

3815-80-3; **6n**, 68657-46-5; **6o**, 68657-43-2; **6p**, 68657-47-6; **6q**, 66947-48-6; **6r**, 3483-16-7; **6s**, 13183-09-0; **6t**, 3815-83-6; **6u**, 6939-12-4; **6v**, 64180-21-8; **6x**, 70377-79-6; **6y**, 20600-69-5; **12a**, 68657-26-1; **12b**, 68657-30-7; **12c**, 68657-31-8; **12d**, 68657-28-3; **12e**, 68657-34-1; **12f**, 68657-29-4; **12g**, 68657-33-0; **12h**, 68657-39-6; **12i**, 68657-36-3; **12j**,

68657-32-9; **12k**, 68657-41-0; **12l**, 68657-27-2; **12m**, 68657-35-2; **12n**, 68657-38-5; **12o**, 68657-25-0; **12p**, 68657-40-9; **12q**, 70415-61-1; **12r**, 70377-80-9; **12s**, 70428-84-1; **12t**, 70377-81-0; **12u**, 70377-82-1; **12v**, 70377-83-2; **12x**, 70377-84-3; **12y**, 70377-85-4; **13a**, 306-18-3; **13b**, 3720-41-0; **13c**, 555-60-2; TCNE, 670-54-2.

Chemistry of Carbanions. 34. Alkylation of a 1-Decalone Enolate with Abnormal Geometry¹

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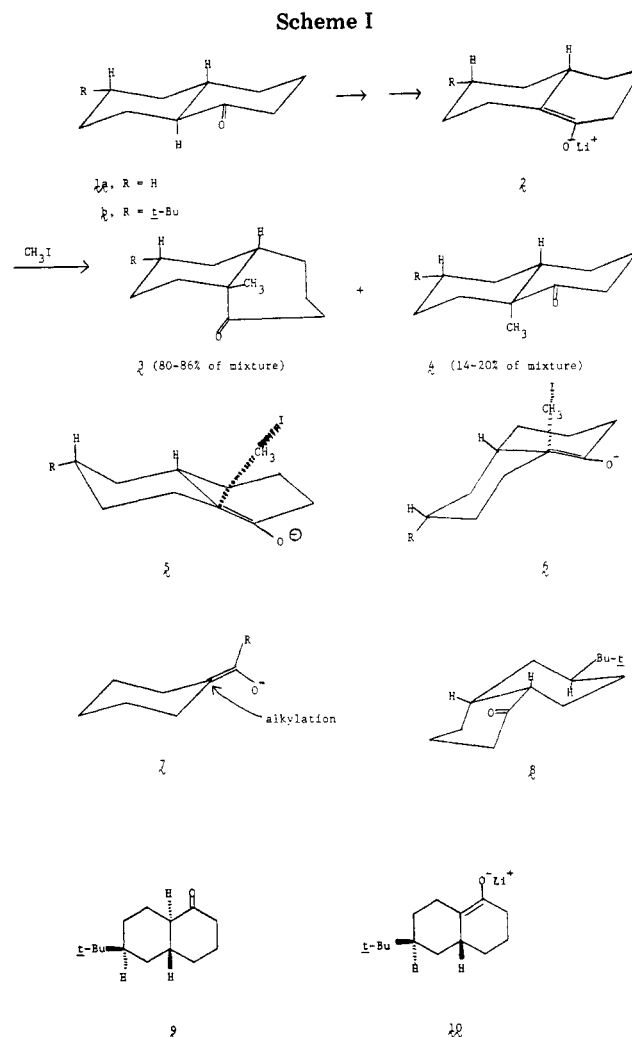
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Solutions of the lithium enolate **10** have been prepared by appropriate transformations of the ketones **8** and **9**. Both an X-ray structure determination of the derived enol ester **26** and conformational calculations on the related olefin **27** suggest that the favored conformations of the enolate **10** are the twist-boat conformers **28a** and **28b**. Reaction of this enolate **10** with methyl iodide formed predominantly the *cis*-fused decalone **17**. This result is in better agreement with an early, reactant-like transition state for the alkylation reaction rather than a late, product-like transition state that resembles the geometry of the products in their initially formed conformations.

The alkylation of the 1-decalone enolates **2** (Scheme I) to form predominantly the *cis*-fused monoalkylated products **3**² conforms to the ideas that the alkylation stereochemistry can be explained by invoking transition states **5** and/or **6** with reactant-like geometries and that the preferred direction for alkylation normally introduces the alkyl substituent equatorial to the saturated cyclohexane ring (see structure **7**). It was of interest to examine the alkylation of a 1-decalone enolate whose geometry was distorted from that normally found (i.e., **5** or **6**) to learn what factor seemed best to account for the alkylation stereochemistry. For that purpose, we have synthesized the 1-decalone derivatives **8** and **9**³ and report here the result of reaction of the corresponding lithium enolate **10** with methyl iodide.

A suitable precursor **11** (Scheme II) for the enolate **10** could be obtained by enol acetylation of ketone **8**³ followed by separation of the enol acetates **11** and **12** by low-pressure liquid chromatography. However, as found in an earlier study,² methylation of the lithium enolate **10** (accompanied by 1 equiv of *t*-BuOLi) formed from the enol acetate **11**, and MeLi was accompanied by the formation of di- and trimethylated products that complicated the separation and analysis of the reaction products. To diminish the amount of polyalkylation, we chose to use the enol silyl ether **14** as a precursor for the enolate **10** in order to avoid excess base (*t*-BuOLi) in the reaction mixture.⁴ Although the direct reaction of the ketone **8** with Me₃SiCl and Et₃N^{4b} formed only the unwanted silyl enol ether **13**, the indirect method, involving generation of the enolate **10** from the enol acetate **11** and subsequent quenching of the enolate **10** with Me₃SiCl,^{4,5} afforded the desired silyl enol ether **14**.



(1) This research has been supported by Public Health Service Grant R01-GM-20197 from the National Institute of General Medical Science. The execution of this research was also assisted by Institution Research Grants from the National Science Foundation for the purchase of a mass spectrometer and a Fourier transform NMR spectrometer.

(2) See H. O. House and M. J. Umen, *J. Org. Chem.*, **37**, 2841 (1972), and references cited therein.

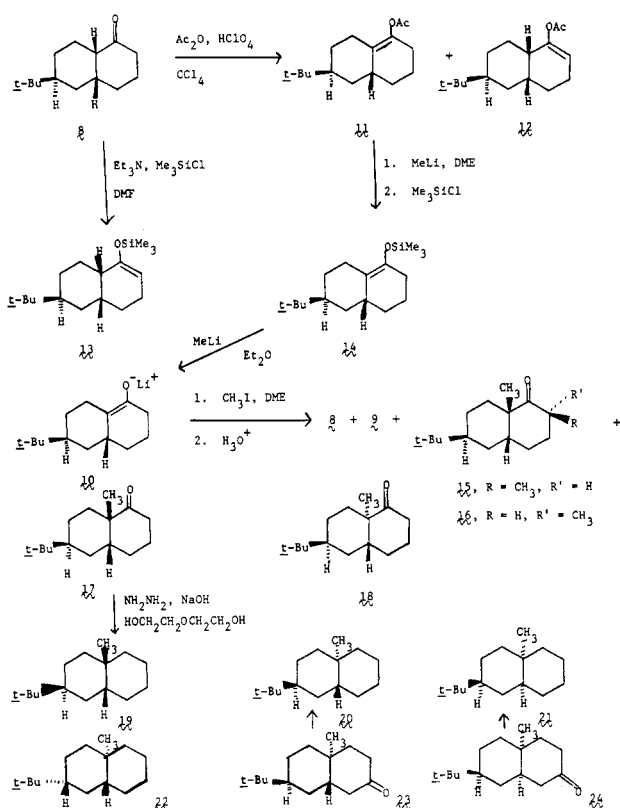
(3) H. O. House and W. V. Phillips, *J. Org. Chem.*, **43**, 3851 (1978).

(4) (a) G. Stork and P. F. Hudrlik, *J. Am. Chem. Soc.*, **90**, 4462, 4464 (1968); (b) H. O. House, L. J. Czuba, M. Gall, and H. D. Olmstead, *J. Org. Chem.*, **34**, 2324 (1969).

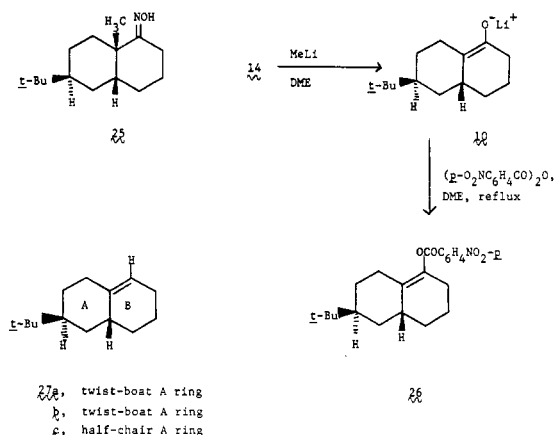
(5) C. R. Krüger and E. G. Rochow, *J. Organomet. Chem.*, **1**, 476 (1964).

Reaction of the enolate **10**, generated from the silyl enol ether **14**, with MeI for a short period of time (40–60 s) afforded mixtures containing small amounts of the recovered unalkylated ketones **8** and **9** and two dialkylated products tentatively assigned structures **15** and **16**. The major product was the monomethylated ketone **17** isolated

Scheme II



Scheme III



as a liquid that appeared to be homogeneous by all the usual criteria. Wolff-Kishner reduction converted this ketone 17 to a hydrocarbon 19 that differed in spectral properties from the previously prepared stereoisomeric hydrocarbons 22 (from ketone 4),² 20 (from ketone 23),⁶ and 21 (from ketone 24).⁶ However, the ¹H NMR spectrum of our hydrocarbon product indicated the presence of a minor impurity (not separated by GLPC) that may be the isomeric hydrocarbon 20 derivable from ketone 18 on Wolff-Kishner reduction.⁶ If this is the case, then the monomethylated product, cis ketone 17 obtained from the enolate 10, could contain as much as 13% of the isomeric trans ketone 18 that we were unable to separate.

To remove any question about the structure and stereochemistry of the major alkylated product, the ketone 17 was converted to its crystalline oxime 25 (Scheme III) for X-ray crystallographic analysis. The structure of this

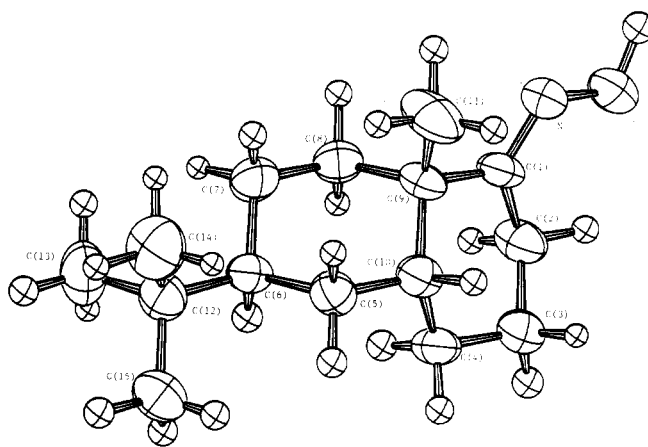


Figure 1. Perspective view of the molecular structure of oxime 25. (For clarity, the H atom thermal parameters have been reduced.)

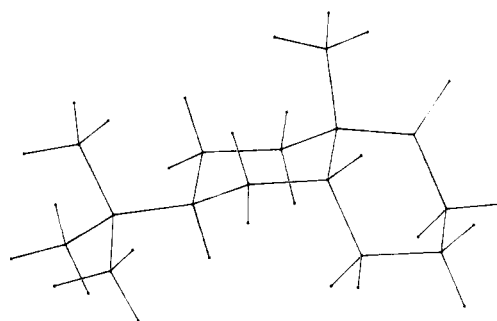


Figure 2. MMI-energy-minimized conformation of the ketone 17.

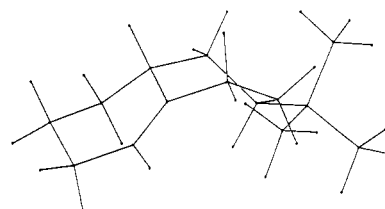


Figure 3. MMI-energy-minimized twist-boat conformation 27a of olefin 27 (calculated steric energy 22.1 kcal/mol).

derivative is presented in Figure 1.

To provide evidence that the conformation determined for the oxime 25 in the solid state is also the probable conformation of the ketone 17 in solution, the appropriate atom coordinates from the crystal structure of oxime 25 were used as input to calculate the conformation of the ketone 17, using the molecular mechanics program (MMI) of Allinger and co-workers.^{7,8} The conformation of ketone 17 calculated to have minimum energy (steric energy 20.79 kcal) is presented in Figure 2.⁹ Comparison of this figure with the analogous figure drawn⁹ from X-ray crystal coordinates for the oxime 25 demonstrated that the two

(7) (a) N. L. Allinger, M. T. Tribble, M. A. Miller, and D. H. Wertz, *J. Am. Chem. Soc.*, **93**, 1637 (1971); (b) N. L. Allinger and J. T. Sprague, *ibid.*, **95**, 3893 (1973); (c) N. L. Allinger, J. T. Sprague, and T. Liljefors, *ibid.*, **96**, 5100 (1974); (d) N. L. Allinger and D. H. Wertz, *Tetrahedron*, **30**, 1579 (1974). A summary of the minimization technique is given in ref 7a; force field parameters are listed in ref 7d. Calculations were performed on an IBM 370 system.

(8) We are most grateful to Professor Allinger and his associates and to the University of Georgia Computer Center for allowing us to use the current version of the MMI program for these calculations.

(9) The plots in these figures are modified ORTEP plots performed on a Calcomp plotter with the CDC Cyber 74 system. The coordinates for these plots were either the final atomic coordinates calculated by the MMI program⁷ after energy minimization or the atomic coordinates derived from the X-ray crystal structure determination.

(6) H. O. House and M. J. Lusch, *J. Org. Chem.*, **42**, 183 (1977).

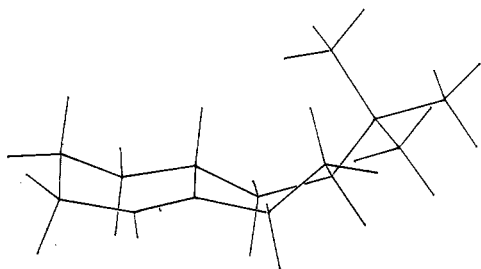


Figure 4. MMI-energy-minimized twist-boat conformation 27b of olefin 27 (calculated steric energy 22.7 kcal/mol).

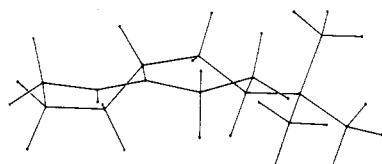


Figure 5. MMI-energy-minimized half-chair conformation 27c of olefin 27 (calculated steric energy 30.7 kcal/mol).

conformers are practically the same. Another indication of the reliability of these calculations in the systems being studied was provided by calculating minimized steric energies for the two unmethylated ketones 8 (18.4 kcal/mol) and 9 (20.3 kcal/mol),¹⁰ using coordinates from molecular models as input. The calculated energy difference between these ketones (1.9 kcal/mol) corresponded reasonably well with the energy difference (1.58 kcal/mol) determined from the equilibrium constant (14.4)³ for the ketones $9 \rightleftharpoons 8$ at 25 °C.

It was clearly desirable to know the favored conformation of the starting enolate 10, in seeking to understand the reaction of the enolate 10 with methyl iodide to form predominantly the cis-fused product 17. The most probable conformations of the enolate have the saturated ring in either a half-chair or a twist-boat arrangement. Utilizing the related olefin 27 as a model, we calculated the relative energies of these conformations.^{7,8} Two twist-boat conformers, 27a (22.1 kcal/mol, Figure 3)⁹ and 27b (22.7 kcal/mol, Figure 4),⁹ of comparable energy were found along with an appreciably less stable half-chair conformer 27c (30.7 kcal/mol, Figure 5).⁹ These calculations clearly suggest a preference for the twist-boat conformers 27a and 27b (Figures 3 and 4) as has been suggested previously.¹¹ To gain additional evidence, we converted the enolate 10 to its crystalline enol *p*-nitrobenzoate 26 as a model of the enolate 10 for X-ray crystallographic analyses. The structure of this derivative is presented in Figure 6.

The conformation of this crystalline enol derivative 26 (Figure 6) matches closely the calculated olefin twist-boat conformation 27b (Figure 4), suggesting that the favored conformers of the enolate 10 are twist-boat conformers 28a and 28b (Scheme IV) analogous to 27a and 27b. In each of these conformers 28a and 28b, attack by methyl iodide from the less hindered convex side would lead to the observed cis-fused ketone 17. Thus, if earlier arguments² supporting an early reactant-like transition state for the alkylation of enolates are accepted, the alkylation of the

(10) Interestingly the lowest energy conformer found for the trans ketone 9 was a conformation with the nonoxygenated cyclohexane ring present as a deformed chair and the *t*-Bu substituent in a pseudoaxial position. The calculated final steric energy of this deformed chair conformer (20.3 kcal) was less than the calculated final steric energy (21.7 kcal) for the conformer with the nonoxygenated cyclohexane ring present as a twist boat with the *t*-Bu group on an equatorial bond.

(11) D. J. Loomes and M. J. T. Robinson, *Tetrahedron*, **33**, 1149 (1977).

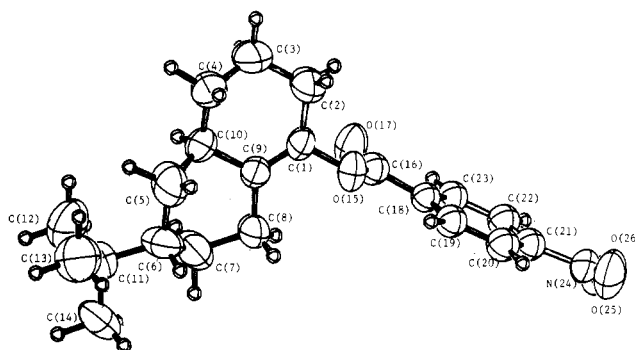


Figure 6. Perspective view of the molecular structure of the enol *p*-nitrobenzoate 26. (For clarity, the H atom thermal parameters have been reduced.)

enolate 10 to form the cis-fused product 17 is to be expected. The argument has also been made that the relative stabilities of the initial alkylated products, formed with the least motion of other atoms during the alkylation step, can be used to predict the stereochemical outcome.¹² In the present case, application of this idea to the two enolate conformers 28a and 28b would lead to the two initial conformers 29a and 29b for the cis ketone 17 and conformers 30a and 30b for the trans ketone. Calculation^{7,8} of the relative steric energies for these conformers gave the following results: 29a, 26.9 kcal/mol; 30a, 29.7 kcal/mol; 29b, 27.2 kcal/mol; 30b, 25.0 kcal/mol. Thus, if a late, product-like transition were involved in this alkylation reaction, one would have expected the trans ketone 18, derived from the initially formed conformer 30b, to be the major product of this reaction. We believe that the failure to observe this stereochemical result provides additional evidence for an early, reactant-like transition state in the alkylation of metal enolates from simple ketones.

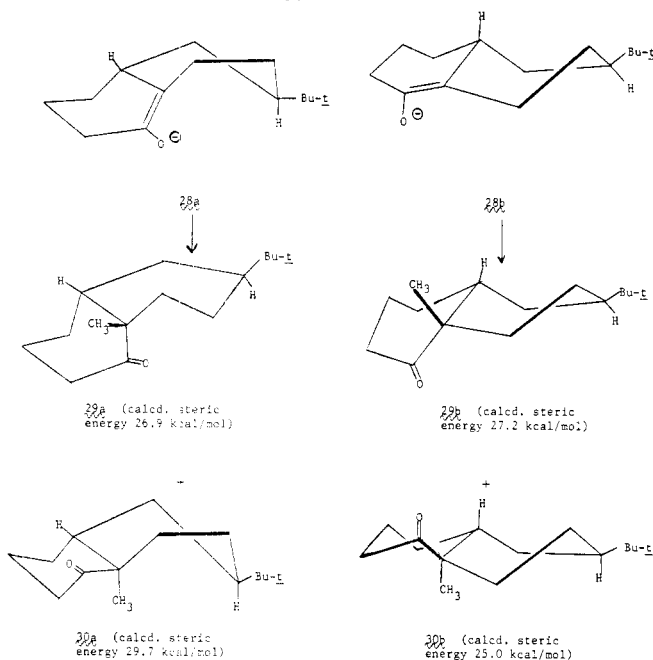
Experimental Section¹³

Preparation of the Enol Acetates 11 and 12. Previously described³ procedures were used to prepare the cis ketone 8 and convert it to the mixture of enol acetates 11 and 12. Thus, acetylation of 6.54 g (31.4 mmol) of the ketone 8 with Ac₂O and HClO₄ in CCl₄ yielded 6.99 g (89%) of the mixture of enol acetates [bp 97–115 °C (0.1 mm)] containing (GLPC, silicone XE-60 on Chromosorb P) ca. 50% of the enol acetate 11 (retention time 39.4 min) and ca. 50% of the enol acetate 12 (51.8 min). This mixture was subjected to preparative low-pressure liquid chromatography on silica gel with an EtOAc–hexane eluent (4:96 (v/v)). Certain of the later chromatographic fractions that were enriched in the unwanted enol acetate isomer 12 were resubjected to the original enol acetylation conditions³ to reequilibrate the enol acetates 11 and 12 to a 1:1 mixture. These mixtures were then rechromatographed. In this way the mixture was separated into 2.80 g (36% yield) of the enol acetate 11 (>98% GLPC analysis) and 2.20 g (28% yield) of the enol acetate 12 (>95%,

(12) This stereochemical argument has been used both for the alkylation of enolates and for the bromination of enols. See H. O. House, "Modern Synthetic Reactions", 2nd ed., W. A. Benjamin, Menlo Park, Calif., 1972, pp 468–471, 586–589.

(13) All melting points are corrected and all boiling points are uncorrected. Unless otherwise stated MgSO₄ was employed as a drying agent. The IR spectra were determined with a Perkin-Elmer Model 257 or Model 299 infrared recording spectrophotometer fitted with a grating. The UV spectra were determined with a Perkin-Elmer Model 202 recording spectrophotometer. The proton NMR spectra were determined at 60 MHz with a Varian Model T-60-A NMR spectrometer and at 100 MHz with a JEOL NMR spectrometer, Model PFT-100. The ¹³C NMR spectra were determined at 25 MHz with a JEOL Fourier transform spectrometer, Model PFT-100. The chemical shift values are expressed in δ values relative to a Me₄Si internal standard. The mass spectra were obtained with a Hitachi Perkin-Elmer Model RMU-7 or a Varian MAT 112S mass spectrometer. All reactions involving strong bases or reactive organometallic intermediates were performed under a nitrogen atmosphere. The anhydrous ethereal solvents were purified by distillation from LiAlH₄, immediately before use.

Scheme IV



GLPC analysis). Both samples were identified with earlier samples by comparison of IR, ^1H NMR, and GLPC data. The ^{13}C NMR (CDCl_3) spectra (δ , multiplicity on off-resonance decoupling) for these two enol acetates follow: enol acetate 11, 167.6 (s), 140.3 (s), 125.0 (s), 42.6 (d), 32.9 (s), 32.0 (d), 30.6 (t), 29.5 (t), 27.0 (q and t, four C atoms), 23.8 (t), 21.7 (t), 21.4 (t), 20.6 (q); enol acetate 12, 168.2 (s), 151.6 (s), 112.5 (d), 41.9 (d), 38.4 (d), 34.2 (d), 32.5 (t), 32.0 (s), 27.7 (t), 27.2 (q, 3 C atoms), 26.8 (t), 24.1 (t), 23.1 (t), 20.8 (q).

Preparation of the Silyl Enol Ether 13. Following a previously described general procedure,^{4b} a solution of 500 mg (2.4 mmol) of the ketone 8,³ 485 mg (4.8 mmol) of Et_3N , and 500 mg (4.6 mmol) of Me_3SiCl in 1 mL of DMF [distilled, dried over No. 4A molecular sieves, and redistilled, bp 43 °C (6 mm)] was refluxed for 48 h. The resulting solution was partitioned between a cold (0 °C) mixture of hexane and aqueous NaHCO_3 . The organic layer was dried, concentrated, and distilled in a short-path still at 0.55 mm to separate 515 mg (77%) of the crude enol ether 13, n_D^{25} 1.4737, containing (GLPC, Carbowax 20M on Chromosorb P) the enol ether 13 (retention time 21.5 min) and three minor unidentified impurities (11.3, 12.2, 18.4 min). Under the conditions of this GLPC analysis, the retention time of the starting ketone 8 was 56.1 min. The product was chromatographed on silica gel with an EtOAc-hexane eluent (1:39 (v/v)) to separate the enol ether 13. Distillation in a short-path still at 0.2 mm afforded the pure enol ether 13 as a colorless liquid, n_D^{25} 1.4738, with IR absorption (CCl_4) at 1662 cm^{-1} ($\text{C}=\text{C}$) and lacking IR absorption at 1679 cm^{-1} characteristic of the isomeric enol ether 14: NMR (CCl_4) δ 4.5–4.8 (1 H, m, vinyl CH), 0.8–2.3 (22 H, aliphatic CH including a *t*-Bu singlet at δ 0.84), and 0.14 (9 H, s, Me_3SiO); mass spectrum m/e (relative intensity) 280 (M^+ , 23), 223 (21), 175 (30), 169 (40), 156 (81), 134 (20), 133 (78), 129 (20), 91 (38), 75 (54), 73 (100), 57 (49), 41 (30).

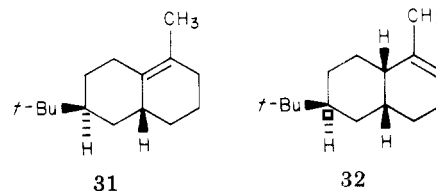
Anal. Calcd for $\text{C}_{17}\text{H}_{32}\text{OSi}$: C, 72.77; H, 11.52; mol wt 280.222. Found: C, 72.75; H, 11.52; mol wt 280.218.

Preparation of the Silyl Enol Ether 14. A solution of 13.9 mmol of MeLi (halide free) and 1 mg of 2,2'-bipyridyl (an indicator) in 11.9 mL of Et_2O was concentrated to dryness under reduced pressure¹⁴ and then 12 mL of anhydrous DME was added. The resulting solution was cooled to 0 °C and a solution of 1.50 g (6.0 mmol) of the enol acetate 11 in 3.0 mL of DME was added, dropwise and with stirring during 10 min. After the resulting red (excess MeLi) solution had been warmed to 25 °C, it was quenched by the rapid addition of 7.4 mL of a solution prepared by mixing 3.0 mL of Me_3SiCl (freshly distilled from a mixture with quinoline;

bp 57 °C), 7.5 mL of DME, and 0.75 mL of Et_3N (freshly distilled from LiAlH_4) and then centrifuging the mixture to separate the solid $\text{Et}_3\text{NH}^+\text{Cl}^-$. The reaction mixture, from which a white precipitate began to separate after 20 s, was stirred at 25 °C for 30 min and then partitioned between pentane and saturated aqueous NaHCO_3 containing excess solid NaHCO_3 . The organic solution was dried and concentrated, and the residual yellow liquid was chromatographed on silica gel with an EtOAc-hexane eluent (1:39 (v/v)) to separate 1.56 g (93%) of the pure silyl ether 14 as a colorless liquid: n_D^{25} 1.4765; IR (CCl_4) 1679 cm^{-1} ($\text{C}=\text{C}$); NMR (CCl_4) δ 0.7–2.4 (23 H m, aliphatic CH including a *t*-Bu singlet at δ 0.83), 0.13 (9 H, s, Me_3SiO); mass spectrum m/e (relative intensity) 280 (M^+ , 22), 223 (27), 195 (28), 133 (33), 91 (23), 75 (50), 73 (100), 57 (32), 41 (25).

Anal. Calcd for $\text{C}_{17}\text{H}_{32}\text{OSi}$: C, 72.77; H, 11.52; mol wt 280.222. Found: C, 72.81; H, 11.50; mol wt 280.220.

Methylation of the Lithium Enolate 10. A solution of 3.75 mmol of MeLi (halide free), 875 mg (3.12 mmol) of the silyl ether 14, and 1 mg of 2,2'-bipyridyl (an indicator) in 3 mL of Et_2O was stirred at 25 °C for 45 min and then concentrated to dryness under reduced pressure.¹⁴ The residue was treated with 3.2 mL of anhydrous DME and the resulting red (excess MeLi) solution was cooled to 0 °C and treated with 741 mg (5.21 mmol) of CH_3I . The resulting mixture was stirred in an ice bath for 40 s and then quenched by the rapid addition of 5 mL of aqueous 5% HCl. After the reaction mixture had been partitioned between pentane and aqueous NaCl, the organic layer was dried and concentrated. The crude residual yellow liquid (618 mg) contained (GLPC, SE-52 on Chromosorb P) two minor components believed to be olefins 31 and 32 (retention times 12.8 and 14.5 min; both together



constituted ca. 2% of the mixture), the previously described³ trans ketone 9 (18.3 min, ca. 15%), the cis ketone 8 (20.0 min, ca. 20%), the monoalkylated ketone 17 (22.0 min, ca. 55%), and an unresolved mixture of two components believed to be dialkylated ketones 15 and 16 (25.1 min, ca. 5%).

A 400-mg aliquot of the crude product was subjected to low-pressure liquid chromatography on silica gel with an EtOAc-hexane eluent (3:97 (v/v)). The first components eluted amounted to 8.6 mg (2% yield) of colorless liquid with spectral properties corresponding to one or both of the olefins 31 and 32: IR (CCl_4), no OH or $\text{C}=\text{O}$ absorption; NMR (CCl_4) δ 5.30 (0.5 H, broad, vinyl CH), 1.0–2.9 (16 H, m, aliphatic CH including a broad singlet at 1.67), 0.87 (9 H, s, *t*-Bu); mass spectrum m/e (relative intensity) 206 (1), 205 (4), 204 (26), 148 (7), 147 (100), 105 (30), 91 (30), 75 (17), 67 (15), 41 (17).

The next fractions from the chromatograph contained varying mixtures of two components believed to be ketones 15 and 16 (total amount 16.7 mg or 3.4% yield). The more rapidly eluted fractions in this group contained (NMR analysis) mainly the product believed to be ketone 15 as a colorless liquid: n_D^{25} 1.4822; IR (CCl_4) 1705 cm^{-1} ($\text{C}=\text{O}$); mass spectrum m/e (relative intensity) 236 (M^+ , 32), 161 (24), 138 (64), 125 (100), 119 (23), 109 (43), 95 (49), 81 (53), 79 (20), 69 (21), 68 (20), 67 (41), 57 (85), 55 (45), 43 (25), 41 (69); NMR (CCl_4) δ 2.0–2.9 (1 H, m, CHCO), 0.8–2.0 [27 H, m, aliphatic CH including a CH_3 singlet at δ 1.11, a CH_3 doublet ($J = 6.6$ Hz) at δ 0.95, and a *t*-Bu singlet at δ 0.87]. In C_6D_6 solution, the locations of the CH_3 singlet, the CH_3 doublet, and the *t*-Bu singlet were δ 1.25 ($\Delta(\delta) = +0.14$), 1.07 ($\Delta(\delta) = +0.12$), and 0.83 ($\Delta(\delta) = -0.04$), respectively. The downfield shift of both methyl signals in C_6D_6 solution is consistent with our tentative assignment 15 with both methyl groups equatorial to the cyclohexanone ring.¹⁵

Anal. Calcd for $\text{C}_{16}\text{H}_{28}\text{O}$: mol wt 236.214. Found: mol wt 236.218.

(14) The technique used for this concentration is described by M. Gall and H. O. House, *Org. Synth.*, 52, 39 (1972).

(15) N. S. Bhacca and D. H. Williams, "Applications of NMR Spectroscopy in Organic Chemistry", Holden-Day, San Francisco, Calif., 1964, pp 165–170.

The more slowly eluted fractions in this group of chromatographic fractions contained (NMR analysis) mainly the product believed to be ketone 16 as a colorless liquid: n_D^{25} 1.4820; IR (CCl₄) 1709 cm⁻¹ (C=O); mass spectrum m/e (relative intensity) 236 (M⁺, 10), 179 (24), 161 (32), 138 (64), 125 (100), 109 (45), 95 (54), 84 (25), 81 (56), 69 (20), 67 (40), 57 (85), 55 (40), 43 (28), 41 (64); NMR (CCl₄) δ 2.0–2.9 (1 H, m, CHCO), 0.8–2.0 [27 H, m, aliphatic CH including a CH₃ singlet at δ 1.07, a CH₃ doublet (J = 6.6 Hz) at δ 1.00, and a *t*-Bu singlet at δ 0.84]. In C₆D₆ solution, the locations of the CH₃ singlet, the CH₃ doublet, and the *t*-Bu singlet were δ 1.04 ($\Delta(\delta)$ = -0.03), 1.05 ($\Delta(\delta)$ = +0.05), and 0.80 ($\Delta(\delta)$ = -0.04), respectively.

The shifts in the methyl signals exhibit no consistent pattern as might be expected for the tentatively assigned structure 16 since the 1,3-diaxial Me-CH₂ interaction present may force the cyclohexanone ring into a boat conformation. The fact that the amounts of both this isomer and the other dialkylated product 15 increased at approximately the same rate as the reaction time was lengthened suggests that both products are derived from the further alkylation of the major monoalkylated product 17.

Anal. Calcd for C₁₆H₂₈O: mol wt 236.214. Found: mol wt 236.216.

Subsequent fractions from the chromatograph contained 192.3 mg (43% yield) of the monoalkylated ketone 17 as a colorless liquid, n_D^{25} 1.4869, that exhibited a single GLPC peak (silicone SE-52 on Chromosorb P): IR (CCl₄) 1709 cm⁻¹ (C=O); mass spectrum m/e (relative intensity) 222 (M⁺, 4.5), 147 (25), 124 (43), 111 (100), 95 (24), 81 (36), 67 (27), 57 (89), 55 (37), 43 (30), 41 (63); ¹³C NMR (CDCl₃, multiplicity of off-resonance decoupling) δ 215.7 (s), 48.6 (s), 42.9 (d), 41.1 (d), 37.7 (t), 32.2 (s), 31.2 (t), 28.0 (t), 27.5 (t), 27.2 (q, three C atoms), 25.4 (t), 22.2 (t), 19.6 (q); ¹H NMR (CCl₄) δ 0.7–2.7 (m, aliphatic CH including a CH₃ singlet at δ 1.10 and a *t*-Bu singlet at δ 0.85). In C₆D₆ solution, the location of the CH₃ and *t*-Bu singlets were δ 1.24 ($\Delta(\delta)$ = +0.14) and 0.80 ($\Delta(\delta)$ = -0.05), respectively. The downfield shift of the methyl signal is consistent with our stereochemical assignment in which the methyl group is equatorial to the cyclohexanone ring.¹⁵

Anal. Calcd for C₁₅H₂₆O: C, 81.02; H, 11.79. Found: C, 81.15; H, 11.87.

Subsequent fractions from the chromatograph contained 48.5 mg (11.5% yield) of the trans ketone 9 followed by 66.7 mg (16% yield) of the cis ketone 8. Both of these products were identified with previously characterized samples⁹ by comparison of IR, NMR, and mass spectra.

A second comparable alkylation experiment was performed with 1.56 g (5.6 mmol) of silyl ether 14, employing the same temperature and molar concentrations of all reactants used in the previous experiment with a total reaction time of 60 s rather than 40 s. The crude liquid product (1.11 g) contained (GLPC analysis) a component thought to be one or both of the olefins 31 or 32 (ca. 3%), the trans ketone 9 (ca. 5%), the cis ketone 8 (ca. 6%), the monomethyl ketone 17 (ca. 74%), and a mixture of dimethyl ketones 15 and 16 (ca. 12%). After following the same chromatographic isolation procedure previously described, the isolated yields were as follows: olefins 31 and/or 32, 43.8 mg or 3.8%; ketones 15 and 16, 126.4 mg or 9.6%; ketone 17, 709.7 mg or 57.2%; trans ketone 9, 53.7 mg or 4.6%; cis ketone 8, 74.4 mg or 6.4%.

Preparation of the Hydrocarbon 19. A solution of 190.8 mg (0.86 mmol) of the ketone 17, 215 mg (4.3 mmol) of hydrazine hydrate, and 2.5 mL of diethylene glycol was refluxed for 75 min and then cooled and treated with 103 mg (2.6 mmol) of NaOH. The reaction mixture was again heated to reflux and the two-phase mixture of H₂O, H₂NNH₂, and hydrocarbon 19 was allowed to distill from the reaction vessel. After the distillate had been partitioned between pentane and aqueous 10% HCl, the organic layer was dried and concentrated to leave 110.7 mg (62%) of the hydrocarbon 19 as a colorless liquid. This material was distilled in a short-path still at 1 mm to separate the hydrocarbon 19 as a colorless liquid: n_D^{25} 1.4770; IR (CCl₄) no OH or C=O absorption; mass spectrum m/e (relative intensity) 208 (M⁺, 7), 152 (38), 151 (37), 150 (30), 137 (57), 109 (33), 96 (31), 95 (100), 83 (24), 81 (47), 69 (22), 67 (28), 57 (52), 55 (32), 41 (40); ¹³C NMR (CDCl₃, multiplicity in off-resonance decoupling) δ 41.6 (d), 41.0 (t and d, 2 C atoms), 32.2 (s), 32.0 (s), 30.4 (t), 28.5 (t), 28.2 (t),

28.0 (q), 27.4 (q, 3 C atoms), 27.2 (t), 22.8 (t), 22.1 (t); ¹H NMR (CCl₄) δ 0.7–2.1 (28 H, m, aliphatic CH including a CH₃ singlet at δ 0.93 and a *t*-Bu singlet at δ 0.83). The ¹H NMR spectrum also exhibited a small peak at δ 0.88 that may be the *t*-Bu signal for the previously described⁹ stereoisomer hydrocarbon 20 (lit.⁶ δ 0.86 for *t*-Bu and δ 0.85 for CH₃). This extra NMR peak was also present in the spectrum of a sample of the hydrocarbon 19 purified by GLPC collection (as noted below, hydrocarbons 19 and 20 were not resolved by any GLPC column we examined). When a sample of the hydrocarbon 19 was mixed with an authentic sample of the hydrocarbon 20, the intensities of the "extra" ¹H NMR signals found in the spectrum of hydrocarbon 19 were enhanced. If this extra peak is attributable to the NMR signal for the *tert*-butyl group of hydrocarbon 20, then the relative heights of the two *tert*-butyl NMR signals in our sample would indicate that the cis hydrocarbon 19 contains ca. 13% of the isomeric trans hydrocarbon 20.

However, it was clear from comparison of the IR, ¹H NMR, and ¹³C NMR spectra for the present sample, hydrocarbon 19, and the previously prepared hydrocarbons 20 and 21 that the three compounds are different. Our hydrocarbon 19 also differs from the previously described² trans hydrocarbon 22 in its IR and NMR absorption.

Anal. Calcd for C₁₅H₂₆: C, 86.43; H, 13.54; mol wt 208.219. Found: C, 86.29; H, 13.67; mol wt 208.223.

Various mixtures of hydrocarbons 19–21 were examined with a variety of GLPC columns. In only two cases columns were found that would resolve hydrocarbons 20 and 21, Apriezon M on Chromosorb P (21, 39.2 min; 20, 41.2 min) and silicone OV-17 on Chromosorb P (21, 35.6 min; 20, 37.1 min). However, with both of these GLPC columns and with all others examined, mixtures of the hydrocarbons 19 and 20 were not resolved.

Preparation of the Oxime 25. A solution of 66.6 mg (0.30 mmol) of the ketone 17, 25.4 mg (0.37 mmol) of HONH₃⁺Cl⁻, and 0.1 mL of aqueous 10% NaOH in 0.7 mL of H₂O and 0.75 mL of EtOH was refluxed for 10 min and then cooled and diluted with 4.5 mL of H₂O. The crude solid oxime that separated (66.2 mg) was recrystallized from EtOH to separate 54 mg (76%) of the crude oxime 25 as colorless needles; mp 152.5–154 °C. A 16.6-mg portion of this oxime was recrystallized from MeOH to separate 11.7 mg (54% yield) of the pure oxime 25; mp 163–164 °C. The oxime 25 was allowed to crystallize slowly from a saturated solution in MeOH to separate crystals of the pure oxime, mp 164–165 °C, that were suitable for X-ray crystallography: IR (CCl₄) 3610, 3290 cm⁻¹ (free and associated OH); NMR (CDCl₃) δ 3.1–3.4 (1 H, broad, OH), δ 0.8–2.7 (26 H, m, aliphatic CH including a CH₃ singlet at δ 1.25 and a *t*-Bu singlet at δ 0.85); mass spectrum m/e (relative intensity) 237 (M⁺, 28), 222 (31), 220 (52), 180 (42), 147 (20), 126 (100), 110 (20), 107 (20), 99 (50), 81 (20), 58 (31), 57 (72), 55 (24), 43 (70), 41 (46).

Anal. Calcd for C₁₅H₂₇NO: C, 75.89; H, 11.47; N, 5.90. Found: C, 75.65; H, 11.25; N, 5.79.

Preparation of the Enol *p*-Nitrobenzoate 26. The solvent was removed¹⁴ from 2.14 mL of an Et₂O solution containing 2.5 mmol of MeLi (halide free), and the MeLi was redissolved in 2.0 mL of DME containing 1 mg of 2,2'-bipyridyl (an indicator). A solution of 560 mg (2.0 mmol) of the silyl enol ether 14 in 0.5 mL of DME was added and the resulting red (excess MeLi) solution was stirred at 25 °C for 1 h. The solution of the enolate 10 was then added, dropwise with stirring, to a refluxing solution of 950 mg (3.0 mmol) of (*p*-O₂NC₆H₄CO)₂O in 12 mL of DME. The resulting mixture was refluxed for an additional 15 min and then cooled to 25 °C and stirred for 12 h. The resulting mixture of a yellow solution and a white precipitate (ArCO₂Li) was filtered and the residue was washed with Et₂O. The combined filtrates were concentrated and a 585-mg aliquot of the residue (total weight 1.185 g) was recrystallized from an EtOAc-hexane mixture to separate 95 mg of unchanged (*p*-O₂NC₆H₄CO)₂O. The remaining material in the mother liquor was chromatographed on silica gel with an EtOAc-hexane eluent to separate 117.2 mg (33%) of the crude enol benzoate 26 as a yellow liquid that solidified on titration with pentane; mp 61–63 °C. Recrystallization from EtOH separated the enol ester 26 as colorless prisms: mp 64–65 °C; IR (CCl₄) 1740 cm⁻¹ (ester C=O); mass spectrum m/e (relative intensity) 357 (M⁺, 1), 151 (22), 150 (100), 134 (36), 133 (94), 120 (26), 119 (46), 104 (26), 57 (34).

Anal. Calcd for $C_{21}H_{27}NO_4$: C, 70.56; H, 7.61; N, 3.92; mol wt 357.1940. Found: C, 70.08; H, 7.63; N, 3.92; mol wt 357.1923.

The Crystal Structure of the Oxime 25. A. Data Collection. A crystal of the oxime **25** with approximate dimensions $0.22 \times 0.30 \times 0.75$ mm was mounted on a glass fiber with epoxy cement such that the longest crystal dimension, 0.75 mm, was approximately parallel to the fiber axis. Unit cell parameters and the orientation matrix were determined on a Syntex $P2_1$ four-circle diffractometer equipped with a graphite monochromator (Bragg 2θ angle 12.2°) using Mo $K\alpha$ radiation at a takeoff angle of 6.75° . Fifteen reflections whose 2θ values ranged from 3.86 to 10.78° were machine centered and used in least-squares refinement of the lattice parameters and orientation matrix. Unit cell parameters obtained were $a = 18.69$ (1) Å,¹⁶ $b = 12.788$ (7) Å, $c = 12.161$ (6) Å, and $V = 2906$ (3) Å³. The calculated density of 1.08 g cm⁻³ for eight formula units per unit cell agrees with the experimental density of 1.08 g cm⁻³ measured by the flotation method using a mixture of H₂O and CsCl. ω scans of several low 2θ angle reflections gave peak widths at half-height of less than 0.18° , indicating a satisfactory mosaic spread for the crystal. Axial photographs indicated that the crystal belonged to the orthorhombic system. Intensity data for zero and upper levels were collected at a rapid scan rate and the intensities examined carefully for systematic absences. The absence of $0kl$ ($l = 2n + 1$), $h0l$ ($l = 2n + 1$), and $hk0$ ($h + k = 2n + 1$) reflections is consistent with only space group $Pccn$ (No. 56).¹⁷

Intensity data were collected by using θ - 2θ scans with X-ray source and monochromator settings identical with those used for determination of the unit cell parameters. A variable scan rate of from 2.93 to 29.3° /min was used and a scan width of 2.0° was sufficient to collect all of the peak intensity. Stationary background counts were measured at the beginning (B_1) and at the end (B_2) of each scan with a total background to scan time ratio, TR, of 1.0. No significant fluctuations were observed in the intensities of three standard reflections (400, 040, 006) monitored every 97 reflections. Intensities were calculated from the total scan count (CT) and background counts by the relationship

$$I = CT - TR(B_1 + B_2)$$

The intensities were assigned standard deviations according to the formula

$$\sigma(I) = [CT + (TR)^2(B_1 + B_2)]^{1/2}$$

from a total of 2583 reflections collected in a complete octant of data out to $2\theta = 50^\circ$; 1507 were accepted as statistically above background on the basis that F was greater than $3\sigma(F)$. Lorentz and polarization corrections were made in the usual way.

B. Solution and Refinement of the Structure. Computations were performed by using standard programs,¹⁸ all computations were carried out on the CDC Cyber 74 system. For structure factor calculations the scattering factors were taken from Cromer and Mann's tabulation.¹⁹ The agreement factors are defined in the usual way as

$$R = (\sum |F_o| - |F_c|) / \sum |F_o|$$

and

$$R_w = [\sum (|F_o| - |F_c|)w^{0.5}] / \sum (|F_o|)w^{0.5}$$

In all least-squares refinements, the quantity minimized was $w(|F_o| - |F_c|)^2$. A weighting scheme based on counting statistics ($w = 2.2 / [\sigma(F)^2 + 0.002F^2]$) was employed for calculating R_w and in least-squares refinement.

The structure was solved by using the automatic centrosymmetric direct methods program of SHELX-76. The total number of parameters varied were 180 for 1507 observations. Parameters varied included a scale factor, coordinates of all atoms except hydrogens, anisotropic thermal parameters for all atoms except

H atoms, and isotropic thermal parameters for H atoms. Hydrogen atoms were refined in the riding mode. The full-matrix least-squares refinement converged at $R = 0.076$ and $R_w = 0.077$. The final atomic coordinates and thermal parameters are available as supplementary material in Table III and the list of bond lengths and bond angles is available as supplementary material in Table I. A list of calculated and observed structure factors is available from the authors.

Crystal Structure of the Enol *p*-Nitrobenzoate 26. A. Data Collection. A crystal of the enol ester **26** with approximate dimensions $0.75 \times 0.45 \times 0.35$ mm was mounted on a glass fiber with epoxy cement such that the longest crystal dimension, 0.75 mm, was approximately parallel to the fiber axis. Unit cell parameters and the orientation matrix were determined on the previously described Syntex $P2_1$ diffractometer using Mo $K\alpha$ radiation at a takeoff angle of 6.75° . Fifteen reflections whose 2θ values ranged from 6.33 to 10.56° were machine centered and used in least-squares refinement of the lattice parameters and orientation matrix. Unit cell parameters obtained were $a = 8.188$ (3) Å,¹⁶ $b = 12.275$ (5) Å, $c = 39.60$ (3) Å, and $V = 3980$ (4) Å³. The calculated density of 1.19 g cm⁻³ for eight formula units per unit cell agrees with the experimental density of 1.17 g cm⁻³ measured by the flotation method using a mixture of CsCl and H₂O. ω scans of several low 2θ angle reflections gave peak widths at half-height of less than 0.24° , indicating a satisfactory mosaic spread for the crystal. Axial photographs indicated that the crystal belonged to the orthorhombic system. Intensity data for zero and upper levels were collected at a rapid scan rate and the intensities examined carefully for systematic absences. The absence of $0kl$ ($k = 2n + 1$), $h0l$ ($l = 2n + 1$), and $hk0$ ($h = 2n + 1$) reflections is consistent with only space group $Pbca$ (No. 61).¹⁷

Intensity data were collected by using θ - 2θ scans with X-ray source and monochromator settings identical with those used for determination of the unit cell parameters. A variable scan rate of from 2.93 to 29.3° /min was used and a scan width of 2.0° was sufficient to collect all of the peak intensity. Stationary background counts were measured at the beginning (B_1) and at the end (B_2) of each scan with a total background to scan time ratio, TR, of 1.0. No significant fluctuations were observed in the intensities of three standard reflections (040, 008, 200) monitored every 97 reflections. Intensities were calculated as previously described.

A total of 3534 reflections were collected in a complete octant of data out to $2\theta = 50^\circ$; 1168 were accepted as statistically above background on the basis that F was greater than $4\sigma(F)$. Lorentz and polarization corrections were made in the usual way. A weighting scheme based on counting statistics ($w = 3.4 / [\sigma(F)^2 + 0.0002F^2]$) was employed for calculating R_w and in least-squares refinement.

B. Solution and Refinement of the Structure. Computations were performed as described previously. The structure was solved by using the automatic centrosymmetric direct methods program of SHELX-76. The total number of parameters varied were 192 for 1168 observations. Parameters varied included a scale factor, coordinates of all atoms except H atoms, anisotropic thermal parameters for all atoms except H atoms, and isotropic thermal parameters for H atoms. Hydrogen atoms were refined in the riding mode. Each type of hydrogen atom was assigned a single temperature factor, using the free-variable parameter of the SHELX-76 program. The full-matrix least-squares refinement converged at $R = 0.083$ and $R_w = 0.068$. The final atomic coordinates and thermal parameters are available as supplementary material in Table IV and the list of bond lengths and bond angles is available as supplementary material in Table II. A list of calculated and observed structure factors is available from the authors.

Registry No. 8, 67238-07-7; 9, 28435-46-3; 10, 70179-43-0; 11, 67238-11-3; 12, 67238-12-4; 13, 70179-44-1; 14, 70179-45-2; 15, 70266-77-2; 16, 70266-78-3; 17, 70179-46-3; 19, 70179-47-4; 20, 60676-29-1; 25, 70179-48-5; 26, 70179-49-6; 31, 70179-50-9; 32, 70179-51-0.

Supplementary Material Available: Tables of atomic coordinates and thermal parameters (Tables III and IV) and tables of bond lengths and bond angles (Tables I and II) (6 pages). Ordering information is given on any masthead page.

(16) Numbers in parentheses here and elsewhere in this paper indicate estimated standard deviations in the least significant digit(s).

(17) "International Tables for X-Ray Crystallography", Vol. I, Kynoch Press, Birmingham, England, 1952.

(18) Programs utilized were Sheldrick's SHELX-76 program and Johnson's ORTEP program.

(19) "International Tables for X-Ray Crystallography", Vol. IV, Kynoch Press, Birmingham, England, 1974, pp 72-98.