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EVIDENCE FOR A SINGLE ELECTRON TRANSFER MECHANISM IN REACTIONS OF LITHIUM DIORGANOCUPRATES WITH ORGANIC HALIDES

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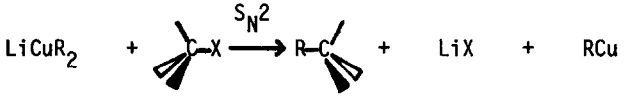
Abstract: It has been demonstrated by means of spectroscopic studies involving cyclizable alkyl halides that lithium dimethylcuprate can react with organic halides by a single electron transfer pathway.

The reaction of lithium diorganocuprates ($LiCuR_2$) with alkyl halides is of major synthetic importance.[1] Since $LiCuR_2$ compounds can be readily prepared from organolithium reagents and copper (I) halides, coupling reactions with alkyl halides have been studied in considerable detail. Perhaps the most significant mechanistic studies have involved stereochemically defined systems. The fact that lithium dialkenylcuprates are known to couple with various alkyl halides with retention of configuration has been used as an argument against the intervention of free radical species as intermediates.[2] Also, it has been demonstrated that $LiCuPh_2$ reacts with optically active 2-bromobutane and 2-butyl tosylate with predominant inversion of configuration.[3,4] Thus, it has been proposed that the coupling reaction of a dialkylcuprate with an alkyl halide proceeds by an S_N2 pathway, as described in equation (1).[1] However, an alternative pathway has been suggested which involves an oxidative addition of the alkyl halide to the cuprate, followed by a reductive elimination of the hydrocarbon product, as described in equation (2).[5-7] The oxidative addition mechanism includes a copper (III) organometallic species, which has also been described as a copper$^{(II)}$-radical complex.[8]

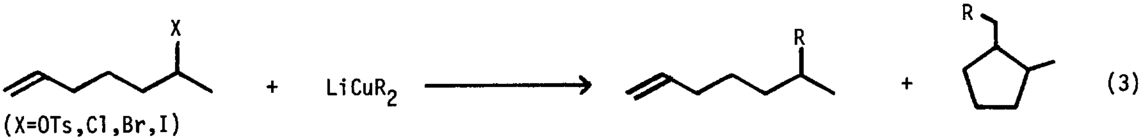


(1)

$$\left[R_2Cu^{(I)}\right]^- \quad + \quad R'X \xrightarrow{-X^-} \left[R_2Cu\overset{(III)}{\text{—}}R'\right] \longrightarrow R\text{-}R' \quad + \quad RCu^{(I)} \qquad (2)$$

In order to determine if cuprate reagents are capable of reacting by an electron transfer pathway, we decided to examine the reaction of $LiCuMe_2$ with trityl halides by EPR. Since the trityl radical is relatively stable, it should be possible to observe it as an intermediate if indeed an electron transfer pathway is operative. Lithium dimethylcuprate was allowed to react with trityl chloride and bromide in ether at 0° to -5°C, and the reactions were followed by EPR spectroscopy at the same temperature. These reactions proceeded rapidly with the development of a yellow-orange color, which increased in intensity with time and then slowly decreased. The reaction solutions were found to be EPR active and exhibited a spectrum in each case consistent with that of the trityl radical.[9] The solutions of the trityl halides under the conditions of these reactions were shown not to be EPR active. The concentration of the radical increased rapidly with time and reached a maximum within a few minutes (estimated intensity ≈3-5%). Beyond the maximum, the radical concentration decreased slowly with the concurrent formation of the product, 1,1,1-triphenylethane, which was formed in 90% yield.

Since it has been demonstrated that $LiCu(CH_3)_2$ is capable of reacting with organic halides by an electron transfer process, as a further test it was decided to examine the reactions of lithium diorganocuprates with cyclizable alkyl halide probes, such as the 6-halo-1-heptenes. Therefore, if indeed an intermediate species having radical character is formed during the coupling reaction, it should be possible to observe cyclized coupled product (eq.3). Hence, the reactions of several lithium diorganocuprates with 6-halo-1-heptenes were examined.

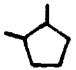
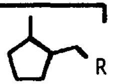


(3)

Earlier we had demonstrated that higher order cuprates, such as Li_2CuMe_3, exhibit enhanced reactivity toward secondary alkyl halides relative to the reactivity of $LiCuMe_2$;[10] therefore, the reactions of the 6-halo-1-heptenes with Li_2CuMe_3 were also investigated.

The results of reactions of several lithium diorganocuprates with several 6-halo-1-heptenes are given in Table 1. Unfortunately, $LiCuEt_2$, $LiCuPh_2$ and $LiCu(n\text{-}C_6H_{13})_2$ gave only elimination products upon reaction with 6-bromo-1-heptene or 6-iodo-1-heptene (exps. 1-4). However, substantial amounts of coupled products were formed in the reactions utilizing the methylcuprates. When X=OTs (exps. 5 and 9) and when X=Br (exps. 7 and 11) the only coupled product is the straight-chain 6-methyl-1-heptene for reactions with either $LiCuMe_2$, or Li_2CuMe_3. However, when X=I (exps 8 and 12), the major product of reaction with either $LiCuMe_2$ or Li_2CuMe_3 is the cyclic coupled product, 1-ethyl-2-methylcyclopentane, in ≈ 65% yield. Also, small amounts of 1,2-dimethylcyclopentane were formed in reactions of the iodo and bromo compounds, which may be an indication of an intermediate radical species which cyclizes and then abstracts a H-atom from the solvent. It should be noted that 6-chloro-1-heptene was found to be completely unreactive toward $LiCuMe_2$ or Li_2CuMe_3. The most striking feature of these results is that the secondary iodo compound reacts with $LiCuMe_2$ and Li_2CuMe_3 by a pathway that is fundamentally different than that of the other secondary halides. Our interpretation of these data is that the iodo compound reacts by a pathway involving predominantly electron transfer, whereas the bromide reacts by a pathway that is predominantly, but not exclusively

Table 1. Reactions of Lithium Diorganocuprates with 6-Halo-1-heptenes in THF[a].

Exp.	X in 	Cuprate	Temp.	Dienes[b]	PRODUCTS (%)  (trans/cis)		 (trans/cis)
1	Br	$LiCuEt_2$	-20^o	96	trace	0.0	0.0
2	Br	$LiCuPh_2$	8^o	98	trace	0.0	0.0
3	Br	$LiCu(n\text{-}Hex)_2$	-30^o	95	0.0	0.0	0.0
4	I	$LiCu(n\text{-}Hex)_2$	-30^o	95	0.0	0.0	0.0
5	OTs	$LiCuMe_2$	8^o	22	0.0	24^c	0.0
6	Cl	$LiCuMe_2$	8^o	trace	0.0	0.0^c	0.0
7	Br	$LiCuMe_2$	8^o	1.1	4.5(3.1)	68	0.0
8	I	$LiCuMe_2$	8^o	1.8	6.0(3.2)	18	65(0.23)
9	OTs	Li_2CuMe_3	8^o	5.0	0.0	20^c	0.0
10	Cl	Li_2CuMe_3	8^o	trace	0.0	0.0^c	0.0
11	Br	Li_2CuMe_3	8^o	2.6	9.6(7.7)	64	0.0
12	I	Li_2CuMe_3	8^o	1.5	10.7(1.1)	14	62(0.22)

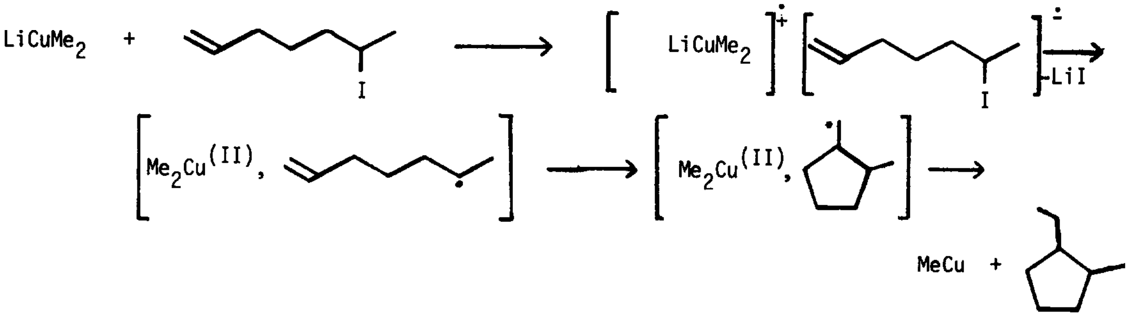
[a] Cuprate reagents were prepared by the addition of the required amount of organolithium compound to CuBr suspended in THF, according to known procedures.[2] Product yields were determined by g.l.c. and all reactions were allowed to proceed for a period of 72 hours.

[b] Mixture of 1,5- and 1,6-heptadienes.

[c] Recovered substrate accounts for material balance.

S_N2. A mechanistic proposal to account for these results is given in Scheme I.

SCHEME I



In conclusion, these studies clearly show that $LiCuMe_2$ and Li_2CuMe_3 do indeed react with organic iodides by an electron transfer pathway. Since we have shown recently that an electron transfer process can proceed with inversion of configuration,[11] we are actively pursuing stereochemical studies of the coupling reactions of organic halides with organocuprate reagents.[12]

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