Reactions of Lithium Diorganocuprates(I) with Tosylates. II. Stereochemical, Kinetic, and Mechanistic Aspects

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Abstract: The reaction of (+)-(*S*)-2-butyl tosylate or mesylate with lithium diphenylcuprate(I) in ether afforded (−)-(*R*)-2-phenylbutane in an optical purity indicating that the reactions had proceeded with 100% inversion of configuration. Reaction of lithium dimethylcuprate(I) with *trans*-4-*tert*-butylcyclohexyl tosylate gave *cis*-1-*tert*-butyl-4-methylcyclohexane (36%) and 4-*tert*-butylcyclohexene (64%), with *cis*-4-*tert*-butylcyclohexyl tosylate gave *trans*-1-*tert*-butyl-4-methylcyclohexane (6%) and 4-*tert*-butylcyclohexene (94%), with *endo*-2-norbornyl tosylate gave *exo*-2-methylnorbornane (65%), norbornene (3%), and nortricyclane (9%), with *exo*-2-norbornyl tosylate gave *exo*-2-methylnorbornane (50%), *endo*-2-methylnorborane (15%), norbornene (2%), and nortricyclane (9%). The reaction of *n*-octyl tosylate with lithium dimethylcuprate(I) in diethyl ether at −42° to yield *n*-nonane was found to have a second-order rate constant of 2.8×10^{-3} l. mol^{-1} sec^{-1}. The order of effectiveness of leaving groups in coupling reactions of lithium diorganocuprates was found to be OTs > I ~ Br > Cl. Various possible mechanisms for these reactions are discussed. It is concluded that these reactions involved the formation of a transient triorganocopper(III) intermediate.

In the preceding paper we have discussed the synthetic aspects of the coupling reactions of lithium diorganocuprates(I) with alkyl tosylates.[2] In the cases of primary tosylates, substitutions to produce new carbon–carbon σ bonds occur in high yield; the yields are somewhat depressed in the cases of secondary tosylates because of competiting elimination reactions. Using difunctional substrates the cuprates were found to react preferentially at the tosylate in a keto tosylate, faster at the tosylate in a bromo tosylate, and with little selectivity in an epoxy tosylate. This paper will be concerned with stereochemistry, kinetics, and mechanism of substitution reactions of tosylates using lithium diorganocuprates(I).

The detailed structures of the organocuprates remain uncertain. Gilman in 1936 had shown that the stoichiometry of the cuprate was 2 equiv of organolithium to 1 equiv of cuprous iodide.[3] House, Respess, and Whitesides have suggested that the equilibrium (eq 1) lies far to the right from the sharpness of the

$$(CH_3Cu)_n + CH_3Li \overset{Et_2O}{\rightleftharpoons} Li^+(CH_3)_2Cu^-(OEt_2)_2 \qquad (1)$$

nmr signal along with the low order of reactivity with carbonyl functions.[4] House and Fischer[5] have suggested that the cuprate is a dimer and exists as a tetrahedral structure analogous to that of methyllithium. van Kolten and Noltes have recently obtained two thermally stable lithium diarylcuprate(I) compounds.[6] They found these compounds to exist in benzene as dimers ($R_4Cu_2Li_2$) by cryoscopy and ebulliscopy. Moreover, examination of their ^{13}C magnetic resonance revealed that the C-1 aryl carbons appear as quartets as a result of ^{13}C–^{7}Li coupling of the C-1 atom with only one Li atom, suggesting a cyclic structure of carbon and metal atoms.

Results

Stereochemical Aspects of the Reaction. Background information on stereochemistry includes the fact that (−)-2-bromobutane reacts with 5 equiv of lithium diphenylcuprate with inversion of configuration to yield (+)-2-phenylbutane[7] (84–92% stereospecificity). There were problems associated with this reaction, the greatest being that secondary bromides react very slowly with the organocuprates and thus require high reaction temperatures (refluxing THF) and long reaction times. Halogen–metal exchange could take place under these conditions and may be responsible for the lack of complete stereospecificity of the reaction. Similarly, *cis*-1-bromo-4-*tert*-butylcyclohexane reacts with 5 equiv of lithium dimethylcuprate to yield a mixture of 45% *trans*-1-methyl-4-*tert*-butylcyclohexane, 10% *cis*-1-methyl-4-*tert*-butylcyclohexane, 4-*tert*-butylcyclohexene (E2 product), and 4-*tert*-butylcyclohexane (from reduction due to halogen–metal exchange).[8] An *endo*-2-norbornylcuprate has been shown to couple with methyl tosylate with retention of configuration to give 2-methylnorbornane (98% endo).[9]

The first example which we investigated was the reaction of an optically active tosylate with a cuprate. A commercial sample of (+)-2-butanol, 69% optically pure and greater than 99% chemically pure, was used to prepare the tosylate by the method of Schleyer;[10] fractional crystallizations were avoided to prevent any resolution of the tosylate. The tosylate was purified by repeatedly oiling it out of petroleum ether at −78°. It was assumed that the (+)-2-butyl tosylate had the same optical purity as the starting alcohol. To an ether solution of lithium diphenylcuprate (5 equiv, −78°) was added an ether solution of (+)-2-butyl tosylate. The reaction mixture was allowed to warm to −20°, and worked up to yield (−)-2-phenylbutane,

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[1] Ethyl Corporation Fellow, 1971–1972.

[2] C. R. Johnson and F. A. Dutra, *J. Amer. Chem. Soc.*, **95**, 7777 (1973).

[3] H. Gilman and J. M. Straley, *Recl. Trav. Chim. Pays-Bas*, **55**, 821 (1936).

[4] H. O. House, W. L. Respess, and G. M. Whitesides, *J. Org. Chem.*, 31, 3128 (1966).

[5] H. O. House and W. F. Fischer, *ibid.*, **33**, 949 (1968).

[6] G. van Kolten and J. G. Noltes, *J. Chem. Soc., Chem. Commun.*, 940 (1972).

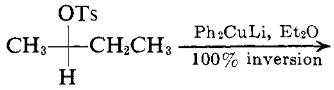
[7] G. M. Whitesides, W. F. Fischer, J. S. Filippo, R. W. Bashe, and H. O. House, *J. Amer. Chem. Soc.*, **91**, 4871 (1969).

[8] E. J. Corey and G. H. Posner, *ibid.*, **89**, 3911 (1967); **90**, 5615 (1968).

[9] G. M. Whitesides, J. S. Filippo, E. R. Stredronsky, and C. P. Casey, *ibid.*, **91**, 6542 (1969).

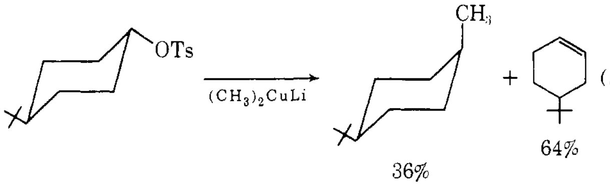
[10] P. v. R. Schleyer, M. M. Donaldson, and W. E. Watts, *ibid.*, **87**, 375 (1965).

whose optical purity (69.4%) indicated that the reaction had proceeded with 100% inversion of configuration (eq 2). The reaction conditions employed in this reaction were very mild, yet the yield could not be increased above 45%.

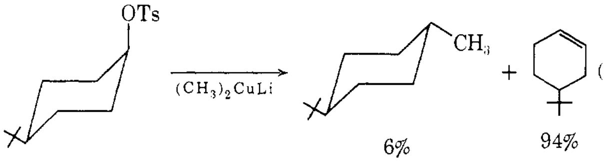
 (2)

$$CH_3\overset{OTs}{\underset{H}{-\!\!\!\!\!+}}CH_2CH_3 \xrightarrow[100\%\ \text{inversion}]{Ph_2CuLi,\ Et_2O} CH_3\overset{H}{\underset{Ph}{-\!\!\!\!\!+}}CH_2CH_3 \quad (2)$$

To rule out any effect of iodide ion on the stereochemistry and product distribution of the reaction, a similar reaction was run, after preparing the cuprate from cuprous bromide. Identical results were obtained. The reaction of lithium diphenylcuprate with the methanesulfonate prepared from the same (+)-2-butanol was also examined; again, within experimental error, the reaction proceeded with 100% inversion of configuration.

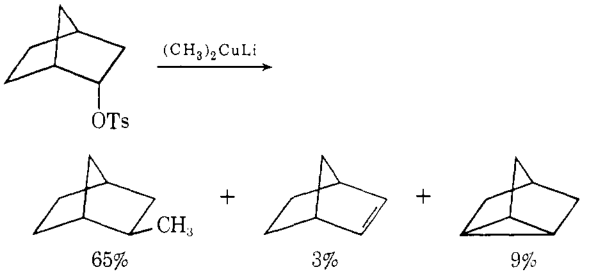


(3)

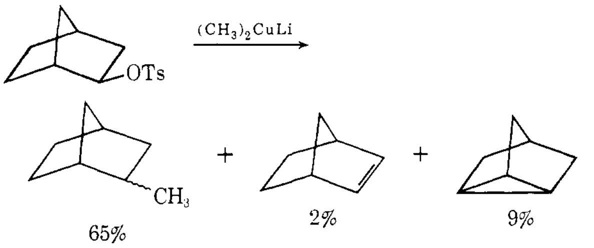


(4)

Addition of *trans*-4-*tert*-butylcyclohexyl tosylate to an ether solution of lithium dimethylcuprate (eq 3) initially at −78°, but allowed to warm to 0° after addition was complete, yielded, after work-up, 36% of *cis*-4-*tert*-butylmethylcyclohexane (no trans isomer could be detected) and 64% of 4-*tert*-butylcyclohexene. Likewise, *cis*-4-*tert*-butylcyclohexyl tosylate was added to lithium dimethylcuprate (eq 4) to give *trans*-4-*tert*-butylmethylcyclohexane (6%) and 4-*tert*-butylcyclohexene (94%). No cis isomer or reduction products could be detected.



(5)



(6)

23% endo, 77% exo

When *endo*-2-norbornyl tosylate was added to lithium dimethylcuprate (eq 5) a 65% yield of *exo*-2-methylnorbornane was obtained. Nortricyclene (9%) and norbornene (3%) were also formed along with several other unidentified products (23%); no *endo*-2-methylnorbornane was found and no reduction of the tosylate to norbornane could be detected. Reaction of *exo*-2-norbornyl tosylate with lithium dimethylcuprate (eq 6) yielded 2-methylnorbornane (65%), nortricyclene (9%) and norbornene (2%) along with several unidentified products (24%). The 2-methylnorbornane formed was 23% endo and 77% exo. The percentage of substitution product (65%) was identical with that obtained with the endo isomer, but there is a significant loss of stereospecificity with the exo isomer.

Table I. Reaction of Lithium Dimethylcuprate with *n*-Octyl Tosylate[a],[b]

Concn of tosylate, *M*	Concn of cuprate, *M*	k, l. mol^{-1} sec^{-1}
0.0457	0.0914	2.60×10^{-3}
0.0236	0.0470	2.35×10^{-3}
0.04717	0.0470	3.04×10^{-3}
0.0893	0.0892	3.20×10^{-3}
		Av 2.8×10^{-3}

[a] Reactions were run in diethyl ether at −42 ± 1.5°. [b] Typical rate plots for these reactions are illustrated by figures in the microfilm edition of this journal; see paragraph at end of paper regarding supplementary material.

The reaction of neopentyl tosylate with lithium diphenylcuprate was examined. This system is prone to rearrange,[11] but an 80% yield of neopentylbenzene (eq 7) was obtained.[2]

$$(CH_3)_3CCH_2OTs + Ph_2CuLi \longrightarrow \underset{80\%}{(CH_3)_3CCH_2Ph} \quad (7)$$

Rate Studies. The stereochemical results prompted an investigation of the kinetics of a cuprate–tosylate reaction. The reaction chosen is typical of the reactions of organocuprates with alkyl tosylates (eq 8).

$$n\text{-}C_8H_{17}OTs + (CH_3)_2CuLi \xrightarrow{Et_2O} CH_3Cu + \text{nonane} + LiOTs \quad (8)$$

The reaction of *n*-octyl tosylate with lithium dimethylcuprate in diethyl ether was studied over a wide range of concentrations of both the tosylate and the cuprate. Lithium dimethylcuprate was chosen because it is one of the more stable cuprates and its concentration could be accurately controlled. The reactions of primary tosylates with cuprates are known to yield only alkanes, and the use of internal standards and vpc techniques provided a moderately accurate method (±3%) for determining the percentage of product formed.

The reaction showed clean second-order kinetics over a wide variety of concentrations and deviated only when the concentration of the tosylate was very high. When using concentrated solutions and a 2 molar excess of the tosylate, the rate of reaction was greatly decreased. No reaction could be detected when a 5 molar excess of the tosylate in a concentrated solution was used. This rate retardation was attributed to the possibility that when the tosylate is present in very high concentrations it competes with the solvent for complexation with the cuprate. This complexation could then be responsible for the rate retardation observed. This postulate was tested by the following experiment.

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[11] I. Dostrovsky, E. D. Hughes, and C. R. Ingold, *J. Chem. Soc.*, 157 (1946).

Table II. Reactions of Lithium Dialkylcuprates with Alkyl Halides and Tosylates[a]

R_2CuLi R	Concn, *M*	R'-X	Concn, *M*	Time, hr	Solvent	Temp, °C	R-R'[b] % yield
n-C_4H_9	0.223	*n*-$C_5H_{11}OTs$	0.0446	0.5	Et_2O	−78	98
n-C_4H_9	0.0892	*n*-$C_5H_{11}OTs$	0.0446	1	Et_2O	−20	96
CH_3	0.2	*n*-$C_8H_{17}I$	0.04	0.5	Et_2O	0	13
				1			18
				2			32
				3			39
				6			60
				17			88

[a] *Cf.* Table IV, ref 7. [b] Vpc yields with internal standards.

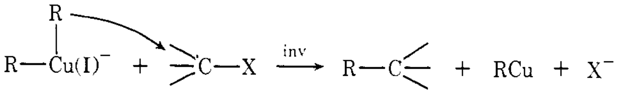
A reaction mixture of the cuprate (0.086 *M*) and the tosylate (0.43 *M*) was prepared; no reaction was observed. However, when 100 ml of ether was added to this reaction mixture, the molarity of the tosylate changed from 0.43 to 0.081 *M* (the latter concentration of tosylate is typical of the concentrations used in this study), and the reaction proceeded with clean second-order kinetics to yield 85% of the theoretical amount of nonane. The results of this study are listed in Table I.

Whitesides, House, and coworkers[7] reported that lithium di-*n*-butylcuprate reacts with almost equal facility with *n*-amyl iodide, bromide, chloride, and tosylate in tetrahydrofuran; the use of diethyl ether resulted in lower yields with *n*-amyl bromide and chloride. We have found that the reaction of the tosylates with the cuprates proceeds much faster in ether than in THF. Also, the displacement reaction with the tosylate as a leaving group is considerably faster than that with the iodide in ether. Our results are given in Table II.

Discussion

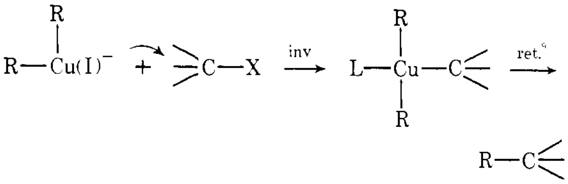
The mechanistic problem in substitution reactions of organocuprates(I) is a complex one; many plausible mechanistic schemes can be envisioned. Four principal mechanistic pathways are illustrated in eq 9–12; subtle and not-so-subtle variations of each are possible.

nucleophilic attack by carbon



(9)

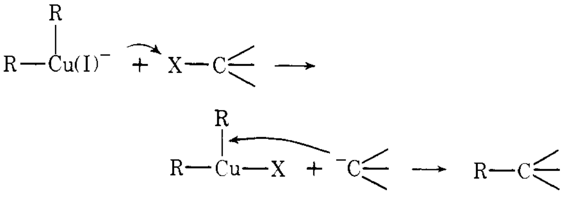
nucleophilic attack by copper



(10)

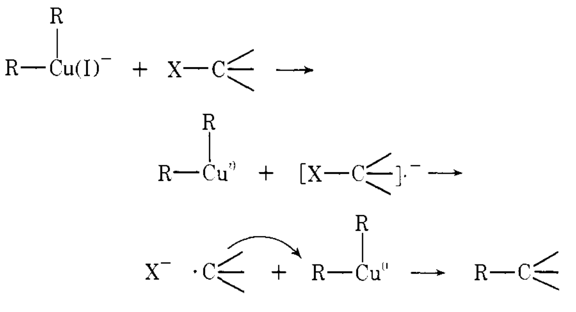
L = solvent or other ligand

nucleophilic attack on the "leaving group" by copper



(11)

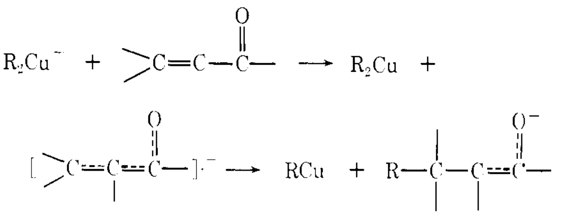
electron transfer process



(12)

Perhaps the easiest to remove from further consideration is represented by eq 11. Such a mechanism is not consistent with the highly stereospecific inversions observed in these substitution reactions. Equation 11 would most likely lead to extensive or total racemization. If any stereochemical integrity was maintained, it would most likely be that of retained configuration. It does not appear that such a reaction would be highly favorable where the leaving group is tosylate.

The task of discriminating between a classical S_N2 mechanism and an electron transfer process involving free radicals as intermediates[12] (eq 12) is more difficult. Such a free-radical process must be considered as a possibility since there is a suggestion for such a mechanism in the conjugate addition reaction of lithium dimethylcuprate to α,β-unsaturated carbonyl compounds (eq 13).[13]



(13)

If the reaction of alkyl tosylates with the cuprates proceeds *via* an electron-transfer mechanism, an intermediate alkyl radical species must be formed. One would therefore expect an alkyl radical to lose its configurational identity if this free radical has any life-

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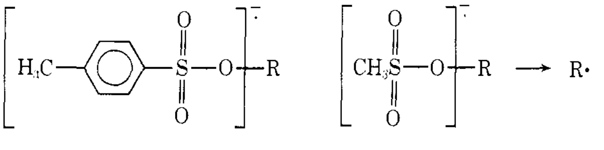
(12) K. A. Bilevitch, N. N. Pubnov, and O. Y. Okhlobystin, *Tetrahedron Lett.*, 3465 (1968).

(13) H. O. House and M. J. Umen [*J. Amer. Chem. Soc.*, **94**, 5495 (1972)] have observed that the yields of reactions of a large variety of electrophilic olefins with lithium dimethylcuprate correlate with the polarographic reduction potential of these substrates. It is their suggestion that this correlation is indicative of the fact that the cuprate reactions proceed by electron transfer. We contend that the polarographic reduction potential measures the affinity of the substrate for electrons and correlation with either an electron transfer process (single electron) or nucleophilic addition process (electron pair) is not unreasonable.

time. However, if the free-radical species exists as a "tight" radical anion pair and is rapidly attacked by the copper(II) species formed,[13] inversion of configuration might be found, although it would appear unlikely that complete stereospecificity could ever be obtained in an electron-transfer mechanism. As a possible probe for an electron-transfer mechanism we compared the stereospecificity of the reaction of lithium diphenylcuprate with (+)-butyl tosylate and methanesulfonate. It seemed to us that the intermediate resulting from electron transfer would not be as stable in the latter case, and reaction might be more likely to involve "free" radicals and hence reduced stereospecificity. However, in both cases, complete inversion of configuration was observed.



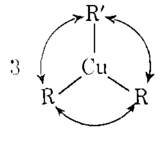
more stable less stable

Baring unusual steric requirements, if considerable free-radical character were present on the alkyl group of the tosylate substrate in the transition state of the reaction, one would expect secondary tosylates to react faster than primary ones. On the other hand, if in an electron-transfer reaction the transition state occurred earlier along the reaction coordinate, one might expect to find little sensitivity of the rate to the nature of the alkyl group of the tosylate. Neither of the above is the case; primary tosylates react faster than secondary tosylates and neopentyl tosylate, for example, is much slower in these reactions than normal primary tosylates.

The most straightforward interpretation of all of the results of substitution reactions of lithium organocuprates(I) seems to be that these are "SN2-like" reactions. The reactions exhibit the appropriate kinetics, first order each in tosylate and cuprate. Primary tosylates are more reactive than secondary tosylates; neopentyl tosylate shows a depressed rate. Our work combined with that of Whitesides, House, and coworkers[7] shows that the order of leaving group effectiveness (in diethyl ether) is that expected for SN2 reactions: OTs > I ~ Br > Cl. The results of stereochemical studies also point to a SN2 mechanism, clean inversion in a simple case of secondary tosylate. In the reaction of *cis-* and *trans*-4-*tert*-butylcyclohexyl tosylate with lithium dimethylcuprate (eq 3 and 4) one finds that in each case substitution occurs exclusively with inversion of configuration and that elimination becomes much more important in the case of the cis tosylate. When the same tosylates were reacted with the highly nucleophilic, but weakly basic, sodium benzenethiolate the results were similar.[14] When lithium dimethylcuprate was reacted with *endo-* and *exo*-2-norbornyl tosylate (eq 3 and 4), E1[15] and E2[16] reactions were in competition with SN2 reactions; the substitution product was exclusively exo in the former case and a mixture of exo and endo in the latter case. The reaction of simple alcohols with triphenylphosphine–bromine gives alkyl bromides with clean inversion of configuration by a mechanism involving nucleophilic attack by bromide ion.[17] When this reagent was reacted with *exo*-2-norbornanol the products were *exo*-2-bromonorbornane (79%), *endo*-2-bromonorbornane (12%), and nortricyclane (9%); *endo*-norbornanol gave exclusively *exo*-2-bromonorbornane.[15]

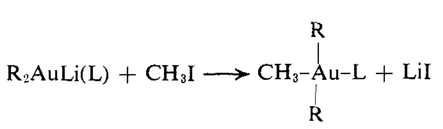
It is our contention that the data available are clearly indicative of a nucleophilic substitution process occurring at the carbon of the substrate (eq 9 or 10). The mechanism represented by eq 10 is attractive in that it offers a substantial explanation for the extraordinary nucleophilicity of these organocuprates which differentiates them from the more typical organometallics such as Grignard reagents or organolithiums. In the cuprate reactions the copper atom is the attacking nucleophilic site, whereas in the more typical organometallic (Li, Mg, etc.) reactions, a carbon atom assumes the role of the attacking nucleophile.

One can conclude that if an intermediate $R_3Cu(III)$ exists, the structure of this intermediate is one that does not allow the various R groups to occupy equivalent structural positions. If R and R′ were similar groups (*e.g.*, *n*-amyl and *n*-butyl) which occupied equivalent structural positions, then product distribution should be as follows in eq 14. The maximum yield of R–R′ would then be 66%. However, *n*-amyl tosylate and lithium di-*n*-butylcuprate(I) couple to give *n*-nonane in 98% yield. This and related observations can be accommodated if one assumes that the copper(III) intermediate has a square planar structure (see below).



$$\longrightarrow 2\mathrm{R{-}R'} + 1\mathrm{RR} + 2\mathrm{RCu} + 1\mathrm{R'Cu} \qquad (14)$$

Recently, Tamaki and Kochi[18] have reported a study of lithium dialkylaurates(I). It was found that dialkylaurates(I) were potent nucleophiles. Reaction of lithium dimethylaurate(I) with methyl iodide to produce the relatively stable trialkylgold(III) complex (R = CH_3) occurs on mixing at 0° in diethyl ether (eq 15). The stereochemistry of the addition reaction to form the gold(III) complex was shown to be predominantly trans (square planar structure with the two alkyl groups originally present in the gold(I) complex occupying trans positions). In an earlier study, Tamaki and Kochi had shown that gold(III) complexes thermolyze to give alkyl coupling products and gold(I) complexes (eq 16).[19]



$$R_2AuLi(L) + CH_3I \longrightarrow CH_3\text{-}\overset{\displaystyle R}{\underset{\displaystyle R}{Au}}\text{-}L + LiI \qquad (15)$$

$$R_3AuL \xrightarrow[\Delta]{} R\text{-}R + RAuL \qquad (16)$$

It is a reasonable assumption that copper(I) and gold(I) complexes show the same fundamental chem-

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(14) E. L. Eliel and R. S. Ro, *J. Amer. Chem. Soc.*, **79**, 5995 (1957).

(15) J. P. Schaefer and D. S. Weinberg, *J. Org. Chem.*, 30, 2635, 2639 (1965).

(16) H. Kwart, T. Takeshita, and J. L. Nyce, *J. Amer. Chem. Soc.*, **86**, 2606 (1964).

(17) D. G. Coe, S. R. Landauer, and H. N. Rydon, *J. Chem. Soc.*, 2281 (1954); H. N. Rydon and B. L. Tonge, *ibid.*, 3043 (1956).

(18) A. Tamaki and J. K. Kochi, *J. Organometal. Chem.*, **51**, C39 (1973).

(19) A. Tamaki and J. K. Kochi, *ibid.*, 40, C81 (1972).

istry in their reactions with electrophilic substrates.[20] We, therefore, conclude that eq 10 involving the transient formation of a square planar copper(III) species (R groups trans) is representative of the reactions of lithium diorganocuprates(I) with electrophilic substrates. Collapse of the copper(II) intermediate results in the coupling of two cis ligands. Copper(III) is an unusual oxidation state of copper, and such intermediates may be expected to have only transitory existence. We further suggest that copper plays a similar role in a host of nucleophilic reactions which occur in the presence of cuprous salts (*e.g.*, eq 17).

$$\mathrm{ArSCu(L)}_n + \mathrm{RX} \longrightarrow \left[\mathrm{ArS}\underset{\underset{\mathrm{R}}{|}}{\mathrm{Cu}}\mathrm{(L)}_n\right] \longrightarrow \mathrm{ArSR} \qquad (17)$$

Experimental Section

(+)-(*S*)-Butyl Tosylate. The (+)-(*S*)-2-butanol, obtained from Norse Laboratories, had $[\alpha]^{20}\mathrm{D}$ +9.6° (neat), 69.2% optically pure (lit.[21] for optically pure $[\alpha]^{20}\mathrm{D}$ +13.9), was shown to be greater than 99% chemically pure by nmr and vpc. The tosylate, prepared by the method of Schleyer,[15] was obtained as an oil, $[\alpha]^{20}\mathrm{D}$ +12.3° (neat), +9.9° (*c* 5.00, ethanol), and was never allowed to crystallize. It was assumed that the optical purity of the tosylate was the same as that of the starting alcohol; however, this is not in agreement with a literature report.[22]

Reaction of (+)-(*S*)-2-Butyl Tosylate with Lithium Diphenylcuprate. To an ether solution of the cuprate prepared from cuprous iodide (3.8 g, 0.02 mol in 30 ml) at −78° was added an ether solution of the tosylate (1.5 g, 6.6 mmol in 10 ml) dropwise over 30 min. The mixture was stirred overnight at −78°. The reaction mixture was warmed to 0° and worked up in the usual manner,[2] yielding an oil which was chromatographed over silica gel–pentane. The product obtained was (−)-(*R*)-2-phenylbutane (45% yield, greater than 99% pure), $[\alpha]^{24}\mathrm{D}$ −19.5° (neat), corresponding to 71.5% optical purity (lit.[23] for enantiomer $[\alpha]^{20}\mathrm{D}$ +27.3°).

Preparation of (+)-(*S*)-2-Butyl Mesylate. The mesylate prepared by the method of Schleyer[10] was an oil, $[\alpha]^{24}\mathrm{D}$ +16.4° (neat). No impurities could be detected by ir or nmr. The mesylate was assumed to have the same optical purity as the starting alcohol.

Reaction of (+)-(*S*)-2-Butyl Mesylate with Lithium Diphenylcuprate. To an ether solution of the cuprate prepared from cuprous iodide (9.35 g, 0.049 mol in 30 ml) at −78° was added an ether solution of the mesylate (2.5 g, 0.0164 mol in 10 ml) over 30 min. The reaction mixture was stirred at −78° for 2 hr and then at −20° for 5 hr, and worked up. The product was chromatographed over silica gel–pentane, yielding a colorless oil (0.73 g, 33%), (−)-(*R*)-2-phenylbutane, $[\alpha]^{25}\mathrm{D}$ −19.65° (neat), corresponding to 71.9% optical purity.

Reaction of *cis*-4-*tert*-Butylcyclohexyl Tosylate with Lithium Dimethylcuprate. To an ether solution of the cuprate prepared from cuprous iodide (3.8 g, 0.02 mol) at −78° was added an ether solution of 0.78 g (2.5 mmol) of the tosylate, mp 78–78.5° (lit.[24] mp 78–80°), over 30 min. The reaction was run for 8 hr at −78°, and was then warmed to 0° and worked up. A mixture of two compounds which could not be separated by column chromatography was isolated. They could be separated by capillary vpc ($^1/_{16}$ in. × 50 ft squalane) and found to be *trans*-4-*tert*-butylmethylcyclohexane[25] (6%) and 4-*tert*-butylcyclohexene (94%). The yield of this mixture was 75%. No cis isomer could be detected.

Reaction of *trans*-4-*tert*-Butylcyclohexyl Tosylate with Lithium Dimethylcuprate. To an ether solution of the cuprate (0.02 mol) at −78° was added an ether solution of 0.78 g (2.5 mmol) of the tosylate, mp 88–89° (lit.[24] mp 89.4–90°). The reaction mixture was stirred for 6 hr at −78°, and then was warmed to −10° and worked up to give a mixture of 4-*tert*-butylcyclohexene (64%) and *cis*-4-*tert*-butylmethylcyclohexane[25] (36%). There was no evidence of the trans isomer.

Preparation of *exo*- and *endo*-2-Methylnorborane. Following the procedure of Wittig and Schoellkopf,[26] norcamphor was added to a THF solution of triphenylphosphonium methylide and after work-up and distillation, 2-methylenenorbornane, bp 122–124°, was obtained. Hydrogenation of this product in methanol over platinum on carbon yielded 2-methylnorbornane, bp 123–125°, $n^{25}\mathrm{D}$ 1.4524. The product was 74% endo and 26% exo, and it was in agreement with literature values: bp 124.5–125°,[27] ratio from hydrogenation 79% endo, 21% exo.[28] The resulting mixture of 2-methylnorbornanes (74% endo, 26% exo) was subjected to normal reaction conditions (lithium dimethylcuprate, 8 hr, 0°) and was quantitatively recovered with no change in the isomer ratio.

Reaction of *exo*-2-Norbornyl Tosylate with Lithium Dimethylcuprate. To an ether solution of the cuprate (4.94 mmol) at 0° was added an ether solution of 0.66 g (2.5 mmol) of the tosylate, mp 55–56° (lit.[29] mp 53.7–54.6°), dropwise over 30 min. Mesitylene was added as an internal standard. After 6 hr at 0°, the reaction was worked up. The yield of 2-methylnorbornane was 58% and the ratio of the isomers was 77% exo, 23% endo. Other products obtained were: nortricyclene,[30] 8.7%; norbornene, 2.4%; unidentified products (more than 8), 18.3%. The reduction product, norbornane, was not found. The isomers of 2-methylnorbornane could be separated by vpc, using a 30 ft × 0.25 in. column, 20% SE-30. All the named products were collected by vpc and their ir's compared with those of authentic samples.

Reaction of *endo*-2-Norbornyl Tosylate with Lithium Dimethylcuprate. Using the endo tosylate, mp 26–27° (lit.[29] mp 27.2–28°), conditions described above were employed, yielding *exo*-2-methylnorbornane (100% exo, 65% yield); 8.5% nortricyclene and 3% norbornene were also obtained. No evidence of the endo isomer could be found.

Reaction of *exo*-2-Norbornyl Tosylate with Lithium Diphenylcuprate. To an ether solution of the cuprate (6.8 mmol in 16 ml) at −20° was added an ether solution of the tosylate (0.9 g, 3.4 mmol in 10 ml). The mixture was allowed to warm to 0°, then worked up in the usual manner, and after chromatography, an oil (0.285 g) was isolated. A vpc analysis indicated this to be a mixture of norbornene, *exo*-2-phenylnorbornane,[31] *endo*-2-norbornanol, and two unidentified products. The 2-phenylnorbornane appeared to be all exo.

Reaction of *endo*-2-Norbornyl Tosylate with Lithium Diphenylcuprate. Results very similar to those above were obtained, and *exo*-2-phenylnorbornane[28] was isolated in 35% yield.

Kinetics of the Reaction of *n*-Octyl Tosylate with Lithium Dimethylcuprate. The *n*-octyl tosylate was purified by oiling it out of petroleum ether three times, then by distillation, bp 170° (0.06 mm). The cuprate was prepared from purified cuprous iodide and fresh methyllithium (Foote). The glassware was flame dried three times; volumes were measured using hypodermic syringes (accuracy ±5%). Mesitylene was used as the internal standard. *n*-Octyl tosylate and cuprous iodide were weighed out to the nearest 0.0001 g. The reaction was followed by taking aliquots and quenching them immediately in an ammonium chloride solution. The ether layers of these aliquots were injected on the gas chroma-

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(20) It is also interesting to note that reaction of alkyl tosylates with the cobaloxime anion results in the production of a carbon–cobalt bond and proceeds with inversion of configuration at carbon: M. Tada and H. Ogawa, *Tetrahedron Lett.*, 2639 (1973); F. R. Jensen, V. Madan, and D. H. Buchnan, *J. Amer. Chem. Soc.*, **92**, 1414 (1970).

(21) R. H. Pickard and J. Kenyon, *J. Chem. Soc.*, **99**, 45 (1911).

(22) J. Kenyon, H. Phillips, and V. Pittman [*ibid.*, 1072 (1935)] reported $[\alpha]^{20}\mathrm{D}$ −11.1° (neat), −5.8° (*c* 5.00 ethanol) for the tosylate considered to be optically pure. This value is not in agreement with our data. This method of purification involved distillation at atmospheric pressure and perhaps some decomposition occurred. It is also possible that some unhydrolyzed tosyl chloride could have distilled over with the tosylate. It has been observed in our laboratories that tosyl chloride and *n*-octyl tosylate codistil. The optical purity of the literature sample may have been 100%, but their chemical purity must have been considerably lower.

(23) J. Kenyon, P. W. B. Harrison, and J. R. Sheppard, *J. Chem. Soc.*, 658 (1926).

(24) S. Winstein and N. J. Holness, *J. Amer. Chem. Soc.*, 77, 5562 (1955).

(25) Authentic samples of *cis*- and *trans*-4-*tert*-butylmethylcyclohexane were prepared by the method of A. L. Liberman, B. M. Lerman, G. N. Zhizhin, and Kh. E. Sterin, *Dokl. Chem.*, **156**, 375 (1964).

(26) G. Wittig and U. Schoellkopf, *Org. Syn.*, 40, 66 (1960).

(27) H. Pledger, *J. Org. Chem.*, **25**, 278 (1960).

(28) N. A. Bellkova, V. G. Berezkin, and A. F. Plate, *Zh. Obshch. Khim.*, **32**, 2942 (1962); *Chem. Abstr.*, **58**, 8925g (1963).

(29) P. v. R. Schleyer, M. M. Donaldson, and W. E. Watts, *J. Amer. Chem. Soc.*, **87**, 375 (1965).

(30) An authentic sample was prepared by the method of K. Alder, H. K. Schafer, H. Esser, H. Krieger, and R. Reubke, *Justus Leibigs Ann. Chem.*, **593**, 23 (1955).

(31) A sample was prepared according to the method of L. Schmerling, U. S. Patent 2,480,267; *Chem. Abstr.*, **44**, 1136i (1950).

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]

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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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(1) (a) A preliminary communication dealing with lithium *tert*-butoxy(alkyl)cuprates has appeared: G. H. Posner and C. E. Whitten, *Tetrahedron Lett.*, 1815 (1973). (b) Parts of this work were presented at the 164th National Meeting of the American Chemical Society, New York, N. Y., Aug 28–Sept 1, 1972, Abstract ORGN 159, and at the 8th Middle Atlantic Regional Meeting of the American Chemical Society, Washington, D. C., Jan 14–17, 1973, Abstract H3.

(2) (a) NDEA fellow 1969–1972; (b) Sonneborn Foundation Fellow, 1972–present.

(3) Enolization of and addition to ketones and esters: (a) J. D. Buhler, *J. Org. Chem.*, **38**, 904 (1973); (b) F. Huet, G. Emptoz, and A. Jubier, *Tetrahedron Lett.*, 479 (1973); (c) "The Chemistry of Carbonyl Compounds," S. Patai, Ed., Interscience, New York, N. Y., 1966.

(4) 1,4 and 1,2 addition to α,β-ethylenic ketones: (a) M. S. Kharasch and O. Reinmuth, "Grignard Reactions of Nonmetallic Substances," Prentice-Hall, Englewood Cliffs, N. J., 1954, pp 196–239; (b) T. Eicher in "The Chemistry of Carbonyl Compounds," S. Patai, Ed., Interscience, New York, N. Y., 1966, pp 624–631, 662–678.

(5) Metal-halogen exchange, α-metalation, α- and β-elimination, and coupling with organic halides: (a) R. G. Jones and H. Gilman, *Org. React.*, **6**, 339 (1951); (b) H. Gilman, *ibid.*, **8**, 258 (1954); (c) D. E. Applequist and D. F. O'Brien, *J. Amer. Chem. Soc.*, **85**, 743 (1963); (d) A. J. S. Winkler and H. Winkler, *ibid.*, **88**, 964, 969 (1966); (e) G. Köbrich, *Angew. Chem., Int. Ed. Engl.*, **6**, 41 (1967); (f) W. Kirsme, "Carbene Chemistry," Academic Press, New York, N. Y., 1964; (g) G. E. Coates, M. L. H. Green, and K. Wade, "Organometallic Compounds," Vol. I, Methuen, London, 1967, p 298 ff; (h) M. Tamura and J. Kochi, *J. Organometal. Chem.*, **29**, 111 (1971); (i) G. M. Whitesides, E. R. Stedronsky, C. P. Casey, and J. San Filippo, Jr., *J. Amer. Chem. Soc.*, **92**, 1426 (1970); (j) L. H. Sommer and W. D. Korte, *J. Org. Chem.*, **35**, 22 (1970); (k) W. D. Korte, L. Kinner, and W. C. Kaska, *Tetrahedron Lett.*, 603 (1970).

(6) H. O. House, "Modern Synthetic Reactions," 2nd ed, W. A. Benjamin, New York, N. Y., 1972, Chapter 9.

(7) G. H. Posner, *Org. React.*, **19**, 1 (1972).

(8) G. H. Posner and D. J. Brunelle, *Tetrahedron Lett.*, 935 (1973); *J. Org. Chem.*, **38**, 2747 (1973).

(9) (a) E. J. Corey and P. L. Fuchs, *J. Amer. Chem. Soc.*, **94**, 4014 (1972); (b) J. A. Marshall and R. A. Ruden, *Tetrahedron Lett.*, 2875 (1971); (c) C. Frejaville and R. Jullien, *ibid.*, 2039 (1971); (d) G. Daviaud and Ph. Miginiac, *ibid.*, 997 (1972); (e) P. A. Grieco and R. Finkelhor, *J. Org. Chem.*, **38**, 2100 (1973).

(10) For a review of substitution reactions using organocopper reagents, see G. H. Posner, *Org. React.*, in press.

(11) (a) E. J. Corey and G. H. Posner, *J. Amer. Chem. Soc.*, **89**, 3911 (1967); **90**, 5615 (1968); (b) G. M. Whitesides, W. F. Fischer, Jr., J. San Filippo, Jr., R. W. Bashe, and H. O. House, *ibid.*, **91**, 4871 (1969).

(12) G. H. Posner, C. E. Whitten, and P. E. McFarland, *J. Amer. Chem. Soc.*, **94**, 5106 (1972), and references therein.