butyl alcohols were chromatoquality grade obtained from Matheson Coleman and Bell, and neopentyl alcohol (99%) was obtained from Aldrich. Lithium aluminum hydride was obtained from Ventron Corp. as solutions in diethyl ether or THF. The solutions were standardized by reaction with iodine according to the method of Felkin,[22] or by measurement of hydrogen on methanolysis.

Gas chromatographic analyses were done on a Hewlett-Packard Model 5750 instrument using the following columns: 12 ft × 0.125 in. 5% Carbowax 20M at 145° for the separation of *cis*- and *trans*-4-*tert*-butylcyclohexanols; 10 ft × 0.25 in. 10% Carbowax 20M (acid washed, silanized) at 140° for *cis*- and *trans*-3,3,5-trimethylcyclohexanols; 16 ft × 0.25 in. ethylene glycol succinate (acid washed, silanized) at 105° for *cis*- and *trans*-2-methylcyclohexanols; 12 ft × 0.25 in. diethylene glycol succinate (acid washed, silanized) for *cis*- and *trans*-3-methylcyclohexanols.

Apparatus and General Procedure. The reactions were carried out in a 250-ml glass reactor (Ace Glass Co.) stirred magnetically and equipped with a condenser and equilibrated dropping funnel. The apparatus was baked and flushed with dry nitrogen. The general procedure is described in detail for the following two reactions.

Reaction of $LiAlH_4$ with 2,6-Dimethylphenol. Reduction of 1. Fifteen milliliters of 0.90 *M* $LiAlH_4$ in ether was transferred by pipet to the reaction flask. Ten milliliters of THF (distilled freshly from $LiAlH_4$) was added dropwise with the apparatus attached to a wet test meter. No hydrogen evolution occurred. A solution of 2,6-dimethylphenol (4.96 g, 0.0406 mol) in 10 ml of THF was added dropwise over 6 min. The volume of hydrogen was recorded (0.045 mol) by means of a wet test meter. The reaction mixture was clear and colorless. The ketone 1 (1.994 g, 0.0129 mol) was added dropwise as a solution in 10 ml of THF over 4 min. The clear, colorless reaction mixture was stirred overnight under a nitrogen atmosphere. After 23 hr, the reaction mixture was hydrolyzed with 10% sulfuric acid, and hydrogen evolution measured. After washing (saturated sodium bicarbonate and salt solution) and drying over anhydrous $MgSO_4$, the product was concentrated by distillation through a 17-in. helix-packed column, using an oil bath. The concentrated product, 29 g, was clear and colorless, and analyzed by GLC before and after the addition of 3,3,5,5-dimethylcyclohexanone as an internal standard.

Reaction of $LiAlH_4$ with 2,6-di-*tert*-Butylphenol and with Neopentyl Alcohol. Reduction of 1. Twenty milliliters of 1.2 *M* $LiAlH_4$ in ether was transferred by pipet to the reaction flask. Fifteen milliliters of THF was added dropwise with no hydrogen evolution. Distilled 2,6-di-*tert*-butylphenol (9.9155 g, 0.048 mol) in 10 ml of THF was added over 20 min, during which hydrogen evolution (0.045 mol) was measured with a wet test meter. The clear, colorless reaction mixture was then stirred under nitrogen for 35 min, and a solution of neopentyl alcohol (2.1279 g, 0.024 mol) in 15 ml of THF was added over 8 min, again measuring hydrogen evolution (0.021 mol). Hydrogen evolution continued after the addition was complete, indicating a rather slow reaction. After 32 min, a solution of 1 (3.0863 g, 0.020 mol) in 15 ml of THF was added dropwise under nitrogen over 8 min. The reaction mixture was clear and pale yellow. It was stirred under nitrogen for 5 hr, cooled, and hydrolyzed with 10% sulfuric acid, with hydrogen evolution measured with the wet test meter. The aqueous layer was extracted with three portions of ether, and combined organic solution washed twice with saturated sodium bicarbonate, twice with saturated salt solution, and dried over anhydrous magnesium sulfate. The filtered solution was concentrated by distillation through a 17-in. helix-packed column using an oil bath (bath temperature to ~90°, bp ~35°). The concentrated product was clear and colorless and was analyzed by GLC before and after the addition of the internal standard, 3,3,5,5-tetramethylcyclohexanone.

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Registry No.—1, 98-53-3.

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Observations on the Steric Requirement of Wittig Reactions with Trialkylphosphonoacetates

Kenn E. Harding* and Chung-Ye Tseng

Department of Chemistry, Texas A&M University, College Station, Texas 77843

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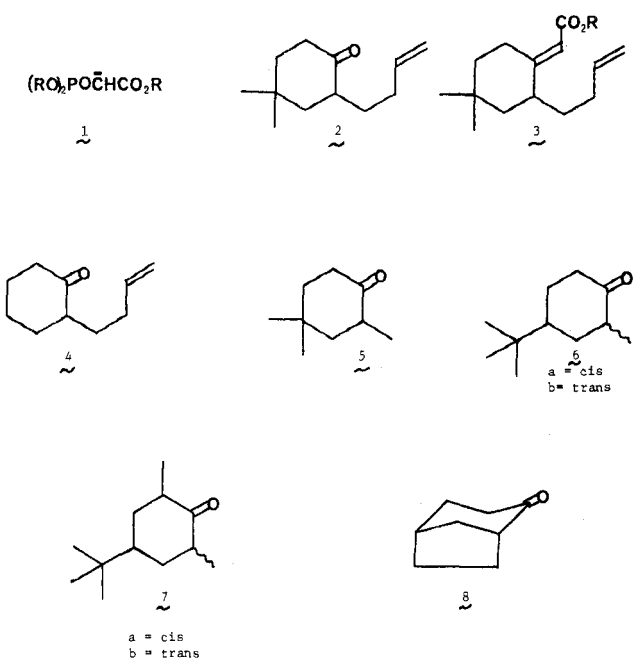
Investigation of the Wittig reaction of trialkylphosphonoacetate anions with several C-2 substituted cyclohexanones has demonstrated the presence of a previously unrecognized steric constraint for this reaction. Cyclohexanones with a C-2 alkyl group constrained to the equatorial orientation proved unreactive to normal treatment with trialkylphosphonoacetate anions. Cyclohexanones which can undergo facile conformational inversion to give an axial C-2 substituent react normally. Conformationally rigid cyclohexanones in which configurational inversion to give an axial C-2 substituent is not energetically prohibitive react slowly and give a mixture of ester products with the alkyl group predominantly axial.

We wish to report some previously unrecognized steric requirements of the Wittig reaction using trialkylphosphonoacetate anions. The observations reported herein further delineate the range of synthetic utility of reactions involving phosphonate anions and substituted cyclohexanones. In the course of another synthetic problem[1] we attempted to convert ketone **2** into the corresponding α,β-unsaturated ester **3** by treatment with anion **1**. Attempts to conduct this

reaction under normal conditions (excess phosphonate anion in glyme or dimethylformamide at room temperature) led to recovery of ketone **2** with no condensation product observed. Since 2-methylcyclohexanone reacts readily with 1,[2] we hypothesized that the restriction of the butenyl side chain to the equatorial position[3] in ketone **2** may be responsible for the lack of reactivity. This hypothesis has been tested by examination of the reaction of **1** with several C-2 alkylated ketones. The ketones used in this study were 2-(3-butenyl)cyclohexanone (**4**), 2,4,4-trimethylcyclohexanone (**5**), 2-methyl-4-*tert*-butylcyclohexanone (**6**), *cis,cis*- and *cis,trans*-2,6-dimethyl-4-*tert*-butylcyclohexanone (**7**), and bicyclo[3.2.1]octan-2-one (**8**).



As expected, reaction with ketone **4** proceeded in a manner similar to the reaction with 2-methylcyclohexanone to give a mixture of the *E* and *Z* isomers of the expected α,β-unsaturated ester (**9** and **10**). Ketone **8**, with an axial C-2 substituent, also reacted readily with anion **1** to give a mixture of the two isomers of the expected α,β-unsaturated ester (**11** and **12**). These results show that the reaction is not hindered by the presence of an axial C-2 substituent or an equatorial C-2 substituent if the alternative conformation with the substituent axial is readily obtainable.

Treatment of either ketone **5** or ketone **7** with anion **1** led to recovery of the starting ketones. Each of these ketones is expected to exist in conformations containing an equatorial C-2 methyl group, since the alternative conformations are quite unfavorable.[3,4]

The reactions with ketone **6** proved to be the most complex. Although the *tert*-butyl substituent at C-4 restricts the cyclohexanone to a single chair conformation, the substituent at C-2 can be interconverted between axial and equatorial orientations by base-catalyzed enolization.

The reactions of ketone **6** with an excess of anion **1a** (generated using sodium hydride or potassium *tert*-butoxide as base) in dimethylformamide at room temperature gave a mixture of esters in good yield. Vapor phase chromatographic analysis showed five peaks with the last one as the major peak (~72% of the total peak area). The individual components of the mixture were partially separated by preparative gas chromatography.

The NMR spectra of these products were instrumental in assigning structures to the isomeric products obtained. The key data which allows differentiation of the isomers

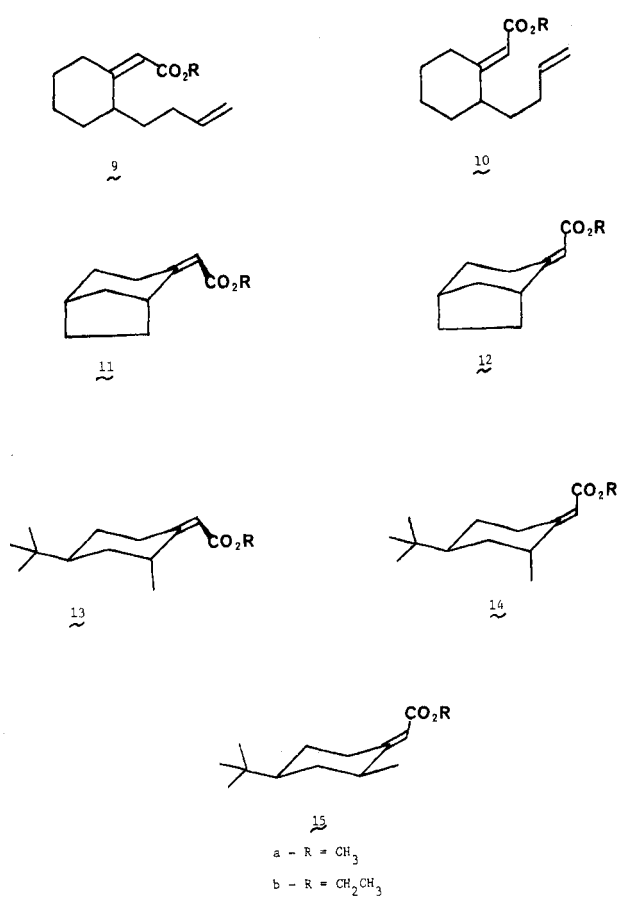
Table I
NMR Assignments for Esters 13, 14, and 15

Compd	δ values: Methyl	Deshielded proton	C–2 methine[a]
13a	1.12	3.84–4.30	~4.0
13b	1.14	~4.01	~3.9–4.0
14a	1.16	3.58–3.98	~2.4
14b		Not isolated pure	
15a	1.05	3.80–4.20	2.18
15b	1.06	~4.01	~2.30

[a] Assigned by determining position of decoupling irradiation which collapsed methyl doublet.

was obtained by use of double-irradiation techniques. The carboalkoxy group of cyclohexylideneacetic acid esters has been shown to strongly deshield the equatorial ring proton which is cis to the carboalkoxy group.[6] In the products from reaction of **1** with ketone **6**, this downfield proton (δ 3.5–4.3) can be established as a C-2 proton (coupled to C-2 methyl) or a C-6 proton (not coupled to C-2 methyl) by double-irradiation techniques.

Specific structural assignments were made for compounds **13**, **14**, and **15**. The key spectral parameters for these compounds are shown in Table I. Structure **13** is easily differentiated from **14** and **15** by the observation that the deshielded ring proton is coupled to the C-2 methyl group. Differentiation between **14** and **15** was made by ozonolysis to the corresponding *cis*- and *trans*-2-methyl-4-*tert*-butylcyclohexanones. Although the reaction with ketone **6** was conducted with both **1a** and **1b**, the separation of isomers was more effective with the products from **1a**. The results appeared essentially identical in the cases in which **1a** and **1b** were compared.



Of the five fractions observed for reaction of **1a** with ketone **6**, fractions 1, 4, and 5 could be isolated in reasonable purity. The spectral data for the first component (~4% of total peak area) showed clearly that it was a β,γ-unsaturated ester. The structure and stereochemistry of this component were not pursued further.[7]

The material in the last fraction (~72% of total peak area) was assigned structure **15a** and that in the fourth fraction was assigned structure **14a** on the basis of the spectral properties (Table I and Experimental Section) and on the observation that ozonolysis of the last fraction gave *cis*-2-methyl-4-*tert*-butylcyclohexanone while ozonolysis of fraction 4 gave *trans*-2-methyl-4-*tert*-butylcyclohexanone. Similar ozonolysis conditions have been used in earlier studies for similar stereochemical assignments.[8,9]

The second and third fractions were not completely separated by gas chromatography. The ir spectrum of the mixture showed absorption expected for an α,β-unsaturated ester. The individual components of the mixture could be characterized by comparisons of relative intensities of peaks in the NMR spectrum and in the gas chromatogram, and use of the double-resonance technique. The spectral data for the major component (higher retention time) clearly indicated that it was the ester **13a**. Ozonolysis of a mixture of these two fractions gave *trans*-2-methyl-4-*tert*-butylcyclohexanone. The minor component was not present in sufficiently large amounts to allow characterization in the mixture.

Although the major product (**15a**) observed in the above reaction contained an equatorial C-2 substituent, it was found that the stereochemistry of the product was quite dependent upon reaction conditions. When ketone **6** was treated with excess phosphonate anion, as above, ester **15a** was found to be the major isomer. However, when less than the theoretical molar quantity of anion **1** was used, the esters **13a** and **14a** were found to be the predominant products, and ester **15a** was distinctly a minor component (~7% of total peak area). The relative amount of ester **15a** was increased (still not the major product), when the amount of phosphonate anion was raised to approximately the theoretical molar quantity. It was determined, however, that the product distribution from this reaction was not affected by the strength of the base used to generate the phosphonate anion, because use of either sodium hydride or potassium *tert*-butoxide (using either **1a** or **1b**) was found to give the same result. In all of the above experiments, the phosphonate reagent, $(RO)_2POCH_2CO_2R$, was present in excess over the base used to generate anion **1**. If excess base was used, the major change observed was a significant increase in the relative amount of the β,γ isomer.

A complete rationalization of the stereochemistry of the phosphonate Wittig reaction with cyclic ketones is not possible at this time. However, the above results clearly show the previously unrecognized importance of an equatorial substituent at C-2 upon the course of this reaction.

The key features to be noted from the results of the present study are (a) the lack of reactivity of ketones **2**, **5**, and **7**; (b) the complex stereochemical result obtained with ketone **6**; and (c) the ease of reactivity of ketone **8**. The facile reactions with 2-methylcyclohexanone and ketone **4** suggest that the conformers with an axial C-2 side chain may be important in their reactivity. The two conformations of 2-methylcyclohexanone differ in energy by only 1.60 kcal/mol.[10] Thus the significant amounts of product with *Z* configuration obtained from reaction with this ketone could be readily accounted for by reaction involving intermediates with an axial methyl group.

Ketones **2** and **5** greatly prefer conformations with an equatorial C-2 substituent, since the alternative chair conformation is highly destabilized by a 1,3-diaxial interaction. Thus, any reaction requiring the C-2 substituent to be axial at the transition state would be quite unfavorable.

However, ketone **6a**, in which conformational inversion is blocked by the bulky *tert*-butyl group, can isomerize to its isomer **6b** with an axial C-2 substituent under basic conditions (**6a** $\rightleftharpoons$ **6b**, $\Delta G = -1.56$ kcal/mol).[11] Taking into account the aforementioned effect of the reagent ratio on product distribution, one might propose the following mechanism to rationalize this reaction. The condensation reaction to give product is assumed to proceed only after ketone **6a** has isomerized to ketone **6b**. The direct reaction of **6a** to give esters with an equatorial C-2 substituent is assumed to be extremely slow, if it occurs at all. The facile reaction of **6b** would be consistent with the observed reactivity of ketone **8**. The reaction with ketone **6b** then gives as initial products the esters **13** and **14** with an axial methyl group. In the presence of excess anion **1** these are isomerized to ester **15** and other isomers.

Thus the present work demonstrates quite clearly that reaction of phosphonate anion **1** with cyclohexanones is subject to severe steric hindrance by the presence of an equatorial substituent at C-2. Reaction will proceed satisfactorily only if this substituent can readily attain a conformational or configurational (epimerization) conversion to an axial position.

Experimental Section

General Procedures. All compounds in this section containing an asymmetric carbon atom are racemic; the prefix *dl* is omitted. Infrared spectra were determined on a Perkin-Elmer grating infrared spectrophotometer, Model 237B, or a Beckman infrared spectrophotometer, Model IR8. Nuclear magnetic resonance (NMR) spectra were determined on Varian Associates Model HA-100 or T-60 spectrometers. Carbon tetrachloride was used as the solvent unless otherwise stated. Tetramethylsilane (Me_4Si) was used as the internal reference. Chemical shifts are reported as δ values in parts per million (ppm) relative to TMS [$\delta(Me_4Si)$ 0.0 ppm]. High-resolution mass spectra were determined on a CEC Model 21-110 spectrometer under the supervision of Dr. R. Grigsby.

The vapor phase chromatographic analyses (VPC) were performed on a Hewlett-Packard instrument, Model 700, equipped with a thermal conductivity detector with a helium flow rate of ~60 ml/min. All percent-composition values are reported as relative peak areas (disk integrator) without correction for relative detector response. Preparative vapor phase chromatographic separations were performed on the same instrument.

Unless otherwise indicated, the elution order used in column chromatography was hexane (pentane, heptane), ether, ethyl acetate. High-pressure liquid chromatographic analyses were performed on a Waters Associates Model ALC 201 equipped with a refractive index detector.

Microanalyses were performed by Chemalytics, Inc., Tempe, Ariz. Melting points were determined on a Thomas-Hoover capillary melting point apparatus.

Tetrahydrofuran was dried over sodium hydroxide pellets and distilled from lithium aluminum hydride just prior to use. Glyme and *N,N*-dimethylformamide were distilled from lithium aluminum hydride and barium oxide, respectively, just prior to use.

A 19-in. spinning band column, Nester-Faust Corp. Model NFT-51, equipped with a Teflon band and rated at 75 theoretical plates was used for fractional distillations. Evaporative distillations refer to bulb-to-bulb (Kugelrohr), short-path distillations in which the bulb was heated by an oven. The temperatures cited for these distillations refer to the maximum temperature attained by the air chamber during the distillation.

The isolation procedure normally consisted of dilution of the product with water and extraction with the solvent indicated. The extractions were usually three in number. The combined organic extracts were then washed with the stated solutions. "Acid" refers to a 10% aqueous solution of hydrochloric acid. "Bicarbonate" refers to a saturated aqueous solution of sodium bicarbonate.

"Brine" refers to a saturated aqueous solution of sodium chloride. After the solution was dried over the stated drying agent, the solvent was removed at ca. 30 mm using a rotary evaporator (Rinco Co.).

Apparatus similar to that described by Johnson and Schneider[12] was used to maintain a nitrogen atmosphere in reactions requiring an inert atmosphere.

Preparation of Materials. 2,4,4-Trimethylcyclohexanone (5). A solution of 0.42 g (4.2 mmol) of cyclohexylamine in 5 ml of dry benzene was added slowly to a solution of 0.5 g (4.0 mmol) of 4,4-dimethylcyclohexanone[13] in 25 ml of dry benzene at room temperature. The mixture was heated to reflux for 12 hr in a flask with a water-separation head. The solvent was removed and the imine was evaporatively distilled (1.8 mm, 135°) to give 0.712 g (92% yield) of colorless liquid. The imine was dissolved in 8 ml of anhydrous ether and added dropwise to a cold, stirred solution of 20 ml of 1 *M* ethylmagnesium bromide over a period of 5 min. The reaction mixture was then refluxed for 5 hr under nitrogen and cooled in an ice bath, and 0.5 g (3.5 mmol) of methyl iodide in 5 ml of anhydrous ether was added dropwise to the reaction mixture. The mixture was refluxed overnight; then the imine salts were decomposed by slow addition of 20 ml of 10% hydrochloric acid and enough water to dissolve the precipitate. The resulting mixture was extracted with ether. The combined ethereal extracts were washed (water, bicarbonate, and brine), dried over anhydrous sodium sulfate, concentrated, and evaporatively distilled (0.1 mm, 65°) to give 0.27 g (48% yield) of ketone **5** [lit.[14] bp 87–89° (30 mmHg)]: ir (film) 1705 cm^{-1} (C=O); NMR (CCl_4, 60 MHz) δ 0.91 (d, 3 H, J = 7.0 Hz, C-2 methyl), 0.97 (s, 3 H, C-4 axial methyl), 1.27 (s, 3 H, C-4 equatorial methyl), 1.42–2.25 ppm (broad absorption, 6 H).

2-Methyl-4-*tert*-butylcyclohexanone (6). A solution of 1.78 g (18 mmol) of cyclohexylamine in 10 ml of dry benzene was added to a solution of 2.5 g (16 mmol) of 4-*tert*-butylcyclohexanone in 30 ml of dry benzene at room temperature. The mixture was heated to reflux for 12 hr in a flask with a water-separation head. The solvent was removed and the imine, without further purification, was dissolved in 20 ml of tetrahydrofuran and added dropwise to a cold, stirred solution of 32 ml of 1 *M* methylmagnesium bromide over a period of 10 min. The reaction mixture was refluxed for 5 hr under nitrogen. Then 2.56 g (18 mmol) of methyl iodide in 10 ml of tetrahydrofuran was added dropwise to the cooled reaction mixture, and the solution was refluxed overnight. The imine salts were decomposed by dropwise addition of 20 ml of 10% hydrochloric acid and enough water to dissolve the precipitate, and the aqueous layer was extracted with ether. The combined ethereal extracts were washed (water, bicarbonate, and brine), dried over anhydrous sodium sulfate, concentrated, and distilled to give 2.33 g (86% yield) of ketone **6**, bp 130° (0.7 mm). VPC analysis on a 10% SE-30 column at 150° indicated the presence of two components with relative peak areas of 94% (retention time 3.4 min) and 6% (retention time 4.0 min). The former fraction proved to be a mixture of ketone **6a** and **6b**; the latter proved to be the mixture of ketones **7a** and **7b**. The two fractions could be separated preparatively by preparative VPC on a 20-ft 20% SE-30 column at 160° or by liquid chromatography (40:1 hexane–ethyl acetate as the solvent). Spectral data for ketone **6**: ir (film) 1710 cm^{-1} (C=O); NMR (CCl_4, 60 MHz) δ 0.92 (s, 9 H, *tert*-butyl), 0.93 (d, 3 H, J = 8.0 Hz, C-2 equatorial methyl[15,16]), 1.10 ppm (d, 3 H, J = 7.0 Hz, C-2 axial methyl[15,16]).

Enamine Equilibration of 2-Methyl-4-*tert*-butylcyclohexanone (6).[15] A solution of 202 mg (1.2 mmol) of ketones **6a** and **6b** (~18:1) and 142 mg of freshly distilled pyrrolidine in 50 ml of dry benzene was refluxed under nitrogen for 24 hr using a water separator. After removal of the solvent under reduced pressure, the mixture was distilled to give the enamine, bp 80–86° (0.15 mm). Then 10 ml of 50% aqueous acetic acid was added dropwise to a solution of the enamine in 25 ml of dry 1,2-dimethoxyethane with stirring under nitrogen over a period of 2 min. The mixture was stirred for 10 min and poured into a mixture of 100 ml of water and 100 ml of ether. The aqueous layer was extracted with ether, and the combined ethereal extracts were washed (water, bicarbonate, and brine), dried over magnesium sulfate, and concentrated. The residue was evaporatively distilled (0.15 mm, 95°) to give 160 mg of a mixture of ketones **6a** and **6b**. The NMR spectrum indicated that the ratio of the two isomers was about 1:1.

2,6-Dimethyl-4-*tert*-butylcyclohexanone (7).[15] A solution of 1.08 g (15 mmol) of freshly distilled pyrrolidine in 20 ml of dry benzene was added dropwise to a solution of 2.00 g (13 mmol) of 4-*tert*-butylcyclohexanone in 20 ml of dry benzene over a period of 15 min. The reaction mixture was heated to reflux in a 200-ml flask with a phase-separation head under nitrogen for 12 hr. The solvent was removed at reduced pressure and the residue was evaporatively distilled (0.15 mm, 90°) to give 2.4 g of the enamine, *N*-(4-*tert*-butylcyclohex-1-enyl)pyrrolidine. A solution of 2.84 g (20 mmol) of methyl iodide in 20 ml of dry benzene was added slowly to a solution of the aforementioned enamine in 20 ml of dry benzene. The mixture was refluxed overnight; then the enamine salt was decomposed by slow addition of 40 ml of 10% hydrochloric acid and water. The reaction mixture was extracted with ether. The ethereal extracts were washed (water, bicarbonate, and brine), dried over anhydrous sodium sulfate, and concentrated. The residue was evaporatively distilled (0.15 mm, 100°) to give 1.43 g of colorless liquid. VPC analysis on a 10% SE-30 column at 135° showed that the product contained 40% starting ketone, 35% ketone **6**, and 25% ketone **7**. Ketone **7** was isolated by preparative VPC on a 20-ft 20% SE-30 column at 150°.

The NMR spectrum of ketone **7** indicated the presence of both isomers, **7a** and **7b**, in a ratio of 2:1. The structural determination was performed by use of lanthanide shift reagent, Eu(fod)$_3$, and was further confirmed by mass spectra. Spectral data follow: ir (film) 1710 cm^{-1} (C=O); NMR (CCl_4, 60 MHz) δ 2.70–1.20 (broad absorption, 7 H), 1.13 (d, 3, J = 10 Hz, axial CH_3), 1.01 (d, 3, J = 7.0 Hz, equatorial CH_3), and 0.88 ppm [5, 9 H, $C(CH_3)_3$]; mass spectrum (6 kV) *m/e* (rel intensity) 182 (25), 126 (50), 57 (100), and 41 (41). The above spectra are consistent with values reported in the literature.[16]

Triethyl Phosphonoacetate. Freshly distilled ethyl bromoacetate (35 g, 0.21 mol) was added dropwise to 35 g (0.21 mol) of triethyl phosphite. After a 30-min induction period the temperature rose and ethyl bromide began to distil. The remainder of the ethyl bromoacetate was then added at a rate to maintain the reaction. After complete addition, the mixture was refluxed at 170° for 9 hr and distilled to give 37 g (80% yield) of triethyl phosphonoacetate, bp 90° (0.2 mm) [lit. bp 152–153° (20 mm),[17] 109–109.5° (0.8 mm)[18]].

Trimethyl Phosphonoacetate. This material was prepared using the same method as described above but using trimethyl phosphite and methyl bromoacetate as reagents.[19]

Phosphonate Wittig Reactions. Reaction with 2-(3-Butenyl)cyclohexanone (4). A solution of 0.9 g (4 mmol) of triethyl phosphonoacetate in 10 ml of dry 1,2-dimethoxyethane was added in a fast stream of drops to a stirred suspension of 192 mg (4 mmol) of 50% sodium hydride in 5 ml of dry 1,2-dimethoxyethane. The mixture was stirred for 30 min under nitrogen at room temperature; then a solution of 0.5 g (3.3 mmol) of ketone **4** in 10 ml of dry 1,2-dimethoxyethane was added over a period of 5 min at room temperature. The mixture was allowed to stand for 30 hr; then 300 ml of water was added to the mixture and the reaction mixture was extracted with ether. The ethereal extracts were washed (water and brine), dried over anhydrous sodium sulfate, and concentrated. The crude product was eluted through a column (silica gel) using the mixture of hexane–ether (4:1) as the eluting solvent to remove excess phosphonate. The resulting material was evaporatively distilled (0.4 mm, 120°) to give 0.51 g (70% yield) of α,β-unsaturated ester. VPC analysis on a 10% SE-30 column at 165° indicated the presence of two components with relative peak areas of 30% (retention time 6.3 min) and 70% (retention time 7.6 min). The two components were separated by preparative VPC. Spectral analysis showed that the former is ester **9** with Z stereochemistry and the latter is ester **10** with E stereochemistry.

Spectral data for ester **9** follow: ir (film) 1710 (C=O), 1640 (conjugated C=C), 3025, 910, 795 cm^{-1} (terminal-CH=CH_2); NMR (CCl_4, 60 MHz) δ 5.58 (s, 1 H, conjugated vinyl proton), 5.30–6.25 (m, 1 H, -C**H**=CH_2), 4.70–5.20 (m, 2 H, -CH=C**H**$_2$), 4.06 (q, 2 H, J = 7.0 Hz, ethoxy methylene, superimposed on a broad multiplet attributable to one α-methine proton), and 1.28 ppm (t, 3 H, J = 7.0 Hz, ethoxy methyl).

Spectral data for ester **10** follow: ir (film) 1710 (C=O), 1640 (conjugated C=C), 3050, 910, 795 cm^{-1} (terminal -CH=CH_2); NMR (CCl_4, 60 MHz) δ 5.55 (s, 1 H, conjugated vinyl proton), 5.30–6.25 (m, 1 H, -C**H**=CH_2), 4.70–5.20 (m, 2 H, -CH=C**H**$_2$), 4.06 (q, 2 H, J = 7.0 Hz, ethoxy methylene), and 1.28 ppm (t, 3 H, J = 7.0 Hz, ethoxy methyl).

Reaction with 2,4,4-Trimethylcyclohexanone (5). A solution of 182 mg (1.0 mmol) of trimethyl phosphonoacetate in 10 ml of dry dimethylformamide was added in a fast stream of drops to a stirred suspension of 48 mg (1.0 mmol) of 50% sodium hydride in 10 ml of dry dimethylformamide. The mixture was stirred for 30 min under nitrogen at 5°, and then a solution of 68 mg (0.49 mmol) of ketone **5** in 5 ml of dry dimethylformamide was added over a 5-

min period at 5°. The reaction mixture was stirred at room temperature for 48 hr. Then 100 ml of water was added to the mixture, and the reaction mixture was extracted with ether. The ethereal extracts were washed (water and brine), dried over anhydrous sodium sulfate, and concentrated. The residue was eluted through a column (silica gel) by using a mixture of hexane–ether (4:1) as the eluting solvent. The resulting material was evaporatively distilled (0.1 mm, 120°) to give 60 mg of colorless oil which was identified as the starting ketone **5**.

Reaction with 2-Methyl-4-*tert*-butylcyclohexanone (6). I. Reactions Using Trimethyl Phosphonoacetate. A. Reaction with Excess Phosphonate Anion (NaH). A solution of 3.5 g (19.2 mmol) of trimethyl phosphonoacetate in 25 ml of dry dimethylformamide was added in a fast stream of drops to a stirred suspension of 888 mg (18.5 mmol) of 50% sodium hydride in 25 ml of dry dimethylformamide. The mixture was stirred for 30 min under nitrogen at 5°; then a solution of 750 mg (4.5 mmol) of ketone **6** in 20 ml of dry dimethylformamide was added over a period of 15 min at 5°. The reaction mixture was stirred at room temperature for 48 hr. Then 300 ml of water was added to the mixture, and the reaction mixture was extracted with ether. The ethereal extracts were washed (water and brine), dried over anhydrous sodium sulfate, and concentrated. The ester product and unchanged ketone were eluted through a column (silica gel) using the mixture of hexane–ether (4:1) as the eluting solvent. The eluate was evaporatively distilled (0.15 mm, 110°) to give 804 mg (80% yield) of ester products. VPC analysis on a 20-ft 20% SE-30 column at 125° showed that the product contained 4% ketone **6** and had five peaks for the ester products with retention times of 2.4, 2.63, 2.75, 3.1, and 3.4 hr. The last fraction was the major isomer (72% relative to total peak area), and the second and third fractions were not completely separated.

The first fraction was isolated and identified as a β,γ-unsaturated ester. The ir spectrum of this ester shows the carbonyl absorption at 1735 cm^{-1} and the absence of conjugated double bond absorption; the NMR spectrum exhibited a vinyl proton absorption at δ 5.50 ppm (broad singlet), a sharp singlet for the methyl ester at δ 3.60 ppm, a singlet at δ 2.88 ppm for the α-methylene group, a doublet at δ 1.00 ppm with coupling constant J = 7.0 Hz for the C-2 methyl group, and a sharp singlet at δ 0.86 ppm for the *tert*-butyl group.

The ir spectrum of the last fraction shows carbonyl absorption at 1710 cm^{-1} and conjugated double bond absorption at 1640 cm^{-1}. The NMR spectrum exhibits a vinyl proton absorption at δ 5.48 ppm, a broad multiplet at δ 4.20–3.80 ppm for a C-2 methylene proton, a sharp singlet at δ 3.60 ppm for the methyl ester, a doublet at δ 1.05 ppm with coupling constant J = 7.0 Hz for the C-2 methyl group, and a singlet at δ 0.86 ppm for the *tert*-butyl group. The methyl doublet collapsed to a singlet upon decoupling irradiation at δ 2.32 ppm, which indicates that the downfield proton is not coupled to the C-2 methyl group. Ozonolysis of this fraction in a 50:50 mixture of ethyl acetate–acetic acid (see below) gave ketone **6a**, as indicated by the presence of a doublet at δ 0.93 ppm in the NMR spectrum. The above data proved that the last fraction is ester **15a**.

The ir spectrum of the fourth fraction shows carbonyl absorption at 1710 cm^{-1} and conjugated double bond absorption at 1640 cm^{-1}. The NMR spectrum exhibits a vinyl proton absorption at δ 5.58 ppm, a broad multiplet at δ 3.98–3.58 ppm for an equatorial methylene proton, a singlet at δ 3.60 ppm for the methyl ester, a doublet at δ 1.16 ppm with a coupling constant of J = 7.0 Hz for the C-2 methyl group, and a *tert*-butyl group absorption at δ 0.86 ppm. The methyl doublet collapses to a singlet upon decoupling irradiation at δ 2.40 ppm, which indicates that the downfield proton is not coupled to the C-2 methyl group. Ozonolysis of this fraction in a 50:50 mixture of ethyl acetate–acetic acid gave ketone **6b**, which shows a doublet at δ 1.10 ppm in the NMR spectrum. Thus, this fraction is proven to be ester **14a**.

The ir spectrum of the mixture of second and third fractions with the latter as the major component shows carbonyl absorption at 1710 cm^{-1} and conjugated double bond absorption at 1640 cm^{-1}. The NMR spectrum of the mixture shows absorptions attributable to both the major and the minor components. Absorptions assigned to the major component are a vinyl proton absorption at δ 5.48 ppm, a broad multiplet at δ 4.30–3.84 ppm for an α-methine proton, a sharp singlet at δ 3.60 ppm for the methyl ester, and a doublet at δ 1.12 ppm with coupling constant J = 7.0 Hz for the C-2 methyl group. The methyl doublet collapsed to a singlet upon decoupling irradiation at δ 4.00 ppm, indicating that the downfield proton was coupled to the C-2 methyl group. Ozonolysis of this mixture in a 50:50 mixture of ethyl acetate–acetic acid gave predominantly ketone **6b** with small amounts of ketone **6a** indicated by the NMR spectrum. Thus the third fraction was assigned structure **13a**.

The NMR spectrum of the minor component in this mixture of the second and third components exhibits a vinyl proton absorption at δ 5.56 ppm, a C-2 methine proton absorption at δ 2.92 ppm, a doublet at δ 1.08 ppm with coupling constant J = 7.0 Hz for the C-2 methyl group, and also a sharp singlet at δ 0.86 ppm for the *tert*-butyl group. The methyl doublet collapsed to a singlet upon decoupling irradiation at δ 2.92 ppm, indicating that the downfield proton was coupled to the C-2 methyl group. The structure of this ester cannot be ascertained with certainty from available data.

B. Use of Potassium *tert*-Butoxide as Base. A solution of 328 mg (1.8 mmol) of trimethyl phosphonoacetate in 5 ml of dry dimethylformamide was added in a fast stream of drops to 202 mg (1.8 mmol) of potassium *tert*-butoxide in 5 ml of dry dimethylformamide with stirring. The mixture was stirred for 30 min under nitrogen at 0°, and then a solution of 150 mg (0.9 mmol) of ketone **6** in 5 ml of dry dimethylformamide was added over a period of 5 min. The reaction mixture was stirred at room temperature for 30 hr. Then 100 ml of water was added to the mixture, and the reaction mixture was extracted with ether. The ethereal extracts were washed (acid, bicarbonate, and brine), dried over anhydrous magnesium sulfate and concentrated. The residue was distilled evaporatively (0.12 mm, 90°) to give 126 mg (63% yield) of ester products. VPC analysis on column A at 130° showed some starting ketone and five peaks for the isomeric ester products with the same retention times as described above. The last fraction was the major isomer.

C. Reaction with One-Half of the Theoretical Molar Quantity of Anion. A solution of 219 mg (1.2 mmol) of trimethyl phosphonoacetate in 5 ml of dry dimethylformamide was added in a fast stream of drops to a stirred suspension of 15 mg (0.3 mmol) of 50% sodium hydride in 5 ml of dry dimethylformamide. The mixture was stirred for 30 min under nitrogen at 5°, and then a solution of 101 mg (0.6 mmol) of ketone **6** in 5 ml of dry dimethylformamide was added over a period of 5 min at 5°. The reaction mixture was stirred at room temperature for 72 hr; then 100 ml of water was added to the mixture, and the reaction mixture was extracted with ether. The ethereal extracts were washed (water and brine), dried over anhydrous sodium sulfate, and concentrated. The ester product and unchanged ketone **6** were eluted through a column (silica gel) using the mixture of hexane–ether (4:1) as the eluting solvent. The eluate was evaporatively distilled (0.15 mm, 110°) to give 104 mg (77% yield) of products. VPC analysis on a 20-ft 20% SE-30 column at 140° showed starting ketone and five peaks for the ester products. The third and fourth fractions were the predominant isomeric products (~45 and ~46%, respectively, relative to total peak area of ester products), and the last fraction was a minor isomeric product (~7% relative to total peak area of ester products.)

D. Reaction with Approximately Equal Theoretical Molar Quantity of Anion. A solution of 219 mg (1.2 mmol) of trimethyl phosphonoacetate in 5 ml of dry dimethylformamide was added in a fast stream of drops to a stirred suspension of 30 mg (0.6 mmol) of 50% sodium hydride in 5 ml of dry dimethylformamide. The mixture was stirred for 30 min under nitrogen at 5°, and then a solution of 101 mg (0.6 mmol) of ketone **6** in 5 ml of dry dimethylformamide was added over a period of 5 min at 5°. The reaction mixture was stirred at room temperature for 48 hr. Then 100 ml of water was added to the mixture, and the reaction mixture was extracted with ether. The ethereal extracts were washed (water and brine), dried over anhydrous sodium sulfate, and concentrated. The ester product and unchanged ketone **6** were eluted through a column (silica gel) using the mixture of hexane–ether (4:1) as the eluting solvent. The eluate was evaporatively distilled (0.15 mm 110°) to give 114 mg (85% yield) of products. VPC analysis showed the same five peaks for ester products. The third and fourth fractions were the predominant isomeric products (~40 and ~39%, respectively, relative to total peak area of ester products), and the last fraction was a minor isomeric product (~19%).

E. Reaction with Excess Sodium Hydride. A solution of 728 mg (4.0 mmol) of trimethyl phosphonoacetate in 20 ml of dry dimethylformamide was added in a fast stream of drops to a stirred suspension of 288 mg (6.0 mmol) of 50% sodium hydride in 10 ml of dry dimethylformamide. The mixture was stirred for 30 min under nitrogen at 5°, and then a solution of 340 mg (2.0 mmol) of ketone **6** in 15 ml of dry dimethylformamide was added over a period of 10 min at 5°. The reaction mixture was stirred at room temperature for 48 hr. Then 300 ml of water was added to the mixture,

and the reaction mixture was extracted with ether. The ethereal extracts were washed (water and brine), dried over anhydrous sodium sulfate, and concentrated. The ester product and unchanged ketone **6** were eluted through a column (silica gel) using the mixture of hexane–ether (4:1) as the eluting solvent. The eluate was evaporatively distilled (0.15 mm, 95°) to give 343 mg (77% yield) of products. VPC analysis showed some starting ketone and five peaks for the ester products. The last fraction was the major one (70% relative to total peak area), but the first fraction (8% relative to total peak area) was increased over the amounts observed in run A.

II. Reaction Using Triethyl Phophonoacetate. A. Use of Sodium Hydride as Base. A solution of 291 mg (1.3 mmol) of triethyl phosphonoacetate in 5 ml of dry 1,2-dimethoxyethane (glyme) was added in a fast stream of drops to a stirred suspension of 58 mg (1.2 mmol) of 50% sodium hydride in 5 ml of dry 1,2-dimethoxyethane. The mixture was stirred for 30 min under nitrogen at room temperature, and then a solution of 101 mg (0.6 mmol) of ketone **6** in 4 ml of dry 1,2-dimethoxyethane was added over a period of 5 min at 25°. The reaction mixture was stirred at room temperature for 12 hr. Then 200 ml of water was added to the mixture, and the reaction mixture was extracted with ether. The ethereal extracts were washed (water and brine), dried over anhydrous sodium sulfate, and concentrated. The ester product and unchanged ketone were eluted through a column (silica gel) using the mixture of hexane–ether (4:1) as the eluting solvent. The eluate was evaporatively distilled (0.25 mm, 90°) to give 128 mg (90% yield) of product. VPC analysis on a 10% SE-30 column at 130° showed some starting ketone (24% of total peak area) and five peaks for the isomeric ester products with retention times of 30.5, 37.5, 45, 50, and 60 min. The last fraction was the major isomer (~75% relative to total peak area of ester products). Three of the components were isolated pure by preparative VPC. The second and fourth fractions were not isolated owing to the overlapping with the third and fifth fractions, respectively.

The ir spectrum of the first fraction shows carbonyl absorption at 1730 cm^{-1} and the absence of conjugated double bond absorption; the NMR spectrum shows one vinyl proton absorption as a multiplet at δ 5.33–5.69 ppm, ethoxy methylene absorption as a quartet at δ 4.06 ppm (J = 7.0 Hz), two α-methylene protons absorption as a singlet at δ 2.86 ppm, ethoxy methyl absorption as a triplet at δ 1.24 ppm (J = 7.0 Hz), α-methyl absorption as a doublet at δ 1.00 ppm (J = 7.0 Hz), and *tert*-butyl absorption as a singlet at δ 0.88 ppm. The above spectral data indicated that the isomer is a β,γ-unsaturated ester.

Anal. Calcd for $C_{15}H_{26}O_2$: 238.193270. Found: 238.192453.

The ir spectrum of the third fraction shows carbonyl absorption at 1710 cm^{-1} and conjugated double bond absorption at 1640 cm^{-1}; the NMR spectrum of this isomer shows one vinyl proton absorption as a singlet at δ 5.46 ppm, ethoxy methylene absorption as a quartet at δ 4.08 ppm (J = 7.0 Hz) superimposed on a broad multiplet attributable to one C-2 methine proton, ethoxy methyl absorption as a doublet at δ 1.16 ppm (J = 8.0 Hz), and *tert*-butyl absorption as a singlet at δ 0.88 ppm. Decoupling irradiation at δ 3.9 ppm caused collapse of the methyl doublet to a singlet. The above spectral data indicate that the isomer is α,β-unsaturated ester **13b.**

Anal. Calcd for $C_{15}H_{26}O_2$: 288.193270. Found: 238.193621.

The ir spectrum of the last fraction shows carbonyl absorption at 1710 cm^{-1} and conjugated double bond absorption at 1640 cm^{-1}; the NMR spectrum of this isomer shows a vinyl proton absorption as a singlet at δ 5.46 ppm, ethoxy methylene absorption as a quartet at δ 4.08 ppm (J = 7.0 Hz) superimposed on a broad multiplet attributable to one α-methylene proton (equatorial), ethoxy methyl absorption as a triplet at δ 1.16 ppm (J = 7.0 Hz), C-2 equatorial methyl absorption as a doublet at δ 1.06 ppm (J = 6.0 Hz), and *tert*-butyl absorption as a singlet at δ 0.88 ppm. The methyl doublet was collapsed to a singlet by decoupling irradiation at δ ~2.30 ppm. The above spectral data indicate that the isomer is the α,β-unsaturated ester **15b.**

Anal. Calcd for $C_{15}H_{26}O_2$: 238.193270. Found: 238.193387.

B. Use of Potassium *tert*-Butoxide as Base. A solution of 2.02 g (9.0 mmol) of triethyl phosphonoacetate in 15 ml of dry dimethylformamide was added in a fast stream of drops to 672 mg (6.0 mmol) of potassium *tert*-butoxide in 15 ml of dry dimethylformamide with stirring. The mixture was stirred for 30 min under nitrogen at 0°; and then a solution of 0.50 g (3.0 mmol) of ketone **6** in 20 ml of dry dimethylformamide was added over a period of 10 min. The reaction mixture was stirred at 0° for 30 min and at room temperature for 30 hr. Then 200 ml of water was added to the mixture, and the reaction mixture was extracted with ether. The ethereal extracts were washed (3*N* hydrochloric acid, bicarbonate, and brine), dried over anhydrous magnesium sulfate, and concentrated. The excess phosphonate was removed by passage through a column (silica gel) using the mixture of hexane–ether (4:1) as the eluting solvent. The eluate was evaporatively distilled (0.12 mm, 90°) to give 355 mg (50% yield) of ester products. VPC analysis on column A at 130° showed some starting ketone (~5% of total peak area) and five peaks for the isomeric ester products with same retention times as described above. The last fraction was the major isomer (~70% relative to total peak area of ester products). The spectral data were the same as described above.

Reaction with 2,6-Dimethyl-4-*tert*-butylcyclohexanone (7). A solution of 291 mg (1.3 mmol) of trimethyl phosphonoacetate in 10 ml of dry dimethylformamide was added in a fast stream of drops to a stirred suspension of 62 mg (1.3 mmol) of 50% sodium hydride in 5 ml of dry dimethylformamide. The mixture was stirred for 30 min under nitrogen at 5°, and then a solution of 85 mg (0.49 mmol) of a mixture of ketones **7a** and **7b** (about 2:1 ratio) in 10 ml of dry dimethylformamide was added over a period of 5 min at 5°. The reaction mixture was stirred at room temperature for 48 hr. Then 150 ml of water was added to the mixture, and the reaction mixture was extracted with ether. The ethereal extracts were washed (water and brine), dried over anhydrous sodium sulfate, concentrated, and evaporatively distilled (0.15 mm, 110°) to give 56 mg of product identified as the starting ketone 7.

Reaction with Bicyclo[3.2.1]octan-2-one (8). A solution of 405 mg (1.8 mmol) of triethyl phosphonoacetate in 10 ml of dry dimethylformamide was added in a fast stream of drops to a stirred suspension of 86 mg (1.8 mmol) of 50% sodium hydride in 10 ml of dry dimethylformamide. The mixture was stirred for 1.5 hr under nitrogen at room temperature, and then a solution of 200 mg (1.6 mmol) of bicyclo[3.2.1]octan-2-one (**8**) (Aldrich) in 5 ml of dimethylformamide was added. The reaction mixture was stirred at room temperature for 48 hr, diluted with 200 ml of water, and extracted with ether. The ethereal extracts were washed (water and brine), dried over anhydrous sodium sulfate, and concentrated. The ester product and unchanged ketone were eluted through a column (silica gel) by using the mixture of hexane–ether (4:1) as the eluting solvent. The eluate was evaporatively distilled (0.25 mm, 86°) to give 235 mg (76% yield) of α,β-unsaturated esters. VPC analysis on a 10% Apiezon L column at 160° showed two peaks in a ratio of 2:3 with the retention times of 15.2 and 17.2 min; the former fraction was shown to be ester **11** and the latter to be ester **12.**

Anal. Calcd for $C_{12}H_{18}O_2$: (ester **11**) 194.130670; (ester **12**) 194.130670. Found: (ester **11**) 194.129943; (ester **12**) 194.129943.

Spectral data for ester **11** follow: ir (film) 1710 (C=O), 1640 cm^{-1} (conjugated double bond); nmr (CCl_4, 100 MHz) δ 5.34 (s, 1 H, vinyl proton), ethoxy methylene superimposed on a broad multiplet (4.10–4.50 ppm) attributable to a methine proton, and 1.22 ppm (t, 3 H, J = 7.0 Hz, ethoxy methyl).

Spectral data for ester **12** follow: ir (film) 1710 (C=O), 1640 cm^{-1} (conjugated double bond); nmr (CCl_4, 100 MHz) δ 5.46 (s, 1 H, vinyl proton), 4.1 (q, J = 3.5 Hz, ethoxy methylene), 3.55–3.88 (m, 1 H, equatorial methylene proton), and 1.22 ppm (t, 3 H, **J** = 7.0 Hz, ethoxy methyl).

When the above reaction was performed in 1,2-dimethoxyethane for 12 hr, a 68% yield of the same products was obtained.

Ozonolysis of Methyl 2-Methyl-4-*tert*-butylcyclohexylideneacetate (15a).[8,9] A solution of 10 mg of ester **15a** in 15 ml of ethyl acetate and 15 ml of acetic acid at ~20° was treated with an excess of ozone. This solution was allowed to stand cold for 20 min and was then stirred for 30 min with 0.4 g of powdered zinc at room temperature. Filtration and concentration of the filtrate under reduced pressure afforded an oily residue which was evaporatively distilled to give *cis*-2-methyl-4-*tert*-butylcyclohexanone (**6a**). The structure and stereochemistry of ketone **6** were confirmed by VPC and NMR spectroscopy in this and the following ozonolyses.

Ozonolysis of Ester 14a. Ester **14a** (~5 mg) was subjected to ozonolysis in a manner as described above to give *trans*-2-methyl-4-*tert*-butylcyclohexanone (**6b**).

Ozonolysis of the Mixture of Esters Containing Predominantly 13a. A mixture containing mainly **13a** and some of the second ester component (~7 mg) was subjected to ozonolysis in a manner as described above to give ketone **6** with the axial methyl doublet of *trans*-2-methyl-4-*tert*-butylcyclohexanone (**6b**) very distinct. A small amount of equatorial methyl doublet of *cis*-2-methyl-4-*tert*-butylcyclohexanone (**6a**) was also present.

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Registry No.—**4,** 16178-83-9; **5,** 2230-70-8; **6a,** 3211-27-6; **6b,** 3211-26-5; **7a,** 20826-63-5; **7b,** 20826-64-6; **8,** 5019-82-9; **9,** 53940-53-7; **10,** 53940-54-8; **11,** 53940-55-9; **12,** 53940-56-0; **13a,** 53940-57-1; **13b,** 53940-58-2; **14a,** 53940-59-3; **15a,** 53940-60-6; **15b,** 53940-61-7; 4,4-dimethylcyclohexanone, 4255-62-3; 4-*tert*-butylcyclohexanone, 98-53-3; pyrrolidine, 123-75-1; *N*-(2-methyl-4-*tert*-butylcyclohex-1-enyl)pyrrolidine, 53940-62-8; triethyl phosphonoacetate, 867-13-0; ethyl bromoacetate, 105-36-2; triethyl phosphate, 122-52-1; trimethyl phosphonoacetate, 5927-18-4; trimethyl phosphite, 121-45-9; methyl bromoacetate, 96-32-2; potassium *tert*-butoxide, 865-47-4.

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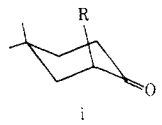

i

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Polyfluoroaryl Carbonyl Chemistry. Benzalacetophenones

Robert Filler,* Victor D. Beaucaire,[1] and H. H. Kang[1]

Department of Chemistry, Illinois Institute of Technology, Chicago, Illinois 60616

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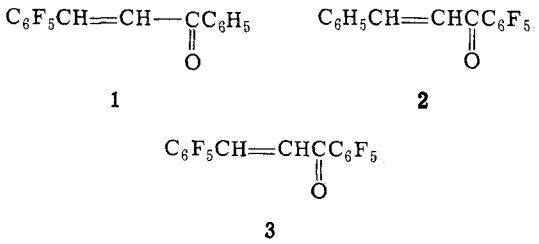
The polyfluorobenzalacetophenones **1, 2,** and **3** have been prepared and the effects of pentafluorophenyl groups on infrared and ultraviolet spectral properties evaluated. When the carbonyl is flanked by C_6F_5, haloform-type cleavage occurs readily in alkaline medium. The subject compounds undergo Michael addition of diethyl malonate with difficulty, but react with C_6H_5MgBr and C_6F_5MgBr to give 1,4-addition products, although in two cases the bimolecular compounds **8** and **9** are formed.

As part of studies on the effects of polyfluoroaryl substitution on the reactivity of neighboring functional groups, we have examined a variety of carbonyl compounds.[2] In this paper we report our observations on the chemistry of polyfluorobenzalacetophenones. The discussion is divided into three parts: preparation, spectral properties, and chemical reactions.

Preparation. Compounds **1, 2,** and **3** were all prepared by the Claisen–Schmidt reaction[3] (eq 1). Pentafluorobenzaldehyde reacted with acetophenone in aqueous ethanolic alkali to give pentafluorobenzalacetophenone (**1**)[4] in 50% yield.

$$ArCHO + Ar'COCH_3 \xrightarrow{OH^-} ArCH{=}CHC(=O)Ar' + H_2O \quad (1)$$

$$Ar = C_6H_5, C_6F_5$$
$$Ar' = C_6H_5, C_6F_5$$



1 **2**

3

2,3,4,5,6-Pentafluoroacetophenone, required for the preparation of benzalpentafluoroacetophenone (**2**) and 2,3-dihydryl-*F*-benzalacetophenone[5] (**3**), was obtained in 56% yield by reaction of bis(pentafluorophenyl)cadmium with acetyl chloride (eq 2). In the subsequent condensation reactions, the concentration of sodium hydroxide was reduced from the usual 6–7% to 1.5% and **2** and **3** were obtained in excellent yield (84–87%). At higher concentrations of alkali, a significant side reaction occurred, which will be discussed later. Compound **3** was prepared previously in 50% yield by a Wittig reaction.[6]

$$2C_6F_5MgBr + CdCl_2 \longrightarrow [(C_6F_5)_2Cd] \xrightarrow{CH_3COCl} C_6F_5COCH_3 \quad (2)$$

Spectral Properties. Infrared and ultraviolet spectral data for the benzalacetophenones are listed in Table I. The influence of neighboring fluorine atoms on carbonyl stretching frequencies has been reported previously.[7] The effect of the pentafluorophenyl group in shifting the ester carbonyl band to higher frequencies has been described.[2a] This trend is also evident in the present study.

Whereas benzalacetophenone exhibits $\nu_{C=O}$ 1667 cm^{-1}, the pentafluorophenyl group in **1** (ν 1674 cm^{-1}) causes an increase in double-bond character of the carbonyl group by minimizing charge delocalization, e.g., **4.** Although the para fluorine alone would enhance the contribution of **4,** the