ilarly treated with phenyllithium which was halogen free.[24] The product isolated was identical with that obtained using phenyllithium prepared from bromobenzene and lithium metal.

Registry No.—**1**, 27377-48-6; **2**, 30514-23-9; **3**, 30514-22-8; **6**, 42297-06-3; **7**, 42297-07-4; **8**, 42297-08-5; **9**, 42297-09-6; **11**, 42297-10-9; **12**, 42297-11-0; **13**, 42297-12-1; *N*-nitrosopyrrolidine, 930-55-2; pyrrolidine, 123-75-1; dimethylnitrosamine, 62-75-9; diethylnitrosamine, 55-18-5; dimethyl acetylenedicarboxylate, 762-42-5; *N*-phenylmaleimide, 941-69-5; *N*-nitrosopiperidine, 100-75-4; *N*-methyl-*N*-*tert*-butylnitrosamine, 7068-83-9.

Supplementary Material Available.—Nmr data for compound **7** freshly dissolved in CCl_4 and after standing for 3 hr and 4 days and for compound **8** in CCl_4 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 JOC-73-4259.

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[24] G. Wittig, F. J. Meyer, and G. Lange, *Justus Liebigs Ann. Chem.*, **571**, 167 (1951).

Reactions of Lithium Diorganocuprates(I) with Oxiranes

CARL R. JOHNSON,* R. WILBUR HERR, AND DONALD M. WIELAND

Department of Chemistry, Wayne State University, Detroit, Michigan 48202

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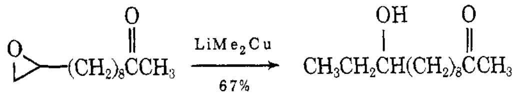
Lithium diorganocuprates have been shown to be highly effective reagents for the nucleophilic ring opening of oxiranes in the trans manner. These reactions occur more rapidly in diethyl ether than in tetrahydrofuran. Evidence and precedent for a mechanism involving the formation of a triorganocopper(III) intermediate is discussed. The selectivity of lithium diorganocuprates in reactions with substrates containing epoxide along with other electrophilic sites is discussed in terms of the hard and soft acid-base theory.

The nucleophilic ring opening of oxiranes by organometallic reagents is a frequently used method for the generation of new carbon-carbon σ bonds;[1] in many cases the utility of the reaction is curtailed owing to competing reactions arising from the Lewis acidity or the basicity of the organometallic reagent. We have observed that lithium diorganocuprates(I) are capable of ring opening of oxiranes under very mild conditions. In a series of preliminary communications,[2-4] we have demonstrated the ability of these reagents to circumvent many of the troublesome side reactions frequently encountered in the reactions of other organometallic reagents with oxiranes. In order to conserve journal space our published results will be summarized in a brief manner in the following paragraphs. The main body of this paper is largely concerned with extensions of our earlier results and mechanistic discussion. The Experimental Section of this paper includes details of certain key experiments described in the earlier communications.

In the introductory communication[2] the reactions of cyclohexene oxide with methyl- and phenyllithium were compared with the corresponding lithium diorganocuprates(I). The results indicated that the cuprates were more reactive toward oxiranes and were somewhat superior in terms of yields of trans nucleophilic addition products. Polymeric methylcopper and methylcopper complexes with trimethyl phosphite or tri-*n*-butylphosphine were unreactive toward cyclohexene oxide, whereas lithium methylcyanobis(triethyl phosphite)copper(I) reacted only slightly. In these ring-opening reactions of oxiranes the lithium ion is undoubtedly lending an electrophilic assist by coordination with the oxirane oxygen. In contrast to the coupling reactions of organocuprates and alkyl halides,[5] these oxirane reactions proceed more rapidly in diethyl ether than in THF. The latter solvates the lithium ion more effectively to the detriment of the lithium ion-oxirane complex. Perhaps the most significant observation was that lithium diorganocuprates could selectively ring open oxiranes in the presence of unprotected carbonyl functions (ester or ketone), *e.g.*, eq 1.



$$\overset{O}{\triangleright}\!-(CH_2)_8\overset{O}{\overset{\|}{C}}CH_3 \xrightarrow[67\%]{LiMe_2Cu} CH_3CH_2\overset{OH}{\overset{|}{C}}H(CH_2)_8\overset{O}{\overset{\|}{C}}CH_3 \qquad (1)$$

In the second communication[3] we compared the reactions of methylmagnesium, methyllithium, and methylcopper reagents with 1,2-epoxybutane and 1,2-epoxy-3-butene.[6] With the latter substrate methylmagnesium reagents gave 16-68% conjugate addition (mixture of *cis*- and *trans*-2-penten-1-ol), methyllithiums gave 20-55%, and lithium dimethylcopper gave 94%. The conjugate mode of addition of lithium dialkylcuprates to α,β-unsaturated carbonyl compounds,[7,8] allylic acetates,[9] and propargylic acetates[10] had already been documented. More recently we reported on the regio- and stereoselectivity of the reactions of methyl-

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[1] (a) A. Rosowsky in "Heterocyclic Compounds with Three- and Four-Membered Rings," Part I, A. Weissberger, Ed., Interscience, New York, N. Y., 1964, pp 386-417; (b) R. E. Parker and N. S. Isaacs, *Chem. Rev.*, **59**, 779 (1959); (c) N. G. Gaylord and E. I. Becker *ibid.*, **49**, 448 (1951).

[2] R. W. Herr, D. M. Wieland, and C. R. Johnson, *J. Amer. Chem. Soc.*, **92**, 3813 (1970).

[3] R. W. Herr and C. R. Johnson, *J. Amer. Chem. Soc.*, **92**, 4979 (1970).

[4] D. M. Wieland and C. R. Johnson, *J. Amer. Chem. Soc.*, **93**, 3047 (1971).

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

[6] For a related study see R. J. Anderson, *J. Amer. Chem. Soc.*, **92**, 4978 (1970).

[7] (a) H. O. House, W. L. Respess, and G. M. Whitesides, *J. Org. Chem.*, **31**, 3128 (1966); (b) H. O. House and W. F. Fischer, Jr., *ibid.*, **33**, 949 (1968); (c) E. J. Corey and J. H. Katzenellenbogen, *J. Amer. Chem. Soc.*, **91**, 1851 (1969); (d) J. B. Siddall, M. Biskup, and J. H. Fried, *ibid.*, **91**, 1853 (1969).

[8] For a review see G. H. Posner, *Org. React.*, **19**, 1 (1972).

[9] (a) P. Rona, L. Tokes, J. Tremble, and P. Crabbe, *Chem. Commun.*, 43 (1969); (b) R. J. Anderson, C. A. Henrick, and J. B. Siddall, *J. Amer. Chem. Soc.*, **92**, 735 (1970).

[10] (a) P. Rona and P. Crabbe, *J. Amer. Chem. Soc.*, **90**, 4733 (1968); (b) *ibid.*, **91**, 3289 (1969).

and phenyllithium and lithium dimethyl-, diphenyl-, and di-*tert*-butylcuprates with 1,2-epoxy-3-cyclohexene.[4,11] The copper reagents were again found to react more rapidly and under milder conditions to give better yields of addition products than their organolithium counterparts. The methyl and phenyl reagents displayed high trans stereoselectivity in both the 1,2 and 1,4 additions. In regard to the 1,4 additions it should be noted that it has been generally accepted that the entering nucleophile bears a cis relationship to the leaving group in an S$_N$2 reaction.[12,13]

Reactions of Cycloalkene Oxides.—Table I summarizes the nucelophilic ring opening reactions of fused ring oxiranes with lithium dimethylcuprate(I). The only significant side reaction appears to be the formation of ketones by rearrangement of the epoxides. In each case the ring opening occurs cleanly in the trans manner. As would be typical of an S$_N$2 process, these reactions were sluggish when back-side attack was sterically encumbered. In the case of *exo*-2,3-epoxynorcamphor and *cis*-cyclooctene oxide this sluggishness could be overcome to some extent by switching from diether ether to dimethoxyethane and increasing the reaction temperature.

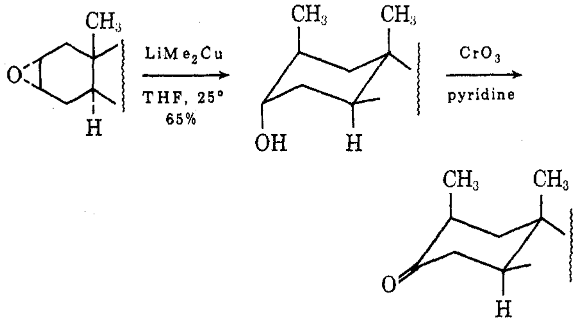
TABLE I

REACTIONS OF LITHIUM DIMETHYLCUPRATE WITH CYCLOALKENE OXIDES[a]

Oxirane	Time, hr	Oxirane recovered, %	Conversion, %	Product distribution: Trans alcohol	Ketone
Cyclopentane oxide	6	0	85[b]	88	12
Cyclohexene oxide	14	0	82[b]	76	24
Cycloheptene oxide	48	11	81[c]	74	26
cis-Cyclooctene oxide	48	79	9[c]	60	40
cis-Cyclooctene oxide	30[d,e]	48	36[c]	60	40
exo-Norbornene oxide	24	100	0[c]		
exo-Norbornene oxide	5[d,f]	1	58[b]	100	
5α-Cholestane 2α,3α-oxide	24	0	86[b]	75[g]	25

[a] The reactions were 0.02 *M* in oxirane and 0.10 *M* in lithium dimethylcuprate (fivefold excess). The lithium dimethylcuprate solution was made at 0°, the oxirane was added dropwise, and then the reaction was allowed to warm to the desired temperature. All reactions were run under an argon or nitrogen atmosphere. The reactions were run in diethyl ether at 25° except where noted. [b] Isolated yield. [c] Vpc yield. [d] In dimethoxyethane. [e] At 70°. [f] At 55°. [g] See eq 2.

The reaction of lithium dimethylcuprate with 5α-cholestane 2α,3α-oxide is of more than passing interest in steroid chemistry. The reaction results in the introduction of a methyl group in the 2 position of the steroid nucleus in the less stable axial orientation (eq 2). Reaction of the same epoxide with a Grignard reagent would most likely lead to ring contraction as the reaction pathway.[14] The same alcohol has recently been



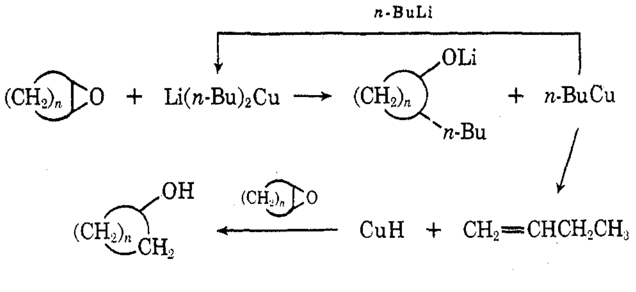
(2)

synthesized from the epoxide in a two-step sequence—reaction with lithio-1,3-dithiane followed by Raney nickel desulfurization.[15] It should be pointed out that, while it is important that lithium dimethylcopper can open sterically hindered epoxides in steroids, the fact that ambient temperatures are required rules out the selective use of this reaction when other reactive function groups are present.

The emergence of a new factor—a competing reduction reaction— is noted in the reactions of lithium di-*n*-butylcuprate with epoxides (Table II). It has recently been shown that the tri-*n*-butylphosphine complex of *n*-butylcopper(I) undergoes thermal decomposition at 0° in ether *via* β elimination of copper(I) hydride.[16] The stability of *n*-butylcopper (the by-product of the reaction of the lithium di-*n*-butylcuprate with an epoxide) in ether solution is not known, but it is likely to be less stable than the complex. Copper hydride is an efficient reducing agent, and we suspect that its formation accounts for the cyclopentanol and cyclohexanol (Table II).[17]

As a possible method to prevent the formation of copper hydride under the reaction conditions it occurred to us to utilize an excess of the *n*-butyllithium, which would in effect "tie up" the *n*-butylcopper as it formed by converting it to the more stable lithium di-*n*-butylcuprate (Scheme I). The second and fourth entry in Table II indicate the excellent success of this approach—the reduction products were completely eliminated. The lithium di-*n*-butylcuprate is itself stable at −40° for an indefinite period. The lower temperatures utilized were not necessary to assure exclusion of reduction products, but were used to prevent rearrangement of the epoxide to ketone. These reactions show that small or even catalytic amounts of cuprous iodide and low temperatures may be used to effect the ring open-

SCHEME I



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[11] For a related study see J. Staroscik and B. Rickborn, *J. Amer. Chem. Soc.*, **93**, 3046 (1971).

[12] G. Stork and W. N. White, *J. Amer. Chem. Soc.*, **78**, 4609 (1956).

[13] For a recent interesting commentary on S$_N$2′ reactions see F. G. Bordwell, *Accounts Chem. Res.*, **3**, 281 (1970).

[14] For a related example see B. G. Christensen, R. G. Strachan, N. R. Trenner, B. H. Arison, R. Hirshmann, and J. M. Chemesda, *J. Amer. Chem. Soc.*, **82**, 3995 (1960).

[15] J. Jones and R. Grayshan, *Chem. Commun.*, 141 (1970).

[16] G. M. Whitesides, E. R. Stedronsky, C. P. Casey, and J. San Filippo, Jr., *J. Amer. Chem. Soc.*, **92**, 1426 (1970).

[17] The reduction of a ketone by lithium di-*n*-butylcuprate has been recently reported by L. T. Scott and W. D. Cotton, *Chem. Commun.*, 320 (1973).

TABLE II

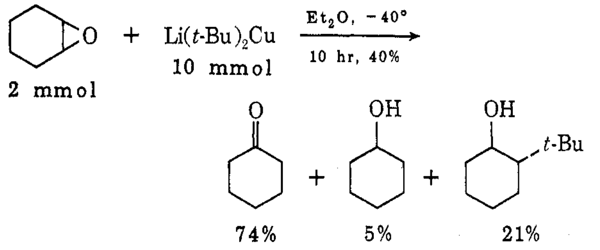
REACTION OF LITHIUM DI-*n*-BUTYLCUPRATE WITH CYCLOALKENE OXIDES[a]

Oxirane	Oxirane, mmol	CuI, mmol	*n*-BuLi, mmol	Time, hr	Temp, °C	Product distribution[b]: *trans*-2-*n*-Butylcycloalkanol	Cycloalkanol	Cycloalkanone
Cyclopentene oxide	1.0	5.0	10.0	4	25	66	22	12
Cyclopentene oxide	1.0	0.5	10.0	4	−40	99	0	1
Cyclohexene oxide	1.0	5.0	10.0	4	25	73	19	8
Cyclohexene oxide	1.0	0.5	10.0	10	0	97	0	3
Cyclohexene oxide	1.0	0	5.0	14	25	13[c]		

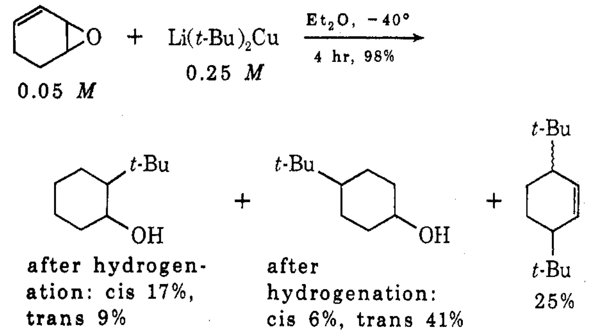
[a] The solvent consisted of 43 mol of diethyl ether and 7 ml of hexane. The lithium *n*-butylcuprate was generated at −40°, the oxirane was added dropwise, and then the mixture was allowed to warm to the desired temperature. The reactions were run under an argon atmosphere. [b] Mesitylene was used as an internal standard. In all cases the conversions to the products shown were in the 80–90% range. [c] The major product was 2-cyclohexenol; for related results see R. L. Letsinger, J. G. Traynham, and E. Bobko, *J. Amer. Chem. Soc.*, **74**, 399 (1952).

ing of epoxides with organolithium reagents. However, these conditions preclude the selective ring opening of epoxides in the presence of such functionalities as keto, ester, or nitrile.

The reactions of lithium di-*tert*-butylcuprate with cyclohexene oxide and 1,2-epoxy-3-cyclohexene are illustrated in eq 3 and 4. The production of 3,6-di-*tert*-butylcyclohexene can be rationalized as involving a dianion[18] which collapses to a carbene or by displacement of LiO⁻. The isolation of this product suggests[19] that the cis products formed in the reaction of lithium di-*tert*-butylcuprate with 1,2-epoxy-3-cyclohexene (eq 4) may arise by equilibration of the initially formed trans products *via* dianions. The vpc of the product mixtures exhibited the same number and relative areas of peaks before and after hydrogenation.

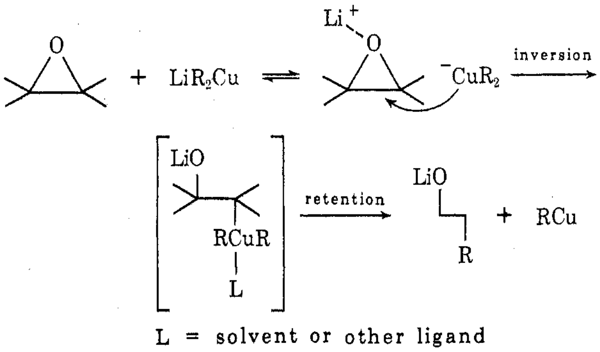


(3)



(4)

Discussion of General Mechanistic Aspects.—Although other mechanisms are certainly conceivable,[20] the reactions of lithium diorganocuprates(I) with oxiranes are most likely to proceed by one of the two possible mechanisms shown below (eq 5 and 6). Lithium ion assistance in the ring opening is suggested by the facts that ether is a better solvent for these reactions than THF (the oxirane competes effectively with ethyl ether for the lithium ion) and sulfide or phosphine solubilized organocopper reagents are not effective in these reactions.



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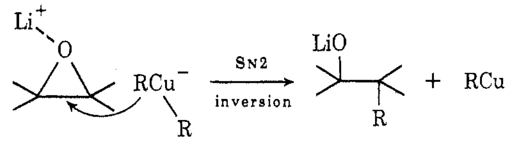

(6)

It is abundantly clear that organocopper reagents are different in their reactivity profile from the run-of-the-mill organometallics such as alkyllithiums and alkylmagnesium halides. The organocopper reagents are more effective at nucleophilic substitution at saturated carbon,[5,20] prefer to add in the conjugate manner to α,β-carbonyl compounds,[7,8] show greater preference for S_N2′ reactions in vinyloxiranes[3,4,6,11] and allylic[9] and propargylic acetates,[10] and prefer reaction at the saturated carbon of an oxirane over addition to a carbonyl.[2] These rather dramatic differences in reactivity can be best explained by the assumption that with a typical organometallic, say an alkyllithium (R^-Li^+), it is the alkyl carbon that is acting as the nucleophile, whereas with a cuprate ($R_2Cu^-Li^+$) the copper atom is the nucleophilic site (eq 5). This latter idea has precedent. Pyridine[bis(dimethyl glyoximate)]cobalt(I) reacts with cyclohexene oxide to give the trans adduct (eq 7).[21a] There is also a good possibility that the so-called deconjugation reactions of substrates, such as isophorone by combinations of Grignard reagents and

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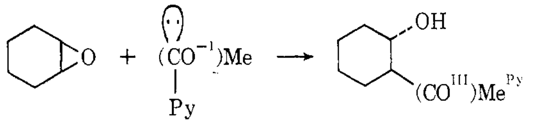
[18] The formation of dianions of allylic alcohols using *n*-butyllithium has been documented: D. R. Dimmel and S. B. Gharpure, *J. Amer. Chem. Soc.*, **93**, 3991 (1971); **94**, 5495 (1972).

[19] For an earlier suggestion see ref 4; H. O. House and M. J. Umen, *J. Amer. Chem. Soc.*, **94**, 5495 (1972), have recently provided new evidence favoring an electron transfer mechanism in the conjugate addition of cuprates to electrophilic olefins.

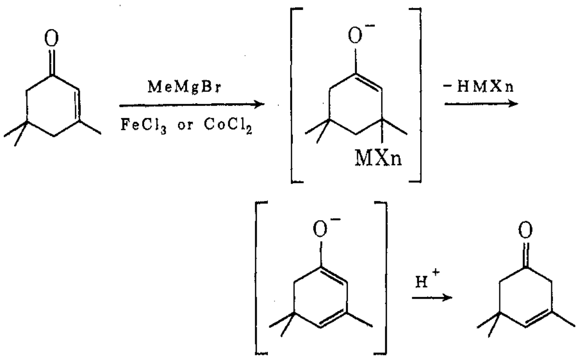
[20] For a related study on the reactions of lithium diorganocuprates and tosylates see C. R. Johnson and G. A. Dutra, *J. Amer. Chem. Soc.*, **95**, 7777, 7783 (1973).

[21] (a) F. R. Jensen, V. Maden, and D. H. Buchanan, *J. Amer. Chem. Soc.*, **92**, 1414 (1970); (b) M. S. Kharasch and P. O. Tawney, *ibid.*, **63**, 2308 (1941); (c) J. Meinwald and L. Hendry, *J. Org. Chem.*, **36**, 1446 (1971).

ferric or cobalt chloride, may occur *via* the formation of a metal–alkyl intermediate followed by elimination (eq 8).[21b,c]

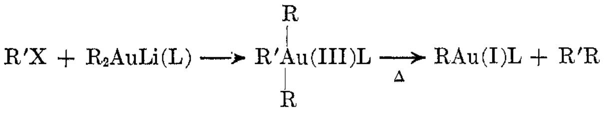


(7)



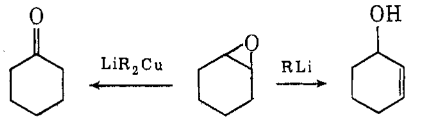
(8)

Clearly, the most pertinent examples of metal atom nucleophiles have been provided by the recent work of Tamaki and Kochi,[22] who found that lithium dialkylaurates(I) react with alkyl halides to provide a relatively stable gold(III) complex in which the original alkyl groups largely assume a trans orientation. The gold(III) complexes undergo thermally induced elimination to produce a new carbon–carbon bond (presumedly by coupling of two cis alkyl groups) (eq 9).



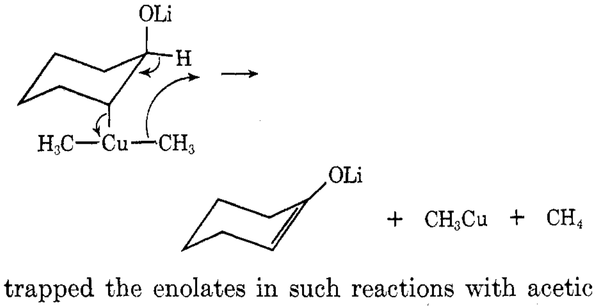
$$R'X + R_2AuLi(L) \longrightarrow R'\underset{R}{\overset{R}{Au}}(III)L \xrightarrow[\Delta]{} RAu(I)L + R'R \quad (9)$$

Major by-products from the reactions of lithium diorganocuprates with epoxides are ketones. For example, cyclohexanone is formed in the reaction of cyclohexene oxide with lithium dimethylcuprate. Note, however, that the typical product from the base-catalyzed rearrangement of cyclohexene oxide is cyclohexen-3-ol (eq 10).[3,23] If it is assumed that the



(10)

mechanism shown in eq 5 obtains, then enolate (and subsequently, ketone) formation can be nicely explained by a cyclic elimination mechanism from an organocopper(III) intermediate (eq 11). We have

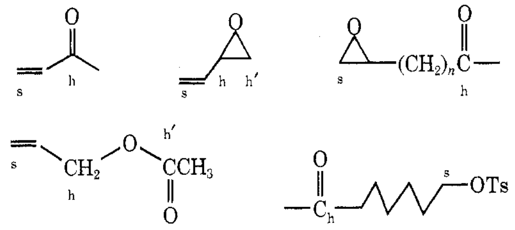


(11)

trapped the enolates in such reactions with acetic anhydride.

In a recent stereochemical, kinetic, and mechanistic study of the coupling reactions of lithium diorganocuprates and alkyl tosylates we concluded that these reactions also involve an initial SN2 reaction with the copper atom of the cuprate as the nucleophilic site.[20]

It appears to us that the hard and soft acid–base principle[24] may be useful to consider, at least from a predictive point of view, in comparing reactions of alkyllithiums and other organometallics with those of lithium organocuprates. If we consider that lithium dimethylcuprate is a softer base than methyllithium and hence prefers to react with the softer acid sites while methyllithium prefers to react at hard acid sites, then a good deal of the difference in their chemistry seems predictable. In the structures shown below we have added labels (s = soft, h = hard, h′ = harder) to indicate what we believe to be reasonable comparative designations of the hardness or softness of the acid sites.



Experimental Section

General.—Infrared spectra were obtained on a Perkin-Elmer 137 B spectrophotometer. The nmr spectra were obtained on a Varian T-60 spectrometer with TMS as the internal standard. The glc work was performed with a Hewlett-Packard Prepmaster, Jr., and a Perkin-Elmer F-11. All organometallic reactions were run under a dry nitrogen atmosphere. Solvents (ether and tetrahydrofuran) were dried by distillation from sodium dispersion. The melting points and boiling points are uncorrected. Elemental analyses were performed by Midwest Microlabs, Inc., Indianapolis, Ind. The 1,2-epoxy-3-butene was obtained from Aldrich Chemical Co. The cyclohexene oxide was obtained from Matheson Coleman and Bell. The methyl- and *n*-butyllithium reagents were obtained from Foote Mineral Co., the phenyllithium was from Alfa Inorganics, and *tert*-butyllithium was from Lithcoa. The methylmagnesium reagents were prepared from magnesium turnings (Fisher) and the methyl halides by the standard procedures. Lithium dimethylcuprate was prepared according to the procedure of House[7a] utilizing cuprous iodide purchases from Alfa Inorganics, Ventron, or Matheson and purified.[25] For details of methods used in the preparation of other cuprates see ref 20.

Reactions of Metallomethyl Reagents with 1,2-Epoxy-3-butene.—A solution of the organometallic reagent (excess) was added to a solution of the oxirane followed by refluxing the mixture in ether for 24 hr. Hydrolysis was effected with saturated ammonium chloride solution and the reaction was worked up in the usual manner.

The reaction of methylmagnesium iodide with 1,2-epoxy-3-butene is representative of the general procedure. To a magnetically stirred solution of 0.361 g (5 mmol) of 1,2-epoxy-3-butene in 10 ml of ether at room temperature, there was added, with a hypodermic syringe, 5 ml of ~3 *M* methylmagnesium iodide in ether (15 mmol). An exothermic reaction occurred upon addition of the Grignard reagent. The mixture was refluxed for 24 hr, cooled, and hydrolyzed with 5 ml of saturated ammonium chloride solution. Following extraction with ether and drying over anhydrous sodium sulfate, the ether was removed by distillation.

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

[23] R. P. Thummel and B. Rickborn, *J. Amer. Chem. Soc.*, **92**, 2064 (1970).

[24] (a) R. G. Pearson, *Science*, 151, 172 (1966); (b) R. G. Pearson and J. Songstad, *J. Amer. Chem. Soc.*, **89**, 1827 (1967); (c) B. Saville, *Angew. Chem., Int. Ed. Engl.*, **6**, 928 (1967); (d) R. G. Pearson, *Chem. Brit.*, **3**, 103 (1967).

[25] G. B. Rauffman and L. A. Teter, *Inorg. Syn.*, **7**, 10 (1963).

TABLE III

NMR DATA FOR THE PRODUCTS FROM THE REACTION OF 1,2-EPOXY-3-BUTENE WITH METALLOMETHYL REAGENTS[a]

Registry no.	Alcohol	Vinyl	CH_3	CH_2	CH	OH
616-25-1	A	5.5 (m, 3)	0.8 (t, 3)	1.4 (m, 2)	3.9 (q, 1)	3.2 (s, 1)
625-31-0	B	5.5 (m, 3)	1.1 (d, 3)	2.1 (t, 2)	3.7 (sex, 1)	3.0 (s, 1)
4516-90-9	C	5.5 (m, 3)	1.0 (d, 3)	3.3 (d, 2)	2.2 (m, 1)	4.0 (s, 1)
1576-96-1 (*E*)	D	5.5 (m, 2)	1.0 (t, 3)	2.0 (m, 2)		4.4 (s, 1)
1576-95-0 (*Z*)				4.0 (m, 2)		

[a] Chemical shift values are given in parts per million from TMS (δ).

The reaction of lithium dimethylcuprate with 1,2-epoxy-3-butene was varied slightly in that the reaction mixture was refluxed for only 30 min.

The reaction mixtures were separated into their components by preparative glc on a 6 ft × 0.75 in., 15% Carbowax 20M, on Chromosorb W, 45–60 mesh column. The column temperature was 85° with a nitrogen flow rate of 400 ml/min.

Product distribution was determined by glc analysis utilizing a 16 ft × 0.25 in., 20% diethylene glycol succinate on Chromosorb W, 60–80 mesh column. The column temperature was 100° with a helium flow rate of 60 ml/min.

Structure assignments of the products were made on the basis of the ir and nmr spectra (Table III). The stereochemical assignment of the cis–trans mixture of 2-penten-1-ol was based on the ir spectra. Two C=C bands were observed for the mixture from each reaction, with the stronger band at 1675 cm^{-1} and the weaker band at 1660 cm^{-1}. The trans/cis ratio was then determined by capillary glc using a 50 ft × 0.020 in. i.d. Perkin-Elmer support coated open tubular (SCOT) column (Carbowax 20M) with a column temperature of 80° and a nitrogen flow rate of ~1.5 cc/min. The product distribution data and reaction parameters are presented in Table II of ref 3.

Refractive indices for the four alcohols are as follows: 1-penten-3-ol (A), n^{25}D 1.4234; 4-penten-2-ol (B), n^{25}D 1.4230; 2-methyl-3-buten-1-ol (C), n^{25}D 1.4257; 2-penten-1-ol (D), n^{25}D 1.4347.

Reactions of Metallomethyl Reagents With 1,2-Epoxy-3-butene in Diethyl Ether.—The same general procedure was used as outlined for the reactions of 1,2-epoxy-3-butene. The product mixture was analyzed and separated by glc (16 ft × 0.25 in., 10% Carbowax 20M, on Chromosorb W, 60–80 mesh column; column temperature 90°, nitrogen flow rate 60 cc/min) and the products were identified by their infrared spectra and glc retention times. The reaction parameters and results are presented in Table I of ref 3.

Reactions of Organometallic Reagents with Cycloalkene Oxides.—The reactions were carried out by adding a solution of cycloalkene oxide to a solution of the organometallic reagent. Work-up and isolation were carried out in the usual manner. Products were usually separated by glc and identified by comparison of ir spectra with those of authentic samples of the compounds. The reaction parameters and results are presented in Table I of ref 2, Table I of ref 4, and Table I of this paper.

The following reaction of lithium dimethylcuprate with cyclohexene oxide illustrates the general procedure. To a solution of 5 mmol of lithium dimethylcuprate in 21 ml of ether, at 0°, there was added dropwise with stirring 0.263 g (2.5 mmol) of cyclohexene oxide in 20 ml of ether over a 10-min period. No reaction was immediately discernible, but after a few minutes a yellow solid began to precipitate from solution. The mixture was stirred for 5 hr at 0°, then hydrolyzed by addition of 20 ml of saturated ammonium chloride solution. This mixture was stirred for 2 hr at room temperature, then the aqueous layer was separated and extracted with two 10-ml portions of ether. The combined ether extracts were washed with 10 ml of saturated sodium chloride solution and dried over anhydrous sodium sulfate. The ether was removed by distillation, and the product mixture was analyzed by glc (8 ft × 0.25 in., 10% Carbowax 20M, on Chromosorb W, 60–80 mesh column, column temperature 125°, helium flow rate 60 ml/min). Three peaks were obtained with retention times of 4.3, 5.5, and 8.1 min. Material was collected from the glc and ir spectra obtained for the three compounds. Comparison with the ir spectra of authentic samples confirmed the following assignments: 4.3 min (8%), cyclohexene oxide; 5.5 min (22%), cyclohexanone. The remaining peak, 8.1 min (70%), was proven to be *trans*-2-methylcyclohexanol by comparison of its ir spectrum with Sadtler ir spectrum 13371. Analysis of the *trans*-2-methylcyclohexanol on a 50 ft × 0.020 in. i.d. Perkin-Elmer diethylene glycol succinate SCOT column (column temperature 85°, nitrogen flow rate ~1.5 ml/min) showed conclusively that no *cis*-2-methylcyclohexanol was present. With the conditions used, a mixture of *cis*- and *trans*-2-methylcyclohexanol was separated cleanly into its components.

By-product from the Reaction of Lithium Di-*tert*-butylcuprate with 1,2-Epoxy-3-cyclohexene.—A white solid (~25%) was observed to precipitate out of the ethereal solution of the crude reaction product. Ice cooling of this solution, filtration of the solid, and recrystallization from ether gave white crystals: mp 161–161.5°; nmr (CCl_4) δ 5.74 (m, 2), 1.70 (m, 6), 0.90 (s, 18); ir (KBr) 3020, 1390, 1360, 770, 685 cm^{-1}; mass spectrum (70 eV) *m/e* 194 (100%), 137, 80, 57. We suggest that this material is either *cis*- or *trans*-3,6-di-*tert*-butylcyclohexene.

Reaction of Methyl 10,11-Epoxyundecanoate with Lithium Dimethylcuprate.—To a solution of 20 mmol of lithium dimethylcuprate in 77 ml of ether there was added 2.161 g (10 mmol) of methyl 10,11-epoxyundecanoate (Aldrich) in 80 ml of ether at 0°. The mixture was stirred at 0° for 13.5 hr, then hydrolyzed and worked up as described for the reaction of cyclohexene oxide with lithium dimethylcuprate. Short-path distillation of the residue gave 0.843 g (37%) of methyl 10-hydroxydodecanoate, bp 114–116° (0.02 mm), white crystals with a broad melting range at about room temperature, ir (film) 3400 and 1725 cm^{-1}.

Anal. Calcd for $C_{13}H_{26}O_3$: C, 67.77; H, 11.40. Found: C, 68.01; H, 11.23.

Reaction of Ethyl 2,3-Epoxybutyrate with Lithium Dimethylcuprate.—To a solution of 20 mmol of lithium dimethylcuprate in 84 ml of ether at 0° there was added over 30 min a solution of 1.309 g (10 mmol) of ethyl 2,3-epoxybutyrate (Aldrich) in 80 ml of ether over 30 min. The reaction was stirred for 3 hr at 0°, then hydrolyzed and worked up as described for the reaction of cyclohexene oxide with lithium dimethylcuprate. There was obtained 1.324 g of residue which analyzed as 74.6% ethyl 2-methyl-3-hydroxybutyrate by glc analysis (8 ft × 0.25 in., 10% Versamid 940 on Chromosorb W, 60–80 mesh column, column temperature 140°, helium flow rate 60 ml/min). The yield of ethyl 2-methyl-3-hydroxybutyrate based on the glc analysis was 67%. A sample of product was collected by preparative glc (6 ft × 0.75 in., Carbowax 20M on Chromosorb W, 45–60 mesh column, column temperature 110°, nitrogen flow rate 400 cc/min), ir (film) 3500 and 1730 cm^{-1}, n^{25}D 1.4245.

Anal. Calcd for $C_7H_{14}O_3$: C, 57.50; H, 9.67. Found: C, 57.51; H, 9.68.

Reaction of Ethyl 2,3-Epoxybutyrate with Methyllithium.—To a solution of 20 mmol of methyllithium (Foote, 1 equiv of LiBr) in 84 ml of ether at 0° there was added a solution of 1.312 g (10 mmol) of ethyl 2,3-epoxybutyrate in 80 ml of ether over 30 min. The reaction was stirred for 3 hr at 0°, then hydrolyzed and worked up. Glc analysis (8 ft × 0.25 in., 10% Versamid 940 on Chromosorb W, 60–80 mesh column, column temperature 125°, nitrogen flow rate 60 ml/min) revealed a mixture consisting of 45% ethyl 2,3-epoxybutyrate, 1% ethyl 2-methyl-3-hydroxybutyrate, and 54% of a complex mixture of unidentified products.

10,11-Epoxy-2-dodecanone.—To a solution of 0.12 mol (21.5 g) of dodecen-11-one[26] in 300 ml of methylene chloride in a 1-l., three-necked flask fitted with mechanical stirrer was added portionwise 0.18 mol (30.5 g) of *m*-chloroperbenzoic acid over a 30-min period while the reaction temperature was maintained at 5–10°. After addition of the acid, the temperature was raised to ambient and stirring was maintained for 19 hr. Excess *m*-chloroperbenzoic acid was reduced with 10% aqueous potassium bisulfite. The methylene chloride layer was separated and shaken with two 200-ml portions of brine solution and then dried over anhydrous magnesium sulfate. Removal of the solvent

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(26) N. A. Sorensen and J. Mehlum, *Acta Chem. Scand.*, **2**, 140 (1948).

and distillation of the oily residue gave 17.5 g (75% yield) of clear, colorless oil: bp 119–123°; mp 27–28°; ir (film) 1720, 915, 835 cm^{-1}.

Anal. Calcd for $C_{12}H_{22}O_2$: C, 72.69; H, 11.18. Found: C, 71.92; H, 11.13.

Reaction of Lithium Dimethylcuprate with 10,11-Epoxy-2-dodecanone.—To a solution of 5.34 mmol of lithium dimethylcuprate in 15 ml of absolute ether at −50° was added dropwise 2.67 mmol (506 mg) of 10,11-epoxy-2-dodecanone in 30 ml of ether. Following the 10-min addition, the reaction mixture was stirred for 30 min and then quenched with 40 ml of saturated ammonium chloride solution. The reaction mixture was warmed to ambient and stirred for 0.5 hr. The ether layer was decanted, shaken with 20 ml of water and 20 ml of brine solution, and then dried over sodium sulfate. Removal of the ether and column chromatography of the residue on silica gel G using 2% ether–98% methylene chloride as eluent gave 372 mg (68% yield) of 11-hydroxy-2-tridecanone: mp 44–45° (recrystallized from hexane); ir (CCl_4) 3500, 1720, 1355, 1160 cm^{-1}.

Anal. Calcd for $C_{13}H_{26}O_2$: C, 72.85; H, 12.23. Found: C, 72.74; H, 12.20.

Reaction of Lithium Diphenylcuprate with 2,3-Epoxy-3-methylbutyronitrile.—To a solution of 10 mmol of lithium diphenylcuprate in 20 ml of ether and 10 ml of benzene at 0° was added 2,3-epoxy-3-methylbutyronitrile[27] (485 mg, 5 mmol) in 10 ml of ether over a 10-min period. After addition was complete the mixture was stirred for an additional 20 min. The usual work-up yielded a liquid residue which upon chromatography on a silica gel column, eluting with pentane–ether, yielded 3-hydroxy-3-methyl-2-phenylbutyronitrile (295 mg, 34%) [ir (film) 3400, 2225, 1150, 730, 690 cm^{-1}, nmr ($CDCl_3$) δ 7.37 (s, 5), 3.80 (s, 1), 2.56 (s, 1), 1.30 (s, 6)] and 2,2-dimethyl-3-benzoyloxirane (50 mg, 6%) [ir (neat) 1690, 1220, 680, 700 cm^{-1}, nmr ($CDCl_3$) δ 7.8 (m, 5), 4.15 (s, 1), 1.63 (s, 3), 1.28 (s, 3)].

Reaction of Lithium Dimethylcuprate with *exo*-Norbornene Oxide.—To a solution of 0.5 mmol (95 mg) of cuprous iodide and 20.0 mmol of methyllithium in 30 ml of anhydrous dimethoxyethane at 0° under nitrogen was added dropwise with stirring 9.0 mm (0.990 g) of *exo*-norbornene oxide. The reaction was warmed to 55° and maintained there for 5 hr. The reaction mixture was cooled to 0° and hydrolyzed with 10 ml of aqueous ammonium chloride. Fifty milliliters of ether and 30 ml of water were added to the mixture and shaken. The ether layer was collected and treated consecutively with 20 ml of water, 20 ml of saturated sodium chloride solution, and solid anhydrous Na_2CO_3. Solvent removal *in vacuo* gave a white solid which after sublimation (60°, 7 mm) gave 0.65 g (58%) of *endo*-3-methyl-*exo*-2-norbornanol: mp 96–100° (lit.[28] mp 95.5–97°); ir (CCl_4) 3300, 1070 cm^{-1}.

Reaction of *exo*-norbornene oxide (9 mmol) with methyllithium (20 mmol) in 30 ml of dimethoxyethane at 70° for 5 hr resulted in a recovery of 93% of starting material and 7% conversion to *endo*-3-methyl-*exo*-2-norbornanol and a trace of norcamphor.

Reaction of Lithium Dimethylcuprate with 5α-Cholestane 2α,3α-Oxide.—To a solution of lithium dimethylcuprate (5 mmol) in 20 ml of ether at 0° was added dropwise 387 mg (1.0 mmol) of 5α-cholestane 2α,3α-oxide[29] in 20 ml of ether. After addition was completed, the reaction mixture was warmed to room temperature and allowed to stir for 24 hr. Work-up gave 341 mg of a white solid which showed two major spots on tlc on silica gel. Column chromatography on silica gel using pentane–ether as eluent gave 5α-cholestan-2-one (82 mg, 22%), mp 128.5–129.5°, $[\alpha]^{25}\mathrm{D}$ +50.6° (*c* 1.97, EtOH) (lit.[29] mp 130°, $[\alpha]\mathrm{D}$ +50.7°), and 2β-methyl-5α-cholestan-3α-ol (260 mg, 65%), mp 117.5–118.0°, $[\alpha]^{25}\mathrm{D}$ +42.9° (*c* 2.0, $CHCl_3$), ir (CCl_4) 3400 cm^{-1}. Oxidation of this alcohol with chromic anhydride–pyridine gave 2β-methyl-5α-cholestan-3-one,[30] mp 98.5–99° (lit.[15] mp 97.5–98.5°), ir (CS_2) 1715 cm^{-1}, $[\alpha]^{25}\mathrm{D}$ +122° (*c* 1.51, $CHCl_3$).

Registry No.—Lithium dimethylcuprate, 15681-48-8; lithium di-*n*-butylcuprate 24406-16-4; 1,2-epoxy-3-butene, 930-22-3; lithium di-*tert*-butylcuprate 23402-75-7; 1,2-epoxy-3-cyclohexene, 6705-51-7; 3,6-di-*tert*-butylcyclohexene, 42334-56-5; methyl 10,-11-epoxyundecanoate, 22663-09-8; methyl 10-hydroxydodecanoate, 27512-78-3; ethyl 2,3-epoxybutyrate, 19780-35-9; ethyl 2-methyl-3-hydroxybutyrate, 27372-03-8; 10,11-epoxy-2-dodecanone, 42334-61-2; dodecen-11-one, 5009-33-6; 11-hydroxy-2-tridecanone, 27372-05-0; lithium diphenylcuprate, 23402-69-9; 2,3-epoxy-3-methylbutyronitrile, 6509-07-5; 3-hydroxy-3-methyl-2-phenylbutyronitrile, 42334-65-6; 2,2-dimethyl-3-benzoyloxirane, 15120-98-6.

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Preparation of Organocalcium Halides in Hydrocarbon Solvents

NARIYOSHI KAWABATA,* AKIRA MATSUMURA, AND SHINZO YAMASHITA

Department of Chemistry, Kyoto Institute of Technology, Matsugasaki, Sakyo-ku, Kyoto 606, Japan

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Contrary to the description in the literature, the reaction of alkyl halides with calcium metal in hydrocarbon solvents was found to give the corresponding alkylcalcium halides in good yields. The reaction was not restricted to primary alkyl iodides. Bromides and chlorides also afforded alkylcalcium halides. Isopropyl halides were also converted into organocalcium halides. In the reaction with *tert*-butyl halides, however, the disproportionation to form the corresponding alkane and alkene far exceeded the formation of *tert*-butylcalcium halides. The reaction of calcium with aryl halides gave arylcalcium halides in poor yields.

In the preceding paper,[1] we demonstrated that the reaction of organic halides with calcium metal in tetrahydrofuran gave the corresponding organocalcium halides in much better yields than those available in the literature. The key ingredient appeared to be the availability of higher purity calcium metal than was previously obtainable. The lower content of sodium in the calcium metal seemed to be an important factor in this improvement. Reaction 1 was shown to be not restricted to aryl and primary alkyl iodides contrary to the description in the literature. Bromides and chlorides also afforded organocalcium halides. In addition, isopropyl halides were first converted into organocalcium halides by the reaction.

$$\mathrm{RX + Ca \longrightarrow RCaX} \qquad (1)$$

Our experimental procedure showed several additional advantages. Previous authors described various approaches to the activation of calcium metal, *e.g.*, treatment with Grignard reagent,[2] amalgamation,[3–5] use of calcium–magnesium alloy,[3] and heating with

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