THE JOURNAL OF Organic Chemistry®

VOLUME 43, NUMBER 2

JANUARY 20, 1978

Reactions of Complex Metal Hydrides of Copper with Alkyl Halides, Enones, and Cyclic Ketones

Eugene C. Ashby,* Jiang-Jen Lin, and Anil B. Goel

School of Chemistry, Georgia Institute of Technology, Atlanta, Georgia 30332

Received May 4, 1977

A series of stable complex metal hydrides of copper of composition Li_nCuH_{n+1} (n = 1–5), prepared by the reaction of $LiAlH_4$ with the corresponding lithium methylcuprates in diethyl ether, has been allowed to react with selected alkyl halides, enones, and cyclic ketones in both diethyl ether and THF. It has been shown that the different hydrides exhibit different regioselectivities toward enones and different stereoselectivities toward cyclic ketones. These data support the integrity of each hydride as a single compound rather than a physical mixture. Tetrahydrofuran-soluble Li_4CuH_5 has been shown to be the most reactive of the complex metal hydrides of copper toward alkyl halides in that this hydride reduced 1-iodo-, 1-bromo-, and 1-chlorodecane in 100, 100, and 99% yields, respectively. The complex metal hydrides of copper reduce enones predominantly 1,4 (Li_2CuH_3, 96%) or 1,2 (Li_4CuH_5, 95%), depending on the hydride. In most cases, the complex metal hydrides of copper reduce 4-*tert*-butylcyclohexanone predominantly from the axial side, as in the case of $LiAlH_4$. Other cyclohexanones are reduced by the complex metal hydrides of copper similarly to $LiAlH_4$, except with less selectivity.

Application of copper hydride reagents in organic synthesis has been a topic of great interest in the past 10 years. Recently, LiCuHR compounds (where R = 1-pentyne, OBu^t, and SPh) have been prepared and used as selective reducing reagents in order to effect conjugate reduction of α,β-unsaturated carbonyl compounds.[1] Almost at the same time, LiCuHR compounds (where R = alkyl and alkynyl) were evaluated as reagents for the selective removal of halo and mesyloxyl groups from RX compounds as well as for the reduction of α,β-unsaturated ketones.[2] More recently, the mixture obtained by the combination of $2LiAlH(OCH_3)_3$ with CuBr or $NaAlH_2(OCH_2CH_2OCH_3)_2$ with CuBr has been demonstrated to possess the ability to reduce conjugated carbonyl compounds to the corresponding saturated derivatives. The intermediates in these reagents were speculated to be "complex copper hydrides", although no evidence was presented to establish this point.[3] We reported the preparation of the first complex metal hydride of copper, $LiCuH_2$, some time ago by the reaction of $LiAlH_4$ with $LiCu(CH_3)_2$.[4] More recently, we have established the existence of some new organocuprates by variable-temperature NMR, namely, $LiCu_2(CH_3)_3$ and $Li_2Cu(CH_3)_3$,[5] and have shown that these new cuprates behave differently from $LiCu(CH_3)_2$ toward enones[6] and organohalides.[7] In continuation of our present investigations in the field of copper chemistry, we have recently been able to prepare a series of complex metal hydrides of copper, $Li_nCu_mH_{n+m}$ (where n = 1–5 and m = 1–2), which are not only stable at room temperature (except for $LiCu_2H_3$ and $LiCu_3H_5$), but also some of which are soluble in THF ($LiCuH_2$ and Li_4CuH_5). These hydrides are pure compounds and not mixtures, according to x-ray and DTA–TGA data[8] as well as evidence that appears in this study. We now wish to report some reactions of the stable new complex metal hydrides of copper (Li_nCuH_{n+1}) with alkyl halides, enones, and cyclic ketones in Et_2O and THF which should be of considerable synthetic interest.

Results and Discussion

When CH_3Li in diethyl ether was added dropwise to a well-stirred slurry of CuI in diethyl ether at −78 °C, a clear and colorless solution resulted when the CH_3Li:CuI ratio was 2:1. When $LiAlH_4$ in Et_2O was added to this solution, no precipitate was observed at −78 °C; however, when the reaction mixture was allowed to warm to room temperature, a white crystalline solid precipitated. The insoluble solid was separated from the ether-soluble $LiAlH_2(CH_3)_2$ by filtration, and the solid was washed with Et_2O, dried, and characterized by elemental analysis and found to be a complex metal hydride of copper. In this way, a series of complex metal hydrides of copper of composition $Li_nCuH_{(n+1)}$ (where n = 1–5) was prepared by the reaction of $LiAlH_4$ with the corresponding lithium methylcuprates (eq 1 and 2). Specifically, the following compounds were prepared for this study: $LiCuH_2$, Li_2CuH_3, Li_3CuH_4, Li_4CuH_5, Li_5CuH_6.

$$(n + 1)CHLi + CuI \xrightarrow[-78°C]{Et_2O} Li_nCu(CH_3)_{n+1} + LiI \quad (1)$$

$$Li_nCu(CH_3)_{n+1} + \left(\frac{n+1}{2}\right) LiAlH_4 \xrightarrow[-78\ °C]{Et_2O} Li_nCuH_{n+1} + \left(\frac{n+1}{2}\right) LiAlH_2(CH_3)_2 \quad (2)$$

The compound $LiCuH_2$ was analyzed as a diethyl ether slurry while other compounds were analyzed as a slurry as well as a solid. It is interesting to note that when the products were dried under vacuum they contained no complexed ether.

Table I. Analyses and Properties of Complex Metal Hydrides of Copper (Li_nCuH_{n+1})

Compd	Anal. (ratio) Li:Cu:H	Solubility in THF	Thermal decomp[a] (0 °C)
$LiCuH_2$	1.07:1.00:2.01	Soluble	70, 300, 400
Li_2CuH_3	2.07:1.00:2.95	Insoluble	90, 110, 120, 145, 290, 440
Li_3CuH_4	3.05:1.00:3.97	Insoluble	110, 120, 140, 308, 410, 450
Li_4CuH_5	3.95:1.00:4.96	Soluble	120, 145, 300, 365, 430, 480–above 500
Li_5CuH_6	5.09:1.00:5.95	Insoluble	140, 305, 440, 400–above 500

[a] Thermal analysis was carried out on a Mettler Thermoanalyzer II under vacuum with simultaneous DTA–TGA recording.

Table II. Reactions of Complex Metal Hydrides of Copper with Organohalides and Tosylates in THF at Room Temperature for 24 h

Expt	Hydride reagent[a]	Registry no.	Halide substrate	Registry no.	Product(s) and yield(s) (%)[b]
1	$LiCuH_2$	53201-99-3	1-Iodododecane	2050-77-3	n-Decane (100)
2	$LiCuH_2$		1-Bromodecane	112-29-8	n-Decane (85)
3	$LiCuH_2$		1-Chlorodecane	1002-69-3	n-Decane (37)
4	$LiCuH_2$		1-Fluorodecane	334-56-5	n-Decane (0)
5	$LiCuH_2$		n-Octyl tosylate	3386-35-4	n-Octane (64)
6	Li_2CuH_3	64010-63-5	1-Iodododecane		n-Decane (100)
7	Li_2CuH_3		1-Bromodecane		n-Decane (100)
8	Li_2CuH_3		1-Chlorodecane		n-Decane (35)
9	Li_2CuH_3		1-Fluorodecane		n-Decane (0)
10	Li_2CuH_3		n-Octyl tosylate		n-Octane (80)
11	Li_2CuH_3		Cyclohexyl chloride	542-18-7	Cyclohexane (0)
12	Li_2CuH_3		1-Chlorocyclohexene	930-66-5	Cyclohexene (0)
13	Li_2CuH_3		3-Chlorocyclohexene	2441-97-6	Cyclohexene (0)
14	Li_2CuH_3		Chlorobenzene	108-90-7	Benzene (0)
15	Li_3CuH_4	64010-64-6	1-Iodododecane		n-Decane (100)
16	Li_3CuH_4		1-Bromodecane		n-Decane (90)
17	Li_3CuH_4		1-Chlorodecane		n-Decane (34)
18	Li_3CuH_4		1-Fluorodecane		n-Decane (0)
19	Li_3CuH_4		n-Octyl tosylate		n-Octane (39)
20	Li_4CuH_5	64010-65-7	1-Iodododecane		n-Decane (100)
21	Li_4CuH_5		1-Bromodecane		n-Decane (100)
22	Li_4CuH_5		1-Chlorodecane		n-Decane (99)
23	Li_4CuH_5		1-Fluorodecane		n-Decane (10)
24	Li_4CuH_5		n-Octyl tosylate		n-Decane (99)
25	Li_4CuH_5		Cyclohexyl chloride		Cyclohexane (0)
26	Li_4CuH_5		1-Chlorocyclohexene		Cyclohexene (0)
27	Li_4CuH_5		3-Chlorocyclohexene		Cyclohexene (10)
28	Li_4CuH_5		Chlorobenzene		Benzene (0)
29	Li_5CuH_6	64010-66-8	1-Iodododecane		n-Decane (100)
30	Li_5CuH_6		1-Bromodecane		n-Decane (100)
31	Li_5CuH_6		1-Chlorodecane		n-Decane (80)
32	Li_5CuH_6		1-Fluorodecane		n-Decane (0)
33	Li_5CuH_6		n-Octyl tosylate		n-Decane (69)

[a] The molar ratio of hydride reagent to substrate is 1:1, except $LiCuH_2$ (2:1) ratio.

Interestingly, $LiCuH_2$ and Li_4CuH_5 were found to be soluble in THF, and Li_4CuH_5 was found to be stable in THF at room temperature. All of the complex metal hydrides of copper, except $LiCu_2H_3$, were found to be stable at room temperature in the solid state or as a slurry in diethyl ether. The thermal stability of these compounds is in the order: $Li_5CuH_6 > Li_4CuH_5 > Li_3CuH_4 > Li_2CuH_3 > LiCuH_2 > LiCu_2H_3$. The hydride, Li_5CuH_6, is stable to 140 °C under vacuum and is stable at room temperature for over 1 month. Elemental analysis, solubility, and thermal stabilities of these complexes are given in Table I.

In order to study the reactions of these hydrides with various organic substrates, either a diethyl ether slurry or a THF solution of the hydride of known concentration was prepared and added to the organic substrate in either diethyl ether or THF.

Reactions of Organohalides and Tosylates. Decyl halides (X = I, Br, Cl and F) and n-octyl tosylate were allowed to react with each of the stable complex metal hydrides of copper (i.e., $LiCuH_2$, Li_2CuH_3, Li_3CuH_4, Li_4CuH_5, and Li_5CuH_6). In preliminary experiments, both THF and diethyl ether were evaluated as solvents with the results indicating that THF is the better solvent. For example, the reaction of Li_2CuH_3 with 1-iodododecane produced 100% n-decane in THF within 1 h of reaction time at room temperature

$$Li_nCuH_{n+1} + C_{10}H_{21}I \xrightarrow{THF} C_{10}H_{22}\ (100\%\ \text{yield}) \qquad (3)$$

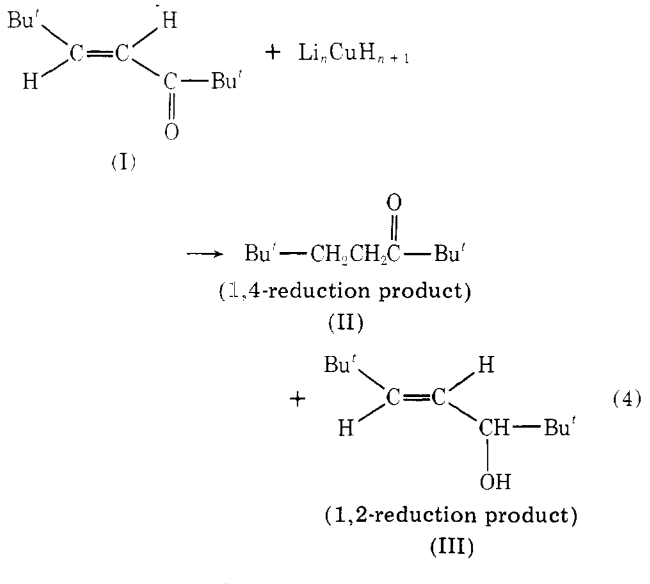
but only 72% n-decane was formed in diethyl ether solvent in a comparable experiment over the same period of time. A further difference in the two solvents was indicated in close observations of the reactions of 1-iodododecane with Li_2CuH_3. In THF, precipitation of a black solid (Cu°) took place immediately when the reagent and substrate were mixed at 22 °C, whereas in diethyl ether the black solid formed more slowly. The results of these studies are summarized in Table II. Each of the five complex metal hydrides of copper react with 1-iodododecane to give 100% n-decane. The reactivity of

Table III. Reactions of Complex Metal Hydrides of Copper with 2,2,6,6-Tetramethyl-*trans*-4-hepten-3-one at Room Temperature

Expt	Hydride reagent	Reaction condition	Enone recovered, %	Products, %	
				1,4	1,2
34	$LiCuH_2$	Et_2O, 24 h	20	60	20
35	$LiCuH_2$	THF, 24 h	0	11	85
36	Li_2CuH_3	Et_2O, 48 h	0	93	6
37	Li_2CuH_3	THF, 48 h	0	88	12
38	Li_3CuH_4	Et_2O, 48 h	70	5	25
39	Li_3CuH_4	THF, 48 h	50	5	45
40	Li_4CuH_5	Et_2O, 24 h	0	5	90
41	Li_4CuH_5	THF, 24 h	0	5	95
42	Li_5CuH_6	Et_2O, 48 h	58	4	33
43	Li_5CuH_6	THF, 48 h	25	4	71

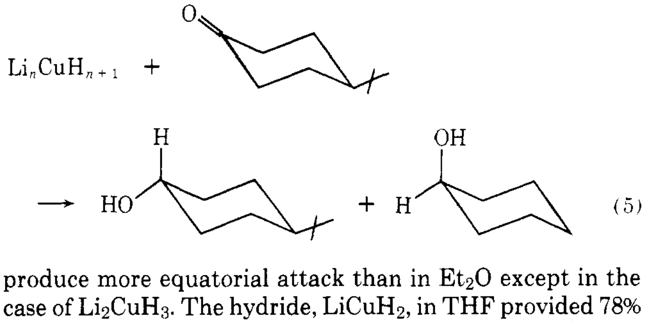
the substrate toward the hydride reagent has been found to decrease in the order of I > Br > OTs > Cl > F. For example, reactions of $LiCuH_2$ in THF with 1-iododecane, 1-bromodecane, *n*-octyl tosylate, 1-chlorodecane, and 1-fluorodecane produced products in 100, 85, 64, 37, and 0% yield, respectively. This order was followed throughout for the five hydride reagents, except for a small deviation involving Li_5CuH_6. Li_4CuH_5 was found to be the most reactive hydride, presumably due to its solubility in THF. This hydride reacted with 1-iododecane, 1-bromodecane, 1-chlorodecane, and *n*-octyl tosylate to give quantitative yields of the reduction product in each case. Only 10% reaction was observed between Li_4CuH_5 and 1-fluorodecane after 24 h at room temperature (with the reagent still active after the 24-h reaction period); however, the other hydrides did not react at all with 1-fluorodecane. Reactions involving Li_2CuH_3 and Li_4CuH_5 were also carried out with other chlorides, namely, cyclohexyl chloride, 1-chlorocyclohexene, 3-chlorocyclohexene, and chlorobenzene; only in the case of the reaction of Li_4CuH_5 with 3-chlorocyclohexene was any reaction observed (10%).

Reactions of 2,2,6,6-Tetramethyl-*trans*-4-hepten-3-one (Enone I). Enone I was chosen as a representative enone for this study. It has been reported that enone I can be reduced quantitatively to the 1,2-reduction product III by $LiAlH_4$ or to the 1,4-reduction product II by H_2AlI. It has also been shown that reaction in THF results in better regioselectivity than in Et_2O solvent.[9] Reactions of each hydride, Li_nCuH_{n+1}, were carried out in THF and Et_2O solvent at room temperature in order to compare the regioselectivity in each solvent (eq 4). The results are shown in Table III.



A comparison of hydride reactivities (i.e., percent enone recovered) and regioselectivity (i.e., the distribution of 1,4:1,2-reduction products) demonstrates the characteristic differences of the different hydrides. Li_2CuH_3 and Li_4CuH_5 both have high reactivities, but exhibit entirely different regioselectivities. Li_4CuH_5 behaves very much like $LiAlH_4$, whereas Li_2CuH_3 produces the exact opposite regioselectivity, behaving as a good conjugate reducing agent. Li_3CuH_4 and Li_5CuH_6 behave similarly both in reactivity and regioselectivity, whereas $LiCuH_2$ behaves very strangely, producing predominant 1,4-reduction in ether (60:20) and predominant 1,2-reduction in THF (11:85). These data also provide more evidence that these complex metal hydrides of copper are not physical mixtures of each other or combinations of $LiCuH_2$ and LiH, since each stoichiometric compound behaves so differently.

Reactions of 4-*tert*-Butylcyclohexanone, 3,3,5-Trimethycyclohexanone, and 2-Methycyclohexanone. The stereoselective reduction of cyclohexanones by metal hydrides has been studied intensively in recent years. $LiAlH_4$ is considered to be the least sterically hindered hydride, since it produces 90, 76, and 20% axial attack on 4-*tert*-butylcyclohexanone, 2-methylcyclohexanone, and 3,3,5-trimethylcyclohexanone, respectively.[10] The more sterically bulky hydrides are subject to "steric approach control" in their approach to any particular cyclohexanone; therefore, the amount of equatorial attack can be considered an indication of the effective bulk of the hydride. Results of the hydride reactions with the cyclohexanones are given in Table IV. Reactions of 4-*tert*-butylcyclohexanone were carried out in both THF and Et_2O solvents (eq 5). It appears that the hydrides in THF produce more equatorial attack than in Et_2O except in the case of Li_2CuH_3. The hydride, $LiCuH_2$, in THF provided 78% equatorial attack, which is very unusual compared to $LiAlH_4$ (10% equatorial attack), but gave only 18% equatorial attack in ether solvent. This result suggests a higher effective bulk for $LiCuH_2$ in THF as compared to ether. The results of Table IV show that the amount of axial alcohol increased in the order: $LiCuH_2 < Li_2CuH_3 < Li_3CuH_4 < Li_4CuH_5 < Li_5CuH_6$.

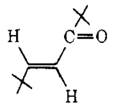
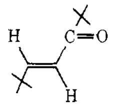
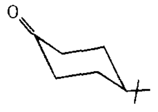


Reaction of 3,3,5-trimethylcyclohexanone and 2-methylcyclohexanane with $LiCuH_2$ in THF and Et_2O and Li_4CuH_5 and Li_5CuH_6 in just THF have also been carried out. In both cases involving $LiCuH_2$, the solvent affects the selectivity in the same way as seen in 4-*tert*-butylcyclohexanone, i.e.,

Table IV. Reactions of Complex Metal Hydrides of Copper with 4-*tert*-Butylcyclohexanone, 3,3,5-Trimethylcyclohexanone, and 2-Methylcyclohexane at Room Temperature

Expt	Hydride reagent	Substituted cyclohexanone	Registry no.	Reaction condition	Ketone recovered	Relative yield, % ax-OH	Relative yield, % eq-OH
44	$LiCuH_2$	4-*tert*-Butyl	98-53-3	Et_2O, 48 h	0	18	82
45	$LiCuH_2$	4-*tert*-Butyl		THF, 48 h	0	78	22
46	Li_2CuH_3	4-*tert*-Butyl		Et_2O, 48 h	17	43	57
47	Li_2CuH_3	4-*tert*-Butyl		THF, 48 h	20	22	78
48	Li_3CuH_4	4-*tert*-Butyl		THF, 72 h	0	31	69
49	Li_4CuH_5	4-*tert*-Butyl		Et_2O, 72 h	16	11	89
50	Li_4CuH_5	4-*tert*-Butyl		THF, 72 h	40	15	85
51	Li_5CuH_6	4-*tert*-Butyl		Et_2O, 72 h	50	9	91
52	Li_5CuH_6	4-*tert*-Butyl		THF, 72 h	55	14	86
53	$LiCuH_2$	3,3,5-Trimethyl	873-94-9	Et_2O, 24 h	0	86	14
54	$LiCuH_2$	3,3,5-Trimethyl		THF, 24 h	0	98	2
55	Li_4CuH_5	3,3,5-Trimethyl		THF, 24 H	1	82	18
56	Li_5CuH_6	3,3,5-Trimethyl		THF, 24 h	0	91	9
57	$LiCuH_2$	2-Methyl	583-60-8	Et_2O, 24 h	0	42	58
58	$LiCuH_2$	2-Methyl		THF, 24 h	0	50	50
59	Li_4CuH_5	2-Methyl		THF, 24 h	0	35	65
60	Li_5CuH_6	2-Methyl		THF, 24 h	0	33	67

Table V. Comparison of Reactivities of $LiAlH_4$ and Li_4CuH_5 in Equal Molar Ratio in THF at Room Temperature

Expt	Hydride	Substrate	Reaction time		$C_{10}H_{22}$	
61	$LiAlH_4$	$C_{10}I$	15 min		98	
62		$C_{10}Br$	15 min		85	
			1 h		95	
63		$C_{10}Cl$	15 min		0	
			1 h		0	
64	Li_4CuH_5	$C_{10}I$	15 min		100	
		$C_{10}Br$	15 min		99	
		$C_{10}Cl$	15 min		0	
			1 h		3	
			24 h		99	
				Enone recovered, %	Products, % 1,4	Products, % 1,2
65	$LiAlH_4$		15 min	0	0	100
66	Li_4CuH_5		15 min	0	5	95
				Ketone recovered, %	Relative yield, % ax-OH	Relative yield, % eq-OH
67	$LiAlH_4$		15 min	0	8	92
68	Li_4CuH_5		15 min	0	45	55

98:86% (THF/Et_2O) equatorial attack in the reduction of 3,3,5-trimethylcyclohexanone. $LiCuH_2$ appears to be more selective (higher effective bulk) than the other complex metal hydrides of copper toward all of the cyclohexanones studied.

We have made a comparison of the reactivity of Li_4CuH_5 to that of the well-known $LiAlH_4$ in order to obtain some idea of the strength of the new complex metal hydrides of copper as reducing agents. It would appear from the results in Table IV that the complex metal hydrides of copper in general, and specifically Li_4CuH_5, are weaker reducing agents than $LiAlH_4$ (experiments 49–50). However, the results in Table IV were obtained for Li_4CuH_5 prepared in diethyl ether (expt 49). The solid Li_4CuH_5 was separated from the ether-soluble $LiAlH_2(CH_3)_2$ by filtration or centrifugation followed by total drying of the solid and reslurrying in ether. When THF was described as the solvent (expt 50) the Li_4CuH_5 was prepared in ether; however, the reaction mixture was filtered, producing a mushy, wet solid, and when THF was added to this mixture all of the solid immediately dissolved. These observations suggest that the product Li_4CuH_5 when prepared contains some complexed ether which can be replaced by the more basic solvent THF, allowing the complex to dissolve. However, if the product Li_4CuH_5 is completely dried under vacuum, the complexed ether is removed, leaving the product in a more stable crystal lattice which exhibits much less solubility in THF. Table V shows the results obtained in a comparison of dissolved Li_4CuH_5 with $LiAlH_4$ in THF. As can be seen from the data, particularly a comparison of reductions of decyl chloride, Li_4CuH_5 is a more powerful reducing agent than $LiAlH_4$. It is also noteworthy that the stereochemistry of reduction of *tert*-butylcyclohexanone by Li_4CuH_5 as a slurry (Table IV, experiment 50; 15:85, axial-OH:equatorial-OH) compared to Li_4CuH_5 in solution (Table V, 45:55, axial-OH:equatorial-OH) is quite different.

In conclusion, results of reactions of new complex metal hydrides of copper with organic substrates have demonstrated their individual integrities and unique properties as reducing agents. In the case of alkyl halides, the new copper hydrides are potentially useful reagents for the reduction to alkanes. Li_4CuH_5, which is soluble in THF, appears to be particularly useful. In the case of enones, it appears that either predominant 1,2- or 1,4-reduction can be obtained depending on the specific hydride used, whereas the new hydrides appear to reduce cyclohexanones similarly to $LiAlH_4$ except in some cases where the reduction is not as selective. A comparison of the rate of reduction for one of the complex metal hydrides of copper (Li_4CuH_5) to $LiAlH_4$ in THF shows that Li_4CuH_5 is a more powerful reducing agent than $LiAlH_4$ toward alkyl halides and possibly toward other substrates as well. The reactivity of the hydrides depends to a large extent on the homogeneous or heterogeneous nature of the hydride, the reactivity being considerably greater when the hydride is soluble in the reaction medium.

Experimental Section

Apparatus and Instrumentation. All operations were carried out either in a nitrogen-filled glove box equipped with a recirculating system[11] to remove oxygen and moisture or at the bench using typical Schlenk tube techniques.[12] All glassware was flash flamed and flushed with nitrogen prior to use. Infrared spectra were recorded in KBr cells using a Perkin-Elmer 621 high-resolution infrared spectrophotometer. The NMR spectra were determined at 60 MHz with a Varian Model T-60-A NMR spectrometer. GLPC analyses were performed on an F and M Model 720 gas chromotograph. Hydrogen analysis was carried out by hydrolyzing samples with hydrochloric acid on a standard vacuum line and collecting the evolved hydrogen with a Toepler pump.[12] Lithium was determined by flame photometry using a Coleman Model 21.[15] Iodide was determined by the Volhard procedure.[16] Copper was determined by electrolytic deposition on a platinum electrode.[17]

Materials. Tetrahydrofuran (Fisher certified reagent grade) was distilled under nitrogen over $NaAlH_4$ and diethyl ether (Fisher Reagent) over $LiAlH_4$ prior to use. Methyllithium in THF and Et_2O was prepared by the reaction of $(CH_3)_2Hg$ with excess lithium metal. Both solutions were stored at −78 °C until ready to use. Cuprous iodide was purified by precipitating from an aqueous KI–CuI solution.[13] The precipitated solid was washed with water, ethanol, and diethyl ether, and then dried at room temperature under vacuum.

A solution of $LiAlH_4$ (Ventron, Metal Hydride Division) was prepared by stirring a diethyl ether slurry overnight, followed by filtration of the slurry through dried Celite analytical grade filter aid. The solution was standardized by aluminum analysis (EDTA).

Halide substrates and authentic samples of products were purchased commercially and used without further purification: iodo-, bromo-, chloro- and fluorodecane (Eastman Organic Chemicals), cyclohexyl chloride (Aldrich Chemical Co.), and 1- and 3-chlorocyclohexene (Friton Laboratories).

n-Octyl tosylate was prepared by reaction of *n*-octanol (7 g, ca. 0.05 M) in pyridine (16 g) with *p*-toluenesulfonyl chloride (10.5 g, ca. 0.055 M) at 20 °C overnight. The workup was by HCl–ice water hydrolysis followed by benzene extraction. The pure product was obtained by distillation: bp 155–156 °C (2 mmHg); NMR ($CDCl_3$) δ 7.66 (2 H, d), 7.25 (2 H, d), 3.94 (2 H, t, CH_2O), 2.40 (3 H, s, benzyl CH_3), 2.0–0.8 (15 H, m, alkyl).

2,2,6,6-Tetramethyl-*trans*-4-hepten-3-one was prepared as previously described.[14] An authentic sample of 1,4-product, 2,2,6,6-tetramethyl-3-heptanone, was synthesized by reaction of 2,2,6,6-tetramethyl-*trans*-4-hepten-3-one with Li/HMPA: bp 108 °C (2 mmHg); NMR (CCl_4) δ 2.36 (2 H, t, $O{=}COCH_2$), 1.40 (2H, t, CH_2), 1.08 (9 H, s, Bu^t), and 0.87 (9 H, s, Bu^t); IR 1710 cm^{-1} ($C{=}O$), no hydroxyl absorption. 2,2,6,6-Tetramethyl-*trans*-4-hepten-3-ol, 1,2-product, was obtained by reaction of 2,2,6,6-tetramethyl-*trans*-4-hepten-3-one with $LiAlH_4$: NMR (CCl_4) δ 5.5 (2 H, m, olefinic), 3.57 (1 H, d, OCH), 1.5 (1 H, s, OH), 0.98 (9 H, s, Bu^t) and 0.78 (9 H, s, Bu^t); IR 3600–3200 (OH), 1485 and 1470 cm^{-1} ($C{=}C$), no carbonyl absorption.

4-*tert*-Butylcyclohexanone (Friton), 3,3,5-trimethylcyclohexanone (Chemical Sample Co.), and 2-methylcyclohexanone (Fisher) were purified by vacuum distillation or sublimation.

Preparation of $Li_nCuH_{(n+1)}$ by the Reaction of $Li_nCu(CH_3)_{n+1}$ with $(n + 1/2)LiAlH_4$ in Diethyl Ether. To a well-stirred slurry of cuprous iodide in diethyl ether at −78 °C was added dropwise CH_3Li in diethyl ether in various ratios (MeLi/CuI = 2:1, 3:1, 4:1, 5:1, or 6:1). A clear solution resulted in every case within a few minutes. These reaction mixtures were stirred at −78 °C for 0.5 h. To these solutions was then added $LiAlH_4$ dropwise with stirring [$Li_nCu(CH_3)_{n+1}/LiAlH_4 = (n + 1):(n + 1/2)$]. No precipitation was observed at −78 °C; however, a white crystalline solid formed in every case when the reaction mixture was allowed to warm to room temperature. These reaction mixtures were stirred at room temperature for 1 h, and the solids were centrifuged, separated, washed with fresh diethyl ether, and made a slurry in ether as well as in THF ($LiCuH_2$ and Li_4CuH_5 dissolved in THF immediately). The products were analyzed before reacting with organic substrates. The supernatant solutions which were washed out in all cases showed Al–H stretching at 1710 cm^{-1} (characteristic of $LiAlH_2(CH_3)_2$).

Reactions of Alkyl Halides, *n*-Octyl Tosylate, Enone I, and Cyclic Ketones with Li_nCuH_{n+1}. A 10-mL Erlenmeyer flask with a Teflon-coated magnetic stirring bar was dried in an oven and allowed to cool under nitrogen flush, and then sealed with a rubber septum and connected by means of a needle to a nitrogen-filled manifold equipped with a mineral oil bubbler. One milliliter of THF or Et_2O solvent was introduced into the reaction vessel; then reactant, e.g., halide substrate (0.5 mL, 0.25 M in THF or Et_2O) with internal standard, was syringed into the vessel. Finally, the calculated amount of the hydride, Li_nCuH_{n+1}, in THF or Et_2O was added. After the designated reaction time, the reaction mixture was quenched with a minimum of distilled water and the resulting solution dried over $MgSO_4$. Analysis of the product and yield data was obtained by GLC, using 6 ft 10% Apiezon L columns. The following oven temperatures and internal standards were used: iododecane, bromodecane, chlorodecane, and fluorodecane, oven temperature 150 °C, internal standard dodecane; *n*-octyl tosylate, 120 °C, decane; cyclohexyl chloride and 1- and 3-chlorocyclohexene, 50 °C, octane; chlorobenzene 50 °C, toluene.

A 10 ft 5% carbowax 20M on Chromosorb W column was used to separate products of enone I. At 90 °C oven temperature and dodecane as the internal standard, recovered enone, 1,4-product, and then 1,2-product were eluted in that order. 4-*tert*-Butylcyclohexanol and 3,3,5-trimethylcyclohexanol were separated by the same column at 150 °C with tetradecane and hexadecane, respectively, as internal standards. The alcohol products of 2-methylcyclohexanone were separated by using a 15-ft 10% diglycerol column (80 °C, internal standard tetradecane). The order of elution for three cyclic ketones was the same—ketone first, axial alcohol second, and equatorial alcohol last.

Acknowledgment. We are indebted to the Office of Naval Research, the donors of the Petroleum Research Fund, administered by the American Chemical Society, and the Aluminum Company of America for the support of this work.

Registry No.—*n*-Octanol, 111-87-5; *p*-toluenesulfonyl chloride, 98-59-9; 2,2,6,6-tetramethyl-3-heptanone, 40239-53-0; 2,2,6,6-tetramethyl-*trans*-4-hepten-3-one, 20859-13-6; 2,2,6,6-tetramethyl-*trans*-4-hepten-3-ol, 55829-99-7; $LiAlH_4$, 16853-85-3.

References and Notes

(1) R. K. Boeckman, Jr., and R. Mackalak, *J. Am. Chem. Soc.*, **96**, 1623 (1974).

(2) S. Masamune, G. S. Bates, and P. E. Georghiou, *J. Am. Chem. Soc.*, **96**, 3686 (1974).
(3) M. F. Semmelhack and R. D. Stauffer, *J. Org. Chem.*, **40**, 3619 (1975).
(4) E. C. Ashby, T. F. Korenowski, and R. D. Schwartz, *J. Chem. Soc., Chem. Commun.* 157 (1974).
(5) E. C. Ashby, and J. J. Watkins, *J. Org. Chem.*, **42**, 1099 (1977).
(7) E. C. Ashby and J. J. Lin, *J. Org. Chem.* (in press).
(8) E. C. Ashby and A. B. Goel, *Inorg. Chem.* (in press).
(9) E. C. Ashby, J. J. Lin, and R. Kovar, *J. Org. Chem.*, **41**, 1939 (1976).
(10) E. C. Ashby and J. B. Boone, *J. Org. Chem.*, **41**, 2890 (1976).
(11) E. C. Ashby and R. D. Schwartz, *J. Chem. Ed.*, **51**, 65 (1974).
(12) D. F. Shriver, "The Manipulation of Air Sensitive Compounds", McGraw-Hill, New York, N.Y., 1969.
(13) G. B. Kauffman and L. A. Teter, *Inorg. Synth.*, **7**, 9 (1963).
(14) H. O. House and P. D. Weeks, *J. Am. Chem. Soc.*, **97**, 2770 (1975).
(15) R. Herrmann and C. T. J. Alkemade, "Chemical Analysis by Flame Photometry", Vol. 14, 2nd ed, Wiley, New York, N.Y., 1963.
(16) F. P. Treadwell and W. T. Hall, "Analytic Chemistry", Vol. II, 9th ed in english, Wiley, New York, N.Y., 1948, p 650.
(17) T. J. Murphy and J. K. Taylor, *Anal. Chem.*, **37** 929 (1965).

Transition-Metal Peroxide Reactions. Synthesis of α-Hydroxycarbonyl Compounds from Enolates

E. Vedejs,* D. A. Engler, and J. E. Telschow

Department of Chemistry, University of Wisconsin, Madison, Wisconsin 53706

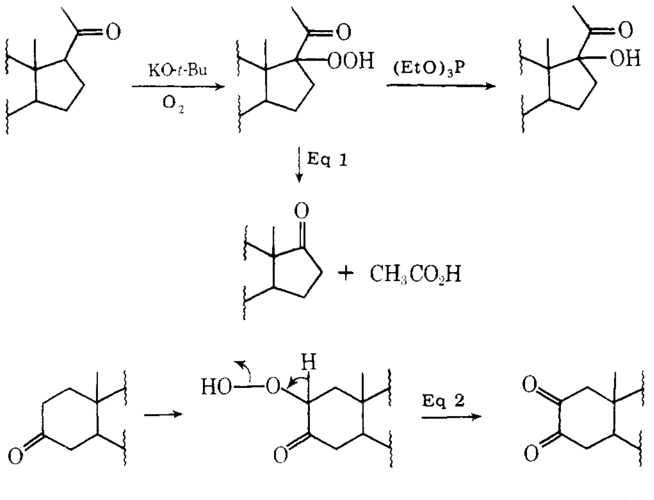
Received June 10, 1977

Enolates of ketones, esters, and lactones are oxidized by MoO_5·Py·HMPA (MoOPH) to give α-hydroxy derivatives. The reaction succeeds with carbonyl compounds having α-methylene or α-methine groups, but enolates from methyl ketones give variable results. The hydroxylation process does not afford products of oxidative C–C cleavage which might be formed from an α-hydroperoxycarbonyl intermediate. If the initial intermediate from an enolate and MoOPH is heated, further oxidation to an α-dicarbonyl compound occurs in poor yield. These results suggest an intermediate having the partial structure $R'C(=O)RCHOMoO_4L_2^-$. Hydroxylation of kinetic enolates derived from unsymmetrical cyclic ketones, cyclohexenones, and certain methyl ketones can be achieved. Acyloin regioisomers are not interconverted under the reaction conditions. Hydroxylation of relatively nonhindered ketones is complicated by aldol condensation between unreacted enolate and the oxidation intermediate. This problem can be minimized by working in dilute solution or by using an inverse addition technique (enolate added to MoOPH). Oxidation of enolate analogues prepared from oximes or *N,N*-dimethylhydrazones has been demonstrated, although yields are low. Stabilized enolates of 1,3-dicarbonyl compounds are not hydroxylated using the typical procedure, and the related dianions afford complex product mixtures.

Introduction

The synthetic problem of enolate hydroxylation has been the object of numerous studies.[1,2,5–7] Barton and co-workers achieved the direct enolate oxygenation of pregnan-20-one, and subsequent hydroperoxide reduction gave the 17α-hydroxy derivative.[1a] Gardner et al. found that modified conditions using in situ triethyl phosphite reduction of the hydroperoxides gave superior yields.[2a,b] In the absence of phosphite, oxidative α-carbon cleavage may occur (eq 1, Scheme I), a reaction which has been studied in several analogous systems.[3] The Barton oxidation cannot be used to introduce a hydroxyl group at an enolizable methyl or methylene group because a second fragmentation pathway (eq 2, Scheme I) is available to the resulting α-hydroperoxy ketone.[4] An α-dicarbonyl compound is formed initially, but further oxidation is facile and complex product mixtures are obtained.

Scheme I



Practical oxygenation of carboxylate dianions can be achieved in a number of examples without in situ peroxide reduction by triethyl phosphite.[5] The carboxylate dianion is apparently sufficiently reactive to attack the peroxide O–O bond so that peroxide does not accumulate as oxygen is introduced. If the dianion is added to excess oxygen, the hydroperoxide can be isolated in moderate yield.[5a,c] Oxidation of amide or lactam enolates by the inverse addition method is also feasible.[6] The same technique can be employed for hydroxylation of α-branched esters,[6a,7] but esters having an α-methylene group behave unpredictably.[5a,6a]

A promising method for synthesis of α-hydroxy derivatives of unbranched carbonyl compounds involves the epoxidation of enol silanes.[8] An α-trimethylsiloxycarbonyl compound can be isolated under nonhydroxylic conditions, and facile hydrolysis to the free alcohol is possible. Acetoxylation of enols with reagents such as mercuric acetate or lead tetraacetate might also be considered,[9] but hydrolysis of α-acetoxy derivatives of ketones is often complicated by interconversion of acyloin regioisomers as will be shown later in this account.

A preliminary report[10] from our laboratory described the direct hydroxylation of enolates with the molybdenum peroxide reagent MoO_5·pyridine·HMPA (MoOPH).[11] Representative ketone and ester enolates were reacted with MoOPH in tetrahydrofuran solution, and hydrolysis of the product gave α-hydroxycarbonyl compounds. The details of the oxidation procedure are the subject of this paper.

0022-3263/78/1943-0188$01.00/0