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NUCLEOPHILIC OPENING OF EPOXIDES BY MIXED CUPRATES

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The reaction of an epoxide with lithium dialkyl cuprates (1) is a well established synthetic route, but usually a large excess of 1 is required and only one of the two alkyl groups of the organometallic reagent is transferred.[1] Mixed cuprates 2 have been developed (e.g.

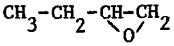
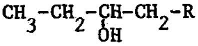
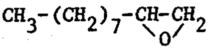
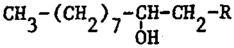
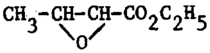
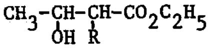
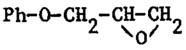
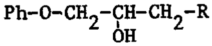
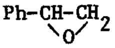
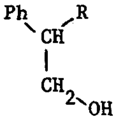
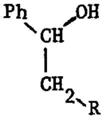
R_2CuLi	$RR'CuLi$	$R(CN)CuLi$
1	2	3, $R=CH_3$ 4, R=n-Bu

R=alkyl, R'=PhS, PhO, t-BuO[2], pentynyl[3]) circumventing these limitations in some type of cuprate reactions but no mixed cuprate has been found for the effective opening of epoxides.[4]

We would like to report that lithium organo(cyano)copper(I) reagents 3 and 4[3,6] react with epoxides to form the corresponding alcohols using stoichiometric amounts of the cuprate reagent 3 or 4 (Table I). The yields are generally comparable to those obtained from reactions with the dialkyl cuprate species (5:88%, 4 equiv. of CH_3Li[7]; 9:67%, 4 equiv. of CH_3Li[5]), the epoxides are attacked at the less steric hindered side[1] (products 5 - 8, 10, 11) or at the more electrophilic carbon atom (products 9, 10).

The conversion of styrene oxide shows an interesting example of product distribution as a function of the organometallic reagent. Treatment of 15 with alkyl Grignard compounds leads to a mixture (approx. 1:1) of 13 and the rearranged alcohol 16, whereas dialkyl magnesium compounds yield 13 as the only product.[8] In the reaction with the cuprates 3 and 4 the formation of the β-alcohol 13 is favored, but the alternative α-alcohol 14 is also detectable (Scheme I).

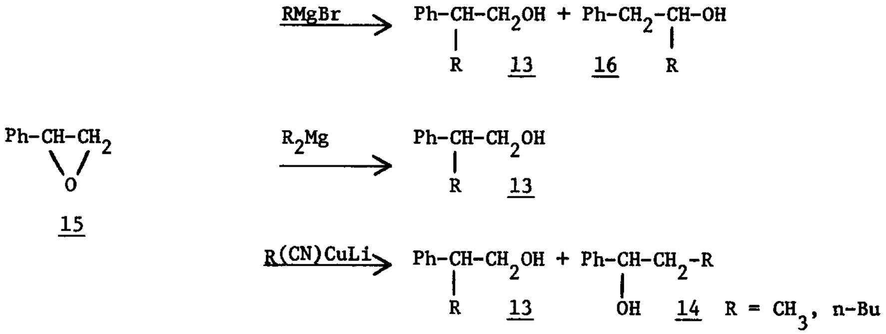
Table I. Reactions of Cyanocuprates with Various Epoxides

Epoxide	R(CN)CuLi	Product	No.	Yield %[a]
 $CH_3-CH_2-\underbrace{CH-CH_2}_{O}$	CH_3	 $CH_3-CH_2-\underset{OH}{CH}-CH_2-R$	5	95[b]
	n-Bu		6	92
 $CH_3-(CH_2)_7-\underbrace{CH-CH_2}_{O}$	CH_3	 $CH_3-(CH_2)_7-\underset{OH}{CH}-CH_2-R$	7	71
	n-Bu		8	83
 $CH_3-\underbrace{CH-CH}_{O}-CO_2C_2H_5$	CH_3	 $CH_3-\underset{OH}{CH}-\underset{R}{CH}-CO_2C_2H_5$	9	43
	n-Bu		10	48
 $Ph-O-CH_2-\underbrace{CH-CH_2}_{O}$	CH_3	 $Ph-O-CH_2-\underset{OH}{CH}-CH_2-R$	11	87
	n-Bu		12	95
 $Ph-\underbrace{CH-CH_2}_{O}$ 15	CH_3	 13  14	13a	81
			14a	18
	n-Bu		13b	74
			14b	21

[a] Isolated yields; [b] yield determined by glc.

The epoxycyclohexenes 17 and 18 are also opened by the cyanocuprates 3 and 4 (Scheme II), in these cases two equivalents of the reagents are necessary to afford reasonable yields. Although 17 and 18 are not converted to the same extent as is reported with dialkyl cuprates,[1,5] 3 and 4 can compete with 1 considering the ratio RLi:epoxide in some of these reactions (Table II).

Scheme I



Scheme II

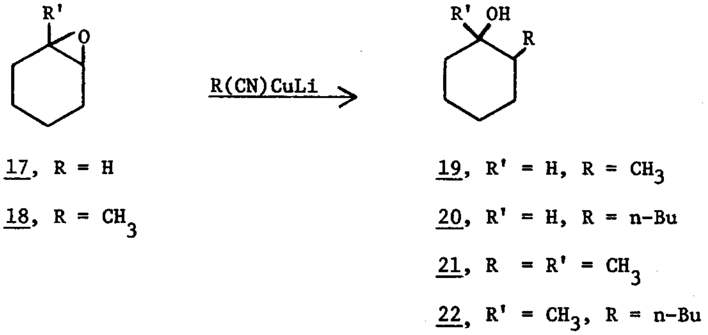


Table II. Reactions of Organocopper Reagents with Cyclohexene Oxides

Cuprate	Epoxide 17 Equiv. RLi	Epoxide 17 Conc. (M)	Epoxide 17 Prod.	Epoxide 17 Yield %	Epoxide 18 Equiv. RLi	Epoxide 18 Conc. (M)	Epoxide 18 Prod.	Epoxide 18 Yield %
$(CH_3)_2CuLi$	10	0.4	19	75[5]	5	0.2	21	65
$CH_3(CN)CuLi$	1	0.4	19	29	1	0.4	21	25
$CH_3(CN)CuLi$	2	0.4	19	58	2	0.4	21	44
$(n\text{-}Bu)_2CuLi$	10	0.1	20	60[1]	5	0.1	22	73
n-Bu(CN)CuLi	1	0.4	20	36	1	0.4	22	34
n-Bu(CN)CuLi	2	0.4	20	66	2	0.4	22	63

General Procedure

To a mixture of 180 mg of cuprous cyanide[9] (2 mmol) and 4.0 ml of ether, 2 mmol of alkyllithium were added under argon at -78°C. The temperature was slowly raised until the cuprous cyanide was completely dissolved (ca. -30°C). After addition of the epoxide in 0.5 ml of ether the reaction mixture was stirred for 0.5-1 h, then warmed up to 0°C and kept at this temperature for additional 5-6 hours. Ammonium chloride or diluted hydrochloric acid[10] was used for the workup followed by extraction of the product with ether.

Acknowledgment

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References and Notes

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4. There is only one attempt of opening epoxides by mixed cuprates reported in literature.[5] The authors stated that "lithium methylcyano(bistriethyl phosphite)copper(I) reacted only slightly with cyclohexene oxide."
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