

*trans*-nitrile **23** corresponding to a 71:29 ratio of the monoalkylated products.

To examine the effect of using a less reactive alkylating agent, a cold ( $-70^\circ$ ) solution of methyl chloride (*ca.* 16 mmol) in 2.0 ml of 1,2-dimethoxyethane was treated with a solution of the anion **26**, prepared from 1.08 mmol of the nitrile **21** and 1.40 mmol of lithium diethylamide in 3.8 ml of 1,2-dimethoxyethane. After the addition was complete, the solution was allowed to warm to room temperature and was stirred for 23 hr and then subjected to the previously described isolation procedure. After a weighed amount of internal standard had been added, analysis<sup>18</sup> indicated the yields of alkylated products to be 67% of **22** and 13% of **23** corresponding to an 84:16 ratio of monoalkylated products.

Samples of each of the alkylated nitriles **22** and **23** were collected<sup>15</sup> for characterization. Sublimation ( $65^\circ$  at 10 mm) of the axial nitrile **22** afforded the material as white plates: mp 48.5–49.5°; ir ( $\text{CCl}_4$ ), 2230  $\text{cm}^{-1}$  ( $\text{C}\equiv\text{N}$ ); nmr ( $\text{CCl}_4$ ),  $\delta$  1.1–2.3 (9 H multiplet, aliphatic CH), 1.37 (3 H singlet,  $\text{CH}_3\text{C}$ ), and 0.94 (9 H singlet,  $(\text{CH}_3)_3\text{C}$ ); mass spectrum, weak molecular ion at  $m/e$  179 with abundant fragment peaks at  $m/e$  123, 108, 95, 57, 41, and 39.

*Anal.* Calcd for  $\text{C}_{12}\text{H}_{21}\text{N}$ : C, 80.38; H, 11.81. Found: C, 80.62; H, 12.04.

The equatorial nitrile **23** sublimed ( $80^\circ$  at 10 mm) as white needles: mp 49.5–50°; ir ( $\text{CCl}_4$ ), 2235  $\text{cm}^{-1}$  ( $\text{C}\equiv\text{N}$ ); nmr ( $\text{CCl}_4$ ),  $\delta$  1.0–2.2 (9 H multiplet, aliphatic CH), 1.40 (3 H singlet,  $\text{CH}_3\text{C}$ ), and 0.90 (9 H singlet,  $(\text{CH}_3)_3\text{C}$ ); mass spectrum, weak molecular ion peak at  $m/e$  179 with abundant fragment peaks at  $m/e$  124, 108, 95, 57, 56, 55, 41, and 39.

*Anal.* Calcd for  $\text{C}_{12}\text{H}_{21}\text{N}$ : C, 80.38; H, 11.81. Found: C, 80.55; H, 11.89.

**The Stereochemistry of Nitriles 22 and 23.** A. **Conversion into Ketones 2 or 3.**—A solution of 62.7 mg (0.35 mmol) of the nitrile **22** and 1.44 mmol of methyllithium in 3.6 ml of ether was refluxed with stirring for 15 hr and then poured into 50 ml of dilute, aqueous hydrochloric acid. The resulting mixture was heated on a steam bath overnight and then extracted with ether. The ethereal solution was dried and concentrated to leave the crude ketone **3**<sup>15</sup> as a residual solid. Sublimation ( $70^\circ$  at 0.12 mm) afforded 62.1 mg (91.7%) of the ketone **3**, mp 47.5–48°,

identified with the previously described sample by a mixture melting point determination and by comparison of gas chromatographic retention times<sup>16</sup> and infrared and mass spectra.

The comparable reaction of 46.3 mg (0.26 mmol) of the nitrile **23** with 1.3 mmol of methyllithium and subsequent hydrolysis yielded, after sublimation ( $70^\circ$  at 10 mm), 44.1 mg (87%) of the ketone **2**, mp 45–46°, identified with the previous sample by all of the criteria listed above.

B. **Conversion into Amides 24 and 25.**—A mixture of 42.0 mg (0.23 mmol) of the nitrile **23**, 0.1 ml (0.87 mmol) of aqueous 30% hydrogen peroxide, 0.15 ml of absolute ethanol, and 9.6  $\mu$ l (0.06 mmol) of aqueous 6 *N* sodium hydroxide was stirred at room temperature for 1 hr and at  $50^\circ$  for 2 hr. Upon dilution with water, the amide separated as a crystalline solid, mp 137–139°, yield 39.8 mg (86%). Recrystallization from aqueous ethanol afforded the pure equatorial amide **25** as white needles: mp 139.5–140° (lit.<sup>6</sup> mp 139.5–140°); ir ( $\text{CHCl}_3$ ) 3510, 3480, and 3390 (NH), 1670 (amide  $\text{C}=\text{O}$ ), and 1580  $\text{cm}^{-1}$  ( $\text{NH}_2$  bending).

Attempts to hydrolyze the axial nitrile **22** by the same procedure resulted in recovery of the starting nitrile, a result consistent with the more hindered nature of the axial cyano group. Consequently, an alternative hydrolysis procedure<sup>19</sup> was employed in which a solution of 26 mg (0.15 mmol) of the nitrile **22** in 0.17 ml of concentrated sulfuric acid was stirred at  $60^\circ$  for 6.5 hr and then diluted with water and extracted with ether. The crude neutral product was recrystallized from aqueous ethanol to separate 18.2 mg (64%) of the amide **24** as white needles: mp 131–132° (lit.<sup>6</sup> mp 129–130°); ir ( $\text{CHCl}_3$ ), 3510, 3480, and 3390 (NH), 1670 (amide  $\text{C}=\text{O}$ ), and 1585  $\text{cm}^{-1}$  ( $\text{NH}_2$  bending).

**Registry No.**—**2**, 15619-08-6; **3**, 15619-21-3; **7**, 15619-09-7; **9a**, 15619-10-0; **9b**, 15619-11-1; **10a**, 15619-12-2; **10b**, 15619-13-3; **11a**, 15619-14-4; **11b**, 15619-15-5; **13**, 15619-16-6; **18**, 15619-17-7; **21a**, 15619-18-8; **21b**, 15619-19-9; **22**, 15619-22-4; **23**, 15619-20-2.

(19) N. Sperber, D. Papa, and E. Schwenk, *J. Amer. Chem. Soc.*, **70**, 3091 (1948).

## The Chemistry of Carbanions. XVII. The Addition of Methyl Organometallic Reagents to Cyclohexenone Derivatives<sup>1a</sup>

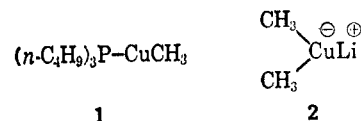
HERBERT O. HOUSE AND WILLIAM F. FISCHER, JR.<sup>1b</sup>

*Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139*

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The additions of methylmagnesium and methylcopper derivatives to the  $\alpha,\beta$ -unsaturated ketones **8**, **19**, and **21** have been studied. The stereochemistry of conjugate addition to the ketone **8** differs for methylcopper and methylmagnesium derivatives. When mixtures of these two metal derivatives are present, both contribute to the over-all stereochemistry of addition. Use of trimethylphosphite as a ligand for methylcopper to give relatively stable, ether-soluble complexes has been found advantageous in certain cases. Although the conjugate addition of lithium dimethylcuprate to  $\alpha,\beta$ -unsaturated ketones appears to require no other species in the reaction solution, trimethyl phosphite and tri-*n*-butylphosphine complexes of methylcopper will undergo conjugate addition only if various salts such as lithium iodide, lithium bromide, magnesium bromide, or lithium cyanide are present in the reaction medium. A possible interpretation of this observation is presented.

Earlier studies of the copper-catalyzed conjugate addition of organomagnesium compounds and organolithium compounds to  $\alpha,\beta$ -unsaturated ketones<sup>2</sup> had provided evidence supporting the idea that the actual reactants in these conjugate addition reactions are organocopper(I) compounds such as the materials



with the stoichiometric compositions **1** and **2**. Although it is probable that these copper(I) derivatives actually exist as associated structures (*e.g.*, tetramers) which may be bonded to solvent molecules as additional ligands, no compelling experimental evidence relating to these questions is currently available. The early data led to the hypothesis that the conjugate addition of the organocopper(I) reactants proceeded *via* a one-electron

(1) (a) This research has been supported by Grant No. AF-AFOSR-573 from the Directorate of Chemical Sciences, Air Force Office of Scientific Research; (b) National Institutes of Health Predoctoral Fellow, 1966–1967.

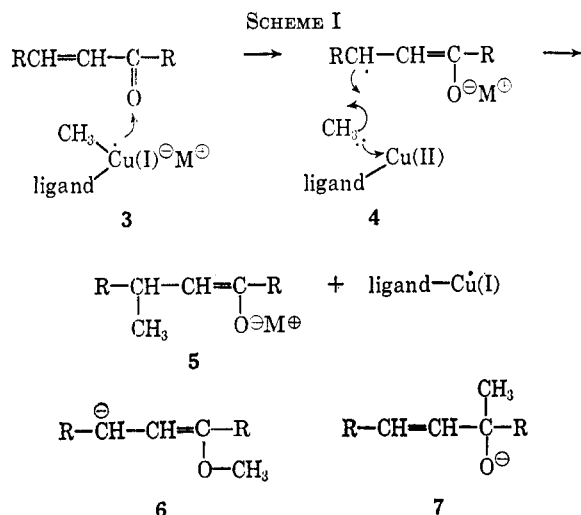
(2) (a) H. O. House, W. L. Reespees, and G. M. Whitesides, *J. Org. Chem.*, **31**, 3128 (1966), and references cited therein; (b) H. O. House, R. A. Latham, and C. D. Slater, *ibid.*, **31**, 2667 (1966); (c) H. O. House and H. W. Thompson, *ibid.*, **28**, 360 (1963); (d) H. O. House, D. D. Traficante, and R. A. Evans, *ibid.*, **28**, 348 (1963); (e) H. O. House and J. E. Oliver, *ibid.*, **33**, 929 (1968).

TABLE I  
THE PRODUCTS OBTAINED FROM ADDITION OF METHYLMAGNESIUM REAGENTS TO 5-METHYL-2-CYCLOHEXENONE (8)  
IN ETHER SOLUTION

Organometallic reagent and any additives (concn, M)	Ketone 8, concn, M	Product composition <sup>a</sup>					
		1,4 addition			1,2 addition		
		% of total product	<i>cis</i> 10, %	<i>trans</i> 9, %	% of total product	<i>cis</i> 11, %	<i>trans</i> 12, %
CH <sub>3</sub> MgBr (0.50-0.54)	0.38-0.41	21	8	92	79	13	87
(CH <sub>3</sub> ) <sub>2</sub> Mg (0.40-0.49)	0.25-0.38	3	10	90	97	12	88
CH <sub>3</sub> Li <sup>c</sup>	c	<1			>99 <sup>b</sup>	33	67
(CH <sub>3</sub> ) <sub>2</sub> Mg (0.51) + [(CH <sub>3</sub> ) <sub>2</sub> N] <sub>3</sub> PO (0.51)	0.36	<1			>99 <sup>b</sup>	13	87
(CH <sub>3</sub> ) <sub>2</sub> Mg (0.38) + (CH <sub>3</sub> ) <sub>2</sub> NCH <sub>2</sub> CH <sub>2</sub> OCH <sub>3</sub> (0.38)	0.33	2			98 <sup>b,d</sup>	15	85
(CH <sub>3</sub> ) <sub>2</sub> Mg (0.38) + (CH <sub>3</sub> ) <sub>2</sub> NCH <sub>2</sub> CH <sub>2</sub> OCH <sub>3</sub> (1.9)	0.33	7			93 <sup>b,d</sup>	15	85
(CH <sub>3</sub> ) <sub>2</sub> Mg (0.40) + (CH <sub>3</sub> ) <sub>2</sub> NCH <sub>2</sub> CH <sub>2</sub> N(CH <sub>3</sub> ) <sub>2</sub> (0.40)	0.33	5			95 <sup>d</sup>	13	87
(CH <sub>3</sub> ) <sub>2</sub> Mg (0.50) + CuI (0.005)	0.42	>99	9	91	<1		
CH <sub>3</sub> MgBr (0.54-0.55) + CuI (0.005)	0.38-0.43	99	7	93	1		

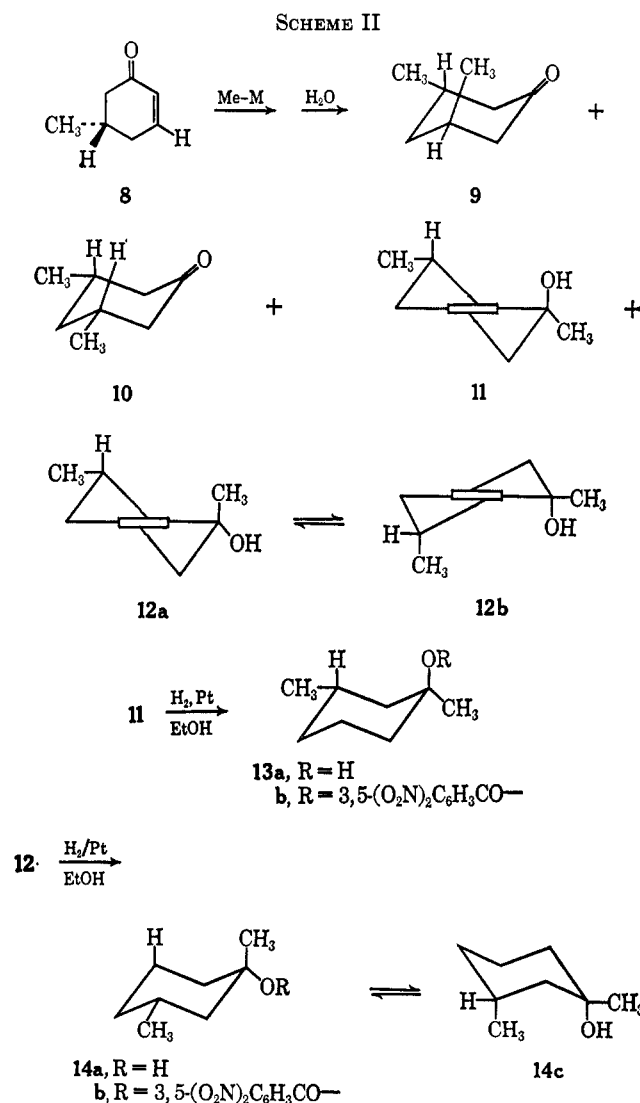
<sup>a</sup> Unless otherwise noted the values listed are average values obtained from two or more reactions and the calculated yields of products exceeded 90%. <sup>b</sup> These data are derived from a single run. <sup>c</sup> A description of this reaction is given in the Experimental Section. <sup>d</sup> In this case the calculated yields were in the range 80-84%.

transfer 3 followed by transfer of an alkyl radical 4 as indicated in Scheme I. This hypothesis presumes that the transition state for the indicated (4) transfer of an alkyl radical to the end of the conjugated anion radical to form an enolate anion 5 will be energetically more favorable than formation of the allylic anion 6 or disruption of the conjugated radical ion system by attack at the carbonyl carbon atom to form 7.



The further question exists of what relationship, if any, exists between the mechanisms of the copper-catalyzed conjugate additions and the presumably uncatalyzed conjugate additions of organomagnesium compounds to  $\alpha,\beta$ -unsaturated ketones. In an earlier study of asymmetric induction, Inouye and Walborsky<sup>3a</sup> provided evidence for different stereochemical requirements in the copper-catalyzed and the uncatalyzed additions of phenylmagnesium bromide to an  $\alpha,\beta$ -unsaturated ester. Some preliminary data from a study by Marshall and Anderson<sup>3b</sup> suggested that different stereochemical outcomes might be observed in the copper-catalyzed and uncatalyzed additions to an  $\alpha,\beta$ -unsaturated ketone. Our earlier study<sup>2c</sup> of an  $\alpha,\beta$ -unsaturated ketone where small differences in stereochemical outcome would not have been detected had indicated that the major stereochemical pathway was the same in the catalyzed and uncatalyzed reactions. To

examine this stereochemical question in more detail, we chose to study the reactions of methyl organometallic reagents with 5-methyl-2-cyclohexenone (8, Scheme II).



A mixture<sup>4</sup> containing 94-96% of the *trans* ketone 9 and 4-6% of the *cis* ketone 10 had been obtained earlier when the unsaturated ketone 8 was treated with ethereal

(3) (a) Y. Inouye and H. M. Walborsky, *J. Org. Chem.*, **27**, 2706 (1962); (b) J. A. Marshall and N. H. Anderson, *ibid.*, **31**, 667 (1966).

(4) N. L. Allinger and C. K. Riew, *Tetrahedron Lett.*, No. 12, 1269 (1966).

TABLE II  
 THE PRODUCTS OBTAINED FROM ADDITION OF METHYLCOPPER(I) DERIVATIVES TO 5-METHYL-2-CYCLOHEXENONE (8)

Methylcopper reagent (concn, M)	Additive (concn, M)	Concn of ketone 8, M	Solvent	Product		Ketone 8 recovery, %
				Yield, %	Composition <sup>a</sup> cis 10, trans 9, %	
CH <sub>3</sub> Cu (0.48-0.58) <sup>b</sup>	LiI (0.48-0.58) <sup>c</sup>	0.22-0.35	Et <sub>2</sub> O	92-99	1 99	
CH <sub>3</sub> Cu (0.41) <sup>b</sup>	(CH <sub>3</sub> ) <sub>2</sub> Mg (0.41) + LiI (0.41) <sup>c</sup>	0.31	Et <sub>2</sub> O	97	5 <sup>d</sup> 95 <sup>d</sup>	
CH <sub>3</sub> Cu (0.41) <sup>b</sup>	MgBr <sub>2</sub> (0.41) + LiI (0.41) <sup>c</sup>	0.31	Et <sub>2</sub> O	97	2 <sup>d</sup> 98 <sup>d</sup>	
CH <sub>3</sub> Cu (0.48) <sup>b</sup>	None	0.27	Et <sub>2</sub> O	<1 <sup>d</sup>		45
CH <sub>3</sub> Cu (0.44) <sup>b</sup>	LiI (0.43) <sup>c</sup>	0.36	Et <sub>2</sub> O	11 <sup>d</sup>	<i>g</i>	<i>f</i>
CH <sub>3</sub> CuPBu <sub>3</sub> (0.37-0.54)	LiI (0.37-0.54) <sup>c</sup>	0.26-0.43	Et <sub>2</sub> O	34	2 98	<i>f</i>
(CH <sub>3</sub> ) <sub>2</sub> CuLi (0.51-0.54)	LiI (0.51-0.54) <sup>c</sup>	0.33-0.43	Et <sub>2</sub> O	90-92	2 98	
(CH <sub>3</sub> ) <sub>2</sub> CuLi (0.47)	None	0.40	Et <sub>2</sub> O	98	2 <sup>d</sup> 98 <sup>d</sup>	
(CH <sub>3</sub> ) <sub>2</sub> CuLi (0.47)	LiI (0.47) <sup>c</sup>	0.40	Et <sub>2</sub> O	97	2 <sup>d</sup> 98 <sup>d</sup>	
CH <sub>3</sub> Cu[P(OBu) <sub>3</sub> ] <sub>3</sub> (0.46)	LiI (0.46) <sup>c</sup>	0.34	Et <sub>2</sub> O	88 <sup>d</sup>	<i>g</i>	
CH <sub>3</sub> Cu[P(OMe) <sub>3</sub> ] <sub>3</sub> (0.47-0.48)	LiI (0.47-0.48) <sup>c</sup>	0.30-0.43	Et <sub>2</sub> O	90-91	2 98	
CH <sub>3</sub> Cu[P(OMe) <sub>3</sub> ] <sub>3</sub> (0.34)	LiI (0.34) <sup>c</sup>	0.29	1,2-Dimethoxyethane	82	2 <sup>d</sup> 98 <sup>d</sup>	
CH <sub>3</sub> Cu[P(OMe) <sub>3</sub> ] <sub>3</sub> (0.38-0.53)	None	0.30-0.43	Et <sub>2</sub> O	<1		<i>f</i>
CH <sub>3</sub> Cu[P(OMe) <sub>3</sub> ] <sub>3</sub> (0.47)	None	0.40	THF	<1 <sup>d</sup>		25 <sup>f</sup>
CH <sub>3</sub> Cu[P(OMe) <sub>3</sub> ] <sub>3</sub> (0.38-0.47)	LiI (0.36-0.48) <sup>c</sup>	0.30-0.40	Et <sub>2</sub> O	71-97	<i>g</i>	
CH <sub>3</sub> Cu[P(OMe) <sub>3</sub> ] <sub>3</sub> (0.47)	MgBr <sub>2</sub> (0.47)	0.40	Et <sub>2</sub> O	73-87	2 98	
CH <sub>3</sub> Cu[P(OMe) <sub>3</sub> ] <sub>3</sub> (0.47)	LiBr (0.47)	0.40	Et <sub>2</sub> O	35 <sup>d</sup>	<i>g</i>	
CH <sub>3</sub> Cu[P(OMe) <sub>3</sub> ] <sub>3</sub> (0.47)	CH <sub>3</sub> Li (0.02)	0.40	Et <sub>2</sub> O	<1 <sup>d</sup>		
CH <sub>3</sub> Cu[P(OMe) <sub>3</sub> ] <sub>3</sub> (0.47)	LiI (0.47) <sup>c</sup>	0.40	THF	48	1 <sup>d</sup> 99 <sup>d</sup>	
CH <sub>3</sub> Cu[P(OMe) <sub>3</sub> ] <sub>3</sub> (0.47)	LiBr (0.47)	0.40	THF	20 <sup>d</sup>	<i>g</i>	8
CH <sub>3</sub> Cu[P(OMe) <sub>3</sub> ] <sub>3</sub> (0.47)	( <i>n</i> -C <sub>6</sub> H <sub>13</sub> ) <sub>4</sub> NI (0.47)	0.40	THF	<1 <sup>d</sup>		<1 <sup>f</sup>

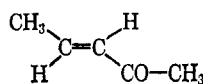
<sup>a</sup> Unless otherwise noted the product compositions listed are average values obtained from two or more reactions. <sup>b</sup> A suspension of the organocopper reagent was employed. The concentration value listed is the calculated value if all the organocopper reagent had been in solution. <sup>c</sup> This LiI was formed in the reaction mixture from methyl lithium and copper(I) iodide or its phosphine or phosphite complex. <sup>d</sup> These data are derived from a single run. <sup>e</sup> This LiI was added to methylcopper which had previously been washed free of halide salts. <sup>f</sup> Uncharacterized higher molecular weight material was also formed in this reaction. <sup>g</sup> The composition of the mixture of stereoisomeric ketones 9 and 10 was not determined in this case.

methylmagnesium iodide in the presence of copper(I) chloride. In the present investigation, we determined the yields of conjugate addition (9 and 10) and 1,2 addition (11 and 12) products and the proportions of stereoisomeric ketones and alcohols. The stereochemistry of the previously unknown alcohols 11 and 12 was established by hydrogenation to form the known<sup>5</sup> saturated alcohols 13a and 14a. The results of these product studies are summarized in Tables I and II.

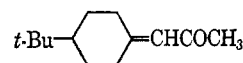
Briefly we found that methylmagnesium derivatives (Table I) gave mixtures of conjugate addition products 9 and 10 in which the less abundant diequatorial *cis* isomer 10 comprised 7-10% of the mixture both in the absence of copper and in the presence of small amounts (1-2 mol %) of a copper catalyst. This result is interesting when considered in the light of our earlier finding<sup>2a</sup> that the conjugate addition reaction is accelerated 10- to 100-fold by the presence of 1-2 mol % of a copper(I) species. The addition of methylcopper derivatives in equimolar amount (Table II) gave mixtures in which the less abundant *cis* isomer 10 comprised 1-2% of the mixture and a mixture of equimolar amounts of methylcopper and dimethylmagnesium gave a value (5% of ketone 10) midway between these two extremes. Thus, it would appear that both metal atoms (magnesium and copper) are present in the aggregate which transfers a methyl group to the  $\beta$ -carbon atom of the  $\alpha,\beta$ -unsaturated ketone and the predominant metal present appears to exert some control over the stereochemistry of addition. However, even in this system we have not detected a stereochemical difference between the apparently uncatalyzed and copper-catalyzed

additions of methylmagnesium derivatives which would be analogous to the difference reported by Inouye and Walborsky. Also of interest was the observation that the stereochemistry of 1,2 addition of various methylmagnesium reagents to the ketone 8 is essentially independent of the other ligands bound to magnesium. A discussion of this observation is presented elsewhere.<sup>2e</sup>

In our earlier studies<sup>2a</sup> involving conjugate additions of methylcopper(I) derivatives to the unsaturated ketones 15 and 16, high yields of conjugate addition



15



16

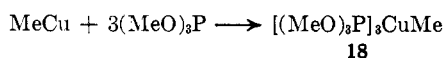
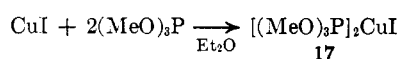
products were obtained with ether solutions of either of the methylcopper(I) complexes 1 or 2 or with the slurry of yellow, insoluble (and presumably polymeric) methylcopper(I) obtained from treatment of copper(I) iodide with 1 equiv of methyl lithium in ether solution. We were therefore surprised to find that, though reaction of the ketone 8 with the dimethylcuprate 2 gave the conjugate addition products 9 and 10 in good yield, the corresponding reaction with the tributylphosphine complex 1 gave relatively poor yields (34%, Table II) accompanied by a viscous, apparently polymeric, material as the major product. We were initially inclined to the view that this polymer formation was the result of the recently described<sup>6</sup> initial conjugate addition of tri-*n*-butylphosphine to the cyclohexenone followed by

(6) (a) R. F. Hudson and P. A. Chopard, *Helv. Chim. Acta*, **46**, 2178 (1963); (b) F. Ramirez, O. P. Madan, and C. P. Smith, *Tetrahedron*, **22**, 567 (1966); (c) R. G. Harvey, *ibid.*, **22**, 2561 (1966); (d) R. G. Harvey and E. V. Jensen, *Tetrahedron Lett.*, 1801 (1963); (e) R. Oda, T. Kawabata, and S. Tanimoto, *ibid.*, 1653 (1964); (f) S. Trippet, *Chem. Commun.*, 468 (1966).

(5) A. V. Kamernitskii and A. A. Akhrem, *J. Gen. Chem. USSR*, **30**, 772 (1960).

further reaction of the intermediate ylide to form high molecular weight products. Although this possibility is difficult to disprove rigorously in the absence of a knowledge of the polymer structure, it was rendered unlikely by control experiments in which the unsaturated ketone **8** was stirred with ether solutions of tri-*n*-butylphosphine or trimethyl phosphite both in the presence and in the absence of copper(I) iodide for periods of time equivalent to the reaction times with methylcopper. In all cases, more than 90% of the unchanged cyclohexenone derivative **8** was recovered.

We subsequently found that an ether-soluble complex of methylcopper(I) could be obtained by reaction of 1 molar equiv of methyllithium with 1 molar equiv of copper(I) iodide in the presence of 3 molar equiv of either tri-*n*-butyl phosphite or trimethyl phosphite. The trimethyl phosphite ester has proved to be a more satisfactory complexing agent than either tri-*n*-butyl phosphite or tri-*n*-butylphosphine because of its volatility (bp 110–111°) and partial water solubility permitting this reagent to be removed readily from the crude reaction products. We have observed that copper(I) iodide can be converted into a crystalline, ether-soluble complex by treatment with 2 molar equiv of trimethylphosphite. This complex has the stoichiometric composition indicated in structure **17**. A cryoscopic deter-



mination of the apparent molecular weight of this complex **17** in benzene solution gave a value of 708 corresponding to 1.62 times the weight of the monomer **17**. This value would be consistent with a dimeric structure (presumably with two halogen bridging atoms) for the complex with partial dissociation in benzene solution. Of course other states of aggregation with partial dissociation could also lead to the observed value.

The observation that 3 molar equiv of trimethyl phosphite are required to obtain complete solution of methylcopper as its complex and that a solution is obtained when equimolar quantities of the copper(I) iodide complex **17**, methyllithium, and trimethyl phosphite are mixed both suggest that the methylcopper complex may have the stoichiometry indicated in structure **18**.<sup>7</sup> Since we have thus far been unable to isolate a pure sample of this complex, it has not been possible to obtain meaningful molecular weight data for a solution of this material. Consequently, the state of aggregation of these soluble phosphite complexes, like the tri-*n*-butylphosphine complex of methylcopper, is not known.

Of interest was the finding that an ether solution of the trimethyl phosphite-methylcopper complex **18** formed from the phosphite, methyllithium, and copper(I) iodide, unlike the phosphite complex **1**, added to the cyclohexenone **8** to form the conjugate addition products **9** and **10** in good yield accompanied by little polymeric material. This observation supports our earlier tentative conclusion that the polymer-forming side reac-

tion with the complex **1** is not the result of the aforementioned conjugated addition of tri-*n*-butylphosphine to the unsaturated ketone **8** since trimethyl phosphite might be expected to undergo a similar side reaction.<sup>6c</sup> In examining this reaction further we were led to prepare an ether suspension of methylcopper(I) from copper(I) iodide and methyllithium and then to separate the insoluble methylcopper. This precipitate was washed with ether at low temperatures until it was free from the lithium iodide which had been present in equimolar amounts in all of the previously studied<sup>2a</sup> ether solutions of copper reagents. Reaction of the unsaturated ketone **8** with an ethereal suspension of this halide-free methylcopper led to the formation of polymeric material; neither of the addition products **9** and **10** could be detected in the crude reaction product. Surprisingly, the same result was obtained when an ether solution of the complex **18** from halide-free methylcopper and 3 molar equiv of trimethyl phosphite was allowed to react with the ketone. Only in the reaction of the unsaturated ketone **8** with the dimethylcuprate **2** were high yields of the conjugate addition products **9** and **10** formed when no lithium iodide was present in the reaction mixture. As indicated in Table II, this tendency of the halide-free methylcopper reagent to polymerize the ketone **8** could be partially avoided by adding 1 molar equiv of lithium iodide to an ether slurry of methylcopper and high yields of conjugate addition products **9** and **10** were obtained when 1 molar equiv of lithium iodide was added to an ether solution of the halide-free phosphite complex **18**. Although added lithium bromide appeared to give poorer yields than lithium iodide, magnesium bromide and lithium iodide were approximately equally effective. In tetrahydrofuran solution similar results were obtained except that poorer yields of addition products **9** and **10** were obtained by adding lithium iodide and lithium bromide to the phosphite complex **18**. However, it was of interest to find that the presence of tetra-*n*-butylammonium iodide in the reaction solution did not lead to the formation of the conjugate addition products **9** and **10**.

Studies of reactions of the unsaturated ketones **19** and **21** with methylcopper derivatives (see Scheme III), summarized in Tables III and IV, offer further evidence for the necessity of some metal derivative (*e.g.*, LiI, MgBr<sub>2</sub>, or CH<sub>3</sub>Li) in the reaction mixture for the successful conjugate addition of a methyl group to an  $\alpha,\beta$ -unsaturated ketone. With ketones **19** and **21**, the absence of such a salt results not in polymerization of the ketone, but in its recovery. Even the solution, presumably containing a complex with the stoichiometry represented by **25**, obtained by reaction of the copper(I) cyanide complex **24**<sup>8</sup> with methyllithium, was capable of adding a methyl group to the end of the conjugated system in ketone **21**. These observations are consistent with our current mechanistic hypothesis (Scheme I) if the further requirement is made that the methylcopper(I) must be complexed (as in **3**) with at least one ligand (*e.g.*, I<sup>−</sup>, CN<sup>−</sup>, CH<sub>3</sub><sup>−</sup>) which places a net negative charge on the copper complex. This additional electron pair supplied by the ligand should facilitate both an electron-donation process (*e.g.*, **3**) and the subsequent transfer of a methyl radical (*e.g.*, **4**).

(7) The alternative possibility exists that the formation constants for these complexes are sufficiently small that an excess of trimethyl phosphite is required in the solutions to prevent separation of the ether-insoluble uncomplexed copper(I) reagents.

(8) Y. Nishiyama, M. Nakagawa, and Y. Suzuki, Japanese Patent 21,321 (Nov 6, 1961); *Chem. Abstr.*, **48**, 4425 (1963).

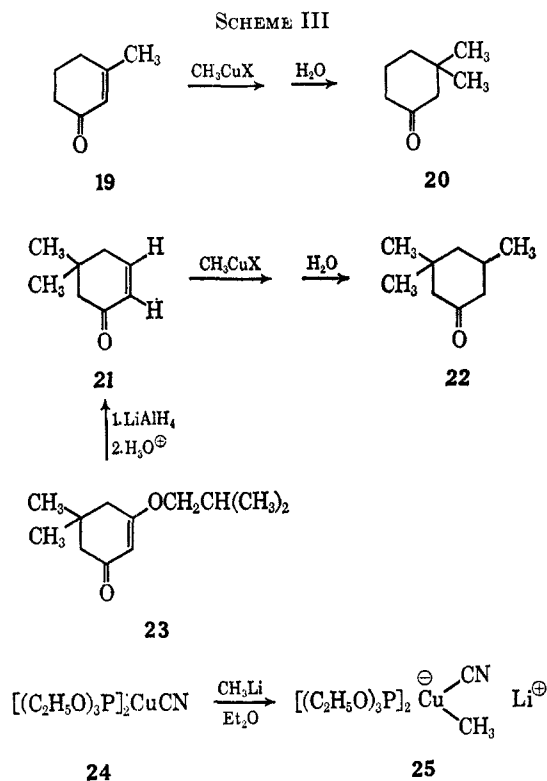


TABLE III

THE PRODUCTS OBTAINED FROM ADDITION OF METHYLCOPPER DERIVATIVES TO 3-METHYL-2-CYCLOHEXENONE (19) IN ETHER SOLUTION

Methylcopper reagent (concn, M)	Concn of lithium iodide, M	Concn of ketone 19, M	Product 20 yield, %	Ketone 19 recovery, %
(CH <sub>3</sub> ) <sub>2</sub> CuLi (0.26)	0.26	0.24	98	1
CH <sub>3</sub> CuPBu <sub>3</sub> (0.31)	0.31	0.24	97	3
CH <sub>3</sub> CuPBu <sub>3</sub> (0.31)		0.24	<1	81
CH <sub>3</sub> Cu[P(OMe) <sub>3</sub> ] <sub>3</sub> (0.31)	0.31	0.24	88	9
CH <sub>3</sub> Cu[P(OMe) <sub>3</sub> ] <sub>3</sub> (0.31)		0.24	<1	70

TABLE IV

THE PRODUCTS OBTAINED FROM ADDITION OF METHYLCOPPER DERIVATIVES TO 5,5-DIMETHYL-2-CYCLOHEXENONE (21) IN ETHER SOLUTION

Methylcopper reagent (concn, M)	Concn of lithium iodide, M	Concn of ketone 21, M	Product 22 yield, %	Ketone 21 recovery, %
CH <sub>3</sub> CuPBu <sub>3</sub> (0.39)	0.39	0.25	92	<1
CH <sub>3</sub> Cu[P(OMe) <sub>3</sub> ] <sub>3</sub> (0.39)	0.39	0.35	93	<1
CH <sub>3</sub> Cu[P(OMe) <sub>3</sub> ] <sub>3</sub> (0.44)		0.33	<1	86
CH <sub>3</sub> Cu <sup>⊖</sup> (CN)[P(OEt) <sub>3</sub> ] <sub>2</sub> Li <sup>⊕</sup> (0.15)		0.11	75	19

The nmr methyl signals for the various methylcopper complexes are summarized in Table V. As would be expected, the methyl signal is found at highest field in those complexes 2 and 25 believed to carry at least a partial negative charge. The observation that the methyl signal is shifted to higher field when lithium iodide is added to the phosphine complex 1 is consistent with the above suggestion that the iodide anion serves to enhance the electron density in the methylcopper complex. The failure to observe any significant shift in the methyl signal of the phosphite complex 18 with added lithium iodide presumably reflects the fact that the metal atom is already tetracoordinate. As a result,

TABLE V  
NUCLEAR MAGNETIC RESONANCE METHYL SIGNALS FOR ETHER SOLUTIONS OF VARIOUS METHYLCOPPER DERIVATIVES

Methylcopper complex <sup>a</sup>	Concn, M	Nmr methyl signal, Hz above TMS at 60 MHz
(CH <sub>3</sub> ) <sub>2</sub> Cu <sup>⊖</sup> Li <sup>⊕</sup> (2)	0.69	82
[(EtO) <sub>3</sub> P] <sub>2</sub> Cu <sup>⊖</sup> (CN)CH <sub>3</sub> Li <sup>⊕</sup> (25)	0.74	80
[(CH <sub>3</sub> O) <sub>3</sub> P] <sub>3</sub> CuMe (18) + LiI <sup>b</sup>	0.70	52
[(CH <sub>3</sub> O) <sub>3</sub> P] <sub>3</sub> CuMe (18)	0.70	55
<i>n</i> -Bu <sub>3</sub> PCuMe (1) + LiI <sup>b</sup>	0.74	47
<i>n</i> -Bu <sub>3</sub> PCuMe (1)	0.62	37

<sup>a</sup> The complexes are written as the simplest formulas which appear to correspond to the correct stoichiometry for formation of the complexes. <sup>b</sup> This lithium iodide was formed during the preparation of the methylcopper.

coordination of the copper with iodide ion would probably require loss of one of the phosphite ligands.

### Experimental Section<sup>9</sup>

**Preparation of the Starting Materials.**—The previously described<sup>10,11</sup> condensation of ethyl crotonate with the sodium enolate of ethyl acetoacetate gave 5-methylcyclohexane-1,3-dione (yield 25%) as white needles from ethyl acetate: mp 126–128° (lit.<sup>11</sup> mp 128–129°); ir (CHCl<sub>3</sub>), 1720 (shoulder), 1705, and 1585 (broad) cm<sup>-1</sup> (partially enolic β-diketone); uv maximum, 254 mμ (ε 18,000); nmr (CDCl<sub>3</sub>), δ 10.98 (1 H singlet, OH), 5.47 (1 H singlet, vinyl CH), 1.7–2.8 (5 H multiplet, aliphatic CH), and 1.08 (1 H multiplet, CH<sub>3</sub>-C).<sup>12</sup> This diketone was converted<sup>10</sup> into 3-ethoxy-5-methyl-2-cyclohexenone isolated in 67% yield as a colorless liquid: bp 78–79.2° (0.3 mm), *n*<sup>20</sup><sub>D</sub> 1.4891 (lit.<sup>10</sup> bp 83° (0.1 mm)); ir (CCl<sub>4</sub>), 1655 (conjugated C=O) and 1610 cm<sup>-1</sup> (conjugated C=C); uv maximum 249 mμ (ε 17,300); nmr (CCl<sub>4</sub>), δ 5.18 (1 H singlet, vinyl CH), 3.92 (2 H quadruplet, *J* = 7 Hz, CH<sub>2</sub>O), 1.5–2.5 (5 H multiplet, aliphatic CH), 1.37 (3 H triplet, *J* = 7 Hz, ethoxy CH<sub>3</sub>), and 1.10 (3 H multiplet, CH<sub>3</sub>C); mass spectrum, molecular ion, *m/e* 154, abundant fragment peaks, *m/e* 112, 84, 69, 68, 43, 29, and 27.<sup>12</sup> Reduction of this enol ether with LiAlH<sub>4</sub> and subsequent acid-catalyzed hydrolysis<sup>10</sup> afforded the **unsaturated ketone 8** in 83% yield: bp 55.5–60° (4.5 mm); *n*<sup>20</sup><sub>D</sub> 1.4742 (lit.<sup>10</sup> bp 60° (8 mm); *n*<sup>25</sup><sub>D</sub> 1.4739); ir (CCl<sub>4</sub>), 1680 (conjugated C=O), 1635, and 1615 cm<sup>-1</sup> (conjugated C=C); uv maximum, 225 mμ (ε 10,900); nmr (CCl<sub>4</sub>), δ 6.7–7.1 (1 H multiplet, vinyl CH), 5.88 (1 H doublet (*J* = 10 Hz) of partially resolved multiplets, vinyl CH), 1.7–2.7 (5 H multiplet, aliphatic CH), and 1.09 (3 H multiplet, CH<sub>3</sub>C); mass spectrum, molecular ion, *m/e* 110, abundant fragment peaks, *m/e* 68, 41, 40, 39, and 27.<sup>12</sup>

Ethereal solutions of dimethylmagnesium (from dimethylmercury), methylmagnesium bromide, and methyl lithium (from methyl bromide) were prepared and standardized (with dimethylphenylsilyl chloride) as described previously.<sup>2</sup> Commercial halide-free ethereal solutions of methyl lithium were also employed.<sup>13</sup> An ether solution of anhydrous magnesium bromide

(9) All melting points are corrected and all boiling points are uncorrected. Unless otherwise stated magnesium sulfate was employed as a drying agent. The infrared spectra were determined with a Perkin-Elmer Model 237 infrared recording spectrophotometer fitted with a grating. Unless otherwise stated, the ultraviolet spectra were determined in 95% ethanol with a Cary recording spectrophotometer, Model 14. The nmr spectra were determined at 60 MHz with a Varian Model A-60 nmr spectrometer. The chemical shift values are expressed either in Hz or δ values (parts per million) relative to a tetramethylsilane internal standard. The mass spectra were obtained with a CEC Model 21-130 or a Hitachi (Perkin-Elmer) mass spectrometer. The microanalyses were performed by Dr. S. M. Nagy and his associates. All transfers and reactions involving organometallic reagents were performed under a nitrogen atmosphere.

(10) J. P. Blanchard and H. L. Goering, *J. Amer. Chem. Soc.*, **73**, 5863 (1951).

(11) A. W. Crossley and N. Renouf, *J. Chem. Soc.*, **107**, 602 (1915).

(12) The characterization of this material in our laboratory was performed by Mr. R. W. Giese.

(13) These solutions, purchased from Foote Mineral Co., were found to be 1.33–1.55 M in methyl lithium (ethylene dibromide standardization procedure) and to be 0.04–0.06 M in halide (Volhard titration).

(from ethylene dibromide) was prepared and standardized as previously described.<sup>2</sup> Ethereal solutions of anhydrous lithium iodide and anhydrous lithium bromide, standardized by Volhard titrations, were prepared by a modification of a previously described procedure.<sup>14</sup> To a suspension of 2.46 g (0.310 mol) of lithium hydride in 100 ml of ether was added, dropwise and with stirring over a 45-min period, a solution of 31.7 g (0.125 mol) of iodine in 250 ml of ether. The resulting mixture was stirred for 10 hr and then filtered to give a clear, colorless solution of lithium iodide which was 0.672 *M* in iodide ion. The solution remained colorless when it was stored in the dark over a small amount of lithium hydride. A comparable reaction of 4.00 g (0.504 mol) of lithium hydride with 28.0 g (0.175 mol) of bromine in 250 ml of ether gave, after filtration, a pale orange solution of lithium bromide which was 1.202 *M* in bromide ion. The preparation and/or purification of the complexing agents *N,N,N',N'*-tetramethylethylenediamine and  $\beta$ -methoxyethylidimethylamine is described elsewhere.<sup>20</sup> Commercial trimethyl phosphite was distilled twice and then stored over Linde Molecular Sieves, No. 5A: bp 110–111°;  $n_D^{25}$  1.4070 (lit. bp 110° (737 mm));<sup>15</sup>  $n_D^{18}$  1.4094<sup>16</sup>). Commercial tri-*n*-butyl phosphite was purified by distillation, bp 138–140° (20 mm) (lit.<sup>17</sup> bp 122° (12 mm)).

Copper(I) iodide was purified according to a previously described procedure;<sup>18a</sup> the reprecipitated salt was washed successively with water, ethanol, and pentane and then dried under reduced pressure. The following procedure was employed to obtain suspensions of halide-free methylcopper. To a cold (–70°) solution of 1.28 g (1.00 mmol) of the crude bis-(di-*n*-butyl sulfide) complex<sup>18b</sup> of copper (I) iodide in 10 ml of ether was added 2.0 ml of an ethereal solution containing 2.36 mmol of methyllithium. The precipitate of methylcopper was separated by centrifugation and the supernatant liquid was removed through a cannula employing a positive nitrogen pressure. The residual methylcopper was washed with four 10-ml portions of cold (0°) ether. Titration for halogen content indicated that 0.9% of the total halide ion remained in the precipitated methylcopper and 98.5% of the total halide ion was in the ethereal solutions. In a second preparation, a cold (–70°) slurry of 315 mg (1.64 mmol) of copper(I) iodide in 10 ml of ether was treated with 1.65 ml of an ethereal solution containing 1.64 mmol of methyllithium. The precipitated methylcopper was separated and washed with four 10-ml portions of cold (0°) ether as previously described. The methylcopper was quenched with water and then dissolved in dilute aqueous HNO<sub>3</sub>; the combined ethereal solutions were concentrated; and the residue was dissolved in dilute, aqueous HNO<sub>3</sub>. Aliquots of each aqueous solution were analyzed for halide ion content (Volhard titration) and for copper content. The copper analyses were performed by conversion of the copper into an aqueous solution of the copper(II)-ammonia complex which was determined photometrically by measuring the optical density of the solution at 650 m $\mu$ .<sup>18c</sup> These results indicated the presence of 1.49 mmol of copper and 0.0151 mmol of halide ion in the precipitate and 0.348 mmol of copper and 1.66 mmol of halide ion in the ether solution.

The tri-*n*-butylphosphine complex of copper(I) iodide and lithium dimethylcuprate (2) were prepared as previously described.<sup>2a</sup> Cryoscopic determination of the molecular weight of a benzene solution (0.135 to 0.359 *m*) of the copper(I) iodide-tri-*n*-butylphosphine complex gave a value of 1206 corresponding to 3.07 times the molecular weight (lit.<sup>19a</sup> 3.36). Ether solutions of the tri-*n*-butylphosphine-methylcopper complex (1) were prepared either by treatment of an ether solution of the copper(I) iodide complex with methyllithium or by treatment of an ether slurry of methylcopper with 1 molar equiv of the phosphine.

(14) M. D. Taylor and L. R. Grant, *J. Amer. Chem. Soc.*, **77**, 1507 (1955).

(15) A. W. Reitz and R. Sabathy, *Z. Phys. Chem. (Leipzig)*, **B**, **41**, 154 (1938).

(16) D. Voigt, *Ann. Chim. (Paris)*, [4] **12**, 429 (1949).

(17) W. Gerrard, *J. Chem. Soc.*, 1464 (1940).

(18) (a) G. B. Kauffman and L. A. Teter, *Inorg. Syn.*, **7**, 9 (1963). (b) This crude, ether-soluble complex was prepared according to the unpublished directions of Professor G. M. Whitesides. Addition of 19.0 g (0.10 mol) of purified copper(I) iodide to 29.2 g (0.20 mol) of di-*n*-butyl sulfide led to solution of the copper salt accompanied by the evolution of heat. The resulting deep red-orange liquid was filtered and stored under a nitrogen atmosphere. (c) A. R. Olson, C. W. Koch, and G. C. Pimentel, "Introductory Quantitative Chemistry," W. H. Freeman and Co., San Francisco, Calif., 1956, p 426.

(19) (a) F. G. Mann, D. Purdie, and A. F. Wells, *J. Chem. Soc.*, 1503 (1936). (b) A. E. Arbutov, *Zh. Russ. Fiz. Khim. Obshchest.*, **38**, 293 (1906); *Chem. Zent.*, **77**, 750 (1906).

To a suspension of 1.62 g (8.5 mmol) of copper (I) iodide in 14 ml of ether was added, dropwise with stirring, 2.12 g (2.00 ml, 17 mmol) of trimethyl phosphite. When the resulting mixture was heated to reflux, a colorless solution resulted. When cooled to 0°, this solution deposited 3.16 g (85%) of the complex 17 as white prisms, mp 68–70.4°. Recrystallization from a small volume of ether afforded 2.81 g (75%) of pure complex 17: mp 70.2–71.4° (lit.<sup>19b</sup> mp 69–70°); nmr (CCl<sub>4</sub>),  $\delta$  3.72 (doublet with *J* = 11.2 Hz, POCH<sub>3</sub>). For comparison, pure trimethyl phosphite has an nmr (CCl<sub>4</sub>) doublet (*J* = 11.4 Hz) at  $\delta$  3.46.

*Anal.* Calcd for C<sub>6</sub>H<sub>18</sub>CuIO<sub>3</sub>P<sub>2</sub>: C, 16.43; H, 4.14; Cu, 14.49; I, 28.94; P, 14.12; mol wt, 439. Found: C, 16.51; H, 4.08; Cu, 14.15; I, 28.67; P, 13.90; mol wt, 708 (1.62 times monomer, cryoscopic in benzene, 0.095–0.0206 *m*).

A cold (0°) ether solution of the complex 17, prepared from 1.40 g (7.3 mmol) of copper(I) iodide, 1.808 g (14.5 mmol) of trimethyl phosphite, and 15 ml of ether, was treated with 6 ml of an ether solution containing 7.2 mmol of methyllithium. An immediate bright yellow precipitate of methylcopper separated and did not redissolve after stirring for 10 min. However, when an additional 904 mg (7.2 mmol) of trimethyl phosphite was added, the precipitated methylcopper dissolved immediately to give a colorless solution of the methylcopper complex 18. Alternatively, a cold (0°) ethereal suspension of methylcopper, prepared from 296 mg (1.56 mmol) of copper(I) iodide and 1.54 mmol of methyllithium in 5 ml of ether was treated, portionwise, with 580 mg (4.68 mmol) of trimethyl phosphite. Although it was evident that part of the methylcopper had dissolved after 1 and 2 molar equiv of the phosphite had been added, it was necessary to add the third molar equivalent of the phosphite before complete solution of the methylcopper was achieved. In trial experiments employing tri-*n*-butyl phosphite, similar behavior was observed. However, since the butyl phosphite complex appeared to offer no advantages over the methyl phosphite complex 18, it was not investigated further. Ether solutions of the methyl phosphite complex 18 were stable at 0° for 5–10 min after which time they began to develop a turbidity.

To a solution of 16.6 g (0.100 mol) of redistilled triethyl phosphite (bp 157–158°) in 25 ml of benzene was added, portionwise with stirring and cooling, 4.45 g (49.8 mmol) of copper(I) cyanide. After the resulting mixture had been stirred for 15 min, it was filtered to remove a small amount of insoluble material and then concentrated under reduced pressure. The residual tan solid (20.8 g or 98%) was recrystallized from hexane to separate the pure copper(I) complex 24 as white prisms: mp 120–120.9° (lit.<sup>8</sup> mp 120°); ir (CCl<sub>4</sub>), 2125 cm<sup>-1</sup> (C≡N); nmr (CCl<sub>4</sub>),  $\delta$  3.99 (12 H broadened quintet, both *J* values of ~7 Hz, P–O–CH<sub>2</sub>) and 1.23 (18 H triplet, *J* = 7 Hz, ethoxy CH<sub>3</sub>). A sample of triethyl phosphite has nmr (CCl<sub>4</sub>) peaks at  $\delta$  3.80 (quintet with both *J* values of ~7 Hz) and 1.22 (triplet, *J* = 7 Hz).

*Anal.* Calcd for C<sub>13</sub>H<sub>30</sub>CuNO<sub>3</sub>P<sub>2</sub>: C, 37.01; H, 7.17; Cu, 15.06; N, 3.32; P, 14.68; mol wt 422. Found: C, 37.20; H, 7.14; Cu, 14.97; N, 3.31; P, 14.40; mol wt, 1462 (3.48 times monomer, cryoscopic in benzene, 0.111–0.172 *m*).

To prepare the methylcopper complex 25, a cold (0°) solution of 1.300 g (3.08 mmol) of the bis(triethyl phosphite) complex (24) of copper(I) cyanide in 10 ml of ether was treated with 2.00 ml of an ether solution containing 3.08 mmol of methyllithium. The resulting colorless solution of the complex 25 is the most stable complex of methylcopper that we have encountered thus far; the ether solution is stable for at least several hours at 25° and for several days at 0°.

The nmr methyl signals for ether solutions of the various methylcopper derivatives at ca. 25° are listed in Table V. In each case, the methyl signal appears as a sharp singlet.

**Preparation of the Epimeric Ketones 9 and 10.** **A. The *cis* Isomer 10.**—Following a previously described procedure,<sup>20</sup> a solution of 100 g of 3,5-dimethylphenol in ethanol was hydrogenated over Raney nickel catalyst at 190° and 2100 psi. Distillation of the crude product gave 98 g (95%) of epimeric alcohols as a colorless liquid, bp 71–75° (5 mm),  $n_D^{25}$  1.4527 (lit.<sup>20</sup> bp 75–76° (10 mm),  $n_D^{25}$  1.4530), which solidified on cooling. Two recrystallizations from petroleum ether (bp 30–60°) separated 71.8 g (69.5%) of one or more of the epimeric 3,5-dimethylcyclohexanols as white needles, mp 36–38.2° (lit.<sup>20</sup> 38–38.5°). Oxidation of 13.0 g of the crystalline alcohol with aqueous chromic acid yielded 6.20 g (51%) of the crude *cis* ketone 10 as a pale

(20) L. Alquist and coworkers, *Ark. Kemi*, **14**, 171 (1958).

yellow liquid: bp 82–83° (35 mm);  $n_D^{25}$  1.4547 (lit.<sup>20</sup> bp 102° (65 mm);  $n_D^{25}$  1.4530). A 5.0-g sample of the crude ketone was converted to the oxime of the *cis* ketone 10 which separated from petroleum ether as 3.05 g (56.6%) of white needles, mp 76.5–77.6° (lit.<sup>20</sup> 76.4–77.2°). Hydrolysis of 2.0 g of this oxime with aqueous oxalic acid followed by distillation of the crude product afforded 1.41 g (79%) of the pure<sup>21</sup> *cis* ketone 10: bp 79° (22 mm);  $n_D^{25}$  1.4412 (lit.<sup>20</sup> bp 102° (60 mm);  $n_D^{25}$  1.4398); ir (CCl<sub>4</sub>), 1715 cm<sup>-1</sup> (C=O); nmr (CCl<sub>4</sub>),  $\delta$  1.00 (multiplet, CH<sub>3</sub>C) superimposed on a multiplet at 1.1–2.5 (aliphatic CH); mass spectrum, molecular ion, *m/e* 126, abundant fragment peaks, *m/e* 111, 69, 56, 55, 42, 41, and 39.

**B. The *trans* Isomer 9.**—Employing a modification of the previously described procedure,<sup>4</sup> a cold (0°) solution of lithium dimethylcuprate (2), from 1.30 g (6.7 mmol) of copper(I) iodide and 12 mmol of methyl lithium in 23 ml of ether, was treated with a solution of 370 mg (3.35 mmol) of the ketone 8 in 3 ml of ether. After the mixture had been stirred for 15 min, it was poured into an aqueous solution (pH 8) of NH<sub>4</sub>Cl and NH<sub>3</sub>. The organic phase was combined with the ethereal extract of the aqueous phase and then washed successively with aqueous NH<sub>4</sub>Cl, water, and aqueous NaCl. After the ethereal solution had been dried and concentrated, distillation in a short-path still separated 368 mg (87%) of the *trans* ketone 9,  $n_D^{25}$  1.4470 (lit.<sup>22</sup>  $n_D^{25}$  1.4465) which contained<sup>21</sup> 2% of the *cis* isomer 10 (eluted first) and 98% of the *trans* isomer 9 (eluted second). A collected<sup>21</sup> sample of the *trans* ketone 9 was used for further characterization: ir (CCl<sub>4</sub>), 1715 cm<sup>-1</sup> (C=O); nmr (CCl<sub>4</sub>),  $\delta$  1.8–2.6 (6 H multiplet, aliphatic CH), 1.57 (2 H triplet, *J* = 5 Hz, CH<sub>2</sub> at C-4), and 0.97 (6 H doublet, *J* = 6 Hz, CH<sub>3</sub>-C); mass spectrum, molecular ion, *m/e* 126, abundant fragment peaks, *m/e* 111, 69, 56, 55, 42, 41, and 39. A 103-mg sample of this *trans* ketone 9 was converted into 178 mg (71%) of the crude 2,4-dinitrophenylhydrazone which was recrystallized from ethanol to separate 129 mg (52%) of the pure 2,4-dinitrophenylhydrazone as orange needles, mp 108.4–110° (lit.<sup>22</sup> mp 109.6–110.3°).

**Preparation of the Epimeric Alcohols 11 and 12.**—To a cold (0°) solution of 90 mmol of methyl lithium in 80 ml of ether was added, dropwise and with stirring over a 30-min period, a solution of 6.00 g (54.6 mmol) of the unsaturated ketone 8 in 10 ml of ether. The resulting mixture was poured into water and the resulting aqueous phase was extracted with ether. After the combined ether solutions had been washed with water and aqueous NaCl, they were dried and concentrated to leave 6.20 g of crude product which was composed<sup>23,24</sup> of 33% of the *cis* alcohol 11 (eluted first) and 67% of the *trans* alcohol 12 (eluted second). Samples of each of the alcohols 11 and 12 were collected<sup>24</sup> for characterization. The *cis* alcohol 11 was obtained as a colorless liquid: ir (CCl<sub>4</sub>), 3620 and 3475 cm<sup>-1</sup> (unassociated and associated OH); nmr (CCl<sub>4</sub>),  $\delta$  5.3–5.5 (2 H multiplet, vinyl CH), 1.1–2.4 (5 H multiplet, aliphatic CH), 1.20 (3 H singlet, CH<sub>3</sub>-C-O) and 0.97 (3 H doublet, *J* = 5.5 Hz, CH<sub>3</sub>-C); mass spectrum, molecular ion, *m/e* 126, abundant fragment peaks, *m/e* 108, 93, 91, 79, 77, and 39.

*Anal.* Calcd for C<sub>8</sub>H<sub>14</sub>O: C, 76.14; H, 11.18. Found: C, 75.80; H, 11.33.

The *trans* alcohol 12, a colorless liquid, has the following spectral characteristics: ir (CCl<sub>4</sub>), 3610 and 3425 cm<sup>-1</sup> (unassociated and associated OH); nmr (CCl<sub>4</sub>),  $\delta$  5.3–5.5 (2 H multiplet, vinyl CH), 1.2–2.4 (5 H multiplet, aliphatic CH), 1.20 (3 H singlet, CH<sub>3</sub>-C-O), and 0.95 (3 H multiplet, CH<sub>3</sub>-C); mass spectrum, molecular ion, *m/e* 126, abundant fragment peaks, *m/e* 106, 105, 93, 91, 78, 77, 44, and 39.

*Anal.* Calcd for C<sub>8</sub>H<sub>14</sub>O: C, 76.14; H, 11.18. Found: C, 76.06; H, 11.02.

The *cis* alcohol 11 would be expected to exist primarily in the indicated conformation with both methyl groups in equatorial or pseudo-equatorial positions. The two conformations 12a and b for the *trans* alcohol 12 are probably of similar energy with some preference for conformation 12a which avoid the 1,3 interaction between an axial methyl group and a pseudo-axial hydroxyl function. The observations that the *cis* alcohol, with a relatively

hindered pseudo-axial hydroxyl function, is eluted more rapidly from gas chromatography<sup>23,24</sup> and has a more abundant fragment peak in its mass spectrum at 108 (M<sup>+</sup> - H<sub>2</sub>O) both are in keeping with the assigned stereochemistry. To establish the stereochemical assignments, a solution of 6.20 g (49.3 mmol) of the mixture of unsaturated alcohols 11 and 12 from the above reaction in 50 ml of ethanol was hydrogenated at 24° and atmospheric pressure over the catalyst from 325 mg of PtO<sub>2</sub> in the presence of 8 mg of NaNO<sub>2</sub>.<sup>25</sup> After 9.0 hr the hydrogen uptake (1100 ml, 45.0 mmol or 0.93 equiv) ceased and the reaction mixture was filtered and concentrated to leave 6.11 g of the crude product as an orange oil: ir (CCl<sub>4</sub>), 3600 and 3350 cm<sup>-1</sup> (unassociated and associated OH). This crude product was composed<sup>24</sup> of the *cis* alcohol 13a (ca. 29%, first eluted) and the *trans* alcohol 14a (ca. 71%, eluted second). Pure samples of each of the saturated alcohols were collected for characterization. The *cis* alcohol 13a was a colorless liquid:  $n_D^{25}$  1.4515 (lit.<sup>5</sup>  $n_D^{25}$  1.4527); ir (CCl<sub>4</sub>), 3600 and 3450 cm<sup>-1</sup> (unassociated and associated OH); nmr (CCl<sub>4</sub>),  $\delta$  1.90 (1 H singlet, OH), 1.0–2.0 (9 H multiplet, aliphatic CH), 1.16 (3 H singlet, CH<sub>3</sub>-C-O) and 0.87 (3 H doublet, *J* = 5.5 Hz, CH<sub>3</sub>-C); mass spectrum, molecular ion, *m/e* 128, abundant fragment peaks, *m/e* 95, 85, 71, 58, 43, 41, and 39. Reaction of a 32-mg sample of this *cis* alcohol 13a with the anhydride from 3,5-dinitrobenzoic acid<sup>26</sup> yielded 69.1 mg (85%) of the crude ester 13b. Recrystallization from petroleum ether afforded 51.3 mg (64%) of the pure 3,5-dinitrobenzoate 13b as white needles: mp 119–120° (lit.<sup>5</sup> mp 118–119°); ir (CCl<sub>4</sub>), 1730 (ester C=O), 1545, and 1330 cm<sup>-1</sup> (NO<sub>2</sub>).

The *trans* alcohol 14a was a colorless liquid:  $n_D^{25}$  1.4575 (lit.<sup>5</sup>  $n_D^{25}$  1.4594); ir (CCl<sub>4</sub>), 3600 and 3350 cm<sup>-1</sup> (unassociated and associated OH); nmr (CCl<sub>4</sub>),  $\delta$  3.39 (1 H singlet, OH), 1.0–1.9 (9 H multiplet, aliphatic CH), 1.17 (3 H singlet, CH<sub>3</sub>-C-O) and 0.89 (3 H doublet, *J* = 5 Hz, CH<sub>3</sub>-C); mass spectrum, molecular ion, *m/e* 128, abundant fragment peaks, *m/e* 95, 85, 71, 58, 43, and 41. Reaction of 35 mg of the *trans* alcohol 14a with the 3,5-dinitrobenzoic anhydride<sup>26</sup> gave 76 mg (85%) of the crude ester 14b as a yellow oil. Recrystallization from petroleum ether separated 60.7 mg (68%) of the 3,5-dinitrobenzoate 14b as white needles: mp 56–59° (lit.<sup>5</sup> mp 59.5–61°); ir (CCl<sub>4</sub>), 1720 (ester C=O), 1540, and 1340 cm<sup>-1</sup> (NO<sub>2</sub>).

In an additional experiment, a solution of 20 mg (0.17 mmol) of the pure<sup>24</sup> *trans* unsaturated alcohol 12 in 0.60 ml of ethanol containing 1  $\mu$ l of aqueous 80% NaNO<sub>2</sub><sup>25</sup> was hydrogenated at 25° and atmospheric pressure over the catalyst from 10 mg of PtO<sub>2</sub>. After 1.3 hr the hydrogen uptake (3.5 ml or 0.94 equiv) ceased and the crude product was isolated as previously described. A collected<sup>24</sup> sample of the single component detected in the crude product was identified with the previously described sample of the *trans* alcohol 14a by comparison of gas chromatographic retention times and infrared and mass spectra. Under conditions where the nmr peak width at half-height was 1.2 Hz for internal tetramethylsilane, the value for the singlet methyl peak in the *cis* alcohol 13a was 1.6 Hz and the corresponding value for the *trans* alcohol 14a was 1.9 Hz. As noted elsewhere,<sup>27</sup> long-range coupling should cause this peak to be broader for an axial methyl group than for an equatorial methyl group. As noted earlier for the unsaturated alcohols 11 and 12, the *cis* alcohol 13a would be expected to exist predominantly in the indicated conformation with two equatorial methyl groups, whereas the *trans* isomer 14a would presumably be composed of a mixture of conformers 14a and 14c in which one of the two methyl groups is axial. Thus, this observation is consistent with the stereochemistry assigned<sup>5</sup> to the two alcohols 13a and 14a for other reasons.

**Reaction of 5-Methyl-2-cyclohexenone (8) with Methyl Organometallic Reagents.**—The results of quantitative product analyses for the mixtures obtained from reaction of the conjugated ketone 8 with methylmagnesium derivatives and methylcopper derivatives are summarized in Tables I and II. In these experiments, a solution (or in certain cases, a suspension) of the organometallic reagent and any additives was prepared in the solvent indicated in the tables. To this cold (0°) solution of organometallic reagent was added with stirring, a solution containing a weighed amount of *n*-butylbenzene (an internal standard for gas chromatographic analysis) and a weighed sample of the ketone 8. The

(21) A gas chromatography column packed with 1,2,3-tris( $\beta$ -cyanoethoxy)propane (TCEP) suspended on Chromosorb P was employed for this analysis.

(22) N. L. Allinger, *J. Amer. Chem. Soc.*, **81**, 232 (1959).

(23) A gas chromatography column packed with Carbowax 20M suspended on Chromosorb P was employed for this analysis.

(24) A gas chromatography column packed with silicone fluid, no. XE-60, suspended on Chromosorb P was employed for this analysis.

(25) M. C. Dart and H. B. Henbest, *J. Chem. Soc.*, 3563 (1960).

(26) The esterification procedure of J. H. Brewster and C. J. Ciotti, Jr. (*J. Amer. Chem. Soc.*, **77**, 6214 (1955)) was employed.

(27) C. W. Shoppee, F. D. Johnson, R. E. Lack, and S. Sternhall, *Chem. Commun.*, 347 (1965).

initial concentrations of the organometallic reagent, any additives, and the ketone **8** after the solutions (total volume 7–15 ml) had been mixed are specified in Tables I and II. The resulting solutions were stirred at 0° for 5–10 min and then poured into saturated aqueous NH<sub>4</sub>Cl adjusted to pH 8–9 by the addition of aqueous NH<sub>3</sub>. After the resulting mixtures had been extracted with ether, the ethereal solutions were washed with aqueous NaCl, dried, concentrated, and analyzed by gas chromatography.<sup>21,24</sup> The gas chromatography equipment was calibrated with known mixtures of authentic samples of the internal standard, the alcohols **11** and **12**, and the ketones **8**, **9**, and **10**. On one column,<sup>21</sup> the alcohols were dehydrated and the ketones and standard were eluted with the following retention times: *n*-butylbenzene, 9.0 min; *cis* ketone **10**, 21.6 min; *trans* ketone **9**, 24.6 min; and unsaturated ketone **8**, 40.4 min. The second column<sup>24</sup> which did not completely resolve the ketones **9** and **10** was used to determine yields and to analyze the mixture of alcohols **11** and **12**. On this column,<sup>24</sup> the following relative retention times were obtained: *n*-butylbenzene, 7.0 min; *cis* alcohol **11**, 10.2 min; *trans* alcohol **12**, 13.2 min, and the mixture of ketones **9** and **10**, 20.3 min. Unless otherwise noted in Table I the calculated yields of products exceeded 90% and in Tables I and II the product compositions are average values from two or more reactions. In all cases the individual values differed from the average values listed by less than 2%.

In order to examine the higher molecular weight products formed when halide-free methylcopper derivatives were mixed with the unsaturated ketone **8**, a cold (0°) solution of the complex **18** (0.52 M concentration), from 20.8 mmol of halide-free methylcopper and 7.74 g (62.4 mmol) of trimethyl phosphite, in 40 ml of ether was treated with 1.65 g (15 mmol) of the ketone **8** and the resulting mixture was stirred at 0° for 20 min. After the reaction solution had been quenched in aqueous NH<sub>4</sub>Cl and NH<sub>3</sub>, the crude organic product, isolated as previously described, was 2.01 g brown viscous oil. Distillation in a short-path still afforded no significant amount of material boiling in the range of ketones **8**–**10**. A fraction of the crude product did distill at higher temperatures as 102 mg of a pale yellow viscous oil (0.1 mm and 150–185° bath) and 120 mg of a pink glassy material (0.1 mm and 185–195° bath). The higher boiling of these two fractions had infrared peaks (CCl<sub>4</sub>) at 1710 (strong), 1685 (shoulder), and 1620 (weak) cm<sup>-1</sup> with broad nmr absorption in the regions  $\delta$  1.2–3.0 and 0.7–1.2.

As control experiments, solutions containing weighed samples of *n*-butylbenzene (an internal standard), 0.500 mmol of the unsaturated ketone **8**, and 0.500 mmol of the phosphorus derivative to be tested were stirred for 15 min at 25° and subjected to the isolation and analysis procedures described above. The following phosphorus derivatives gave the per cent recovery of unchanged ketone **8**: tri-*n*-butylphosphine, 100% recovery; tri-*n*-butylphosphine complex of copper(I) iodide, 96% recovery; trimethyl phosphite, 98% recovery; bis(trimethyl phosphite) complex of copper(I) iodide, 94% recovery.

**3,3-Dimethylcyclohexanone (20).**—To a cold (0°) solution of lithium dimethylcuprate (**2**), prepared from 9.00 g (47 mmol) of copper(I) iodide and 111 mmol of methyl lithium in 138 ml of ether, was added, dropwise and with stirring over a 15-min period, a solution of 5.00 g (45.5 mmol) of redistilled 3-methyl-2-cyclohexenone (**19**), bp 84.5–85° (13 mm), during which some methylcopper separated from the reaction mixture as a yellow precipitate. The resulting mixture was stirred at 25° for 15 min and then poured in an aqueous solution (pH 8–9) of NH<sub>3</sub> and NH<sub>4</sub>Cl. The ethereal extract of the mixture was washed with aqueous NaCl, dried, concentrated, and distilled to separate 4.8 g of colorless liquid, bp 71–71.5° (19 mm), which contained<sup>24</sup> ca. 10% of an unknown component eluted first and ca. 90% of the saturated ketone **20**.<sup>28</sup> A collected<sup>24</sup> sample of the pure ketone **20** has the following spectral peaks: ir (CCl<sub>4</sub>), 1715 cm<sup>-1</sup> (C=O); nmr (CCl<sub>4</sub>),  $\delta$  1.2–2.4 (8 H multiplet, aliphatic CH) and 0.96 (6 H singlet, CH<sub>3</sub>C); mass spectrum, molecular ion peak, *m/e* 126, abundant fragment peaks, *m/e* 111, 83, 69, 56, 55, 42, 41, and 39.

(28) G. Buchi, O. Jeger, and L. Ruzicka (*Helv. Chim. Acta*, **31**, 245 (1948)) report the ketone **20** to boil at 62–65° (13 mm).

Reaction of 110 mg of this ketone **20** with excess 2,4-dinitrophenylhydrazine in acidic methanol yielded 213 mg (86%) of the 2,4-dinitrophenylhydrazone as orange needles from ethanol, mp 139.6–140.6° (lit.<sup>28</sup> mp 139°).

**5,5-Dimethyl-2-cyclohexenone (21).**—Following the general procedure described earlier,<sup>29</sup> reaction of 50 g (0.357 mol) of 5,5-dimethylcyclohexane-1,3-dione with 10 ml of isobutyl alcohol and 1.1 g of *p*-toluenesulfonic acid in 275 ml of refluxing benzene for 3.5 hr yielded 63.0 g (90%) of 3-isobutoxy-5,5-dimethyl-2-cyclohexenone (**23**) as a colorless liquid: bp 79–83° (0.07 mm); *n*<sup>20</sup><sub>D</sub> 1.4777 (lit.<sup>29</sup> bp 76° (0.1 mm); *n*<sup>18</sup><sub>D</sub> 1.4810); ir (CCl<sub>4</sub>), 1665 (conjugated C=O) and 1615 cm<sup>-1</sup> (conjugated C=C); nmr (CCl<sub>4</sub>),  $\delta$  5.15 (1 H singlet, vinyl CH), 3.58 (2 H doublet, *J* = 6 Hz, CH<sub>2</sub>O), 1.5–2.5 (5 H multiplet, aliphatic CH); 1.03 (6 H singlet, CH<sub>3</sub>C) and 0.96 (3 H doublet, *J* = 6 Hz, CH<sub>3</sub>C); mass spectrum, weak molecular ion peak at *m/e* 196, abundant fragment peaks at *m/e* 124, 68, 58, 44, and 43.

Reduction of 60 g (0.306 mol) of this enol ether **23** with 5.00 g (0.132 mole) of LiAlH<sub>4</sub> in 350 ml of ether and subsequent hydrolysis with aqueous sulfuric acid following previously described procedures<sup>10,29a,30</sup> yielded 33.6 g (88%) of crude neutral product. Fractional distillation through a 90-cm spinning-band column separated 27.1 g of pure<sup>24</sup> material, bp 74–75° (11 mm), and *n*<sup>20</sup><sub>D</sub> 1.4680 (lit. bp 75° (15 mm),<sup>29a</sup> *n*<sup>20</sup><sub>D</sub> 1.4710,<sup>29a</sup> *n*<sup>22</sup><sub>D</sub> 1.4699<sup>29c</sup>), as well as 6.45 g of higher boiling fractions which were contaminated<sup>11</sup> with a higher boiling impurity. The pure unsaturated ketone **21** has the following spectral peaks: ir (CCl<sub>4</sub>), 1710 (shoulder), 1680 (conjugated C=O), 1640 and 1615 cm<sup>-1</sup> (conjugated C=C); nmr (CCl<sub>4</sub>),  $\delta$  6.76 (1 H doublet of triplets, *J* = 10.5 and 4 Hz, vinyl CH), 5.89 (1 H doublet of triplets, *J* = 10.5 and 2 Hz vinyl CH), 2.1–2.5 (4 H multiplet, aliphatic CH), and 1.05 (6 H singlet, CH<sub>3</sub>C); mass spectrum, molecular ion peak at *m/e* 124, abundant fragment peaks at *m/e* 68, 58, and 43.

**Addition of Methylcopper Derivatives to 3-Methyl-2-cyclohexenone (19) and to 5,5-Dimethyl-2-cyclohexenone (21).**—The product data for these additions are summarized in Tables III (ketone **19**) and IV (ketone **21**). Solutions of the methylcopper reagents in ether were prepared as previously described; in certain cases the methylcopper was washed free of lithium iodide prior to addition of the complexing ligand. Ether solutions of the ketone **19** or **21** and pentamethylbenzene (an internal standard) were added to cold (0°) solutions of the methylcopper derivative. The concentrations of reactants listed in Tables III and IV are the initial concentrations after mixing. After the reaction solutions had been stirred at 0° for 10–15 min, they were poured into an aqueous solution (pH ~8) of NH<sub>4</sub>Cl and NH<sub>3</sub>. The combined ether phase and ethereal extract of the aqueous phase were washed with aqueous NaCl, dried, concentrated, and analyzed by gas chromatography<sup>24</sup> employing equipment which had been previously calibrated with known mixtures of authentic samples. For reactions with the ketone **19**, the retention times<sup>24</sup> were as follows: saturated ketone **20**, 18.3 min; pentamethylbenzene, 31.3 min; and unsaturated ketone **19**, 35.9 min. For reactions with the ketone **21**, the retention times<sup>24</sup> were as follows: saturated ketone **22**, 21.1 min; triethyl phosphite (present in certain reactions), 22.5 min; the unsaturated ketone **21**, 24.2 min; and pentamethylbenzene, 32.0 min. A collected<sup>24</sup> sample of the product ketone **22** was identified with an authentic sample<sup>31</sup> by comparison of gas chromatographic retention times and infrared spectra.

**Registry No.**—**8**, 15466-88-3; **9**, 15466-89-4; **10**, 15466-90-7; **11**, 15466-91-8; **12**, 15466-92-9; **13a**, 15466-93-0; **14a**, 15466-94-1; **17**, 15523-81-6; **19**, 1193-18-6; **20**, 2979-19-3; **21**, 4694-17-1; **22**, 873-94-9; **23**, 15466-96-3; **24**, 15523-82-7; **25**, 15523-83-8.

(29) (a) R. Frank and H. Hall, *J. Amer. Chem. Soc.*, **72**, 1645 (1950); (b) A. Eschenmosher, J. Schreiber, and S. Julia, *Helv. Chim. Acta*, **36**, 482 (1953); (c) A. W. Allan, R. P. A. Sneeden, and J. M. Wilson, *J. Chem. Soc.*, 2186 (1959).

(30) W. F. Gannon and H. O. House, *Org. Syn.*, **40**, 14 (1960).

(31) Obtained from the Aldrich Chemical Co., Milwaukee, Wis.