tograph, and the areas of the nonane and mesitylene peaks were measured by a Hewlett-Packard electronic integrator (Model 3370A). The reproducibility of this method was ±3%.

All of the rate constants reported were calculated from the slopes of the plot of either $1/(a - b) \ln [b(a - x)/a(b - x)]$ ($a = b$, $a =$ [cuprate], $b =$ [tosylate], and $x =$ [nonane]) *vs.* time or $(1/c) - (1/c)$ ($c =$ [tosylate]) *vs.* time.

Reaction of *n*-Octyl Iodide with Lithium Dimethylcuprate. *n*-Octyl iodide (0.240 g, 1 mmol) in ether (10 ml) was added to an ether solution of the cuprate (0.952 g, 5 mmol in 15 ml). After 20 hr at 0°, the reaction had proceeded to 88% completion (Table II). The reaction did not proceed when less than 5 equiv of the cuprate was employed or at temperatures lower than 0°.

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Supplementary Material Available. Figures 1 and 2 will appear following these pages in the microfilm edition of this volume of the journal. Photocopies of the supplementary material from this paper only or microfiche (105 × 148 mm, 20× reduction, negatives) containing all of the supplementary material for the papers in this issue may be obtained from the Journals Department, American Chemical Society, 1155 16th St., N.W., Washington, D. C. 20036. Remit check or money order for $3.00 for photocopy or $2.00 for microfiche, referring to code number JACS-73-7783.

A New Class of Mixed Cuprate(I) Reagents, Het(R)CuLi, Which Allow Selective Alkyl Group Transfer[1]

Gary H. Posner,* Charles E. Whitten,[2a] and Jeffrey J. Sterling[2b]

Contribution from the Department of Chemistry, The Johns Hopkins University, Baltimore, Maryland 21218. *Received June 28, 1973*

Abstract: Five different alkylhetero(alkyl)cuprate(I) and arylhetero(alkyl)cuprate(I) reagents of the form Het(R)-CuLi have been prepared from the corresponding heterocopper species (Het-Cu) and organolithium reagents (RLi): Het = *t*-BuO, PhO, *t*-BuS, PhS, Et_2N. The stability of these mixed cuprate reagents follows the order PhS > PhO > *t*-BuO > *t*-BuS ~ Et_2N. Of these five, PhS(R)CuLi is most effective for selective conjugate addition and substitution reactions using secondary and tertiary alkyl R groups. Acid chlorides have been converted to the corresponding secondary and tertiary butyl ketones in high isolated yields, and α,α'-dibromo ketones have been transformed cleanly into α-secondary and α-tertiary butyl ketones. Substitution of primary alkyl iodide by secondary and tertiary butyl groups is achieved in 67–98% yields using PhS(R)CuLi, and cyclohexenone undergoes conjugate addition of the *tert*-butyl group in 86% yield. Some of these reactions have been achieved using only a slight (*e.g.*, 20–30%) excess of organocopper reagent over substrate. The utility of these new mixed cuprate reagents is compared with that of other organocopper reagents.

Carbon–carbon σ-bond formation, one of the most fundamental operations in organic chemistry, is often accomplished by interaction of an organometallic reagent with an organic substrate. Highly nucleophilic organometallic reagents (*e.g.*, lithium and magnesium alkyls) are usually also strongly basic and therefore often undergo two or more competing modes of reaction.[3–5] Less nucleophilic organometallic reagents derived from charge-delocalized carbanions (*e.g.*, lithium enolates) are often more selective and useful in formation of carbon–carbon σ bonds, but these reagents do not generally allow direct attachment of two *hydrocarbon* groups.[5i,6] Alkyl, alkenyl, and aryl organocuprate(I) reagents, R_2CuLi, are now being used effectively for highly selective conjugate addition reactions to various α,β-unsaturated carbonyl[7] and sulfonyl[8] compounds and homoconjugate addition reactions to certain cyclopropyl carbonyl compounds,[9] and for highly selective substitution reactions[10] with alkyl,[11] alkenyl,[11] aryl,[11] and acyl[12] halides, with α,α'-

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dihalo ketones,[13] with epoxides,[14] with allylic[15] and propargylic[16] acetates, and with alkyl tosylates.[17] Several of these organocopper reactions have been used as one of the key steps in syntheses of such natural products as nootkatone[18a] and fukinone,[18b] fulvoplumierin,[19] zizaene,[20] a codling moth sex pheromone,[21] the boll weevil sex attractant,[22] insect juvenile hormone,[15b,23] and various prostaglandins.[9a,14f,24]

Two limitations on the broad utility of these organocopper reagents have often been the difficulty in using thermally unstable *sec*- and *tert*-alkylcuprates(I)[11b] and the need for a large (*e.g.*, 300–500%) excess of organocuprate(I) to achieve complete conversion of substrate to product.[7,10,11] To circumvent these limitations, several types of mixed cuprates RR′CuLi have been prepared recently in which both R and R′ are hydrocarbon groups.[25,26] Certain cuprous alkoxides and phenoxides,[27] cuprous mercaptides,[28] and cuprous amides[29] are known to be relatively stable; we expected, therefore, that a mixed cuprate Het(R)CuLi in which the hetero group is alkoxy or aryloxy (R′O), alkylthio or arylthio (R′S), or dialkylamino ($R_2'N$) might transfer the hydrocarbon group R selectively in many organocopper addition and substitution reactions. Such selective transfer would allow economical use of the hydrocarbon group and would release the heterocopper species (or Het-H after hydrolysis) which should not complicate product isolation.

We report now preparation of a series of mixed cuprate(I) reagents of the form Het(R)CuLi, their reactions with several diverse types of organic substrates, and comparison of the reactions of these mixed cuprates and of other organocopper reagents.

Results and Discussion

Preparation and Properties of Several Hetero(alkyl)cuprate Reagents Het(R)CuLi. Five different mixed hetero(alkyl)cuprate(I) reagents were prepared according to eq 1–3. The appropriate alcohol, mercaptan,

$$\text{Het-H} + n\text{-BuLi} \xrightarrow{\text{THF}} \text{Het-Li} + n\text{-BuH} \qquad (1)$$

$$\text{Het-Li} + \text{CuI} \xrightarrow{\text{THF}} \text{Het-Cu} + \text{LiI} \qquad (2)$$

$$\text{Het-Cu} + \text{RLi} \xrightarrow[-78^\circ]{\text{THF}} \text{Het(R)CuLi} \qquad (3)$$

$$\text{Het} = t\text{-BuO, PhO, } t\text{-BuS, PhS, Et}_2\text{N}$$

or amine in tetrahydrofuran was treated with 1 equiv of *n*-butyllithium. Such solutions of lithium *tert*-butoxide and lithium thiophenoxide, for example, are stable at 0° under inert atmosphere for up to 1 week. Addition of these solutions to suspensions of cuprous iodide in tetrahydrofuran produces the corresponding alkylheterocopper or arylheterocopper species which are immediately cooled to −78° and then treated with the appropriate organolithium reagent.[30]

The reactivity of these mixed cuprate reagents at −78° in tetrahydrofuran was then determined by allowing each to react with 1 equiv of benzoyl chloride.[31] Lithium diethylamino(*tert*-butyl)cuprate produced a mixture of diethylamide (20%), *tert*-butyl ketone (pivalophenone, 50%), and reactant acid chloride (30%);[32] the substantial amount of unreacted benzoyl chloride even after long reaction times suggests that the amino(alkyl)cuprate decomposes even at −78°. Lithium *tert*-butylthio(*tert*-butyl)cuprate gave pivalophenone (75%) and *tert*-butyl thiobenzoate (25%), which probably indicates that *tert*-butylthio group transfer from the mixed cuprate competes with alkyl group transfer.[33]

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(30) Attempts to prepare *tert*-butoxy(alkyl)cuprate reagents in ether solution or to prepare lithium *tert*-butoxy(*methyl*)cuprate were unsuccessful.

(31) An acid chloride was chosen for calibration of the reactivity of these mixed cuprates rather than, for example, an α,β-unsaturated ketone because substitution of chlorine proceeded rapidly at −78° whereas conjugate addition was relatively slow at this temperature.

(32) Benzoyl chloride was detected as methyl benzoate due to the methanol added at the end of the reaction.

(33) An equilibrium between a mixed cuprate and the corresponding two symmetrical cuprates ($2RR'CuLi \rightleftarrows R_2CuLi + R'_2CuLi$) has been suggested in several cases.[11b,34] It is possible that lithium di-*tert*-butylcuprate and lithium di-*tert*-butylthiocuprate are formed and that they react at different rates with benzoyl chloride; absence of any phenyldi-*tert*-butylcarbinol among the products, as is produced in reaction

Table I. Properties of Het(*t*-Bu)CuLi Reagents in Tetrahydrofuran[a]

	Het				
Property	*t*-BuO	PhO	*t*-BuS	PhS	Et_2N
Color of solution	Yellow-brown	Orange-brown	Pale green	White ppt (−78°) Colorless (0°)	Green-brown
Homogeneous solution	Yes	No	No	No (−78°) Yes (0°)	No
Selectivity of alkyl group transfer at −78°	Complete	Complete	Low	Complete	Low
Highest temperature at which stable for 1 hr	−50°	−30°	<−78°	0°	<−78°
Minimum number of equiv needed to consume 1.00 equiv of PhCOCl	1.16	1.30		1.10	
Het-H	Volatile	Base soluble	Volatile	Base soluble	Volatile

[a] The solvent actually is approximately a 2:1 mixture of THF–pentane; pentane is the solvent in commercial *tert*-butyllithium which is used to prepare the mixed cuprates.

Transfer of alkylthio groups from alkylthiocopper reagents to organic substrates has been noted previously.[28] Lithium *tert*-butoxy-, phenoxy-, and phenylthio(*tert*-butyl)cuprates, however, all produced pivalophenone in high yields without any detectable amounts of *tert*-butyl or phenyl esters. This completely selective transfer of only the alkyl group in these mixed reagents (*i.e.*, the absence of esters) indicates that formation of the mixed reagent probably had been complete before benzoyl chloride was added.[35]

The thermal stabilities of lithium *tert*-butoxy-, phenoxy-, and phenylthio(*tert*-butyl)cuprates were determined qualitatively as follows. Each reagent was prepared at −78°, stored for 1 hr at a given temperature between −78 and 0°, and then recooled to −78°. One equivalent of benzoyl chloride was added and the amount of pivalophenone formed from these aged cuprate solutions was determined. At −50° all three mixed cuprates give pivalophenone in good yield. At −30° pivalophenone is formed in high yield using phenoxy- and phenylthio(*tert*-butyl)cuprates(I), but lithium *tert*-butoxy(*tert*-butyl)cuprate(I) decomposes at this temperature as indicated by complete recovery of benzoyl chloride.[32] At 0° pivalophenone is produced using lithium phenylthio(*tert*-butyl)cuprate, but phenyl benzoate (90%) is formed using lithium phenoxy(*tert*-butyl)cuprate.[27b] At present we have no good explanation for this order of thermal stability, which also appears to hold for the corresponding mixed *sec*-butylcuprates.

Using lithium *tert*-butoxy, phenoxy, and phenylthio(*tert*-butyl)cuprates, we attempted to ascertain which of these three reagents would convert benzoyl chloride to pivalophenone in the highest yield, *with yield being based on the tert-butyl group.* A series of experiments was set up in which 1.00 equiv of benzoyl chloride was allowed to react at −78° in tetrahydrofuran separately with 1.10, 1.20, and 1.30 equiv of each of the three hetero(*tert*-butyl)cuprates. The best results were obtained with lithium phenylthio(*tert*-butyl)cuprate; only 1.10 equiv of this reagent was needed to convert all of the benzoyl chloride to pivalophenone. The high efficiency of this substitution reaction is in sharp contrast to all lithium diorganocuprate substitution reactions, in which the maximum yield of product is 50% based on the organic group transferred.[7,10] The economic use of the alkyl group in this and other (see below) substitution and addition reactions suggests that these mixed hetero(alkyl)cuprate reagents may be especially useful for transfer of valuable alkyl groups as, for example, in synthesis of prostaglandins.[14f]

Finally it should be emphasized that during the course of reaction between benzoyl chloride and the mixed hetero(alkyl)cuprates, the corresponding heterocopper species and lithium chloride are formed (eq 4). In

$$\mathrm{PhCOCl + Het(R)CuLi \longrightarrow PhCOR + Het\text{-}Cu + LiCl} \quad (4)$$

contrast to the substantial difficulties encountered in product isolation when R_2CuLi–Lig species (Lig = phosphine or sulfide) are used,[11b] *tert*-butoxycopper and phenoxycopper are easily hydrolyzed; *tert*-butyl alcohol is removed under vacuum and phenol is soluble in aqueous base. Phenylthiocopper[28b] is insoluble in a tetrahydrofuran–water solution containing ammonium chloride and can be isolated as a yellow powder simply by suction filtration. Upon treatment with aqueous mineral acid it produces a clear yellow solution having the distinctive odor of thiophenol. On several occasions using a slight excess of lithium phenylthio(*tert*-butyl)cuprate, product isolation involved simply suction filtration, extracting with diethyl ether, drying the organic extracts, and evaporating solvent *in vacuo* to afford the desired product having spectral and physical data *identical* with those of authentic compounds.

Some properties of the five lithium hetero(*tert*-butyl)-cuprate reagents studied are summarized in Table I.

Reactions with Acid Chlorides. The large number of new methods for converting carboxylic acid derivatives to ketones reflects the importance of this type of synthetic transformation.[38] In addition to the more

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of preformed lithium di-*tert*-butylcuprate with benzoyl chloride, argues against the intermediacy of lithium di-*tert*-butylcuprate in reaction of the mixed lithium *tert*-butylthio(*tert*-butyl)cuprate.

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Table II. Reaction of Various *tert*-Butylcopper Reagents with 1.00 Equiv of Benzoyl Chloride

Reagent	No. of equiv	Temp, °C	Time, min	Solvent	Product % yield[a]: PhCO-*t*-Bu	Product % yield[a]: $PhCO_2CH_3$[b]	Product % yield[a]: Other
PhS(*t*-Bu)CuLi	1.10	−78	20	THF	99 (87[c])	0	0
t-BuO(*t*-Bu)CuLi	1.16	−78	20	THF	98 (82[c])	0	0
PhO(*t*-Bu)CuLi	1.30	−30	60	THF	87	13	0
t-BuS(*t*-Bu)CuLi	1.00	−78	60	THF	75	3	22[d]
Et_2N(*t*-Bu)CuLi	1.00	−78	60	THF	50	30	23[e]
t-Bu_2CuLi	2.00	−78	20	THF	76	8	7[f]
(CH_3)(*t*-Bu)CuLi	3.00	−78	15	Ether	72	0	9[g]
t-BuCu	3.00	−78	30	Ether	37	49	0
t-BuMgCl + CuI (100 mol %)	1.10	−78, 20	30, 30	Ether	34	<1	~20[i]
t-BuMgCl + CuI (10 mol %)	1.10	−78, 20	30, 30	Ether	33	3	~20[i]
t-BuLi[h] + CuI (10 mol %)	1.10	−78, 20	30, 30	Ether	5	3–5	~20[i]

[a] The yields were determined by glpc using calibrated internal standards and are based on benzoyl chloride. [b] Addition of absolute methanol at the end of the reaction converted any remaining benzoyl chloride to methyl benzoate. [c] Yield of pure product after distillation. [d] PhCOS-*t*-Bu. [e] $PhCONEt_2$. [f] PhC(*t*-Bu)$_2$OH. [g] $PhCOCH_3$. [h] Reaction of 3.0 equiv of *t*-BuLi with 1.0 equiv of benzoic acid produces pure pivalophenone in only 67% yield: H. O. House and T. M. Bare, *J. Org. Chem.*, **33**, 943 (1968); M. J. Jorgenson, *Org. React.*, **18**, 1 (1970). [i] Nonvolatile organic residue remaining after vacuum distillation.

classical organometallic reagents which have been used (*e.g.*, organocadmium,[39] organozinc,[39] organoaluminum,[40] organolithium[41]), new approaches have involved organoiron,[42] organorhodium,[43] organoboron,[44] organosilicon,[45] and organocopper[12,46] species. Functional group specificity, high yields, and simplicity and mildness of experimental conditions are noteworthy characteristics of many organocuprate reactions with carboxylic acid chlorides.[12] As noted previously, however, 3 equiv of R_2CuLi (6 equiv of R) is usually needed for optimal yields of ketones, and secondary and tertiary organocopper reagents are generally more difficult to prepare than primary ones.[12] Using 1.2–1.3 equiv of mixed lithium *tert*-butoxy(*sec*-butyl)- and (*tert*-butyl)-cuprates per equivalent of acid chloride, we have been able to overcome these difficulties and to prepare in high yields (based on the alkyl group) a variety of secondary and tertiary alkyl ketones bearing remote halogen, keto, and ester groups (eq 5 and 6).[46f] This functional group specifity and economic use of the alkyl group characterize reactions also of lithium phenylthio(*tert*-butyl)cuprate (eq 7). This reagent, for example, has been used successfully in preparative scale (20 mmol) conversion of benzoyl chloride to pivalophenone. Furthermore, although aldehydes are unstable toward lithium dimethylcuprate even at −90°,[12] a mixture of 1 equiv of benzaldehyde and 1 equiv of benzoyl chloride reacts at −78° with 1 equiv of lithium phenylthio(*tert*-butyl)cuprate to form pivalophenone in 90% yield with 73% recovery of benzaldehyde.

$$Br(CH_2)_{10}COCl \xrightarrow[\text{THF, }-78°\text{, 15 min}]{\text{1.2 equiv of }t\text{-BuO}(t\text{-Bu})\text{CuLi}} Br(CH_2)_{10}CO\text{-}t\text{-Bu} \quad 78\% \qquad (5)$$

$$n\text{-}BuCO(CH_2)_4COCl \xrightarrow[\text{THF, }-78°\text{, 15 min}]{\text{1.3 equiv of }t\text{-BuO}(sec\text{-Bu})\text{CuLi}} n\text{-}BuCO(CH_2)_4CO\text{-}sec\text{-}Bu \quad 86\% \qquad (6)$$

$$EtO_2CCH_2CH_2COCl \xrightarrow[\text{THF, }-78°\text{, 15 min}]{\text{1.2 equiv of PhS}(t\text{-Bu})\text{CuLi}} EtO_2CCH_2CH_2CO\text{-}t\text{-}Bu \quad 65\% \qquad (7)$$

We have made an extensive comparison of the relative effectiveness of various *tert*-butylcopper reagents in converting benzoyl chloride to pivalophenone. The results are summarized in Table II. The main conclusion is quite clear: neither copper-catalyzed *tert*-butylmagnesium chloride[47] nor lithium di-*tert*-butylcuprate is so effective as the mixed lithium phenylthio(*tert*-butyl)cuprate or *tert*-butoxy(*tert*-butyl)cuprate. The greater effectiveness of these two hetero(*tert*-butyl)-cuprate reagents relative to other *tert*-butylcopper reagents is expected to be even more pronounced in reactions with many functionalized acid chlorides.

These results using hetero(alkyl)cuprate reagents for conversion of acid chlorides to ketones are more than simply an improved procedure based on refinement of known techniques; they involve a new class of mixed cuprate reagents which allow considerably more *selective* and more *economical* transfer of secondary and especially tertiary alkyl groups than can be achieved using any other procedure.

Reactions with α,α′-Dibromo Ketones. The ease with which ketones undergo α-alkylation makes them important synthetic intermediates. Much experimentation has led to several useful methods which allow control over the regioselectivity and the amount of alkylation (*i.e.*, monoalkylation rather than dialkylation or polyalkylation) of ketones.[6] Many of these methods involve formation of enol derivatives (enol acetates,[48] enol silyl ethers,[49] enol phosphorylated species,[50] enol stannyl ethers,[51] and enamines[52]) which

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(39) D. A. Shirley, *Org. React.*, **8**, 28 (1958).

(40) H. Reinheckel, K. Haage, and D. Jahnke, *Organometal. Chem. Rev., Sect. A*, **4**, 55 (1969).

(41) M. J. Jorgenson, *Org. React.*, **18**, 1 (1970).

(42) (a) J. P. Collman and N. W. Hoffman, *J. Amer. Chem. Soc.*, **95**, 2689 (1973); (b) Y. Sawa, M. Ryang, and G. Tsutsumi, *J. Org. Chem.*, **35**, 4183 (1970).

(43) L. S. Hegedus, S. M. Lo, and D. E. Bloss, *J. Amer. Chem. Soc.*, **95**, 3040 (1973).

(44) A. Pelter, M. G. Hutchings, and K. Smith, *Chem. Commun.*, 1529 (1970).

(45) S. P. Dent, C. Eaborn, and A. Piddock, *Chem. Commun.*, 1703 (1970).

(46) (a) G. M. Whitesides, C. P. Casey, J. San Filippo, Jr., and E. J. Panek, *Trans. N. Y. Acad. Sci.*, **29**, 572 (1967); (b) G. H. Posner and C. E. Whitten, *Tetrahedron Lett.*, 4647 (1970); (c) C. Jallabert, N. T. Luong-Thi, and H. Rivière, *Bull. Soc. Chim. Fr.*, 797 (1970); (d) N. T. Luong-Thi, H. Rivière, J.-P. Bégué, and C. Forestier, *Tetrahedron Lett.*, 2113 (1971); (e) J. Schwartz, *ibid.*, 2803 (1972); (f) G. H. Posner and C. E. Whitten, *ibid.*, 1815 (1973).

(47) (a) J. E. Dubois, M. Boussu, and C. Lion, *Tetrahedron Lett.*, 829 (1971), and references therein; (b) J. A. McPhee and J. E. Dubois, *ibid.*, 467 (1972).

(48) H. O. House, M. Gall, and H. O. Olmstead, *J. Org. Chem.*, **36**, 2361 (1971), and references therein.

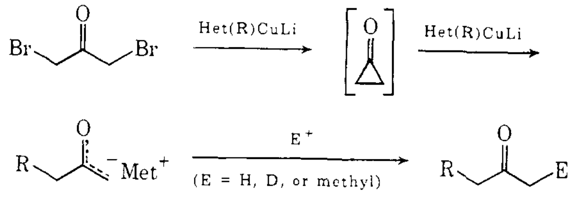
(49) G. Stork and P. Hudrlick, *J. Amer. Chem. Soc.*, **90**, 4462 (1968).

(50) I. J. Borowitz, E. W. R. Casper, R. K. Crouch, and K. C. Yee, *J. Org. Chem.*, **37**, 3873 (1972).

(51) P. A. Tardella, *Tetrahedron Lett.*, 1117 (1969).

(52) A. G. Cook, Ed., "Enamines: Their Synthesis, Structure, and Reactions," Marcel Dekker, New York, N. Y., 1969.

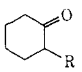
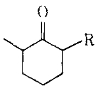
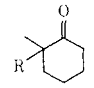
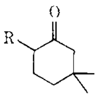
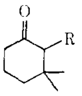
subsequently are converted to lithium enolates or allowed to react directly with suitable alkyl halides.[53] These displacement reactions falter with most secondary alkyl halides and fail with tertiary alkyl halides. We have recently reported a new method for α-secondary and α-tertiary alkylation of ketones which involves reaction between α,α′-dibromo ketones and nucleophilic lithium *tert*-butoxy(alkyl)cuprate reagents.[13] The reaction is represented in eq 8, and its effectiveness is



(8)

exemplified by conversion of 2,6-dibromocyclohexanone to 2-*tert*-butylcyclohexanone in 50% isolated yield.[13] A complete summary of results obtained in α-butylation of two symmetrical and four unsymmetrical ketones is given in Table III.

Table III. α-Alkyl Ketones from 1.0 Equiv of α,α′-Dibromo Ketones and 5.0 Equiv of Lithium *tert*-Butoxy(alkyl)cuprate Reagents in Tetrahydrofuran at −78°

		R, % yield[a]		
Substrate	Products	*n*-Bu	*s*-Bu	*t*-Bu
2,6-Dibromocyclohexanone		77 (81)[b]	73	65 (50)[c]
4,6-Dibromo-5-nonanone	*n*-$C_4H_9COCH(R)C_3H_7$-*n*	75	67	60
2,6-Dibromo-2-methylcyclohexanone[d]		48	61	31
		16	8	2
1,3-Dibromo-2-heptanone	*n*-$C_5H_{11}COCH_2R$	37	49	53
	n-$C_4H_9CH(R)COCH_3$	11	8	6
1,3-Dibromo-3-methyl-2-butanone	$(CH_3)_2CHCOCH_2R$	55	42	56
	$R(CH_3)_2CCOCH_3$	25	8	10
2,6-Dibromo-3,3-dimethylcyclohexanone		31		33
		5		0

[a] The yields were determined by glpc using calibrated internal standards and are based on substrate. [b] 5 equiv of *n*-Bu_2CuLi were used instead of *t*-BuO(*n*-Bu)CuLi. [c] Yield of isolated product; see ref 13. [d] 10 equiv of cuprate reagent were used.

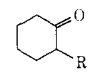
The data in Table III require several comments. Unsymmetrical α,α′-dibromo ketones react with lithium *tert*-butoxy(butyl)cuprate reagents to give mixtures of α- and α′-monoalkylated products. Alkylation of the less substituted α-carbon atom predominates, and the degree of regioselectivity increases from normal butylation to secondary butylation to tertiary butylation. This regioselectivity is apparently due mainly to steric effects; butylation of 2,6-dibromo-3,3-dimethylcyclohexanone, in which a bulky group is on the carbon atom β to the carbonyl group, proceeds with the largest regioselectivity we have observed in α-alkylation of any unsymmetrical ketone. On the other hand, treatment of 2α,4α-dibromo-5α-cholestan-3-one with lithium dimethylcuprate gives a mixture of 2α- and 4α-methyl-5α-cholestan-3-one.

The optimum ratio of mixed cuprate to dibromo ketone substrate was studied briefly. Yields of α-butyl ketones decreased by a small amount (∼10%) when 3 equiv rather than 5 equiv of cuprate reagent was used and increased by a small amount (∼10%) when 10 equiv rather than 5 equiv of cuprate reagent was used. Although the need for a large excess of cuprate to achieve complete conversion of substrate to product has been noted previously,[7,10,11] no explanation of this phenomenon is apparent.

The major side products observed in these α-alkylation reactions of dibromo ketones are small amounts (∼10%) of the parent ketone and varying amounts of polymeric material. The largest amounts of polymer appear in the tertiary butylation reactions; the *tert*-butyl absorptions which are evident in the nmr spectrum of this polymer are probably due to the *tert*-butyl group and not the *tert*-butoxy group because polymer formed in reactions of lithium *tert*-butoxy(*sec*-butyl)cuprate show no *tert*-butyl absorption. The infrared spectrum of polymer shows a broad carbonyl absorption at about 1700 cm^{-1}. Attempts to reduce polymer formation by varying the ratio of reagent to substrate or by using different solvents (diethyl ether, pentane) were not highly successful.

We have compared the relative effectiveness of various butylcuprate reagents in converting 2,6-dibromocyclohexanone into 2-butylcyclohexanones. The results are summarized in Table IV. Lithium *tert*-butoxy(*tert*-butyl)cuprate and phenylthio(*tert*-butyl)cuprate are clearly the best reagents for α-tertiary alkylation. Mixed hetero(alkyl)cuprates also work better than the corresponding dialkylcuprates for α-secondary alkylation. Normal butylation, however, is achieved in

Table IV. Reaction of 5.0 Equiv of Various Butylcopper Reagents with 1.0 Equiv of 2,6-Dibromocyclohexanone (at −78° for 30 min)

		Product	
Reagent	Solvent		% yield[a]
PhS(*t*-Bu)CuLi	THF	R = *t*-Bu	63
t-BuO(*t*-Bu)CuLi	THF	R = *t*-Bu	65 (50[b])
CH_3(*t*-Bu)CuLi	Ether	R = *t*-Bu	20
t-Bu_2CuLi	Ether	R = *t*-Bu	18
t-BuO(*sec*-Bu)CuLi	THF	R = *sec*-Bu	75
sec-Bu_2CuLi	Ether	R = *sec*-Bu	38
t-BuO(*n*-Bu)CuLi	THF	R = *n*-Bu	77
n-Bu_2CuLi	Ether	R = *n*-Bu	81

[a] The yields were determined by glpc using calibrated internal standards and are based on 2,6-dibromocyclohexanone. [b] Yield of isolated product.

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[53] Cyclopropylamines have also been used recently for alkylation of ketones: M. E. Kuehne and J. C. King, *J. Org. Chem.*, **38**, 304 (1973).

slightly better yield using dialkylcuprates than using mixed hetero(alkyl)cuprates.

As noted previously,[13] α,α'-dibromo ketones react with lithium dimethylcuprate in diethyl ether to give α-methyl ketones consistently in high yield upon aqueous work-up. We have now found that methylmagnesium iodide (2 mol equiv) produces the same transformations albeit generally in lower yields (Table V).[54]

Table V. α-Methyl Ketones from α,α'-Dibromo Ketones and Methylmagnesium Iodide and Lithium Dimethylcuprate(I) in Diethyl Ether

Substrate	% yield of isolated α-methyl ketone using CH_3MgI^a	% yield of isolated α-methyl ketone using $(CH_3)_2CuLi^b$
cis-2,12-Dibromocyclododecanone	86	97
2,8-Dibromocyclooctanone	65	80^c
trans-2,6-Dibromocyclohexanone	<1	98
cis-2,6-Dibromocyclohexanone	<10	$95^{c,d}$
4,6-Dibromo-5-nonanone	17	70
2,4-Dibromo-2,4-dimethyl-3-pentanone	70^d	$54^{d,e}$
1,3-Dibromo-1,3-diphenyl-2-propanone	<20	72^f

[a] 25° reaction temperature; the substantial variation in yield of α-methyl ketone as a function of α,α'-dibromo ketone structure is not yet fully understood. [b] −78° reaction temperature. [c] Reaction temperature −78° for 5 min and then 25° for 1 hr. [d] Yield was determined by analytical glpc using a calibrated internal standard and is based on substrate. [e] Reaction was performed in pentane as solvent at −50°. [f] 18% dimer: 1,3,4,6-tetraphenyl-2,5-hexanedione.

A cyclopropanone (or allene oxide or oxyallyl carbonium ion) intermediate has been trapped in reaction of 1,3-dibromo-1,3-diphenyl-2-propanone with lithium dimethylcuprate and with methyl Grignard.[13] Reaction of *tert*-butylmagnesium chloride with 2,6-dibromocyclohexanone does not produce any appreciable amount of 2-*tert*-butylcyclohexanone.

This new method for α-alkylation of ketones complements our procedure for preparing unsymmetrical ketones from acid chlorides and organocuprate reagents. Although the efficiency of alkyl group transfer in these reactions between α,α'-dibromo ketones and hetero(alkyl)cuprates is not high, the effective α-secondary and α-tertiary alkylation of ketones represents a novel, significant synthetic operation which cannot be achieved directly by other means.

Reactions with Alkyl Halides. The scope and limitations of coupling reactions between organic halides and organocopper reagents have been reviewed.[10] This method for formation of carbon–carbon σ bonds allows selective substitution of halogens by various hydrocarbon groups in many different types of organic halide substrates. Although methyl and primary alkyl groups can be introduced using the corresponding lithium dialkylcuprate reagents,[10,11] introduction of secondary and tertiary alkyl groups has been more difficult. Until now phosphine-complexed secondary and tertiary dialkylcuprates have been used most often, despite the difficulty of product isolation.[11b] Recently secondary and tertiary alkylation of *n*-alkyl tosylates using R_2CuLi species have been reported,[17] and we have shown that *n*-alkyl iodides undergo replacement of halogen by secondary and tertiary alkyl groups when treated with lithium *tert*-butoxy(alkyl)cuprates.[46f] Comparison of the relative effectiveness of various organocopper reagents in these secondary and tertiary alkylation reactions (Table VI) shows that lithium phenylthio(alkyl)cuprates are substantially superior to the corresponding lithium *tert*-butoxy(alkyl)cuprates but that these mixed hetero(alkyl)cuprates are not always more effective than other organocopper reagents. It is noteworthy that tertiary alkylation is achieved more effectively than secondary alkylation using the mixed hetero(alkyl)cuprates.

Table VI. Reaction of Various Organocuprate Reagents with 1.0 Equiv of Primary Alkyl Halides or Tosylates

Substrate	Solvent	Reagent	No. of equiv	Product (% yield[a])		
					R = *sec*-Bu	R = *t*-Bu
n-$C_8H_{17}I$	THF	PhS(R)CuLi	2.0	*n*-$C_8H_{17}R$	67	98
n-$C_8H_{17}I$	THF	*t*-BuO(R)CuLi	3.0	*n*-$C_8H_{17}R$	52	82
n-$C_5H_{11}I^b$	Ether	R_2CuLi	5.0	*n*-$C_5H_{11}R$	7	0
n-$C_8H_{17}Br$	THF	*t*-BuO(R)CuLi	5.0	*n*-$C_8H_{17}R$	0^c	83
n-$C_5H_{11}Br^b$	THF–pentane	$R_2CuLiPBu_3$	5.0	*n*-$C_5H_{11}R$	94	92
n-$C_8H_{17}OTs^d$	Ether	R_2CuLi	5.0	*n*-$C_8H_{17}R$	85^e	90^e

[a] The yields were determined by glpc using calibrated internal standards and are based on substrate. [b] These data are from ref 11b. [c] 1-Bromooctane was recovered. [d] These data are from ref 17. [e] Yield of isolated product.

Coupling of secondary and tertiary dialkylcuprates with *secondary* alkyl halides[10,11] and tosylates[17] proceeds in poor yield. Likewise, lithium phenylthio(*tert*-butyl)cuprate does not consume any 2-iodooctane even after 2 hr at 30°, and lithium *tert*-butoxy(*tert*-butyl)cuprate converts 2-octyl tosylate into 2,2,3-trimethylnonane is less than 25% yield.[55]

Reactions with α,β-Ethylenic Ketones. Conjugate addition reactions of organocopper reagents to α,β-unsaturated carbonyl compounds have been reviewed recently.[7] Although 1,4-addition of primary alkyl groups is common, conjugate addition of secondary and especially tertiary alkyl groups has been achieved in only several instances.[56] Recently a mixed alkynyl(*tert*-butyl)cuprate reagent has been used for conversion of 2-cyclohexenone to 3-*tert*-butylcyclohexanone,[25d] and we have reported using lithium *tert*-butoxy(*tert*-butyl)cuprate also for this conversion.[46f] Although the data in Table VII indicate that lithium phenylthio(*tert*-butyl)cuprate is the most effective hetero(*tert*-butyl)cuprate for this conversion, *n*-propylethynyl(*tert*-butyl)cuprate affords the conjugate adduct in highest yield; this alkynyl(alkyl)cuprate reagent, however, is considerably more difficult to prepare than the corresponding hetero(alkyl)cuprate.

Prodigious efforts are now being applied in various laboratories to effect conjugate addition of various alkenyl groups to 2-cyclopentenones. These efforts

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(54) There are reports from only one research group on reaction of an α,α'-dibromo ketone with a Grignard reagent to give an α-substituted ketone: J. Umnowa, *J. Russ. Phys. Chem. Soc.*, **44**, 1395 (1912); **45**, 881 (1913); *Chem. Zentralbl.*, **1**, 1402 (1913).

(55) Work is progressing in these laboratories on development of new methods for formation of carbon–carbon σ bonds between two secondary alkyl groups.

(56) (a) J. A. Marshall and H. Roebke, *J. Org. Chem.*, **31**, 3109 (1966); **33**, 840 (1968); (b) V. K. Andersen and J. Munch-Petersen, *Acta Chem. Scand.*, **16**, 947 (1962); (c) C. A. Henrick and J. B. Siddall, Zoecon Corp., unpublished results (see ref 7).

Table VII. Reaction of Various *tert*-Butylcopper Reagents with 1.00 Equiv of 2-Cyclohexen-1-one in Tetrahydrofuran

Reagent	No. of equiv	Temp, °C	Time, hr	3-*tert*-Butylcyclohexanone (% yield[a])
PhS(*t*-Bu)CuLi	1.06	−78	1	27
PhS(*t*-Bu)CuLi	1.25	0	1	50
PhS(*t*-Bu)CuLi	2.54	0	2	86
PhO(*t*-Bu)CuLi	2.50	−30	2	66
t-BuO(*t*-Bu)CuLi	1.47	−50	8	53[b]
t-BuO(*t*-Bu)CuLi	2.42	−50	4	62[c]
n-PrC≡C(*t*-Bu)CuLi	1.04	−78	0.25	>95[d]

[a] The yields were determined by glpc using calibrated internal standards and are based on 2-cyclohexen-1-one. [b] After 8 hr at −50°, the reaction mixture was allowed to warm to 0° during 2 hr. [c] After 4 hr at −50°, the reaction mixture was allowed to warm to 25° during 2 hr. [d] These data are from ref 25d; reaction was done in ether.

are justified because some of them already have led to syntheses of several prostaglandins.[24] Although reaction of 2-cyclopentenone with lithium *tert*-butoxy(vinyl)cuprate failed to give any appreciable amount of conjugate adduct,[46f] results using lithium phenylthio(vinyl)cuprate are somewhat more promising. Using 1.05 equiv of lithium phenyl(vinyl)cuprate in tetrahydrofuran for 30 min at −78°, all 2-cyclopentenone is consumed and 3-vinylcyclopentanone can be isolated by column chromatography in approximately 30% yield. This yield compares reasonably well with the yields obtained using lithium dialkenylcuprates which have been roughly 50% based on enone but 25% based on the alkenyl group transferred.[24c,d,g]

Conclusion

Of the five lithium hetero(alkyl)cuprate reagents studied, lithium phenylthio(alkyl)cuprates are the most useful. They are easily prepared and are stable up to 0°. They allow easy work-up after reaction with substrate, and they provide the highest efficiency in terms of the alkyl group which is transferred. They react with acid chlorides, α,α'-dibromo ketones, primary alkyl halides, and enones to form ketones, α-alkyl ketones, hydrocarbons, and β-alkyl ketones in higher yields than the other hetero(alkyl)cuprates. Compared with other organocopper reagents, lithium phenylthio(alkyl)cuprates are equally useful in reactions with most enones and primary alkyl iodides and are substantially more useful in reactions with α,α'-dibromo ketones and acid chlorides.

Experimental Section

General Procedure. Infrared spectra were obtained with Perkin-Elmer 337 and 457 infrared spectrophotometers, as liquid films, KBr pellets, or in $CHCl_3$ or CCl_4 solution. Nmr spectra were obtained with a Varian A-60 or a Jeol MH-100 spectrometer in CCl_4 or $CDCl_3$ solutions, with TMS internal standard. Mass spectra were recorded with a Hitachi-Perkin Elmer RMU-6 mass spectrometer. Melting points, determined with a Mel-Temp melting point apparatus, and boiling points are uncorrected. Analytical glpc were performed on a Varian Aerograph series 1200 gas chromatograph, using the following columns: (A) 10 ft × 0.25 in. FFAP on Chrom W (60–80); (B) 18 ft × 1/8 in. Reoplex on Anachrom AS (80–90); (C) 7 ft × 1/8 in. 5% SE-30 on Chrom G (100–120); (D) 10 ft × 0.25 in. 10% Carbowax 20-M on Chrom W (60–80). Preparative glpc was performed on a Varian Aerograph Model 90-P gas chromatograph, using the following columns: (E) 20 ft × 3/8 in. QF-1 on Chrom W (45–60); (F) 20 ft × 3/8 in. 20% Carbowax 20-M on Chrom W (45–60); (G) 10 ft × 0.25 in. 5% SE-30 on Chrom W (60–80); (H) 20 ft × 1/8 in. 20% SE-30 on Chrom W (45–60). Analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn., or by Chemalytics, Inc., Tempe, Ariz.

All reactions involving organocopper compounds were performed in three-neck round-bottom flasks charged with cuprous iodide and equipped with serum stoppers and a nitrogen filled balloon. Prior to the introduction of solvent, the apparatus was dried with a Bunsen burner flame while being evacuated.

Reagents and Solvents. The following reagents were obtained from commercial sources and were used without purification: cyclooctanone, 2-methylcyclohexanone, 2,4-dimethyl-3-pentanone, 5-nonanone, 2-heptanone, 1,3-diphenylpropanone, 5α-cholestan-3-one, 11-bromoundecanoic acid, *n*-octyl iodide, and adipic acid.

The following reagents were obtained from commercial sources and were purified as indicated: 2,12-dibromocyclododecanone (recrystallized twice from ether to mp 123–124°), cyclohexanone (distilled at 155° (760 mm)), *tert*-butyl alcohol (distilled from CaH_2),3 -methylcyclohexenone (distilled at 59° (4 mm)), thiophenol (distilled at 46° (8 mm)), *tert*-butylmercaptan (distilled at 64° (760 mm)), phenol (recrystallized from petroleum ether–chloroform to mp 43°), diethylamine (distilled at 55° (760 mm)), *tert*-butyl chloride (distilled at 51° (760 mm)), 3-carbomethoxypropionyl chloride (distilled at 39° (0.13 mm)), benzoyl chloride (distilled at 32° (0.15 mm)), benzaldehyde (distilled at 62° (10 mm)), 2-cyclohexen-1-one (distilled at 56–58° (13 mm)), 2-cyclopenten-1-one (distilled at 64° (20 mm)).

Commercial solvents were used from freshly opened bottles without further treatment except that tetrahydrofuran was distilled from lithium aluminum hydride and stored under N_2 and furan was distilled immediately prior to use.

Cuprous iodide (Fisher Chemical Co.) was continuously extracted with tetrahydrofuran in a Soxhlet extractor for 12 hr and dried *in vacuo* at 25°; the cuprous iodide thus purified remained pure on standing for several months, and aliquots were used for reaction with organolithium reagents to generate cuprates(I). For comparison, some commercial cuprous iodide was recrystallized,[57] but this purification procedure was found to be unnecessary because the yields in several reactions using THF-washed or recrystallized cuprous iodide were virtually the same.

Alkyllithium reagents were obtained from Foote Mineral Co. and Alfa Inorganics, and were used directly from the bottle. Methyllithium was about 2.0 *M* in diethyl ether solution and was stored at ambient temperature. *n*-Butyllithium and *sec*-butyllithium were about 2.0 and 1.2 *M*, respectively, in hexane solutions and *tert*-butyllithium and vinyllithium were about 2.0 *M* in pentane and tetrahydrofuran solutions, respectively. These were stored at 0°. Molarity was determined by a double titration procedure.[58]

Lithium Phenylthio(*tert*-butyl)cuprate. Preparation and Reaction with Benzoyl Chloride. A stirred suspension of 4.19 g (22.0 mmol) of cuprous iodide in 45 ml of tetrahydrofuran was treated at 25° with 18.3 ml of 1.20 *M* (22.0 mmol) lithium thiophenoxide in 1:1 tetrahydrofuran–hexane.[59] A clear, yellow solution formed within 5 min but became a cloudy suspension upon cooling to −78°. Dropwise addition of 10.6 ml of 2.06 *M* (21.8 mmol) *tert*-butyllithium in pentane to the cold (−78°) suspension gave a fine, nearly white precipitate. Into this cold (−78°) suspension was injected after 5 min 15.0 ml of a precooled (−78°) solution of 2.81 g (20.0 mmol) of benzoyl chloride in tetrahydrofuran. Addition of the substrate regenerated the cloudy, yellow suspension, and the reaction was stirred for 20 min before quenching was effected by injection of 5.0 ml (125 mmol) of absolute methanol. The reaction mixture was allowed to warm to room temperature and poured into 200 ml of saturated, aqueous ammonium chloride, and the yellow precipitate thus formed was removed by suction filtration. The aqueous phase was extracted with three 100 ml portions of ether and the combined ether phases were washed twice with 50 ml of 1 *N* sodium hydroxide and dried with magnesium sulfate. Solvent was removed *in vacuo* to afford 3.21 g (99%) of a slightly yellow oil with spectral properties essentially identical with those of pure pivalo-

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(57) G. B. Kauffman and L. A. Teter, *Inorg. Syn.*, 7, 9 (1963).

(58) G. M. Whitesides, C. P. Casey, and J. K. Krieger, *J. Amer. Chem. Soc.*, **93**, 1379 (1971), and references cited therein.

(59) Lithium thiophenoxide was prepared by reaction of equimolar quantities of *n*-butyllithium and thiophenol at 0° under nitrogen in sufficient tetrahydrofuran to form a ≈1.0 *M* solution. Lithium *tert*-butoxide, lithium *tert*-butylmercaptide, and lithium phenoxide were prepared by similar procedures.

phenone. Short path distillation gave 2.82 g (87% yield based on benzoyl chloride) of colorless pivalophenone: bp 105–106° (15 mm) (lit.[60] 103–104° (13 mm)); n^{20}D 1.5092 (lit.[61] n^{20}D 1.5090); ir (CCl$_4$) 1680 cm^{-1} (C=O); nmr (CCl$_4$) δ 7.6–7.8 (m, 2 H), 7.2–7.5 (m, 3 H), 1.33 (s, 9 H).

Lithium *tert*-Butoxy(*tert*-butyl)cuprate. Preparation and Reaction with Benzoyl Chloride. To a stirred suspension of 457 mg (2.40 mmol) of cuprous iodide in 3.0 ml of tetrahydrofuran at 25° was added 2.18 ml of 1.10 *M* (2.40 mmol) lithium *tert*-butoxide in 1:1 tetrahydrofuran–hexane.[59] After 15 min all solid, gray cuprous iodide had disappeared and a cloudy green-brown suspension had formed. The mixture was cooled to −78°, and 2.10 ml of 1.12 *M* (2.33 mmol) *tert*-butyllithium in pentane was injected dropwise. A solution of 290 mg (2.06 mmol) of benzoyl chloride in 2.0 ml of tetrahydrofuran was precooled to −78° and rapidly added to the reaction mixture. After 20 min the reaction was quenched by addition of 1.0 ml (25 mmol) of absolute methanol. After warming to room temperature the mixture was poured into 50 ml of saturated, aqueous ammonium chloride and extracted with three 50 ml portions of ether. The combined ether phases were washed with 50 ml of 1% sodium thiosulfate and dried with magnesium sulfate, and the solvent was evaporated to leave 332 mg (99%) of a yellow oil. Microdistillation afforded 274 mg (82%) of colorless pivalophenone: n^{20}D 1.5084 (lit.[61] n^{20}D 1.5090); ir (CCl$_4$) 1680 cm^{-1} (C=O); nmr (CCl$_4$) δ 7.6–7.8 (m, 2 H), 7.3–7.5 (m, 3 H), 1.32 (s, 9 H).

Lithium Phenoxy(*tert*-butyl)cuprate. Preparation and Reaction with Benzoyl Chloride. To a stirred suspension of 190 mg (1.00 mmol) of cuprous iodide in 1.5 ml of tetrahydrofuran was added at 25° 1.00 ml of 1.00 *M* (1.00 mmol) lithium phenoxide in 1:1 tetrahydrofuran–hexane.[59] After 15 min the mixture was cooled to −50° and 0.45 ml of 2.12 *M* (0.96 mmol) *tert*-butyllithium in pentane was added dropwise. The mixture was stirred for 1 hr at −50° and cooled to −78°, and a precooled (−78°) solution of 135 mg (0.96 mmol) of benzoyl chloride in 1.0 ml of tetrahydrofuran was injected. After 15 min the reaction was quenched with 1.0 ml (25 mmol) of absolute methanol. Normal work-up (ether–ammonium chloride extraction) including washing with 1 *N* sodium hydroxide gave 169 mg (109%) of a yellow oil. The nmr spectrum (CCl$_4$) of the crude product indicated the relative yields of products to be 87% pivalophenone, δ 1.33 (s), and 13% methyl benzoate, δ 3.86 (s).

13-Bromo-2,2-dimethyl-3-tridecanone. Into a cold (−78°), stirred suspension of 2.40 mmol of lithium *tert*-butoxy(*tert*-butyl)cuprate was injected slowly a cold (*ca.* −50°) solution of 567 mg (2.00 mmol) of 11-bromoundecanoyl chloride (bp 117–119° (0.22 mm); lit.[62] bp 130–132° (1 mm)) in 2.0 ml of tetrahydrofuran. The reaction was stirred for 15 min at −78° and then quenched by addition of 1.0 ml (25 mmol) of absolute methanol. Normal work-up afforded 611 mg (100%) of a slightly yellow oil. The crude product was filtered through a 5 × 50 mm column of F-20 Alumina (ether solvent) and microdistilled to give 514 mg (84%) of a colorless liquid. The nmr spectrum indicated the product to be 93% of the desired ketone (78% based on consumed starting material) and 7% of the corresponding methyl ester. A sample of the pure 13-bromo-2,2-dimethyl-3-tridecanone was obtained by column chromatography on a 1.5 × 10 cm column of F-20 Alumina using hexane and 5% ether–hexane as eluant followed by microdistillation: ir (CCl$_4$) 1707 cm^{-1} (C=O); nmr (CCl$_4$) δ 3.37 (t, 3 H), 2.38 (t, 3 H), 1.2–2.0 (m, 16 H), 1.10 (s, 9 H).

Anal. Calcd for C$_{15}$H$_{29}$BrO: C, 59.01; H, 9.57; Br, 26.17. Found: C, 59.19; H, 9.51; Br, 26.10.

3-Methyl-4,9-tridecanedione. A cold (−78°) suspension of 1.30 mmol of lithium *tert*-butoxy(*tert*-butyl)cuprate was treated with a precooled (−78°) solution of 201 mg (0.98 mmol) of 6-oxadecanoyl chloride[63] (bp 86–87.5° (0.23 mm)) in 1.0 ml of tetrahydrofuran. After 20 min the reaction was quenched by the addition of 1.0 ml (25 mmol) of absolute methanol and worked up by the normal procedure to afford 230 mg of slightly yellow 3-methyl-4,9-tridecanedione. Microdistillation gave 194 mg (87%) of colorless liquid which was more than 98% pure by nmr and glpc. An analytical sample was obtained by preparative glpc (column A, 180°, 35 min): ir (CCl$_4$) 1716 cm^{-1} (C=O); nmr (CCl$_4$) δ 2.35 (m, 7 H), 0.7–1.9 (m, 19 H), doublet apparent at 1.03.

Anal. Calcd for C$_{14}$H$_{26}$O$_2$: C, 74.29; H, 11.58. Found: C, 74.24; H, 11.36.

Methyl 5,5-Dimethyl-4-oxohexanoate. To 2.40 mmol of lithium phenylthio(*tert*-butyl)cuprate at −78° was added 303 mg (2.02 mmol) of 3-carbomethoxypropionyl chloride as a cold (−78°) solution in 1.0 ml of tetrahydrofuran. After 20 min the reaction was quenched by injection of 1.0 ml (25 mmol) of absolute methanol. Analytical glpc (column A, 180°, butyrophenone internal standard) indicated one major product (7.5 min) and two minor products (5 min and 6.8 min, each less than 3%). The major product is methyl 5,5-dimethyl-4-oxohexanoate (226 mg, 65%) which was obtained pure by preparative glpc (column H, 190°, 18 min): ir (CCl$_4$) 1741 cm^{-1} (ester C=O), 1710 cm^{-1} (ketone C=O); nmr (CCl$_4$) δ 3.63 (s, 3 H), 2.62 (m, 4 H), 1.15 (s, 9 H).

Anal. Calcd for C$_9$H$_{16}$O$_3$: C, 62.77; H, 9.36. Found: 63.07; H, 9.29.

Competition between Benzoyl Chloride and Benzaldehyde for a Limited Amount of Lithium Phenylthio(*tert*-butyl)cuprate. To a cold (−78°) suspension of 2.0 mmol of lithium phenylthio(*tert*-butyl)cuprate was added a cold (−78°) solution of 212 mg (2.0 mmol) of benzaldehyde and 281 mg (2.00 mmol) of benzoyl chloride in 2.0 ml of tetrahydrofuran. After 5 min the reaction was quenched by injection of 1.0 ml (25 mmol) of absolute methanol and worked up by the normal procedure including washing of the combined ether extracts with 1 *N* sodium hydroxide. The nmr (CCl$_4$) spectrum indicated the crude product (510 mg) to contain pivalophenone (292 mg, 90%, δ 1.32 (s)), methyl benzoate (27 mg, 10%, δ 3.83 (s)), and benzaldehyde (155 mg, 73% recovery, δ 10.5 (s)).

Pivalophenone. A. Using Lithium *tert*-Butylthio(*tert*-butyl)cuprate. To a stirred suspension of 190 mg (1.00 mmol) of cuprous iodide in 1.5 ml of tetrahydrofuran at 25° was added 1.0 ml of 1.00 *M* (1.00 mmol) lithium *tert*-butylmercaptide.[59] After 15 min the reaction mixture was cooled to −78° and 0.47 ml of 2.12 *M* (1.00 mmol) *tert*-butyllithium in pentane was added dropwise. After 1 hr at −78° a solution of 140 mg (1.00 mmol) of benzoyl chloride in 1.0 ml of tetrahydrofuran was cooled to −78°, injected into the reaction mixture, and was followed after 15 min by 1.0 ml (25 mmol) of absolute methanol. Normal work-up gave 174 mg of a yellow oil. The nmr spectrum (CCl$_4$) indicated the products to be pivalophenone (112 mg, 69%, δ 1.33 (s)), methyl benzoate (11 mg, 8%, δ 3.85 (s)), and *tert*-butyl thiobenzoate (45 mg, 23%, δ 1.55 (s)).

B. Using Lithium Diethylamino(*tert*-butyl)cuprate. To a suspension of 381 mg (2.00 mmol) of cuprous iodide in 4.5 ml of tetrahydrofuran at −30° was added 2.0 ml of freshly prepared (−30°) 1.00 *M* (2.00 mmol) lithium diethylamide. After 5 min the red-brown mixture was cooled to −78° and 0.93 ml of 2.12 *M* (2.00 mmol) *tert*-butyllithium in pentane was added dropwise. The mixture was stirred for 1 hr at −78° before a cold (−78°) solution of 281 mg (2.00 mmol) of benzoyl chloride in 2.0 ml of tetrahydrofuran was injected. Quenching with 1.0 ml (25 mmol) of absolute methanol followed by normal work-up gave 262 mg of yellow liquid. The nmr spectrum (CCl$_4$) indicated the products to be pivalophenone (146 mg, 45%, δ 1.32 (s)), methyl benzoate (16 mg, 6%, δ 3.85 (s)), and benzoic acid diethyl amide (81 mg, 23%, δ 3.33 (q) and δ 1.11 (t)).

C. Using Lithium Di-*tert*-butylcuprate. To a cold (−78°) suspension of 381 mg (2.00 mmol) of cuprous iodide in 4.0 ml of tetrahydrofuran was added dropwise 1.89 ml of 2.12 *M* (4.00 mmol) *tert*-butyllithium in pentane. After 5 min a cold (−78°) solution of 281 mg (2.00 mmol) of benzoyl chloride in 2.0 ml of tetrahydrofuran was injected, and after 20 min the reaction was quenched with 1.0 ml (25 mmol) of absolute methanol. Ether–ammonium chloride work-up afforded 302 mg of a yellow oil. The nmr spectrum (CCl$_4$) indicated the products to be pivalophenone (249 mg, 77%, δ 1.32 (s)), methyl benzoate (23 mg, 8%, δ 3.82 (s)), and phenyldi-*tert*-butylcarbinol (29 mg, 7%, δ 1.07 (s)).

D. Using *tert*-Butylcopper. To a suspension of 1.14 g (6.00 mmol) of cuprous iodide in 17 ml of ether at −40° was added dropwise 5.30 ml of 1.12 *M* (5.94 mmol) *tert*-butyllithium in pentane. After 5 min the reaction mixture was cooled to −78°, and 295 mg (2.10 mmol) of benzoyl chloride dissolved in 2.0 ml of ether was cooled to −78° and injected into the reaction mixture. After 15 min the reaction was quenched with 1.0 ml (25 mmol) of absolute methanol and worked up by the usual procedure to give 251 mg of a yellow oil. Analysis of the crude product by nmr (CCl$_4$) indicated the principal products to be pivalophenone [118 mg, 35%, δ 1.32 (s)] and methyl benzoate [133 mg, 47%, δ 3.83 (s)].

E. Using *tert*-Butylmagnesium Chloride and 100 Mol % of Cuprous Iodide.[64] To a cold (−78°) mixture of 419 mg (2.20 mmol)

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(60) A. Haller and E. Bauer, *C. R. Acad. Sci.*, **148**, 73 (1909).

(61) C. Cherrier and J. Metzger, *C. R. Acad. Sci.*, **226**, 797 (1948).

(62) N. Rabjohn and M. S. Cohen, *J. Amer. Chem. Soc.*, **76**, 1280 (1954).

(63) Prepared by the action of oxalyl chloride on 6-oxodecanoic acid.

(64) The procedure followed is that outlined in ref 47.

of cuprous iodide and 273 mg (1.94 mmol) of benzoyl chloride in 7.0 ml of ether was added dropwise 0.92 ml of 2.38 M (2.20 mmol) *tert*-butylmagnesium chloride[65] and the mixture was stirred for 30 min at −78°. The reaction was allowed to warm slowly to 20° over 1.5 hr and then quenched by the addition of 1.0 ml (25 mmol) of absolute methanol. Normal ether–ammonium chloride work-up gave 251 mg of yellow oil. Analytical glpc (column D, 200°, butyrophenone as internal standard) indicated the major product to be pivalophenone (4.9 min, 104 mg, 34%) with one minor product also present. The nmr spectrum confirmed the presence of pivalophenone (δ 1.35 (s)) and showed the minor product to be methyl benzoate (δ 3.88 (s)). Vacuum distillation left 75 mg of a nonvolatile, organic residue which was not identified.

F. Using *tert*-Butyllithium and 10 Mol % of Cuprous Iodide.[64] To a mixture of 42 mg (0.22 mmol) of cuprous iodide and 273 mg (1.94 mmol) of benzoyl chloride in 7.0 ml of ether was added dropwise 1.07 ml of 2.12 M (2.37 mmol) *tert*-butyllithium in pentane and the mixture was stirred for 30 min at −78°. The reaction was allowed to warm slowly to 20° over 1.5 hr and then was quenched by the addition of 1.0 ml (25 mmol) of absolute methanol. The usual work-up procedure afforded 268 mg of yellow oil, but analytical glpc (column D, 200°, butyrophenone as internal standard) indicated only a small amount of pivalophenone (4.9 min, 16 mg, 5%). The nmr spectrum (CCl$_4$) confirmed the presence of pivalophenone (δ 1.33 (s)) and also displayed a resonance characteristic of methyl benzoate ($\sim$15 mg, $\sim$5%, δ 3.83 (s)).

General Procedure for Reaction of α,α'-Dibromo Ketones with Lithium *tert*-Butoxy(alkyl)cuprate Reagents. To 970 mg (5.1 mmol) of cuprous iodide in 10 ml of tetrahydrofuran at 0° was added 4.5 ml of 1.1 M (5.0 mmol) lithium *tert*-butoxide. After stirring for 5 min, the green mixture was cooled to −78°, and the following reagents were added successively: 5.0 mmol of the appropriate alkyllithium reagent, 1.0 mmol of the α,α'-dibromo ketone in 1 ml of tetrahydrofuran, and after 30 min 1 ml of absolute methanol. Normal work-up involved pouring the reaction mixture into a stirring aqueous solution of ammonium chloride, adding 0.7–0.8 g of sodium thiosulfate to remove any color due to halogen, and extracting with ether. Volatile products were analyzed and isolated by glpc, and nonvolatile products were isolated by solvent removal under reduced pressure.

2-*n*-Butylcyclohexanone. A. Using Lithium *tert*-Butoxy(*n*-butyl)cuprate. Following the general procedure, to 5.0 mmol of lithium *tert*-butoxy(*n*-butyl)cuprate at −78° was added 256 mg (1.0 mmol) of 2,6-dibromocyclohexanone (Table VIII) in 1 ml of tetrahydrofuran and, after 30 min, 1 ml of absolute methanol. Normal work-up was followed by solvent removal under reduced pressure. Analytical glpc (column A, 120°, cyclooctanone internal standard) indicated one major peak, at 9 min, which corresponds to 2-*n*-butylcyclohexanone (117 mg, 77%). The crude product was distilled at a bath temperature of about 130° (25 mm) to give 90 mg (59%) of pure 2-*n*-butylcyclohexanone: n^{25}D 1.4538 (lit.[66] n^{25}D 1.4545); nmr (CCl$_4$) δ 0.7–2.5 (broad m); ir (CCl$_4$) 1718 cm^{-1} (C=O); mass spectrum (70 eV) *m/e* 154, 111, 98, 93, 70.

B. Using Lithium Di-*n*-butylcuprate. To 970 mg (5.1 mmol) of cuprous iodide in 14 ml of diethyl ether at −45° was added 5.5 ml of 1.81 M (10.0 mmol) *n*-butyllithium. The dark solution was cooled to −78° and 250 mg (1.0 mmol) of 2,6-dibromocyclohexanone was added in 1 ml of ether. After 30 min, 1 ml of absolute methanol was added followed by normal work-up and solvent removal under reduced pressure. Analytical glpc (column A, 120°, cyclooctanone internal standard) indicated one major peak at 9 min, which was identified as 2-*n*-butylcyclohexanone (125 mg, 81%) by comparison to an authentic sample.

2-*sec*-Butylcyclohexanone. A. Using Lithium *tert*-Butoxy(*sec*-butyl)cuprate. To 5.0 mmol of lithium *tert*-butoxy(*sec*-butyl)cuprate at −78° was added 256 mg (1.0 mmol) of 2,6-dibromocyclohexanone in 1 ml of tetrahydrofuran and, after 30 min, 1 ml of methanol. Normal work-up was followed by solvent removal under reduced pressure leaving 152 mg of a yellow oil. Analytical glpc (column A, 120°, cyclooctanone internal standard) indicated one major peak at 11.5 min which corresponds to 2-*sec*-butylcyclohexanone (112 mg, 73%). Distillation at a bath temperature of about 120° (25 mm) afforded 80 mg (54%) of pure 2-*sec*-butylcyclohexanone: n^{20}D 1.4603 (lit.[67] n^{20}D 1.4586); nmr (CCl$_4$) δ 0.7–2.5 (broad m); ir (CCl$_4$) 1718 cm^{-1} (C=O); mass spectrum (70 eV) *m/e* 154, 125, 98, 83, 70.

Table VIII. Preparation and Properties of α,α'-Dibromo Ketones

α,α'-Dibromo ketone	Ref[a]	Bp/mp, °C (lit.)	Ir (C=O)[b] (lit.)
cis-2,6-Dibromocyclohexanone	*e*	mp 108–110 (110–111)[f]	1750 (1750)[e]
trans-2,6-Dibromocyclohexanone	*e*	mp 32–35 (36)[e]	1740 (1736)[e]
4,6-Dibromo-5-nonanone	*g*	bp 130–133 (15 mm) (132–135 (20 mm))[g]	1727
trans-2,6-Dibromo-2-methylcyclohexanone	*e*	mp 40–42 (39)[h]	1740
1,3-Dibromo-2-heptanone	*i*	bp 126–132 (25 mm) (111–114 (9 mm))[i]	1725
1,3-Dibromo-3-methyl-2-butanone	*k*	bp 87 (10 mm) (87 (10 mm))[j]	1723
cis- and *trans*-2,6-Dibromo-3,3-dimethylcyclohexanone[c]	*l*	bp 99–100 (0.5 mm)	1736 and 1753 (trans, 1736 and 1742; cis, 1750)[l]
2,4-Dibromo-2,4-dimethyl-3-pentanone	*m*	bp 109–114 (41 mm) (84.5–86.5 (10 mm))[m]	1700
1,3-Dibromo-1,3-diphenylpropanone	*k*	mp 75–85 (79–97)[k]	1745
2,8-Dibromocyclooctanone[d]	*h*	mp 72.5–74	1740
2α,4α-Dibromo-5α-cholestan-3-one	*n*	mp 196–198 (194–194.5)[n]	1758

[a] Source of general procedure used for preparation of dibromo ketones. [b] CCl$_4$ solvent, numbers given in cm^{-1}. [c] 90% pure; contains some mono- and tribrominated contaminants. [d] *Anal.* Calcd for $C_8H_{12}OBr_2$: C, 33.85; H, 4.23; Br, 56.29. Found: C, 33.99; H, 4.32; Br, 56.14. [e] D. Q. Quan, *C. R. Acad. Sci., Ser. C*, **267**, 1074 (1968). [f] E. J. Corey, *J. Amer. Chem. Soc.*, **75**, 3297 (1953). [g] R. Breslow, L. J. Altman, and A. Krebs, *J. Amer. Chem. Soc.*, **87**, 1326 (1965). [h] E. Garbisch, *J. Org. Chem.*, **30**, 2109 (1965). [i] C. Rappe and R. Adelström, *Acta Chem. Scand.*, **19**, 383 (1965). [j] R. G. Doerr and P. S. Skell, *J. Amer. Chem. Soc.*, **89**, 4684 (1967). [k] R. Breslow, T. Eicher, A. Krebs, R. Peterson, and J. Posner, *J. Amer. Chem. Soc.*, **87**, 1320 (1965). [l] H. Durr, G. Ourisson, and B. Waegell, *Chem. Ber.*, **98**, 1859 (1965). [m] G. Claeson and A. Thalen, *Acta Chem. Scand.*, **17**, 1172 (1963). [n] C. Djerassi and A. L. Wilds, *J. Amer. Chem. Soc.*, **68**, 1712 (1946).

B. Using Lithium Di-*sec*-butylcuprate. To 970 mg (5.1 mmol) of cuprous iodide in 11 ml of diethyl ether at −45° was added 8.0 ml of 1.24 M (10.0 mmol) *sec*-butyllithium. The dark solution was cooled to −78° and 256 mg (1.0 mmol) of 2,6-dibromocyclohexanone was added in 1 ml of ether. After 30 min 1 ml of methanol was added followed by normal work-up and solvent removal under reduced pressure leaving 110 mg of a yellow oil. Analytical glpc (column A, 120°, cyclooctanone internal standard) indicated three minor peaks (1.5–2.5 min) and a major peak at 11.5 min which was identified as 2-*sec*-butylcyclohexanone (66 mg, 43%) by comparison to authentic material.

6-*n*-Propyl-5-decanone. To 5.0 mmol of lithium *tert*-butoxy(*n*-butyl)cuprate at −78° was added 3.16 mg (1.0 mmol) of 4,6-dibromo-5-nonanone in 1 ml of tetrahydrofuran and, in 30 min, 1 ml of absolute methanol. Normal work-up was followed by solvent removal under reduced pressure leaving 230 mg of a yellow oil. Analytical glpc (column C, 160°, cyclododecanone internal standard) indicated 2 minor peaks (*ca.* 1.5 min) and a major one (4.5 min). One of the minor peaks was identified as 5-nonanone (10 mg, 7%) by comparing its retention time with that of authentic material. The major peak corresponds to 6-*n*-propyl-5-decanone (149 mg, 75%) which was isolated by preparative glpc (column E, 180°, 24 min): nmr (CCl$_4$) δ 2.2–2.6 (m, 3 H), 1.05–1.7 (m, 14 H),

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(65) *tert*-Butylmagnesium chloride was prepared by the method of F. C. Whitmore and D. Badertsher, *J. Amer. Chem. Soc.*, **55**, 1559 (1933), and standardized by the method of H. Gilman, E. Zoellner, and J. Dickey, *ibid.*, **51**, 1576 (1929).

(66) H. Holmquist, H. Rothrock, C. Theobold, and B. Englund, *J. Amer. Chem. Soc.*, **78**, 5339 (1956).

(67) V. Barkhash, G. Smiranova, A. Prudchenko, and I. Machinskaya, *Zh. Obshch. Khim.*, **33**, 2202 (1963); *Chem. Abstr.*, **59**, 1383h (1963).

0.7–1.05 (m, 9 H); ir (CCl_4) 1720 cm^{-1} (C=O); mass spectrum (70 eV) *m/e* 198, 169, 156, 142, 127, 113, 110.

Anal. Calcd for $C_{13}H_{26}O$: C, 78.72; H, 13.21. Found: C, 78.98; H, 13.06.

4-*tert*-Butyl-5-nonanone. To 5.0 mmol of lithium *tert*-butoxy(*tert*-butyl)cuprate at −78° was added 316 mg (1.0 mmol) of 4,6-dibromo-5-nonanone in 1 ml of tetrahydrofuran and, after 30 min, 1 ml of absolute methanol. Normal work-up was followed by solvent removal under reduced pressure leaving 210 mg of a yellow oil. Analytical glpc (column C, 160°, cyclododecanone internal standard) indicated two major peaks: A, 1.5 min; B, 3.5 min. A was identified as 5-nonanone (*ca.* 10 mg, 7%) by comparing its retention time with that of authentic material. B is 4-*tert*-butyl-5-nonanone (118 mg, 60%) which was isolated by preparative glpc (column E, 165°, 13 min): nmr (CCl_4) δ 2.15–2.45 (m, 3 H), 0.85–1.9 (m, 14 H) superimposed on 0.9 (s, 9 H); ir (CCl_4) 1710 cm^{-1} (C=O); mass spectrum (70 eV) *m/e* 198, 156, 113, 100, 85.

Anal. Calcd for $C_{13}H_{26}O$: C, 78.72; H, 13.21. Found: C, 78.76; H, 13.28.

2-*n*-Butyl-6-methylcyclohexanone and 2-*n*-Butyl-2-methylcyclohexanone. To 10.0 mmol of lithium *tert*-butoxy(*n*-butyl)cuprate at −78° was added 270 mg (1.0 mmol) of *trans*-2,6-dibromo-2-methylcyclohexanone in 1 ml of tetrahydrofuran and, in 30 min, 1 ml of absolute methanol. Normal work-up was followed by solvent removal under reduced pressure leaving 200 mg of a yellow oil. Analytical glpc (column C, 125°, cyclooctanone internal standard) indicated three major components: A, 2 min; B, 4 min; C, 11 min. A was identified as 2-methylcyclohexanone (4 mg, 3%) by comparing its retention time with that of authentic material. B was not identified. C was isolated *via* preparative glpc (column H, 200°) as a mixture of *cis*- and *trans*-2-*n*-butyl-6-methylcyclohexanone and 2-*n*-butyl-2-methylcyclohexanone (107 mg, 64%) in the following relative amounts by analytical glpc (column B, 130°): *cis*-2-*n*-butyl-6-methylcyclohexanone (32 min, 43%); *trans*-2-*n*-butyl-6-methylcyclohexanone (36 min, 27%); and 2-*n*-butyl-2-methylcyclohexanone (38 min, 30%). *cis*-2-*n*-Butyl-6-methylcyclohexanone was isolated *via* preparative glpc (column E, 170°, 24 min): nmr (CCl_4) 0.6–2.5 (m with apparent doublet at 0.94, $J = 6$ Hz) consistent with literature[50] nmr data); ir (CCl_4) 1709 cm^{-1} (C=O). 2-*n*-Butyl-2-methylcyclohexanone collected *via* preparative glpc (column E, 170°, 28 min) was contaminated with *ca.* 10% *trans*-2-*n*-butyl-6-methylcyclohexanone but still gave nmr (CCl_4) data consistent with the literature:[50] δ 0.6–2.2 (broad m with 0.98 (s)); ir (CCl_4) 1709 cm^{-1} (C=O). The following data were obtained from the mixture of isomers: mass spectrum (70 eV) *m/e* 168, 126, 112, 87.

Anal. Calcd for $C_{11}H_{20}O$: C, 78.51; H, 11.98. Found: C, 78.58; H, 12.01.

2-*sec*-Butyl-6-methylcyclohexanone and 2-*sec*-Butyl-2-methylcyclohexanone. To 10 mmol of lithium *tert*-butoxy(*sec*-butyl)cuprate at −78° was added 270 mg (1.0 mmol) of *trans*-2,6-dibromo-2-methylcyclohexanone and, after 30 min, 1 ml of absolute methanol. Normal work-up was followed by solvent removal under reduced pressure leaving 184 mg of a yellow oil. Analytical glpc (column C, 125° cyclooctanone internal standard) indicated three major components: A, 2 min; B, 9.5 min; C, 11 min. A was identified as 2-methylcyclohexanone (4 mg, 3%) by comparing its retention time with an authentic sample. Preparative glpc (column H, 200°) gave pure samples of B (35 min) and C (40 min). B is 2-*sec*-butyl-6-methylcyclohexanone (100 mg, 61%): nmr (CCl_4) δ 1.05–2.5 (broad m, *ca.* 11 H), 0.7–1.05 (spikey m, *ca.* 9 H) with apparent methyl doublet at 0.95 ($J = 6$ Hz); ir (CCl_4) 1713 cm^{-1} (C=O); mass spectrum (70 eV) *m/e* 168, 153, 139, 112, 97.

Anal. Calcd for $C_{11}H_{20}O$: C, 78.51; H, 11.98. Found: C, 78.28; H, 12.07. r

C is 2-*sec*-butyl-2-methylcyclohexanone (13 mg, 8%): nms (CCl_4) similar to above compound except that the methyl doublet i replaced by a singlet at δ 0.83; ir (CCl_4) 1709 cm^{-1} (C=O); mass spectrum (70 eV) *m/e* 168, 166, 139, 127, 112, 97.

2-*tert*-Butyl-6-methylcyclohexanone and 2-*tert*-Butyl-2-methylcyclohexanone. To 10.0 mmol of lithium *tert*-butoxy(*tert*-butyl)cuprate at −78° was added 270 mg (1.0 mmol) of *trans*-2,6-dibromo-2-methylcyclohexanone and, after 30 min, 1 ml of absolute methanol. Normal work-up was followed by solvent removal under reduced pressure leaving 180 mg of a yellow oil. Analytical glpc (column C, 110°, cycloheptanone internal standard) indicated three major components: A, 3 min; *B*, 11 min; *C*, 12 min. A was identified as 2-methylcyclohexanone (20 mg, 13%) by comparing its retention time with that of authentic material. Preparative glpc (column H, 200°) gave pure B (33 min) and C (38 min). B is 2-*tert*-butyl-6-methylcyclohexanone (52 mg, 31%): nmr (CCl_4) δ 1.0–2.3 (m, 8 H), 1.0 (s, *t*-Bu), 0.85 (s, CH_3), which is the upfield component of the methyl doublet partially obscured by the *tert*-butyl singlet; ir (CCl_4) 1714 cm^{-1} (C=O); mass spectrum (70 eV) *m/e* 168, 153, 112, 69.

Anal. Calcd for $C_{11}H_{20}O$: C, 78.51; H, 11.98. Found: C, 78.46; H, 12.03.

C is 2-*tert*-butyl-2-methylcyclohexanone (3 mg, 2%): nmr (CCl_4) δ 1.0–2.5 (m, 8 H), 0.95 (s, 3H), 0.85 (s, 9 H); ir (CCl_4) 1713 cm^{-1} (C=O); mass spectrum (70 eV) *m/e* 168, 153, 125, 111, 97, 83, 69.

6-Hendecanone and 3-*n*-Butyl-2-heptanone. To 5.0 mmol of lithium *tert*-butoxy(*n*-butyl)cuprate at −78° was added 272 mg (1.0 mmol) of 1,3-dibromo-2-heptanone in 1 ml of tetrahydrofuran and, after 30 min, 1 ml of absolute methanol. Normal work-up was followed by solvent removal under reduced pressure leaving 200 mg of a green oil. Analytical glpc (column C, 125°, cyclooctanone internal standard) indicated two major products: A, 7 min; B, 9.5 min. Preparative glpc (column H, 200°) was used to isolate A (25 min) and B (31 min). A is 3-*n*-butyl-2-heptanone (19 mg, 11%) which has spectral data fully consistent with those in the literature.[68a] B is 6-hendecanone (63 mg, 37%): $n^{25}D$ 1.4270 (lit.[68b] $n^{25}D$ 1.4268); nmr (CCl_4) δ 2.15–2.0 (m, 4 H), 1.05–1.85 (m, 12 H), 0.75–1.05 (m, 6 H); ir (CCl_4) 1720 cm^{-1} (C=O); mass spectrum (70 eV) *m/e* 170, 127, 114, 99, 71.

3-Methyl-5-decanone and 2-*sec*-Butyl-2-heptanone. To 5.0 mmol of lithium *tert*-butoxy(*sec*-butyl)cuprate at −78° was added 272 mg (1.0 mmol) of 1,3-dibromo-2-heptanone in 1 ml of tetrahydrofuran and, after 30 min, 1 ml of absolute methanol. Normal work-up was followed by solvent removal under reduced pressure leaving 188 mg of a green oil. Analytical glpc (column C, 125°, cyclooctanone internal standard) indicated two major peaks: A, 6 min; B, 7.5 min. Preparative glpc (column H, 200°) was used to isolate A (24 min) and B (27 min). A is 2-*sec*-butyl-2-heptanone (14 mg, 8%): nmr (CCl_4) δ 2.15–2.4 (m, 1 H), 2.05 (s, 3 H), 1.05–1.9 (m, 9 H), 0.65–1.05 (m, 9 H); ir (CCl_4) 1715 cm^{-1} (C=O); mass spectrum (70 eV) *m/e* 170, 114, 99, 85, 71. B is 3-methyl-5-decanone (83 mg, 49%): nmr (CCl_4) δ 2.1–2.5 (m, 4 H), 1.05–1.90 (m, 9 H), 0.7–1.05 (m, 9 H); ir (CCl_4) 1720 cm^{-1} (C=O); mass spectrum (70 eV) *m/e* 170, 99, 71, 59, 58.

Anal. Calcd for $C_{11}H_{22}O$: C, 77.58; H, 13.02. Found: C, 77.28; H, 12.86.

2,2-Dimethyl-4-nonanone and 3-*tert*-Butyl-2-heptanone. To 5.0 mmol of lithium *tert*-butoxy(*tert*-butyl)cuprate at −78° was added 272 mg (1.0 mmol) of 1,3-dibromo-2-heptanone and, after 30 min, 1 ml of absolute methanol. Analytical glpc (column C, 110°, cycloheptanone internal standard) indicated two major peaks: A, 8 min; B, 9 min. Preparative glpc (column H, 170°) was used to isolate A (41 min) and B (45 min). A is 3-*tert*-butyl-2-heptanone (10 mg, 6%): nmr (CCl_4) δ 2.1–2.4 (m, 1 H), 2.05 (s, 3 H), 1.05–1.70 (m, 6 H), 0.85–1.05 (m, 3 H) superimposed on 0.90 (s, 9 H); ir (CCl_4) 1715 cm^{-1} (C=O); mass spectrum (70 eV) *m/e* 170, 155, 114, 99, 85, 71. B is 2,2-dimethyl-4-nonanone (90 mg, 53%): nmr (CCl_4) 2.15–2.45 (m, 4 H), 1.1–1.55 (m, 6 H), 1.05–0.85 (m, 3 H) superimposed on 1.00 (s, 9 H); ir (CCl_4) 1720 cm^{-1} (C=O); mass spectrum (70 eV) *m/e* 170, 99, 71. The samples were combined for microanalysis.

Anal. Calcd for $C_{11}H_{22}O$: C, 77.58; H, 13.02. Found: C, 77.27; H, 12.65.

2-Methyl-3-octanone and 3,3-Dimethyl-2-heptanone. To 5.0 mmol of lithium *tert*-butoxy(*n*-butyl)cuprate at −78° was added 244 mg (1.0 mmol) of 1,3-dibromo-3-methyl-2-butanone in 1 ml of tetrahydrofuran and, after 30 min, 1 ml of absolute methanol. Normal work-up was followed by careful solvent removal using a 15-cm vigreux column. Analytical glpc (column A, 130°, 5-nonanone as internal standard) indicated four major products: A, 3 min; B, 5 min; C, 5.5 min; D, 16 min. A could not be cleanly resolved from solvent. Preparative glpc (column F, 120°) gave pure samples of B (31 min) and C (41 min). B is 3,3-dimethyl-2-heptanone (35 mg, 25%): bp 173–174° (760 mm) (lit.[69] bp 169.5 (735 mm)); nmr (CCl_4) δ 2.0 (s, 3 H), 1.05 (s, 6 H) superimposed on 0.8–1.6 (m, 9 H); ir (CCl_4) 1708 cm^{-1} (C=O); mass spectrum (70 eV) *m/e* 142, 99, 86, 71. C is 2-methyl-3-octanone (75 mg, 55%): bp 180–181° (760 mm) (lit.[70] bp 182–184° (760

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mm)); nmr (CCl_4) δ 2.2–2.8 (m, 3 H), 1.05 (d, 6 H, J = 7 Hz) superimposed on 0.8–1.7 (m, 9 H); ir (CCl_4) 1714 cm^{-1} (C=O); mass spectrum (70 eV) *m/e* 142, 86, 71. A was not identified.

2,5-Dimethyl-3-heptanone and 3,3,4-Trimethyl-2-hexanone. To 5.0 mmol of lithium *tert*-butoxy(*sec*-butyl)cuprate at −78° was added 244 mg (1.0 mmol) of 1,3-dibromo-3-methyl-2-butanone in 1 ml of tetrahydrofuran and, after 30 min, 1 ml of absolute methanol. Normal work-up was followed by careful solvent removal through a 15-cm vigreux column. Analytical glpc (column A, 120°, nonanone internal standard) indicated two major products: A, 4 min; B, 5.5 min. Preparative glpc (column E, 145°) was used to isolate B (18 min) and C (21 min). B is 2,5-dimethyl-3-heptanone (60 mg, 42%): nmr (CCl_4) δ 1.7–2.7 (m, 4 H), 0.7–1.4 (m, 8 H) superimposed on 1.05 (d, J = 7 Hz, 6 H); ir (CCl_4) 1713 cm^{-1} (C=O); mass spectrum (70 eV) *m/e* 142, 113, 99, 86, 71.

Anal. Calcd for $C_9H_{18}O$: C, 75.99; H, 12.76. Found: C, 76.29; H, 12.52.

C is 3,3,4-trimethyl-2-hexanone (11 mg, 8%): nmr (CCl_4) δ 2.0 (s, 3 H), 0.95 (s, 6 H), superimposed on 0.7–1.6 (m, 9 H), which is fully consistent with the literature nmr spectrum;[71] ir (CCl_4) 1708 cm^{-1} (C=O); mass spectrum (70 eV) *m/e* 142, 99, 71.

2,5,5-Trimethyl-3-hexanone and 3,3,4,4-Tetramethyl-2-pentanone. To 5.0 mmol of lithium *tert*-butoxy(*tert*-butyl)cuprate at −78° was added 244 mg (1.0 mmol) of 1,3-dibromo-3-methyl-2-butanone in 1 ml of tetrahydrofuran and, after 30 min, 1 ml of methanol. Normal work-up was followed by careful solvent removal through a 15-cm vigreux column. Analytical glpc (column A, 135°, cycloheptanone internal standard) indicated three major products: A, 2.7 min; B, 4 min; C, 6.5 min. Preparative glpc (column E, 150°) was used to isolate the products: A, 8 min; B, 12 min; C, 20 min. A is 2,5,5-trimethyl-3-hexanone (81 mg, 56%): $n^{20}{}_D$ 1.4137 (lit.[72] $n^{20}{}_D$ 1.4114–1.4129); nmr (CCl_4) δ 2.2–2.8 (heptuplet, J = 6.5 Hz, 1 H), 2.3 (s, 2 H), 1.05 (d, J = 6.5 Hz, 6 H) overlapping 1.0 (s, 9 H); ir (CCl_4) 1712 cm^{-1} (C=O); mass spectrum (70 eV) *m/e* 142, 99, 86, 71. B is 3,3,4,4-tetramethyl-2-pentanone (13 mg, 10%): bp 163–164° (760 mm) (lit.[73] bp 165.5–166.5 (760 mm)); nmr (CCl_4) δ 2.05 (s, 3 H), 1.1 (s, 3 H), 0.95 (s, 3 H), 0.85 (s, 9 H); ir (CCl_4) 1720 cm^{-1} (C=O); mass spectrum (70 eV) *m/e* 142, 137, 127, 109, 85, 71. C was unidentified.

3,3-Dimethylcyclohexanone. To 8.60 g (45.1 mmol) of cuprous iodide in 135 ml of diethyl ether at 0° was added 45.5 ml of 1.98 *M* (90 mmol) methyllithium. The clear colorless solution was cooled to −78° and 3.3 g (30 mmol) of 3-methyl-2-cyclohexenone was added in 3 ml of diethyl ether. After 1 hr at −78°, the reaction was allowed to warm to 0° for 45 min at which time 1 ml of absolute methanol was added. Normal work-up was followed by solvent removal leaving 3.36 g of a green oil. Analytical glpc (column A, 150°) showed one peak (4 min). The crude product was distilled at 73–74° (26 mm) (lit. bp 71–71.5 (19 mm))[74] to give clear colorless 3,3-dimethylcyclohexanone (2.9 g, 77%): nmr (CCl_4) δ 1.4–2.3 (m, 8 H), 0.95 (s, 6 H); ir (CCl_4) 1717 cm^{-1} (C=O). Spectral data were fully consistent with those in the literature.[74]

2-*n*-Butyl-5,5-dimethylcyclohexanone and 2-*n*-Butyl-3,3-dimethylcyclohexanone. To 5.0 mmol of lithium *tert*-butoxy(*n*-butyl) cuprate at −78° was added 284 mg (1.0 mmol) of 2,6-dibromo-3,3-dimethylcyclohexanone in 1 ml of tetrahydrofuran and, after 30 min, 1 ml of absolute methanol. Normal work-up was followed by solvent removal under reduced pressure leaving 177 mg of a yellow oil. Analytical glpc (column C, 160°, cyclododecanone internal standard) indicated three major peaks: A, 1.7 min; B, 2 min; C, 5.2 min. A was identified as 3,3-dimethylcyclohexanone (22 mg, 17%) by comparing its retention time with that of authentic material. Preparative glpc (column E, 195°) was used to isolate B (8 min) and C (28 min): B[75] is apparently a mixture of methyl esters (22 mg, 16%): nmr (CCl_4) δ 3.6 (s, 3 H); ir (CCl_4) 1734 cm^{-1} (C=O). C is an 85:15 mixture of 2-*n*-butyl-5,5-dimethylcyclohexanone and 2-*n*-butyl-3,3-dimethylcyclohexanone as revealed by analytical glpc (column B, 150°, 26 and 27.5 min, respectively). They could not be completely separated, so the following data are for the isolated mixture (66 mg, 36%): nmr (CCl_4) δ 0.8–2.2 (m), 2.1 (s), 1.6 (m), 1.2 (m), 1.0 (s), 0.85 (s); ir (CCl_4) 1712 cm^{-1} (C=O); mass spectrum (70 eV) *m/e* 182, 167, 139, 126, 111.

Anal. Calcd for $C_{12}H_{22}O$: C, 79.06; H, 12.16. Found: C, 79.27; H, 11.93.

2-*tert*-Butyl-5,5-dimethylcyclohexanone. To 5.0 mmol of lithium *tert*-butoxy(*tert*-butyl)cuprate at −78° was added 285 mg (1.0 mmol) of 2,6-dibromo-3,3-dimethylcyclohexanone and, after 30 min, 1 ml of absolute methanol. Normal work-up was followed by solvent removal under reduced pressure leaving 170 mg of a yellow oil. Analytical glpc (column C, 160°, cyclododecanone internal standard) indicated three major products: A, 1.7 min; B, 1.9 min; C, 3.5 min. A was identified as 3,3-dimethylcyclohexanone (20 mg, 15%) by comparing its retention time with that of authentic material. Preparative glpc (column E, 185°) was used to isolate B (18 min) and C (23 min). B[75] is 5,5-dimethyl-2-cyclohexenone (20 mg, 15%): nmr (CCl_4) δ 6.7 (m, 1 H), 5.85 (m, 1 H), 2.2 (m, 4 H), 1.05 (s, 6 H); ir (CCl_4) 1682 (C=O); mass spectrum (70 eV) *m/e* 124, 109, 96, 81, 68. Spectral data are completely consistent with those in the literature.[76] C is 2-*tert*-butyl-5,5-dimethylcyclohexanone (60 mg, 33%): mp 37–38°; nmr (CCl_4) δ 1.4–2.4 (m, 7 H), 1.0 (s, 3 H), 0.95 (s, 9 H), 0.85 (s, 3 H); ir (CCl_4) 1714 cm^{-1} (C=O); mass spectrum (70 eV) *m/e* 182, 168, 139, 127.

Anal. Calcd for $C_{12}H_{22}O$: C, 79.06; H, 12.16. Found: C, 78.83; H, 12.27.

2α- and 4α-Methyl-5α-cholestan-3-one. To 305 mg (1.6 mmol) of cuprous iodide in 4 ml of diethyl ether at 0° was added 1.4 ml of 2.06 *M* (3.0 mmol) methyllithium. The clear colorless solution was cooled to −78° and 163 mg (0.3 mmol) of 2α,4α-dibromo-5α-cholestan-3-one was added through a side arm. After 30 min, 1 ml of absolute methanol was added to the yellow suspension, followed by normal work-up and solvent removal under reduced pressure, leaving 118 mg (99%) of white crystals, mp 102–109°. These were recrystallized twice from absolute methanol to give a material of mp 122–123°; however, nmr (CCl_4) still indicated the methyl doublet peaks from both 2α- and 4α-methyl-5α-cholestan-3-one (2α-methyl-5α-cholestan-3-one (mp 119–120°[77]) absorbs at δ 0.94 (J = 6 Hz) in an authentic sample, and 4α-methyl-5α-cholestan-3-one (mp 121–123°[78]) is reported[79] to absorb at δ 0.90 (J = 7 Hz)).

General Procedure for Reaction of α,α′-Dibromo Ketones with Lithium Dimethylcuprate. To 970 mg (5.1 mmol) of cuprous iodide in 14 ml of anhydrous diethyl ether at 0° was added 5.6 ml of 1.72 *M* (10.0 mmol) methyllithium. The resulting clear solution was cooled to −78° and 1.0 mmol of α,α′-dibromo ketone was added by syringe. After 30 min 1 ml of absolute methanol was added followed by a normal work-up which involved pouring the reaction mixture into a stirring aqueous solution of ammonium chloride and extracting with ether.

2-Methylcyclododecanone. A. **Using Lithium Dimethylcuprate.** Using the general procedure, to 40.0 mmol of lithium dimethylcuprate at −78° was added through a side arm 3.44 g (10.0 mmol) of solid *cis*-2,12-dibromocyclododecanone. After 15 min, 10 ml of methanol was added to the yellow suspension followed by normal work-up and solvent removal leaving 1.88 g (99% yield) of a yellow oil. Analytical glpc (column A, 200°) indicated two peaks: A, 7 min; B, 8 min. A was identified as cyclododecanone by comparing its retention time with that of authentic material and accounted for *ca.* 1% of the mixture. B corresponds to 2-methylcyclododecanone. Distillation at a bath temperature of *ca.* 100° (0.2 mm) gave a clear colorless oil: nmr (CCl_4) δ 2.5 (broad m, 3 H), 1.3 (m, 18 H), 1.02 (d, J = 7 Hz, 3 H); ir (CCl_4) 1710 cm^{-1} (C=O); mass spectrum (70 eV) *m/e* 196; semicarbazone mp 211–213°.

Anal. Calcd for $C_{14}H_{27}N_3O$: C, 66.36; H, 10.74; N, 16.59. Found: C, 66.62; H, 10.53; N, 16.43.

B. **Using Methylmagnesium Iodide.** To 107 mg (4.0 mmol) of magnesium turnings in 6 ml of diethyl ether was added 0.25 ml (4.0 mmol) of neat methyl iodide. After the reaction was initiated 10 ml more of diethyl ether was added and in *ca.* 15 min 680 mg (2.0 mmol) of dry *cis*-2,6-dibromocyclododecanone was added *via* a side arm. After 30 min at ambient temperature the reaction was poured

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into brine and extracted with ether, the combined organic layers were dried ($MgSO_4$), and solvent was removed under reduced pressure leaving 350 mg of a yellow oil. Analytical glpc (column C, 200°) indicated three peaks: A, 3.5 min; B, 4.5 min; C, 5.5 min. Each was identified by comparing retention times (and ultimately nmr data) to authentic material. A is cyclododecanone (7 mg, 2%); B is 2-methylcyclododecanone (335 mg, 86%); C is 2,12-dimethylcyclododecanone (7 mg, 2%).

2,12-Dimethylcyclododecanone. To 10.0 mmol of lithium dimethylcuprate at −78° was added through a side arm 680 mg (2.0 mmol) of solid *cis*-2,12-dibromocyclododecanone. After 30 min 3.6 ml (50 mmol) of neat methyl iodide was added and the reaction allowed to stir at ambient temperature overnight. Normal work-up was followed by solvent removal leaving 420 mg of a yellow oil. Analytical glpc (column C, 180°) indicated three products: A, 6 min; B, 7 min, C, 8 min. A was identified as 2-methylcyclododecanone by comparing its retention time with that of authentic material. Preparative glpc (column H, 215°) was used to isolate B (30 min) and C (34 min). B is 2,12-dimethylcyclododecanone (285 mg, 68%) recrystallized from absolute methanol: mp 43–44°; nmr (CCl_4) δ 2.72 (broad m, 2 H), 1.31 (m, 18 H), 1.00 (d, J = 7 Hz, 6 H); ir (CCl_4) 1710 cm^{-1} (C=O); mass spectrum (70 eV) *m/e* 210. C is 2,12-dimethylcyclododecanone (122 mg, 29%): nmr (CCl_4) δ 2.72 (broad m, 2 H), 1.33 (m), 1.04 (d, J = 7 Hz, 6 H); ir (CCl_4) 1700 cm^{-1} (C=O); mass spectrum (70 eV) *m/e* 210. The isomeric nature of A and B was confirmed by combining them for microanalysis. They are apparently *cis-* and *trans*-2,12-dimethylcyclododecanone.

Anal. Calcd for $C_{14}H_{26}O$: C, 79.93; H, 12.46. Found: C, 80.05; H, 12.37.

2-Deuterio-12-methylcyclododecanone. To 5.0 mmol of lithium dimethylcuprate at −78° was added *via* a side arm 240 mg (5.0 mmol) of solid 2,12-dibromocyclododecanone. After 15 min a 10% deuterium oxide (25.0 mmol) solution in tetrahydrofuran was added followed by normal work-up and solvent removal under reduced pressure leaving 178 mg of a green oil. Comparison with an nmr (CCl_4) of 2-methylcyclododecanone indicated that this product was predominantly 2-deuterio-12-methylcyclododecanone because of the decrease in size of the δ 2.5 multiplet relative to the rest of the absorption and the continued presence of a methyl *doublet* at δ 1.02. The mass spectrum (70 eV) confirms this analysis indicating a 95% d_1 peak.

2-Methylcyclooctanone. A. Using Lithium Dimethylcuprate. To 10.0 mmol of lithium dimethylcuprate at −78° was added *via* a side arm 284 mg (1.0 mmol) of solid 2,8-dibromocyclooctanone. After 5 min, the reaction was allowed to warm to ambient temperature for 90 min before adding 1 ml of absolute methanol. Normal work-up and solvent removal under reduced pressure left 123 mg of a yellow oil. Analytical glpc (column C, 180°) indicated four products: A, 1.5 min; B, 1.6 min; C, 2.3 min; D, 3.3 min. A was identified as cyclooctanone (*ca.* 3 mg, 2%) by comparing its retention time to authentic material. B is 2-methylcyclooctanone (111 mg, 80%) isolated by preparative glpc (column H, 190°): n^{25}D 1.4670 (lit.[80] n^{25}D 1.4654–1.4657); nmr (CCl_4) δ 2.33 (m, 3 H), 1.52 (m, 10 H), 0.95 (d, J = 6 Hz, 3 H); ir (CCl_4) 1705 cm^{-1} (C=O); mass spectrum (70 eV) *m/e* 140. C (*ca.* 2% of mixture) was unidentified. D was identified as 2-bromocyclooctanone (*ca.* 3 mg 2%) by comparing its retention time with that of authentic material.

B. Using Methylmagnesium Iodide. To 107 mg (4.0 mmol) of magnesium turnings in 6 ml of diethyl ether was added 0.25 ml (4.0 mmol) of neat methyl iodide. After the reaction was initiated 10 ml more of diethyl ether was added and in *ca.* 15 min 568 mg (2.0 mmol) of solid 2,8-dibromocyclooctanone was added *via* a side arm. After 30 min at ambient temperature the reaction was poured into brine and extracted with ether, the combined organic layers were dried ($MgSO_4$), and solvent was removed under reduced pressure leaving 210 mg of a yellow oil. Analytical glpc (column C, 180°) indicated two major peaks: A, 2 min; B, 3.5 min. Both were identified by comparing retention times with those of authentic material and corroborated by nmr (CCl_4) of the mixture. A is 2-methylcyclooctanone (178 mg, 65%) and B is 2-bromocyclooctanone (32 mg, 8%).

4-Methyl-5-nonanone. To 5.0 mmol of lithium dimethylcuprate at −78° was added 600 mg (2.0 mmol) of 4,6-dibromononanone in 10 ml of diethyl ether. After 30 min, 2 ml of absolute methanol was added followed by normal work-up and solvent removal under reduced pressure leaving 315 mg of a yellow oil. Analytical glpc (column A, 135°, cyclooctanone internal standard) indicates one major product: 4-methyl-5-nonanone (109 mg, 70%) which was isolated *via* preparative glpc (column F, 160°): bp 192° (760 mm) (lit.[81] 189–190° (745 mm)); nmr (CCl_4) δ 2.4 (m, 3 H), 0.9–1.8 (m, 10 H), 0.9 (d, 3 H); ir (CCl_4) 1715 cm^{-1} (C=O); mass spectrum (70 eV) *m/e* 156.

2,2,4-Trimethyl-3-pentanone. A. Using Lithium Dimethylcuprate. Having taken the usual precautions for the exclusion of moisture, a flask was charged with 12.8 ml of 1.58 *M* (20 mmol) methyllithium. The ether was then evaporated off at aspirator pressure (with a calcium chloride trap) at 0° and replaced by 50 ml of pentane followed by 1.92 g (10.1 mmol) of cuprous iodide added *via* a side arm. The reaction was cooled at −50° and 544 mg (2.0 mmol) of 2,4-dibromo-2,4-dimethyl-3-pentanone with 125 mg of chlorobenzene internal glpc standard was added in 15 ml of pentane over 20 min. After 30 min of further stirring, 1 ml of absolute methanol was added followed by normal work-up. Analytical glpc (column B, 100°) indicated 11 peaks between 3 and 12 min of which none accounted for more than 15% of the mixture except that one at 6 min. This corresponds to 2,2,4-trimethyl-3-pentanone (138 mg, 54%) which was isolated by preparative glpc (column E, 110°, 33 min): by 137° (760 mm) (lit.[82] bp 135° (760 mm)); n^{25}D 1.4054; nmr (CCl_4) δ 3.00 (q, J = 6 Hz, 1 H), 1.12 (s, 9 H); 1.00 (d, J = 6 Hz, 6 H); ir (CCl_4) 1705 cm^{-1} (C=O); mass spectrum (70 eV) *m/e* 128.

B. Using Methylmagnesium Iodide. To 107 mg (4.0 mmol) of magnesium turnings in 6 ml of diethyl ether was added 0.25 ml (4.0 mmol) of neat methyl iodide. After the reaction was initiated 10 ml more of diethyl ether was added and in *ca.* 15 min 544 mg (2.0 mmol) of 2,4-dibromo-2,4-dimethyl-3-pentanone in 1 ml of ether. After 30 min at ambient temperature the reaction was poured into brine and extracted with ether and the combined organic layers were dried ($MgSO_4$). Analytical glpc (column B, 100°, 2-heptanone internal standard) indicated that the product was almost entirely 2,2,4-trimethyl-3-pentanone (180 mg, 70%) by comparing its retention time with that of authentic material.

2-Methylcyclohexanone. A. From *trans*-2,6-Dibromocyclohexanone. To 10.0 mmol of lithium dimethylcuprate at −78° was added 512 mg (2.0 mmol) of *trans*-2,6-dibromocyclohexanone in 1 ml of ether. After 30 min 1 ml of absolute methanol was added followed by normal work-up and solvent removal under reduced pressure leaving 222 mg of a yellow oil. Analytical glpc (column C, 100°, cymene internal standard) indicated this oil to be almost entirely 2-methylcyclohexanone (220 mg, 98%, 4 min), with a small amount of cyclohexanone (<1%), by comparing retention times with authentic material. Nmr and ir were also fully consistent with those of an authentic sample of 2-methylcyclohexanone.

B. From *cis*-2,6-Dibromocyclohexanone. The above procedure was exactly repeated for *cis*-2,6-dibromocyclohexanone, except that the reaction was allowed to warm to ambient temperature over 30 min before adding 1 ml of methanol. In this case analytical glpc (column C, 100°, cycloheptanone internal standard) indicated 2-methylcyclohexanone as the major product (212 mg, 95%) and cyclohexanone as the only observable side product (*ca.* 1%).

1,3-Diphenyl-2-butanone. To 5.0 mmol of lithium dimethylcuprate at −78° was added *via* a side arm 368 mg (1.0 mmol) of solid 1,3-dibromo-1,3-diphenyl-2-propanone. After 30 min 1 ml of absolute methanol was added followed by normal work-up and solvent removal under reduced pressure leaving 219 mg of a yellow oil containing some solid material which showed only one peak on analytical glpc (column C, 180°, 5 min). The solid was removed by filtration and recrystallized twice from a methanol–chloroform–ether solution to give *ca.* 10 mg of fine white powder which is 1,3,4,6-tetraphenyl-2,5-hexanedione: mp 199–201° (lit.[83] mp 202–203°); nmr (CCl_4) δ 7.28 (m, 20 H), 4.69 (s, 2 H), 3.40 (s, 4 H); ir (CCl_4) 1710 cm^{-1} (C=O); mass spectrum (70 eV) *m/e* (no parent) 209, 119, 91. The remaining oil was distilled at a bath temperature of *ca.* 120° (0.2 mm) to give 1,3-diphenyl-2-butanone (150 mg, 67%) as a clear colorless oil: n^{20}D 1.5621 (lit.[84] n^{20}D 1.5652); nmr (CCl_4) δ 7.25 (m, 10 H), 3.75 (q, J = 7 Hz, 1 H), 3.52 (s, 2 H), 1.30 (d, J = 7 Hz, 3 H); ir (CCl_4) 1710 cm^{-1} (C=O).

2α,4β-Diphenyl-8-oxabicyclo[3.2.1]octen-3-one. To 60.0 mmol of lithium dimethylcuprate in 170 ml of furan at −78° was added *via*

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a side arm 5.5 g (15.0 mmol) of dry 1,3-dibromo-1,3-diphenyl-2-propanone. After 15 min methanol was added, followed by normal work-up and solvent removal leaving 2.5 g of a yellow semisolid oil. This material was column chromatographed on *ca.* 150 g of alumina as follows: 50:50 ligroin–benzene eluted with 1,3-diphenyl-2-butanone; 9:1 benzene–ligroin eluted 2α,4β-diphenyl-8-oxabicyclo[3.2.1]octen-3-one which was recrystallized from ether and ether–$CHCl_3$ to give white crystals: mp 150–151° (lit.[85] mp 152–153°); nmr ($CDCl_3$) δ 7.2 (m, 10 H), 6.51 (s, 2 H), 5.32 (d, J = 1 Hz, 1 H), 5.02 (d of d, J = 1 and 4 Hz, 1 H), 4.18 (d, J = 4 Hz, 1 H), 3.60 (s, 1 H); ir (Nujol) 1710 (C=O), 1695 cm^{-1}; uv (EtOH) λ (max) 260 (ϵ 515) and 298 nm (ϵ 320); mass spectrum (70 eV) *m/e* 276. These spectral data are fully consistent with those reported in the literature.[85]

Examination of the nmr spectrum ($CDCl_3$) of the original crude material revealed additional absorptions at δ 6.3 (s), 4.90 (d, J = 4.5 Hz) and 4.05 (d, J = 4.5 Hz) which correspond to peaks from 2α,4α-diphenyl-8-oxabicyclo[3.2.1]octen-3-one according to the literature.[85] Based on the nmr spectrum of the crude material, the combined yield of both Diels–Alder adducts is *ca.* 20%.

2α,4α-Diphenyl-8-oxabicyclo[3.2.1]octen-3-one. To 107 mg (4.0 mmol) of magnesium turnings in 6 ml of furan was added 0.25 ml (4.0 mmol) of neat methyl iodide. After the reaction was initiated 10 ml more of furan was added and in *ca.* 15 min solid 1,3-dibromo-1,3-diphenyl-2-propanone (736 mg, 2.0 mmol) was added *via* a side arm. After 30 min at ambient temperature the reaction was poured into brine and extracted with ether, the combined organic layers were dried ($MgSO_4$), and solvent was removed under reduced pressure leaving 455 mg of an orange oil. This material was column chromatographed on 50 g of silica as follows: 50:50 hexane–benzene eluted 1,3-diphenyl-2-butanone; benzene eluted 2α,4α-diphenyl-8-oxabicyclo[3.2.1]octen-3-one as an orange oil (50 mg) which was recrystallized twice from cold diethyl ether to give a few milligrams of white crystals: mp 126–127° (lit.[85] mp 134–135°); nmr ($CDCl_3$) δ 7.2 (m, 10 H), 6.35 (s, 2 H), 4.90 (d, J = 4.5 Hz, 2 H), 4.05 (d, J = 4.5 Hz, 2 H); ir (Nujol) 1705 cm^{-1} (C=O); mass spectrum (70 eV) *m/e* 276. These spectral data were consistent with those in the literature.[85]

Examination of the nmr spectrum of the original crude material reveals no absorption at δ 5.32, 5.02, 4.18, or 3.60, indicating no 2α,4β-diphenyl-8-oxabicyclo[3.2.1]octen-3-one; thus, the trans Diels–Alder adduct isolated in the analogous lithium dimethylcuprate reaction was not formed during this reaction. The yield of the cis Diels–Alder adduct was *ca.* 25%.

2,2-Dimethyldecane. Into a cold (−78°) suspension of 2.00 mmol of lithium phenylthio(*tert*-butyl)cuprate at −78° was injected a solution of 240 mg (1.00 mmol) of *n*-octyl iodide in 1.0 ml of tetrahydrofuran. After 2 hr at −78°, the reaction was warmed slowly over 1 hr to 0°. Excess organometallic was quenched by addition of 1.0 ml (25 mmol) of absolute methanol, and normal work-up including sodium hydroxide washing of the combined ether extracts gave a yellow oil. Analytical glpc (column C, 115°, *p*-cymene as internal standard) indicated one product (5.8 min) which was 2,2-dimethyldecane (167 mg, 98%). An analytically pure sample was obtained by preparative glpc (column F, 200°, 7.5 min): $n^{19}D$ 1.4195 (lit.[86] $n^{19}D$ 1.4192); ir (CCl_4) 2978, 2963, 2928, 1458, 1362 cm^{-1}; nmr (CCl_4) δ 1.05–1.40 (broad m, 14 H), 0.90 (s over t, 12 H).

3-*n*-Butylcyclohexanone. To a suspension of 495 mg (2.60 mmol) of cuprous iodide in 4.6 ml of tetrahydrofuran at 25° was added 2.36 ml of 1.10 *M* (2.60 mmol) lithium *tert*-butoxide in 1:1 tetrahydrofuran–hexane. After 15 min all solid, gray cuprous iodide had disappeared, the suspension was cooled to −78°, and 1.40 ml of 1.81 *M* (2.54 mmol) *n*-butyllithium in hexane was added dropwise followed in 15 min by a solution of 198 mg (2.06 mmol) of 2-cyclohexen-1-one in 2.0 ml of tetrahydrofuran. The reaction was then maintained at −50° for 2 hr, quenched with 1.0 ml (25 mmol) of absolute methanol, and poured into 50 ml of saturated, aqueous ammonium chloride. The aqueous phase was extracted with three 50 ml portions of ether, and the combined ether phases were washed with 1% sodium thiosulfate and dried with magnesium sulfate. Removal of the solvent *in vacuo* left 339 mg (106%) of a yellow oil which was microdistilled to afford 269 mg (84%) of pure 3-*n*-butylcyclohexanone: $n^{20}D$ 1.4563 (lit.[87] $n^{20}D$ 1.4555); ir (CCl_4) 1715 cm^{-1} (C=O); nmr δ 1.6–2.5 (m), 1.33 (broad s), 0.90 (t).

3-*tert*-Butylcyclohexanone. To a stirred suspension of 952 mg (5.00 mmol) of cuprous iodide in 11.0 ml of tetrahydrofuran was added at 25° 4.70 ml of 1.06 *M* (4.98 mmol) lithium thiophenoxide in 1:1 tetrahydrofuran–hexane. A clear, yellow solution formed within 5 min but became a cloudy, heterogeneous mixture upon cooling. Into the cold (−78°) suspension was injected dropwise 2.35 ml of 2.12 *M* (4.98 mmol) *tert*-butyllithium in pentane followed after 5 min by 189 mg (1.97 mmol) of 2-cyclohexen-1-one dissolved in 2.0 ml of tetrahydrofuran. The reaction mixture was warmed to 0° and, after 2 hr, was poured into 50 ml of rapidly stirred, saturated, aqueous ammonium chloride. The yellow precipitate thus formed was removed by suction filtration, and the aqueous phase was extracted with three 50-ml portions of ether. The ether phases were combined, washed with 1 *N* sodium hydroxide and dried with magnesium sulfate, and solvent was removed *in vacuo* to leave 322 mg (104%) of a yellow oil. Analytical glpc (column A, 150°, 3-*n*-butylcyclohexanone as internal standard) indicated one major product (10.8 min) which was 3-*tert*-butylcyclohexanone (260 mg, 86%). Microdistillation afforded 220 mg (72%) of the pure ketone: $n^{25}D$ 1.4612 (lit.[88] $n^{25}D$ 1.4611); ir (CCl_4) 1715 cm^{-1} (C=O); nmr (CCl_4) δ 1.1–2.4 (broad m, 9 H), 0.92 (s, 9 H).

3-Vinylcyclopentanone. To a cold (−78°) suspension of 21 mmol of lithium phenylthio(vinyl)cuprate[89] was added a cold (−78°) solution of 1.64 g (20.0 mmol) of 2-cyclopenten-1-one in 5.0 ml of tetrahydrofuran. After 20 min the reaction was quenched with 5.0 ml (125 mmol) of absolute methanol and worked up by the usual procedure including both a 1 *N* sodium hydroxide and a 1% sodium thiosulfate wash. Analytical glpc (column D, 130°, cymene as internal standard) indicated one volatile product (8.5 min) which was 3-vinylcyclopentanone (725 mg, 33%). The crude product was distilled under vacuum to afford 682 mg (31%) of colorless liquid (bp 80–90° (34 mm), 90–95% pure by glpc). Substantial amounts of high boiling residue, principally tetra-*n*-butyltin from the vinyllithium, remained in the distilling flask. A pure sample was obtained by preparative glpc (column H, 180°, 15 min): ir (CCl_4) 3080, 1748 (C=O), 1642 (C=C), 912 cm^{-1}; nmr (CCl_4) δ 5.86 (m, 1 H), 5.12 (m, 1 H), 4.95 (m, 1 H), 2.5–3.1 (m, 7 H); mass spectrum (70 eV) *m/e* 110 (molecular ion), 95, 82, 81, 68, 67, 54, 53, 39.

Anal. Calcd for $C_7H_{10}O$: C, 76.33; H, 9.15. Found: C, 76.55; H, 9.26.

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