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The Chemistry of Carbanions. 30. Stereochemistry of the Metal–Ammonia Reduction of 7-*tert*-Butyl-10-methyl-$\Delta^{1,9}$-octal-2-one[1]

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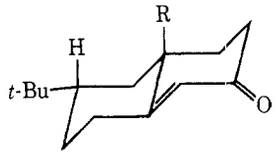
Several different routes, including reactions of several preformed metal enolates with methyl vinyl ketone, have been explored as synthetic routes to the octalone derivative **5**. This octalone **5** is held in an atypical conformation by a suitably placed *tert*-butyl substituent. As a result of this atypical conformation, reduction of the octalone **5** with Li in NH_3 produces mainly the cis-fused decalone derivative **6** (70% of the product) rather than a trans-fused decalone, the usual product of a metal–NH_3 reduction.

We are interested in exploring the use of a sterically bulky substituent to control the conformation of polycyclic systems and, as a result of this conformational control, to control the stereochemistry of reactions at sites remote from the location of the bulky substituent. This procedure for achieving stereochemical control would be an extension of the idea of conformational transmission.[2] An example of the use of this procedure to control reaction stereochemistry is provided by the reductions of enones **1** and **2** with Li and an alcohol in liquid NH_3. While reduction of the enone **1** (R = H[3] or CH_3[4]) produced the usual[5] trans-fused decalin derivative **3**, reduction of the epimer **2**[4,5] formed the atypical cis-fused decalin derivative **4**. Thus, the stereochemistry of this reduction is controlled by the location and stereochemistry of the remote *t*-Bu group.



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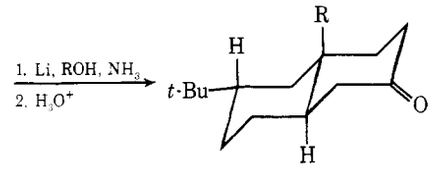

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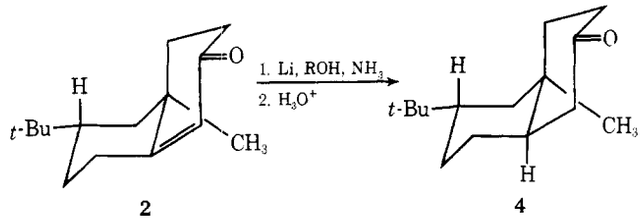
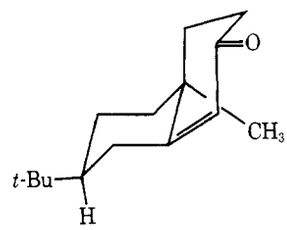


2 **4**

If this type of stereochemical control by a remote substituent is applicable to a number of reactions, it would clearly be profitable to find other substituents comparable to a *t*-Bu group in steric bulk (e.g., Me_3Si)[6] that could be introduced into a synthetic intermediate, used to control the stereochemistry of a reaction, and then removed. However, before exploring such groups that might be introduced temporarily to control conformation, it was clearly appropriate to examine other cases in which a remote *t*-Bu substituent might be effective in controlling reaction stereochemistry. This paper describes our study of another metal–NH_3 reduction, the conjugate reduction of the enone **5** to form either the cis or trans decalone derivatives **6** or **7**, and subsequent publications will describe stereochemical studies of other reactions.



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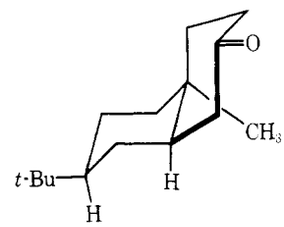

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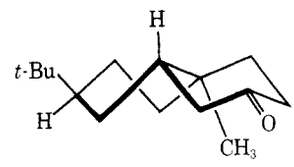

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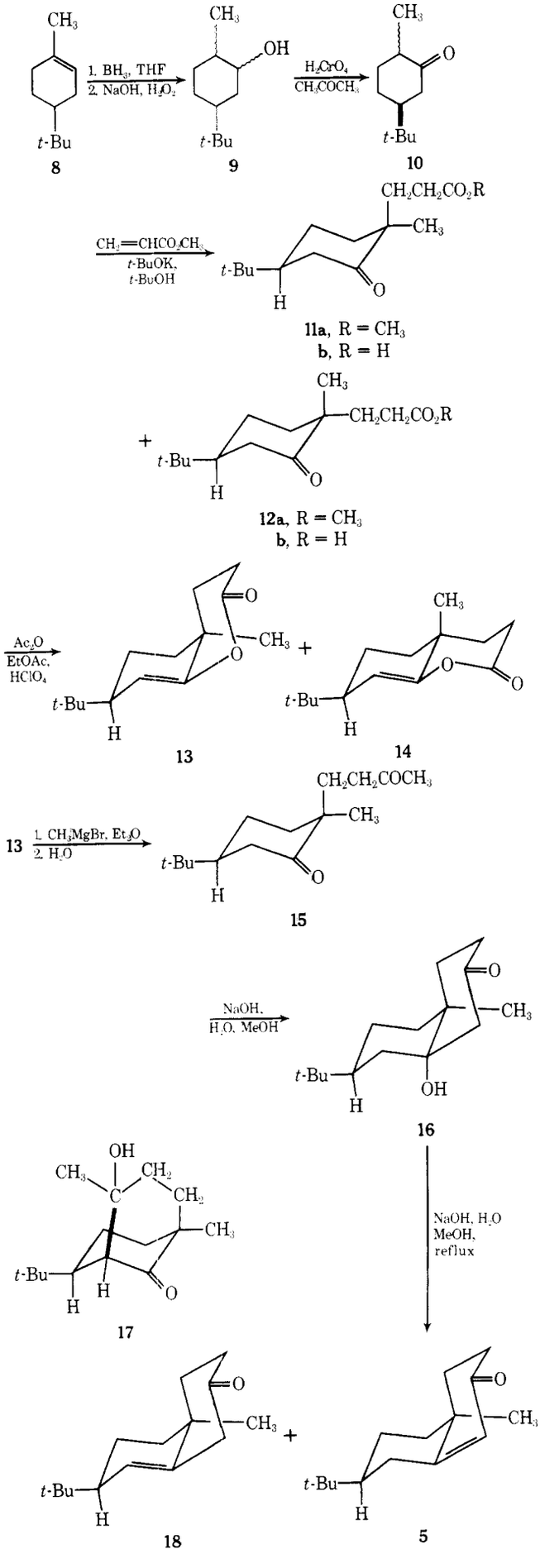
In order to prepare a sample of the enone **5** of known stereochemistry we made use of a previously studied sequence[7] in which the olefin **8** (Scheme I) was converted successively to the alcohol **9**, the ketone **10**, and the two epimeric Michael adducts **11a** and **12a**. In the last step of this sequence,

Scheme I



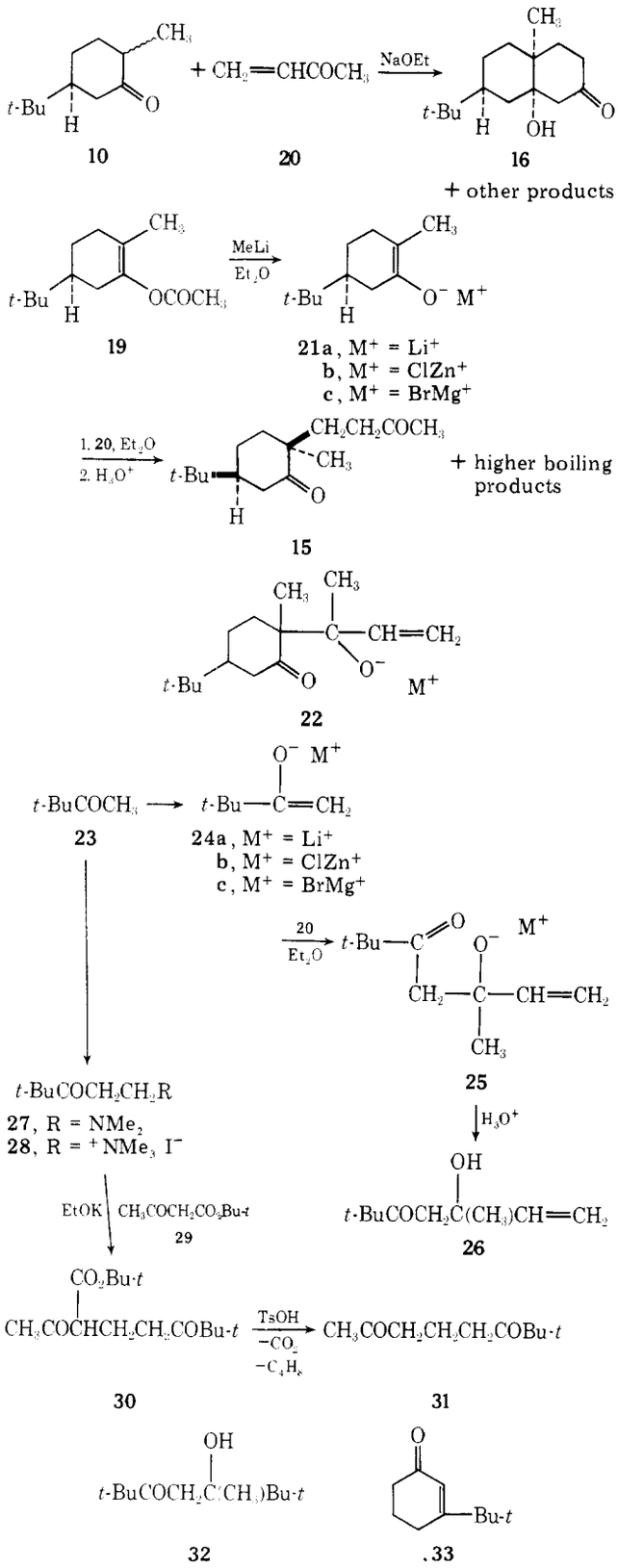
more than 85% of the Michael adduct was the epimer **11a** with an axial carbomethoxyethyl group.[7] Reaction of the corresponding mixture of keto acids **11b** and **12b** either with Ac_2O in EtOAc containing a catalytic amount of $HClO_4$[8] or with refluxing Ac_2O containing a catalytic amount of NaOAc[9] produced a mixture of epimeric enol lactones **13** and **14** from which the more abundant stereoisomer **13** was readily isolated by crystallization. Reaction of the enol lactone **13** with an equimolar amount of MeMgBr followed by hydrolysis[9,10] gave the diketone **15** with the desired stereochemistry. Reaction of this diketone with dilute NaOH at 25 °C yielded the corresponding ketol **16**; interestingly, we obtained no evidence indicating the formation of the isomeric ketol **17**. Reaction of the ketol **16** with excess NaOH in refluxing MeOH produced the desired enone **5** accompanied by 4–5% of its double bond isomer **18**.

In agreement with the stereochemical assignment given (Scheme I) for compound **16** in which the bridgehead Me group is axial to the cyclohexanone ring, the ^1H NMR signal for this Me group was shifted upfield 14 Hz when the solvent was changed from CCl_4 to C_6D_6.[11] By contrast, in the diketone **15** where the Me group is equatorial to the cyclohexanone ring, the NMR Me signal exhibited the expected[11] slight downfield shift (4.5 Hz) when the solvent was changed from CCl_4 to C_6D_6. Although conversion of the keto ester **11** of known stereochemistry via intermediates **13**, **15**, and **16** to the enone **5** served to establish the stereochemistry of this enone, it was clearly desirable to find a more direct synthetic route to the enone **5**. The fact that the desired ketol stereoisomer **16** was a relatively high-melting crystalline solid permitted us to obtain this ketol **16** in 24–31% yield by fractional crystallization of the product mixtures obtained from direct reaction of the ketone **10** and methyl vinyl ketone (**20**, Scheme II) in the presence of a catalytic amount of NaOEt.[12]

In an effort to improve the overall yield of the enone **5**, we also examined the reaction of methyl vinyl ketone **20** with the preformed metal enolates **21**. The Li enolate **21a** was obtained from the enol acetate **19**[13] and the ClZn (**21b**) and BrMg (**21c**) enolates were prepared by reaction of the Li enolate (**21a**) with $ZnCl_2$ or $MgBr_2$.[14] The best yields of the diketone **15** (54–55%) were obtained by reaction of either the Li enolate **21a** or the BrMg enolate **21c** with 1 equiv of methyl vinyl ketone (**20**) in Et_2O solution at −35 to −45 °C; the other products were the ketone **10** and higher molecular weight products from multiple condensation reactions. Thus, in this case the kinetically favored aldol product **22** evidently is sufficiently sterically congested that it dissociates to allow the slower (but energetically favored) formation of the Michael adduct (the enolate of **15**) to proceed. Although we observed similar results in reactions of the analogous metal enolates of 2-methylcyclohexanone with methyl vinyl ketone, the formation of Michael adducts from preformed metal enolates and methyl vinyl ketone is not a general reaction. In particular, with the less sterically congested metal enolates **24**, the same reaction conditions described above yield largely the kinetically favored aldol adduct **25**. This less sterically congested adduct **25** does not dissociate significantly under the reaction conditions described so that only very small amounts (<1%) of the Michael product **31** were formed. A similar reaction of the relatively unhindered Li enolate **24a** with cyclohexenone was previously observed to form only the aldol adduct.[15] Thus, the use of preformed metal enolates as precursors for Michael adducts from enones appears to be limited to situations in which the kinetic favored aldol adducts (e.g., **22**) have sufficient steric congestion to favor their dissociation.[16]

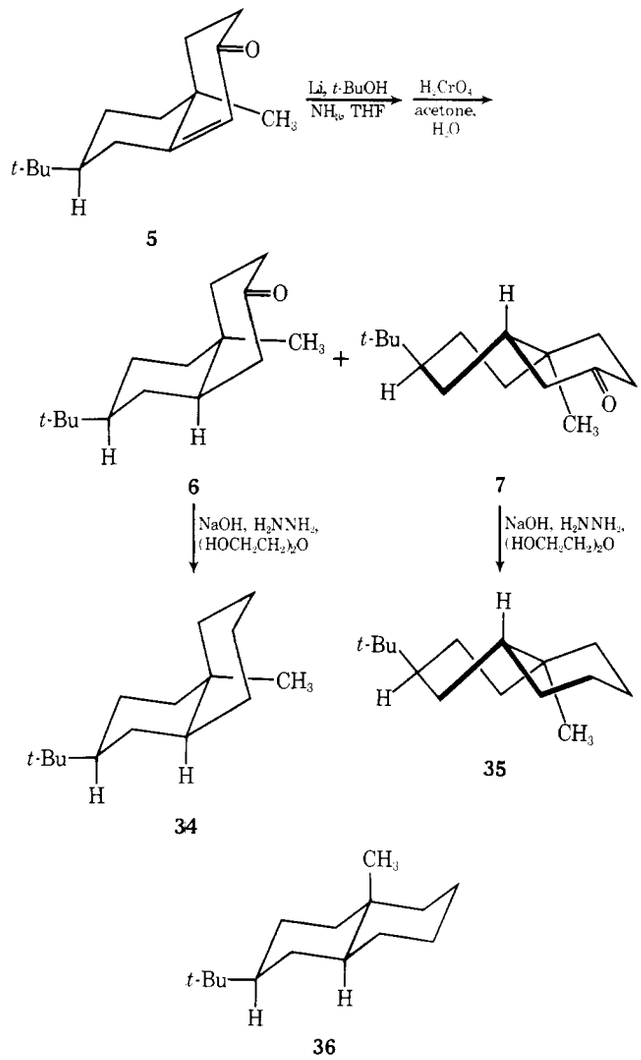
Although the foregoing studies demonstrated that a somewhat better yield of the diketone **15** could be obtained by employing a Michael reaction of the preformed BrMg enolate **21c** with methyl vinyl ketone (**20**), this benefit was offset

Scheme II



by the fact that three steps (**10** → **19** → **15** → **16**) were needed to convert the ketone **10** to the ketol **16**. Consequently, we utilized the NaOEt-catalyzed reaction of the ketone **10** with the enone **20** to obtain the bulk of the ketol **16** needed for preparing the enone **5**. Reduction of this enone **5** with the usual Li–NH_3–*t*-BuOH system produced a mixture containing mainly the cis-fused ketone **6** (70% of the product) accompanied by lesser amounts of the trans-fused ketone **7** (30% of the product, see Scheme III). To establish the stereochemistry of the ketone products **6** and **7**, the products were converted to the corresponding hydrocarbons **34** and **35** by Wolff–Kishner reduction. The product from the major ketone product **6** was shown to be identical with the previously characterized[17] cis-fused hydrocarbon **34**. The trans-fused hydrocarbon **35** was clearly different from the previously described[17] isomeric trans-fused decalin **36**.

Scheme III



Thus, the Li–NH_3 reduction of the enone **5** gives results similar to those indicated[4] for the reduction of the enone **2**. In both cases, the unusual conformation conferred upon the molecules by the bulky *tert*-butyl group in an appropriate stereochemical arrangement leads to the predominant formation of cis-fused decalone derivatives in spite of the very large preference for trans-fused decalones normally expected in a metal–NH_3 reduction.[5]

Experimental Section[18]

Preparation of the Keto Esters 11a and 12a. Reaction of 31.54 g (207 mmol) of the olefin **8** with 114 mmol of BH_3[19] in 146 ml of THF for 1 h at 3–25 °C followed by the addition of 10 ml of H_2O and oxidation with 25 ml of aqueous 3 M NaOH and 25 ml (250 mmol) of aqueous 30% H_2O_2 at 35–55 °C for 1 h yielded 38.66 g of the crude mixture of stereoisomeric alcohols **9**.[20] These alcohols **9** in 20 ml of H_2O and 100 ml of acetone were oxidized with 69.0 ml (1.33 equiv) of Jones reagent[21] for 45 min to yield, after fractional distillation, 25.11 g (72% based on the olefin **8**) of the ketone **10**, bp 88–90 °C (4.4 mm), $n^{25}D$ 1.4570 [lit.[7] bp 99–105 °C (10 mm), $n^{25}D$ 1.4562], containing (GLC, TCEP on Chromosorb P) the two stereoisomers of ketone **10** [retention times 7.5 (major) and 8.0 min (minor)] as well as a small amount of 4-*tert*-butylcyclohexanone (9.2 min). To a solution of *t*-

BuOK, from 237 mg (6.05 mg-atoms) of K, and 9.255 g (55.0 mmol) of the ketone **10** in 50 ml of *t*-BuOH was added 5.208 g (60.5 mmol) of methyl acrylate, dropwise during 5 min with stirring and cooling (mixture kept at 25–30 °C). After the mixture had been stirred for an additional 5 min, it was neutralized with aqueous 2 M HOAc and subjected to the usual isolation procedure to separate 11.29 g (81%) of the product as a colorless liquid, bp 106–112 °C (0.23 mm) [lit.[7] bp 92–99 °C (0.2 mm)], containing (GLC, LAC-728 on Chromosorb P) the known[7] keto esters **11a** (ca. 88%, retention time 13.8 min) and **12a** (ca. 12%, 21.7 min).

Preparation of the Enol Lactone 13. A mixture of 5.087 g (20.0 mmol) of the keto esters **11a** and **12a** and 60 ml of aqueous 20% HCl was refluxed with stirring for 18 h and then cooled and extracted with Et_2O. An Et_2O solution of the acidic product (from extraction with $NaHCO_3$) was dried and concentrated to leave 4.536 g (93.8%) of a mixture of keto acids **11b** and **12b** as a white solid: mp 88–93.5 °C; IR (CCl_4), 1710 cm^{-1} (carboxyl C=O); UV max (95% EtOH) 290 nm (ϵ 34.5); NMR (CCl_4) δ 11.57 (1 H, s, OH), 1.2–2.7 (11 H, m, aliphatic CH), 0.90 (9 H, s, *t*-Bu), and two singlets (total 3 H) at 1.14 (minor, axial CH_3 of **12b**) and 0.97 (major, equatorial CH_3 of **11b**). Although this product recrystallized easily from hexane, the recrystallized product (mp 88.5–104 °C) contained (NMR analysis) the same mixture of isomers **11b** and **12b** present in the initial product.

After a solution of 51.07 g (0.50 mol) of Ac_2O, 0.05 ml (0.6 mmol) of aqueous 70% $HClO_4$, and 5.153 g (21.4 mmol) of the mixture of keto acids **11b** (major) and **12b** (minor) in 500 ml of EtOAc[8] had been stirred at 25 °C for 15 min, it was partitioned between EtOAc and aqueous $NaHCO_3$ and the organic layer was separated, dried, and concentrated. The residue was treated with MeOH and pyridine to remove the residual Ac_2O and again concentrated. A solution of the residual yellow liquid (4.828 g, a mixture of lactones **13** and **14**) in pentane when cooled to 0 °C deposited 2.805 g (59%) of the pure (GLC) enol lactone **13** as white plates: mp 52.5–53.5 °C; IR (CCl_4) 1764 (enol ester C=O) and 1679 cm^{-1} (enol C=C); UV (95% EtOH) end absorption with ϵ 5440 at 210 nm; NMR (CCl_4) δ 5.30 (1 H, d, J = 2.5 Hz, vinyl CH), 2.4–2.7 (2 H, m, CH_2CO), 1.3–2.2 (7 H, m, aliphatic CH), 1.13 (3 H, s, CH_3), and 0.88 (9 H, s, *t*-Bu); mass spectrum *m/e* (rel intensity) 222 (M^+, <1), 207 (1), 166 (24), 165 (100), 137 (50), 109 (29), 55 (36), and 41 (17); calcd for $C_{14}H_{22}O_2$, 222.1620; found, 222.1605. When the NMR spectrum was measured in C_6D_6, the CH_3 singlet was shifted upfield 14 Hz (to 53 Hz) relative to its position (67 Hz) in CCl_4 solution. This upfield shift is consistent with the CH_3 group being axial to the lactone ring.[11]

Anal. Calcd for $C_{14}H_{22}O_2$: C, 75.63; H, 9.97. Found: C, 75.61; H, 9.97.

The lactone **13** was very sensitive to air oxidation and was best stored under an N_2 atmosphere in a refrigerator. In an alternative preparation, a solution of 3.382 g (14.1 mmol) of the mixture of keto acids **11b** and **12b** and 30 mg of NaOAc in 25 ml of Ac_2O was refluxed[9] for 5 h and then subjected to the usual isolation procedure to yield 2.824 g of pale yellow liquid, bp 111–120 °C (0.05 mm), that solidified on standing. This crude product contained (GLC, Carbowax 20M on Chromosorb P) the lactones **13** (ca. 90%, retention time 43.3 min) and **14** (ca. 10%, 48.1 min). The NMR spectrum (CCl_4) of this product differed from the spectrum of the pure lactone in exhibiting two vinyl CH doublets at δ 5.30 (major, attributable to **13**) and 5.22 (minor, attributable to **14**). The NMR CH_3 signal for the minor enol lactone isomer **14** was not resolved from the *t*-Bu signal. In C_6D_6 solution, the NMR CH_3 signals for the lactones were found at δ 0.95 (lactone **13**) and 0.92 (lactone **14**). When a 2.561-g portion of this lactone mixture was recrystallized from pentane at 0 °C, 1.451 g of the pure lactone **13** was obtained, mp 52.5–53.5 °C.

Preparation of the Diketone 15 and the Ketol 16. A. From the Lactone 13. A cold (0 to −2 °C) solution of 454 mg (2.04 mmol) of the enol lactone **13** in 25 ml of Et_2O was treated with 1.5 ml of an Et_2O solution containing 2.04 mmol of MeMgBr,[9,10] stirred at 0 to −3 °C for 3 h, and then partitioned between Et_2O and aqueous NH_4Cl. The Et_2O layer was washed with aqueous NaCl, dried, and concentrated to leave 491 mg of a pale yellow liquid that contained (IR and NMR analysis, GLC, Carbowax 20M on Chromosorb P) primarily the diketone **15** (retention time 40.8 min) accompanied by several minor unidentified components (6.0, 7.6, 14.0, 17.0, and 48.2 min). A collected (GLC) sample of the pure diketone **15** was obtained as a colorless liquid: $n^{25}D$ 1.4756; IR (CCl_4), 1719 and 1703 cm^{-1} (C=O); mass spectrum *m/e* (rel intensity) 238 (M^+, <1), 168 (13), 95 (22), 69 (16), 57 (30), 55 (23), 43 (100), and 41 (48); NMR (CCl_4) δ 2.0–2.5 (7 H, m, CH_2CO and a $COCH_3$ singlet at 2.08), 1.2–2.0 (7 H, m, aliphatic CH), and 0.90 (12 H, s, CH_3 and *t*-Bu). In C_6D_6 solution, the NMR CH_3 singlets were found at δ 1.67 (CH_3CO), 0.98 (CH_3), and 0.70 (t-Bu). The shift, $\delta_{CCl_4} - \delta_{C_6D_6}$, for the CH_3 singlet is −4.5 Hz, consistent with the methyl group being equatorial[11] in the diketone **15**.

Anal. Calcd for $C_{15}H_{26}O$: C, 75.58; H, 11.00. Found: C, 75.66; H, 11.01.

A solution of 504 mg of the crude diketone **15** [from 454 mg (2.04 mmol) of the lactone **13**] and 1.041 g (26 mmol) of NaOH in 60 ml of MeOH and 10 ml of H_2O was stirred at 25 °C under an N_2 atmosphere for 24 h. The resulting yellow solution was concentrated and the residual slurry was partitioned between Et_2O and H_2O. After the Et_2O solution had been washed with aqueous NaCl and dried, concentration left 404 mg of the crude product as a pale yellow solid, mp 90–125 °C. Recrystallization from hexane separated 173 mg (35.6% based on the lactone **13**) of ketol **16** as white plates, mp 145–147 °C. Recrystallization gave the pure ketol **16**: mp 146.5–147.5 °C; IR (CCl_4) 3598, 3440 (OH), and 1719 cm^{-1} (C=O); UV (95% EtOH) maximum at 281.5 nm (ϵ 21) with end absorption, ϵ 385 at 210 nm; mass spectrum *m/e* (rel intensity) 238 (M^+, 2), 181 (16), 168 (100), 111 (28), 69 (36), 57 (77), 55 (58), 43 (84), and 41 (94); NMR ($CDCl_3$) δ1.1–3.0 [17 H, m, aliphatic CH including a CH_3 singlet at 1.21 and an OH singlet (exchanged with D_2O) at 1.62] and 0.83 (9 H, s, *t*-Bu). In C_6D_6 solution, the NMR CH_3 singlets were at δ 0.97 (CH_3) and 0.75 (*t*-Bu). The absence of a third CH_3 singlet in these NMR spectra indicates that the ketol has the structure **16** rather than the alternative structure **17**.

Anal. Calcd for $C_{15}H_{26}O_2$: C, 75.58; H, 11.00. Found: C, 75.64; H, 11.01.

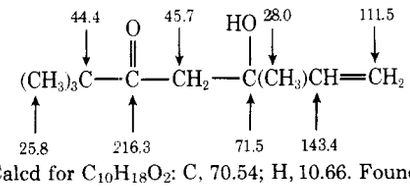
B. From the Ketone 10. A 0.25-ml (0.75 mmol) sample of a NaOEt slurry [from 1.724 g (75 mg-atoms) of Na with 25 ml of EtOH] was added to 1.683 g (10.0 mmol) of the cold (10 °C) ketone **10** and then 0.734 g (10.5 mmol) of $MeCOCH{=}CH_2$ was added, dropwise with stirring and cooling. Since the analysis of the crude reaction mixture indicated that unchanged ketone **10** remained, an additional 0.25 ml (0.75 mmol) of NaOEt slurry was added followed by the dropwise addition of a second equivalent (0.734 g or 10.5 mmol) of $MeCOCH{=}CH_2$. The resulting mixture was allowed to stand at −15 °C for 3 days and then partitioned between Et_2O and aqueous NH_4Cl. The Et_2O solution was washed with aqueous NaCl, dried, and concentrated to leave 3.20 g of crude product as a viscous orange liquid. Fractional crystallization from an Et_2O–hexane mixture separated 515 mg of the crude ketol **16**, mp 141–147 °C. The residue from the mother liquors was extracted with boiling hexane and the extract was decolorized with charcoal, concentrated, and chromatographed on silica gel with PhH as eluent to separate an additional 400 mg of the crude ketol **16** (total yield 0.91 g or 38%). Recrystallization from hexane separated 748 mg (31%) of the pure ketol **16** as white plates, mp 146.5–148.5 °C, identified with the previously described sample by a mixture melting point determination and comparison of IR spectra. In several additional experiments employing two 7.5–10 mol % portions of NaOEt with temperatures in the range −20 to −10 °C, the isolated yields of the recrystallized ketol **16** ranged from 24 to 30%. When two 1.9 mol % portions of NaOEt were employed, as recommended[12] for the preparation of the ketol from 2-methylcyclohexanone, the yield of ketol **16** was only 4%.

C. From the Metal Enolates 21. Previously described procedures were used to prepare a 0.73 M solution of anhydrous $ZnCl_2$ in Et_2O[14] and the enol acetate **19**, bp 63–65 °C (0.07 mm), $n^{25}D$ 1.4620–1.4626 [lit.[7] bp 70–76 °C (0.1 mm), $n^{25}D$ 1.4629]. Reaction of 169.1 (0.90 mol) of $BrCH_2CH_2Br$ with 24.3 g (1.00 g-atom) of triply sublimed Mg in 450 ml of Et_2O afforded a two-phase mixture of $MgBr_2$ and Et_2O from which some $(Et_2O)_2MgBr_2$ crystallized on standing. This mixture was diluted with 50 ml of PhH and 100 ml of Et_2O and the resulting solution was cooled on dry ice to deposit white, crystalline $(Et_2O)_2$-$MgBr_2$. This solid was recrystallized from a PhH–Et_2O mixture (1:2 v/v) and then redissolved in 250 ml of anhydrous Et_2O to again give a mixture of two liquid phases. The lower, more abundant phase was filtered through a Celite pad and then aliquots of the colorless to pale yellow solution were quenched in H_2O and titrated for Mg and Br. The concentration of $MgBr_2$ in the more dense liquid phase was 2.45 M.

A solution of the Li enolate **21a** was prepared[13,14] from 1.016 g (4.83 mmol) of the enol acetate **19** and 10.62 mmol of halide-free MeLi in 30 ml of Et_2O containing 387 mg of n-$C_{16}H_{34}$ (an internal standard) and then divided into three 10-ml aliquots, each containing 1.6 mmol of the enolate **21a**. One aliquot was treated with 3.6 mmol of $ZnCl_2$ in 5.0 ml of Et_2O and the resulting pale yellow suspension was stirred at 5 °C for 45 min. A second aliquot of solution was treated with 3.62 mmol of $MgBr_2$ in 1.5 ml of Et_2O and stirred at 0 °C for 30 min. Each of the three solutions, containing 1.6 mmol of one of the enolates **21**, was cooled to −40 to −45 °C and a solution of 121 mg (1.73 mmol) of $CH_3COCH{=}CH_2$ in 11.5 ml of Et_2O was added dropwise with stirring and cooling during 10 min. After the resulting mixtures had been stirred at −35 to −45 °C for 15 min, a 5-ml aliquot of the reaction

solution was withdrawn and quenched in a cold MeOH–Et_2O mixture. A second equivalent (1.73 mmol) of $CH_3COCH{=}CH_2$ in 11.5 ml of Et_2O was added to the remaining cold (−40 °C) reaction solutions. After the resulting solutions had been stirred at −35 to −40 °C for 5 min, a second aliquot was removed and quenched in cold MeOH–Et_2O. Each of the six reaction mixture aliquots from the above experiments was acidified with HOAc, and partitioned between Et_2O and aqueous NH_4Cl. The organic layers were washed successively with aqueous $NaHCO_3$ and aqueous NaCl, dried, concentrated, and analyzed by GLC (silicone SE-52 on Chromosorb W, apparatus calibrated with known mixtures). The GLC retention times for the various products follow: ketone **10**, 3.9 min; *n*-$C_{16}H_{34}$, 17.5 min; and diketone **15**, 32.2 min. Collected (GLC) samples of the diketone **15** from the reaction mixtures were identified with the previously described authentic sample by comparison of GLC retention times and NMR and IR spectra. The yields of diketone **15** from the various enolates **21** and 1 and 2 equiv of the enone **20** follow: **21a**, 54 and 7%; **21b**, 9 and 6%; **21c**, 55 and 45%. In a similar experiment where the lithium enolate **21a** was generated in THF solution and the cold (−40 to −45 °C) solution was treated with 1.1 equiv of MeCOCH=CH, the yield of diketone **15** was 42%.

Preparation of the Ketol 26. Following previously described procedures, a solution of the enolate **24a** was prepared[13,14] by adding a solution of 8.44 g (84 mmol) of the ketone **23** in 22 ml of Et_2O to a cold (−35 to −40 °C) solution of *i*-Pr_2NLi, from 11.19 g (111 mmol) of *i*-Pr_2NH in 80 ml of cold (−35 to −40 °C) Et_2O and 61 ml of a hexane solution containing 110 mmol of *n*-BuLi, and several milligrams of 2,2′-bipyridyl (an indicator). The resulting solution of enolate **24a** was warmed to −10 °C and treated with 76 ml of an Et_2O solution containing 55 mmol of anhydrous $ZnCl_2$. After the resulting pale orange solution of the enolate **24b** had been stirred at −10 to 0 °C for 15 min, it was divided into two equal aliquots each containing 42 mmol of the enolate **24b**. One portion of this enolate solution was kept at 3–5 °C while 5.525 g (78.8 mmol) of the enone **20** was added, dropwise and with stirring during 10 min. The resulting mixture, from which a white, granular precipitate separated, was stirred at 3–5 °C for 5 min and then partitioned between Et_2O and cold aqueous 1 M HCl. After the ethereal phase had been washed successively with aqueous $NaHCO_3$ and with aqueous NaCl, it was dried and concentrated to leave 7.78 g of a pale yellow liquid product that contained (IR and NMR analyses) the ketol **26**. Distillation in a short-path still separated 5.019 g (70.2%) of the pure ketol **26** as a colorless liquid: bp 48–58.5 °C (1.6 mm); $n^{25}D$ 1.4391–1.4400; IR (CCl_4), 3480 (associated OH), 1694 (C=O with intramolecular H bonding), 1643 (weak, C=C), and 930 cm^{-1} ($CH{=}CH_2$); UV max (95% EtOH) 288.5 nm (ϵ 41); NMR (CCl_4) δ 5.86 (1 H, d of d, J = 10.3 and 17.5 Hz, vinyl CH), two overlapping doublets of doublets at 5.14 (1 H, J = 17.5 and 2.0 Hz, vinyl CH) and 4.92 (1 H, J = 10.3 and 2.0 Hz, vinyl CH), 4.20 (1 H, broad s, OH, exchanged with D_2O), an AB pattern with J = 17.5 Hz at 2.83 and 2.49 (2 H, $COCH_2$), 1.21 (3 H, s, CH_3), and 1.07 (9 H, s, *t*-Bu); mass spectrum *m/e* (rel intensity) 170 (M^+, <1), 100 (20), 70 (21), 57 (100), 55 (54), 43 (74), 41 (53), and 39 (16). The natural abundance ^{13}C NMR spectrum ($CDCl_3$ solution) of the product is summarized in the following formula.

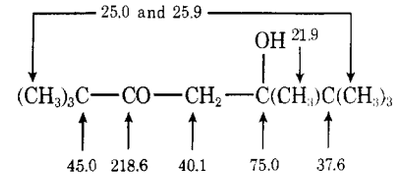


Anal. Calcd for $C_{10}H_{18}O_2$: C, 70.54; H, 10.66. Found: C, 70.55; H, 10.68.

The second aliquot of the solution containing 42 mmol of the enolate **24b** was maintained at −60 °C while 78.8 mmol of the enone **20** was added, dropwise and with stirring during 20 min. After following the previously described isolation procedure, distillation of the crude product separated 4.36 g (65.2%) of the ketol **26**, bp 50–57 °C (1.6 mm), $n^{25}D$ 1.4386–1.4392. In a comparable experiment, the reaction mixture obtained from the enone **20** and an Et_2O solution of the enolate **24b** was stirred for 2 h at 24–25 °C with periodic removal of aliquots for hydrolysis and NMR and IR analysis. No appreciable change in the nature of the crude product was evident during the prolonged reaction period. When a sample of the granular white precipitate present in the reaction mixture was separated and hydrolyzed, analysis (IR and NMR) again indicated the presence of the crude ketol **26**. A portion of the supernatant liquid from the reaction mixture appeared to contain (IR and NMR) mainly the ketone **23** after hydrolysis.

To learn whether a significant amount of the Michael adduct **31** could be obtained from reaction of one of the metal enolates **24** with the enone **20**, a cold (−35 to −40 °C) solution of the Li enolate **24a** was prepared using 3.97 g (39.2 mmol) of *i*-Pr_2NH, 7.2 ml of THF, 19.9 ml of Et_2O, 24.9 ml of a hexane solution containing 37.8 mmol of *n*-BuLi, and 3.627 g (36.2 mmol) of ketone **23** in 10 of Et_2O containing 604 mg of *n*-$C_{17}H_{36}$ (an internal standard). This solution was divided into three 24-ml aliquots, each containing 12 mmol of the enolate **24a**. One aliquot was mixed (at −5 to 0 °C) with 8.7 ml of an Et_2O solution containing 6.3 mmol of anhydrous $ZnCl_2$, stirred at 0 °C for 15 min. A second aliquot of the enolate solution was treated with 8.7 ml of Et_2O containing 12.7 mmol of anhydrous $MgBr_2$, and the resulting solution (containing some suspended solid) was stirred at −5 to 0 °C for 15 min. Each of the three enolate solutions was cooled to −50 to −60 °C, treated with 18.5 mmol of the enone **20**, stirred at −55 to −60 °C for 5 min, and then siphoned into cold aqueous 1 M HCl. From each of these reactions, the combined organic layer and ethereal extract of the aqueous phase were washed with aqueous $NaHCO_3$, concentrated, and subjected to GLC analysis (ethylene glycol adipate on Chromosorb P) employing apparatus calibrated with known mixtures of *n*-$C_{17}H_{36}$ (retention time 12.3 min) and the diketone **31** (18.8 min). When the ketol **26** was injected on this GLC apparatus, it dissociated to the rapidly eluted ketones **23** and **20**, and consequently did not interfere with the analysis for the diketone **31**. In the three reaction mixtures (each containing mainly the ketol **26**, NMR analysis), the calculated yields of diketone **31** were 0.08% from enolate **24a**, 0.47% from enolate **24b**, and 0.57% from enolate **24c**.

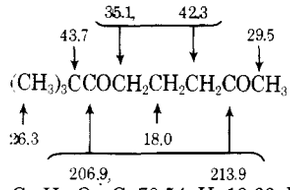
Preparation of the Ketol 32. A pale yellow solution of the enolate **24a**, from 5.49 g (54.3 mmol) of the ketone **23** and 54.3 mmol of *i*-Pr_2NLi in 90 ml of Et_2O and 30 ml of hexane, was maintained at −1 to 1 °C for 30 min while a solution of 5.49 g (54.3 mmol) of the ketone **23** in 15 ml of Et_2O was added, dropwise and with stirring. The resulting pale yellow solution was partitioned between Et_2O and cold aqueous 1 M HCl and the organic phase was washed successively with aqueous $NaHCO_3$ and with aqueous NaCl and then dried and concentrated. The residual pale yellow liquid (10.7 g) containing (IR and NMR analysis) the crude ketol was fractionally distilled to separate 8.66 g (79.6%) of fractions containing the pure ketol **32** as a colorless liquid: bp 60–67.5 °C (1.6 mm); $n^{25}D$ 1.4374–1.4390 [lit. bp 64–65 °C (0.9 mm),[22a] 89–90 °C (5 mm),[22b] 77 °C (3 mm);[22c] $n^{25}D$ 1.4378,[22a] 1.4384,[22b] 1.4390[22c]]; IR (CCl_4), 3488 (associated OH), and 1694 cm^{-1} (C=O with H bonding); UV max (95% EtOH) 290 nm (ϵ 44); NMR (CCl_4) δ 4.14 (1 H, s, OH, exchanged with D_2O), an AB pattern (J = 17 Hz) with signals at 2.82 and 2.37 (2 H, CH_2CO), 1.09 singlet with a partially resolved second signal at ca. 1.08 (total 12 H, *t*-Bu and CH_3), 0.89 (9 H, s, *t*-Bu); mass spectrum *m/e* (rel intensity) 185 (1), 143 (7), 100 (15), 85 (15), 57 (100), 43 (26), and 41 (33). The natural abundance ^{13}C NMR spectrum ($CDCl_3$ solution) of the product is summarized in the following formula.



Preparation of the Diketone 31. After a solution of 50.08 g (0.50 mol) of the ketone **23**, 17.57 g (0.585 mol) of paraformaldehyde, 47.7 g (0.585 mol) of Me_2NH_2Cl, and 0.8 ml of aqueous 12 M HCl in 65 ml of EtOH had been refluxed for 6 h, the solution was cooled to deposit 39.32 g (41%) of the hydrochloride of the amino ketone **27** as white plates. This material was partitioned between Et_2O and excess aqueous Na_2CO_3 and the organic phase was washed with aqueous NaCl, dried, and concentrated to leave 28.78 g (37%) of the crude amino ketone **27** as a pale yellow liquid: IR (CCl_4) 1703 cm^{-1} (C=O); NMR (CCl_4) δ 2.3–2.7 (4 H, m, CH_2), 2.14 (6 H, s, CH_3N), and 1.08 (9 H, s, *t*-Bu). A solution of this amine **27** (28.78 g, 183 mmol) in 100 ml of Et_2O was treated, portionwise and with stirring, with 32.5 g (229 mmol) of CH_3I. The white precipitate that separated was collected, washed with Et_2O, and dried to leave 48.66 g (89%) of the crude salt **28**, mp 184–188 °C dec. Recrystallization from absolute EtOH afforded 45.68 g (84%) of the methiodide **28** as fine, colorless crystals: mp 188–190 °C dec (lit.[23] mp 196 °C); IR (KBr pellet), 1703 cm^{-1} (C=O); NMR (D_2O) δ 3.15 (9 H, s, CH_3N), 2.8–3.1 (4 H, m, CH_2), and 1.17 (9 H, s, *t*-Bu).

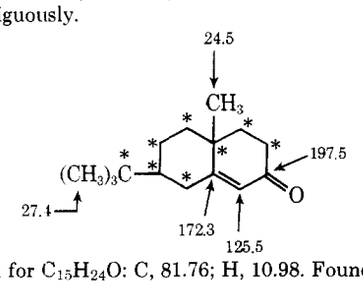
To a cold (0–2 °C) mixture of 16.46 g (55 mmol) of the methiodide **28**, 7.91 g (50 mmol) of the keto ester **29**, and 55 ml of PhH was added, dropwise and with stirring during 25 min, a solution of $KOEt$[24] prepared from 2.05 g (53 mg-atoms) of K and 29.3 ml of EtOH. After the resulting pale yellow to colorless suspension had been stirred at 0–2 °C for 3 h, it was filtered and the filtrate was concentrated under re-

duced pressure. The residual yellow semisolid was partitioned between H_2O and Et_2O and the organic phase was washed successively with aqueous $NaHCO_3$ and with aqueous NaCl, and then dried and concentrated. The residual crude diketo ester **30** amounted to 13.5 g of pale yellow liquid: IR (CCl_4), 1739 (ester C=O) and 1714 cm^{-1} (C=O); NMR (CCl_4) δ 3.1–3.5 (1 H, m, CHCO), 1.7–2.7 (7 H, m, aliphatic CH including a CH_3CO singlet at 2.15), 1.43 (9 H, s, *t*-BuO), and 1.08 (9 H, s, *t*-Bu). A mixture of 6.76 g (25 mmol) of the crude diketo ester **30** and 48 mg (2.5 mmol) of *p*-TsOH was heated to 120–140 °C with stirring for 1 h at which time the gas evolution had subsided. The residual yellow liquid was distilled to separate 2.84 g (67%) of the diketone **31** as colorless to pale yellow fractions, bp 98–102 °C (5.5 mm), $n^{25}D$ 1.4365–1.4370. These fractions contained (GLC, ethylene glycol adipate on Chromosorb P) mainly the diketone **31** (retention time 15.5 min) accompanied by ca. 4% of an impurity believed to be the enone **33** (18.3 mm). A sample containing (GLC) mainly this impurity **33** was obtained by GLC collection: IR (CCl_4) 1671 (conjugated C=O) and 1614 cm^{-1} (conjugated C=C).[25] To separate the pure diketone **31**, a portion of the product containing ca. 96% of the diketone **31** was crystallized from hexane at ca. −25 °C and the resulting white needles (mp ca. −10 °C) were collected, allowed to melt, and rapidly distilled in a short-path still at 1.4 mm. The pure diketone **31** was obtained as a colorless liquid; $n^{25}D$ 1.4358; IR (CCl_4) 1713 and 1701 cm^{-1} (C=O); UV max (95% EtOH) 282 nm (ϵ 49); NMR (CCl_4) δ 2.2–2.7 (4 H, M, CH_2CO), 2.05 (3 H, s, CH_3CO), 1.5–2.0 (2 H, m, CH_2), and 1.08 (9 H, s, *t*-Bu); mass spectrum *m/e* (rel intensity) 170 (M^+, 1), 155 (2), 113 (100), 85 (75), 58 (30), 57 (82), 55 (24), 43 (93), and 41 (34). The natural abundance ^{13}C NMR spectrum ($CDCl_3$) of the diketone **31** is summarized in the following formula.



Anal. Calcd for $C_{10}H_{18}O_2$: C, 70.54; H, 10.66. Found: C, 70.54; H, 10.68.

Preparation of the Enone 5. A solution of 29.76 g (744 mmol) of NaOH, 300 ml of H_2O, and 17.74 g (74.4 mmol) of the ketol **16** (mp 146.5–147.5 °C) in 1800 ml of MeOH was refluxed for 18 h and then diluted with 500 ml of aqueous NaCl, concentrated, and extracted with Et_2O. The ethereal extract was washed with aqueous NaCl, dried, and concentrated to leave 16.13 g (98%) of the crude product as a yellow liquid that contained (IR analysis) practically pure enone **5**. This product exhibited one major GLC peak (silicone SE-52 on Chromosorb W) corresponding to the conjugated enone **5** (retention time 25.2 min) accompanied by a small amount (ca. 4%) of the β,γ isomer **18** (13.7 min). Distillation afforded 14.70 g (89.7%) of the enone **5** as a pale yellow liquid, bp 93–105 °C (0.03 mm). Redistillation gave the pure enone **5** as a very pale yellow liquid; bp 106–110 °C (0.03 mm); $n^{25}D$ 1.5130 [lit.[26] bp 85 °C (0.1 mm)]; IR (CCl_4) 1670 (conjugated C=O) and 1626 cm^{-1} (conjugated C=C); UV max (95% EtOH) 244 nm (ϵ 14 900) and 314.5 (74) [lit.[26] 242 nm (ϵ 12 600)]; ^1H NMR (CCl_4) δ 5.66 (1 H, broad, vinyl CH), 1.3–2.6 (11, H, m, aliphatic CH), 1.22 (3 H, s, CH_3), and 0.84 (9 H, s, *t*-Bu); mass spectrum *m/e* (rel intensity) 220 (M^+, 9), 164 (14), 149 (17), 121 (19), 91 (23), 79 (23), 77 (18), 57 (100), 55 (39), 43 (23), 41 (88), and 39 (31). The ^{13}C NMR spectrum of the enone **5** ($CDCl_3$ solution) is summarized in the following structure; the indicated assignments are consistent with off-resonance decoupling measurements. The additional peaks at 21.3, 31.7, 33.9 (2 C atoms), 35.7, 36.0, 37.4, and 44.8 ppm correspond to the designated (*)C atoms; however, we are unable to make the assignments unambiguously.



Anal. Calcd for $C_{15}H_{24}O$: C, 81.76; H, 10.98. Found: C, 81.81; H, 11.17.

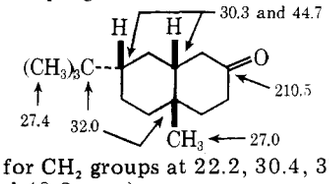
The enone **5** formed a 2,4-dinitrophenylhydrazone that crystallized from MeOH as crimson needles: mp 172–173.5 °C [lit.[26] mp 166–167.5 °C); IR ($CHCl_3$) 1619 (C=N, C=C), 1508, and 1339 cm^{-1} (NO_2); NMR ($CDCl_3$) δ 11.2 (1 H, broad, NH), 9.13 (1 H, d, J = 2.5 Hz, aryl CH), 8.32 (1 H, d of d, J = 2.5 and 9.5 Hz, aryl CH), 7.97 (1 H, d, J = 9.5 Hz, aryl CH), 6.13 (1 H, broad, vinyl CH), 1.2–2.8 (11 H, m, aliphatic CH), 1.17 (3 H, s, CH_3), and 0.88 (9 H, s, *t*-Bu).

The crude enone **5** (558 mg containing ca. 4% of the β,γ isomer **18**) from another preparation was subjected to preparative low-pressure liquid chromatography employing a column packed with silica gel and eluted with Et_2O–hexane (1:9 v/v). The more rapidly eluted fractions contained a few milligrams of the crude β,γ isomer **18** that was distilled in a short-path still to separate the β,γ isomer **18** as a pale yellow liquid that solidified when cooled below 30 °C: IR (CCl_4) 1721 (C=O) and 1658 cm^{-1} (weak, C=C); NMR (CCl_4) δ 5.42 (1 H, broad, vinyl CH), 1.3–3.3 (11 H, m, aliphatic CH), 1.23 (3 H, s, CH_3), and 0.85 (9 H, s, *t*-Bu); mass spectrum *m/e* (rel intensity) 220 (M^+, 7), 164 (100), 163 (23), 149 (40), 107 (27), 91 (27), 79 (22), 57 (99), 55 (45), 41 (64), and 39 (21); calcd for $C_{15}H_{24}O$, 220.1827; found, 220.1826.

The latter fractions from this chromatograph contained 549 mg of the enone **5** as a pale yellow liquid identified with the previously described material by comparison of IR spectra.

Reduction of the Enone 5. To a cold (−33 °C) solution of 586 mg (84.4 mg-atoms) of Li in 150 ml of liquid NH_3 was added, dropwise and with stirring, a solution of 4.658 g (21.1 mmol) of the enone **5** and 3.144 g (42.4 mmol) of *t*-BuOH in 30 ml of THF. After the resulting mixture had been stirred under reflux for 20 min, solid NH_4Cl was added to consume the excess Li and the NH_3 was allowed to evaporate. The residue was partitioned between H_2O and Et_2O and the Et_2O solution was washed with aqueous NaCl, dried, and concentrated. The crude roduct, a yellow liquid containing (IR analysis) mainly the ketones **6** and **7** accompanied by some alcohol by-products, was dissolved in 100 ml of cold (0 °C) acetone, treated with a slight excess of aqueous 8 N H_2CrO_4,[24] and then treated with *i*-PrOH, diluted with H_2O, concentrated under reduced pressure, and again partitioned between H_2O and Et_2O. After the Et_2O solution had been washed successively with aqueous $NaHCO_3$ and with aqueous NaCl, it was dried and concentrated to leave 4.639 g (99%) of the crude product as an orange liquid. Distillation at 0.02 mm in a short-path still afforded 4.22 g (90%) of the mixture of ketones **6** and **7** as a pale yellow liquid. This mixture contained (GLC, silicone XE-60 on Chromosorb P) ca. 70% of the ketone **6** (retention time 21.8 min) and ca. 30% of the ketone **7** (25.9 min).

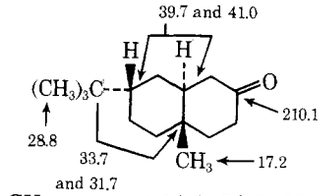
A collected (GLC) sample of the major isomer, ketone **6**, was obtained as a colorless liquid that solidified on standing, mp 48.5–50.5 °C. Recrystallization from pentane at dry ice temperature afforded the pure ketone: mp 50.8–51.8 °C; IR (CCl_4) 1712 cm^{-1} (C=O); ^1H NMR (CCl_4) δ 1.0–2.9 (17 H, m, aliphatic CH including a CH_3 singlet at 1.22) and 0.84 (9 H, s, *t*-Bu); in C_6D_6 solution the ^1H NMR singlets were at δ 0.91 (CH_3) and 0.75 (*t*-Bu); mass spectrum *m/e* (rel intensity) 222 (M^+, 27), 167 (21), 166 (48), 109 (22), 108 (28), 96 (100), 95 (30), 81 (22), 57 (79), 55 (32), and 41 (43). The natural abundance ^{13}C NMR spectrum of the ketone **6** ($CDCl_3$ solution) is summarized in the following structure; the indicated assignments are consistent with off-resonance decoupling measurements.



(signals for CH_2 groups at 22.2, 30.4, 37.5, 39.8, 44.5, and 48.2 ppm)

Anal. Calcd for $C_{15}H_{26}O$: C, 81.02; H, 11.79. Found: C, 81.10; H, 11.95.

A collected (GLC) sample of the minor isomer, ketone **7**, was distilled in a short-path still at 0.02 mm to obtain the pure ketone as a colorless liquid: $n^{25}D$ 1.4893; IR (CCl_4) 1714 cm^{-1} (C=O); ^1H NMR (CCl_4) δ 1.2–2.5 (14 H, m, aliphatic CH), 1.08 (3 H, s, CH_3), and 0.89 (9 H, s, *t*-Bu); in C_6D_6 solution the ^1H NMR singlets were at δ 0.74 (CH_3) and 0.79 (*t*-Bu); mass spectrum *m/e* (rel intensity) 222 (M^+, 13), 167 (35), 166 (49), 109 (20), 96 (24), 95 (29), 57 (100), 55 (24), and 41 (34). The natural abundance ^{13}C NMR spectrum of the ketone **7** ($CDCl_3$ solution) is summarized in the following formula; the indi-



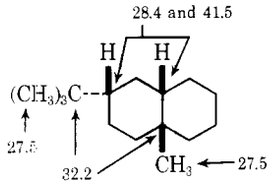
(signals for CH_2 groups at 21.2, 29.2, 37.8, 38.2, 41.4, and 44.9 ppm)

cated assignments are consistent with off-resonance decoupling measurements.

Anal. Cacld for $C_{15}H_{26}O$: C, 81.02; H, 11.79. Found: C, 81.31; H, 11.97.

To obtain quantitative data concerning the yields and product distributions of the ketones **6** and **7** from reduction of enone **5**, a series of small-scale reductions were performed in which the crude neutral product was mixed with an internal standard (n-$C_{19}H_{40}$) and subjected to GLC analysis (silicone XE-60 on Chromosorb P, apparatus calibrated with known mixtures). The retention times for the various components follow: n-$C_{19}H_{40}$, 9.2 min; β,γ enone **18**, 19.0 min; ketone **6**, 22.4 min; ketone **7**, 27.0 min; α,β enone **5**, 46.2 min. In a typical reduction, a solution of 881 mg (4.0 mmol) of the enone **5** and 593 mg (8.0 mmol) of t-BuOH in 5.0 ml of THF was added to a solution of 111 mg (16.0 mg-atoms) of Li in 25 ml of liquid NH_3. After the resulting mixture had been stirred under reflux for 30 min, it was subjected to the previously described isolation procedure including treatment with aqueous H_2CrO_4 in acetone. The crude liquid product was mixed with a known weight of n-$C_{19}H_{40}$ and subjected to GLC analysis. In three independent runs the total yield of ketones **6** and **7** were 91, 97, and 98% and the average composition of the product was 70.0 ± 0.5% of ketone 6 and 30.0 ± 0.7% of ketone **7**.

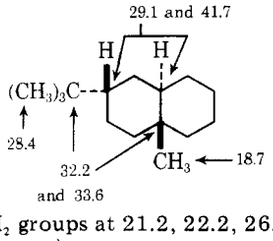
Preparation of the Hydrocarbon 34. A mixture of 607 mg (2.73 mmol) of the ketone **6**, 804 mg (13.7 mmol) of aqueous 85% H_2NNH_2, and 6.0 ml of $(HOCH_2CH_2)_2O$ was refluxed (N_2 atmosphere) for 1.25 h and then cooled and treated with 328 mg (8.19 mmol) of NaOH. The mixture was again heated to boiling, the H_2O and H_2NNH_2 were allowed to distill from the mixture, and the resulting solution was refluxed (N_2 atmosphere) for 3 h. The reaction mixture was partitioned between pentane and aqueous 10% HCl and the organic layer was washed with aqueous NaCl, dried, and concentrated to leave 527 mg (93%) of the crude hydrocarbon **34** (IR and GLC analysis, silicone DC-710 on Chromosorb P). Distillation separated 426 mg (75%) of the hydrocarbon **34** as a colorless liquid, bp 72.5–74 °C (0.14 mm), $n^{25}D$ 1.4798–1.4801 (lit.[20] $n^{25}D$ 1.4792), that was identified with an authentic sample by comparison of IR, NMR, and mass spectra and GLC retention times. The natural abundance ^{13}C NMR spectrum of the hydrocarbon ($CDCl_3$ solution) is summarized in the following structure; the indicated assignments are consistent with off-resonance decoupling measurements.



(signals for CH_2 groups at 20.6, 22.2, 22.8, 28.1, 29.9, 42.1, and 48.7 ppm)

Preparation of the Hydrocarbon 35. The same reduction procedure was followed with 308 mg (1.38 mmol) of the ketone **7**, 406 mg (6.9 mmol) of aqueous 85% H_2NNH_2, 3.0 ml of $(HOCH_2CH_2)_2O$, and 166 mg (4.14 mmol) of NaOH. The crude neutral product, 260 mg (90%) of pale yellow liquid containing (IR and GLC analysis) the hydrocarbon **35**, was distilled in a short-path still at 1.5 mm to separate 222 mg (77%) of the pure hydrocarbon **35** as a colorless liquid: $n^{25}D$ 1.4792; IR (CCl_4) no OH or C=O absorption; ^1H NMR (CCl_4) δ 1.0–2.0 (16 H, m, aliphatic CH), 0.86 (9 H, s, t-Bu), and 0.85 (3 H, s, CH_3); mass spectrum m/e (rel intensity) 208 (M^+, 2), 152 (52), 137 (31), 109 (39), 96 (45), 95 (100), 83 (32), 81 (49), 67 (32), 57 (73), 55 (43), and 41 (52).

The IR, NMR, and mass spectra of this hydrocarbon **35** were clearly different from the corresponding spectra of the known[17] hydrocarbons, **34** and **36**. The natural abundance ^{13}C NMR spectrum of the hydrocarbon **35** ($CDCl_3$ solution) is summarized in the following structure; the indicated assignments are consistent with off-resonance decoupling measurements.



(signals for CH_2 groups at 21.2, 22.2, 26.9, 29.0, 39.3, 39.4, and 42.7 ppm)

Anal. Calcd for $C_{15}H_{28}$: C, 86.46; H, 13.54. Found: C, 86.44; H, 13.50.

After a number of GLC columns were examined, one GLC column (silicone OV-17 on Chromosorb P) was found that would partially resolve the cis hydrocarbon **34** (retention time 22.5 min) from the trans hydrocarbon **35** (23.2 min). On this same column, the previously described[17] trans hydrocarbon **36** had a retention time between those of hydrocarbons **34** and **35** so that a mixture of all three hydrocarbons exhibited a single broad GLC peak.

Registry No.—**5**, 13547-64-3; **5** DNPH, 60676-13-3; **6**, 60676-14-4; **7**, 60676-15-5; **8**, 3419-74-7; **9**, 15822-55-6; *cis*-**10**, 5951-22-4; *trans*-**10**, 5937-40-6; **11a**, 37818-70-5; **11b**, 60676-16-6; **12a**, 37786-90-6; **12b**, 60676-17-7; **13**, 60676-18-8; **15**, 60676-19-9; **16**, 60676-20-2; **18**, 60676-21-3; **19**, 37786-83-7; **20**, 79-94-4; **21a**, 37786-85-9; **21b**, 60676-22-4; **21c**, 60676-23-5; **23**, 75-97-8; **24a**, 34865-75-3; **24b**, 60676-24-6; **25**, 60676-25-7; **27**, 22700-73-8; **28**, 60676-26-8; **29**, 1694-31-1; **30**, 60676-27-9; **31**, 60676-28-0; **32**, 3205-30-9; **33**, 17299-35-3; **34**, 35096-26-5; **35**, 60676-29-1; methyl acrylate, 96-33-3; MeLi, 917-54-4; $ZnCl_2$, 7646-85-7; $MgBr_2$, 7789-48-2; i-Pr_2NLi, 4111-54-0.

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Stereochemistry of Organophosphorus Cyclic Compounds. 6.[1] Stereochemistry of the Reaction between Sulfenyl Chlorides and Trivalent Phosphorus Compounds[2]

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cis- and *trans*-2-methylthio-2-oxo-4-methyl-1,3,2-dioxaphosphorinanes (**3**) have been synthesized and their conformations studied by ^1H and ^{31}P NMR. *trans*-**3** is found to exist as a chair-form conformer with the ring methyl and phosphoryl group equatorial. *cis*-**3** adopts most likely a chair conformation with the ring methyl equatorial and phosphoryl group axial. It has been demonstrated that *cis*- and *trans*-2-methoxy-4-methyl-1,3,2-dioxaphosphorinanes (**1**) and 2-hydro-2-oxo-4-methyl-1,3,2-dioxaphosphorinanes (**2**) react with a variety of sulfenyl chlorides stereospecifically with retention at phosphorus. The same steric course has been observed for reaction between optically active *O*-isopropyl ethylphosphinate (**12**) and *O*-isopropyl *O*-trimethylsilyl ethylphosphonite (**15**) and methylsulfenyl chloride. The mechanism of reaction of trivalent phosphorus compounds with sulfenyl chlorides is discussed.

The reaction between alkyl- and arylsulfenyl chlorides and trialkyl phosphites, which takes place to give the corresponding thiophosphates and alkyl chlorides according to eq 1, was first studied by Morrison[3] in 1955.

$$(RO)_3P + R'SCl \longrightarrow (RO)_2P(=O)-SR' + RCl \qquad (1)$$

Dialkyl phosphites react analogously although in this case thiophosphate formation is accompanied by the elimination of hydrogen chloride in place of the alkyl chloride.

Reaction 1 is usually regarded as an Arbuzov-type process involving decomposition of an intermediate phosphonium chloride.[4] However, neither the mechanism nor the steric course of this reaction has been investigated in detail.[5] We were prompted to undertake a detailed study of the mechanism of reaction 1 by consideration of the fact that the phosphite molecule can attack either the sulfur or the halogen atom of the sulfenyl halide molecule. Formally, this corresponds to the two possible modes of sulfur–chlorine bond polarization.

$$R-\overset{\delta^+}{S}(Cl^{\delta^-}) \overset{1}{\leftarrow} \ddot{P}(OR)_3 \overset{2}{\rightarrow} \overset{\delta^+}{Cl}-\overset{\delta^-}{SR} \qquad (2)$$

One possible ionic mechanism consists in the nucleophilic attack of phosphite on sulfur leading to the formation of an intermediate "quasi-phosphonium salt" A (eq 3). Subsequent

$$(RO)_3P: + \overset{\delta^+}{R}\overset{\delta^-}{S}-Cl \longrightarrow \underset{A}{\left[(RO)_2\overset{+}{P}(-O-R)-SR'\ Cl^-\right]} \longrightarrow (RO)_2P(=O)-SR' + RCl \qquad (3)$$

nucleophilic attack of chloride ion on the alkoxy group yields the thiol ester and alkyl chloride. According to this mechanism formation of the thiol ester should take place with retention of configuration around the phosphorus atom.

An alternative mechanism consists in nucleophilic attack of the phosphorus atom on the "electropositive" halogen atom[6] of the sulfenyl chloride molecule leading to the formation of a chlorophosphonium salt B. Displacement of

$$(RO)_3P: + \overset{\delta^+}{Cl}-\overset{\delta^-}{SR'} \longrightarrow \underset{B}{[(RO)_3\overset{+}{P}-Cl\ R'S^-]} \longrightarrow \underset{A}{\left[(RO)_2\overset{+}{P}(-O-R)-SR'\ Cl^-\right]} \longrightarrow (RO)_2P(=O)-SR' + RCl$$

$$+ (R'S)_2 + (RO)_2P(=O)-Cl \qquad (4)$$

chloride ion by attack of mercaptide ion at phosphorus would convert intermediate B to the same "quasi-phosphonium salt" A which would then undergo the normal decomposition.

The stereochemical consequence of this mechanism is that the thiol ester should have a configuration opposite to that of the initial phosphite or be formed as a racemate. Inversion of configuration around the phosphorus atom would take place during the exchange of chlorine for the thioalkyl group in the chlorophosphonium salt B whereas chloride–chloride exchange in phosphonium salt B or the mercaptide–mercaptide exchange in phosphonium salt A would be responsible for racemization.

A third mechanism involving "biphilic" addition of the trivalent phosphorus atom to the S–Cl bond might also be considered[7] (eq 5). This would lead to the formation of a