparently homogenous. Various conversion products (aldehyde, mesylate, and iodide) all had spectral properties consistent with the assigned structures. Also, reaction with *tert*-butyldimethylchlorosilane regenerated the ether which did give acceptable analytical data.

Stereochemical Control of Reductions. 8.[1] Exploration of the Inner Limits of the Haptophilic Effect with 2-Exo-Substituted 7-Methylenenorbornanes[2]

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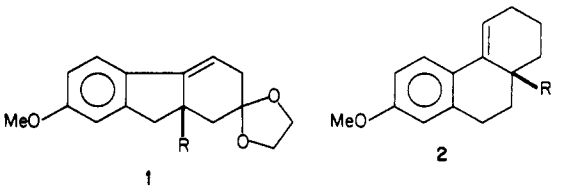
Catalytic hydrogenations over a Pd/C catalyst have been conducted on a series of 2-*endo*-methyl-7-methylenenorbornanes bearing a variable functional group in the 2-exo position. In this system (3), R groups previously found in other systems to have a strong haptophilic attraction to the catalyst surface produced mixtures of reduction products containing 18–63% anti epimer resulting from catalyst adsorption assisted by R ($CH_2OH \sim CHO < CH_2NH_2$). Six carboxyl derivatives used as R groups and previously found to have low to moderate haptophilicities gave pure syn epimers in the hydrogenation of 3. These results are interpretable in terms of a group's ability to bind to the catalyst surface by electron donation vis-à-vis the steric interference to such adsorption generated by the group's bulk. For R = CH_2NH_2 this interpretation is consistent with the known behavior of amines as mild catalyst poisons. However, it is concluded that the geometry of system 3 decreases the effective catalyst-binding properties of all R groups by placing R where it partially blocks one face of the alkene. Attempted reductions of 3, R = CH_2OH, with $LiAlH_4$, with B_2H_6, and with a chelative iridium catalyst are described. The terms proximofacial and distofacial are defined to specify processes occurring at molecular faces respectively nearest to and remote from a reference group.

The stereochemical outcome of a catalytic hydrogenation can be influenced not only by interference with catalyst adsorption arising from bulky groups within the substrate molecule but also, in an opposite sense, by the haptophilic effect[3] of certain substrate groups. This effect, although well documented,[4] is not well understood but is thought to operate by relatively prolonged adsorption of such a group at the catalyst surface, tending to ensure addition of hydrogen to that group's own face of the molecule. We have previously examined this effect in two model systems, 1 and 2, using Pd and Pt[4b,5] catalysts.



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In expanding our original heterogeneous study on the tetrahydrofluorene system 1[3,4a,5] to the related hexa-

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