A Highly Stereoselective Preparation of 1,4- and 1,5-Alkadienes

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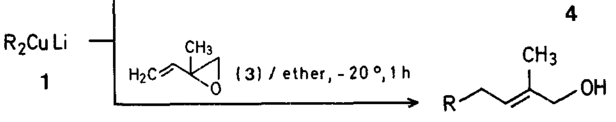
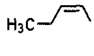
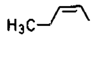
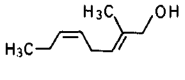
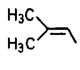
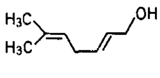
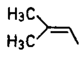
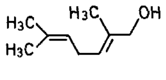
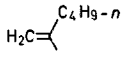
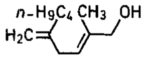
The construction of a diene system is often a problem in organic synthesis. Unsymmetrical 1,4- and 1,5-alkadienes are usually obtained either by reduction of the corresponding enynes or via the Wittig reaction. We now report on a direct preparation of these dienes by the reaction of olefinic organocopper reagents with alkenyl oxiranes[1]. Thus, reactions of alkenyl cuprates **1** with butadiene monoepoxide (**2**) or isoprene epoxide (**3**) lead to 2,5-dienols **4** and **5**, respectively (see Scheme A and Table 1).



Scheme A

Table 1. Preparation of 2,5-Dienols **4** and **5** (Scheme A)

R in **1**	Epoxide	Product No.	Product Structure	Yield [%]	(*E*/*Z*)-Ratio[a]
 [b]	**2**	**4a**		70	96:4
 [b]	**3**	**5a**		82	86:14
	**2**	**4b**		82	96:4
	**3**	**5b**		95	92:8
	**3**	**5c**		91	91:9

[a] The major product is easily isolated by distillation; isomers at newly formed double bond.

[b] From $(C_2H_5)_2CuLi + 2HC{\equiv}CH$ according to Ref. [7].

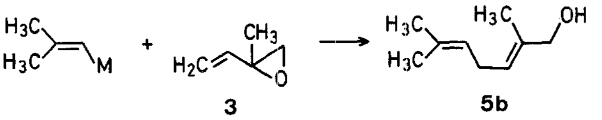
The stereochemistry of the alkenyl group in R is unchanged and the high degree of *trans* selectivity for the newly formed C—C double bond is still unexplained. Anderson[2] and Herr and Johnson[3] observed similar results on reaction of lithium dimethylcuprate (2–5 equivalents) or lithium diphenylcuprate (5 equivalents) with butadiene monoepoxide. In the present reaction *both* alkenyl groups of the organocuprate are transferred.

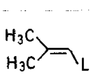
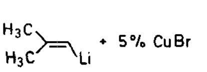
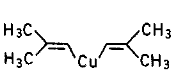
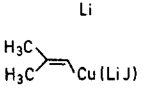
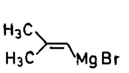
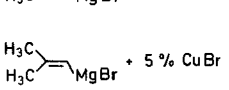
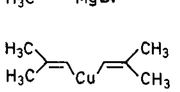
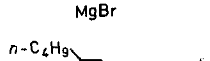
A more detailed study of the reaction of isoprene epoxide (**3**) with various isocrotyl organometallic derivatives (see Table 2) indicates that:

(a) the regioselectivity (conjugate versus direct attack) depends on the presence or absence of a copper salt, and

(b) the substitution pattern at the newly formed double bond is influenced by the nature of the copper reagent.

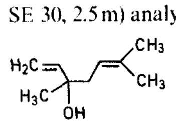
Table 2. Reaction of Isoprene Epoxide **3** with Isocrotyl Organometallic Reagents



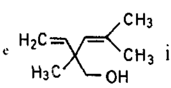
Organometallic Reagent	Reaction Conditions Temp./time/solvent	Yield[a] [%] of **5b**	(*E*/*Z*)-Ratio[b] of **5b**
	20°/10 h/ether 20°/10 h/THF	63[c] 9	80:20 26:74
	−15°/1.5 h/ether −10°/1.5 h/THF	94 86	88:12 90:10
	−25°/1.5 h/ether	95	92:8
	−20°/4 h/ether −20°/5 h/THF	82 30	67:33 65:35
	20°/2 h/THF	32[d]	20:80
	−15°/1.5 h/THF	79[e]	96:4
	−20°/3 h/THF	34	97:3
	−20°/2 h/ether −10°/5 h/THF	78[g] 35[g]	58:42 60:40

[a] Yield of product isolated by distillation.

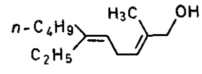
[b] Determined by ^{13}C-N.M.R., ^{1}H-N.M.R., and G.L.C. (conditions: SE 30, 2.5 m) analysis of crude mixture.

[c]  is obtained in 25% yield in ether and 57% yield in THF.

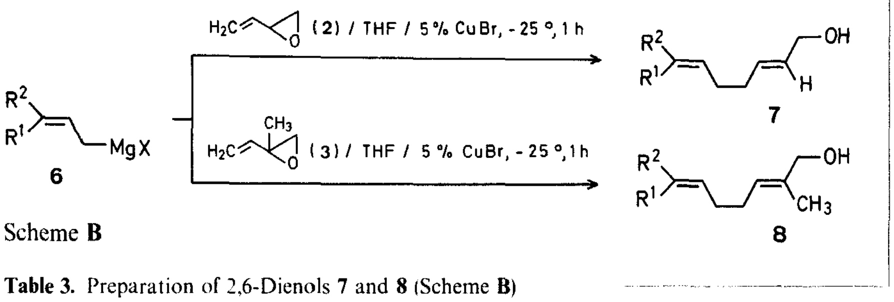
[d] Mixture of by-products is also obtained.

[e]  is obtained in 19% yield.

[f] Prepared by addition of ethylcopper-magnesium dibromide to 1-hexyne according to Ref. [8].

[g]  (**5d**) is the product.

From the results in Table 2 it is seen that the copper(I)-catalysed reaction of the organolithium or the Grignard reagent is preferable for the synthesis of the dienes from both economical and practical points of view. An extension of this reaction to allylic organometallic derivatives gives rise to the 2,6-dienol system (see Scheme **B** and Table 3).

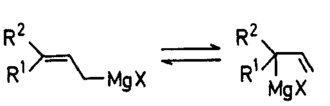


Scheme **B**

Table 3. Preparation of 2,6-Dienols **7** and **8** (Scheme **B**)

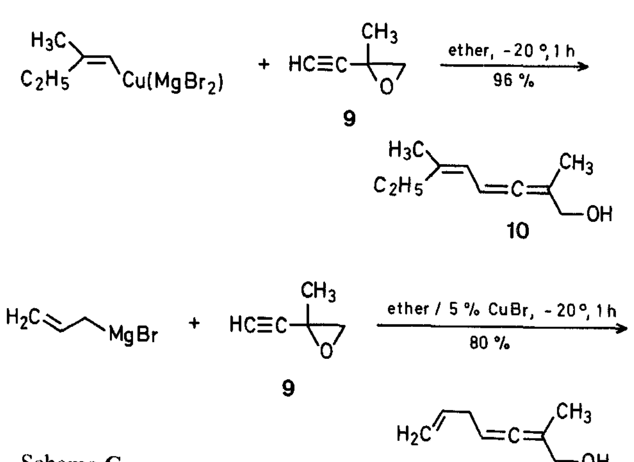
R^1	R^2	Oxirane	Product	Yield [%]	(*E*/*Z*)-Ratio
H	H	**3**	**8a**	90	92:8
CH_3	H	**3**	**8b**	95	95:5
$n\text{-}C_3H_7$	$n\text{-}C_3H_7$	**2**	**7c**	92	94:6

In this case tetrahydrofuran seems to be a better solvent than diethyl ether (41 % yield and several by-products). In spite of the supposed equilibrium of substituted allylic Grignard reagents this reaction occurs only at the primary carbon atom.



Further extension of the reaction to ethynyl epoxides (e.g. **9**) gives rise to the en-allenol systems (see Scheme **C**).

The catalytic procedure [4] can be used with allylic Grignard reagents whereas with alkyl Grignard reagents or vinyl-



Scheme **C**

Table 4. Physical and Spectral Data of All Products **4**, **5**, **7**, **8**, **10** and **11**

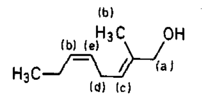
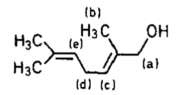
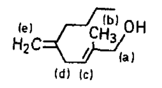
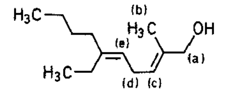
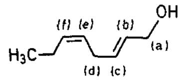
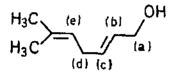
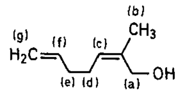
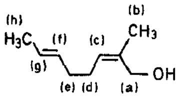
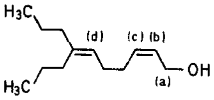
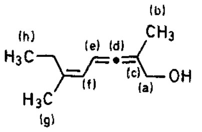
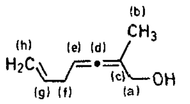
Product No.	Structure	b.p./torr (Lit. b.p./torr)	Molecular formula[a]	I.R. (neat) ν_{max} [cm^{-1}]	^{1}H-N.M.R. (CCl_4/TMS)[b] δ [ppm]	^{13}C-N.M.R. ($CDCl_3$/TMS)[c] δ [ppm]
5a		56–59°/0.05	$C_9H_{16}O$ (140.2)	3320 (OH), 1650 (C=C)	5.34 [m, 3H, H(c), H(e), H(f)]; 4.05 [s, *E*-H(a)]; 3.88 [s, *Z*-H(a)]; 2.77 [dd, 2H(d)]; 1.66 [s, 3H(b)]	68.5 [*Z*-C(a)]; 61.1 [*E*-C(a)]
5b		105°/15	$C_9H_{16}O$ (140.2)	3320 (OH); 1670 (C=C)	5.34 [t, H(c)]; 5.11 [t, H(e)]; 4.06 [s, *E*-H(a)]; 3.90 [s, *Z*-H(a)]; 2.70 [dd, 2H(d)]; 1.66 [s, 3H(b)]	68.3 [*Z*-C(a)]; 60.7 [*E*-C(a)]
5c		64°/0.01	$C_{11}H_{20}O$ (168.3)	3310 (OH); 1645 (C=C)	5.44 [t, H(c)]; 4.75 [s, 2H(e)]; 4.05 [s, *E*-H(a)]; 3.94 [s, *Z*-H(a)]; 2.72 [d, 2H(d)]; 1.65 [s, 3H(b)]	68.3 [*Z*-C(a)]; 61.0 [*E*-C(a)]
5d		100–105°/1	$C_{13}H_{24}O$ (196.3)	3310 (OH), 1670 (C=C)	5.44 [t, H(c)]; 5.07 [t, H(e)]; 4.05 [s, *E*-H(a)]; 3.88 [s, *Z*-H(a)]; 2.72 [dd, 2H(d)]; 1.65 [s, 3H(b)]	–
4a		47–50°/0.05	$C_8H_{14}O$ (126.2)	3310 (OH), 1670, 1650 (C=C)	5.57 [m, H(b), H(c)]; 5.34 [m, H(e), H(f)]; 3.99 [m, 2H(a)]; 2.75 [dd, 2H(d)]	63.0 [*Z*-C(a)]; 58.0 [*E*-C(a)]
4b		50–51°/0.05	$C_8H_{14}O$ (126.2)	3320 (OH), 1660 (C=C)	5.50 [m, H(b), H(c)]; 5.05 [t, H(e)]; 3.96 [m, 2H(a)]; 3.96 [m, 2H(d)]	63.2 [*Z*-C(a)]; 58.2 [*E*-C(a)]
8a		93°/15	$C_8H_{14}O$ (126.2)	3320 (OH), 1670 (C=C), 1640	5.80 [m, H(f)]; 5.40 [m, 1H(c)]; 5.06 + 4.78 [2d, 2H(g)]; 4.05 [s, *E*-H(a)]; 3.92 [s, *Z*-H(a)]; 2.54 [2d, 2H(d) + 2H(e)]; 1.64 [s, 3H(b)]	68.2 [*Z*-C(a)]; 60.7 [*E*-C(a)]

Table 4. (Continued)

Product No.	Structure	b.p./torr (Lit. b.p./torr)	Molecular formula[a]	I.R. (neat) ν_{max} [cm^{-1}]	^{1}H-N.M.R. (CCl$_4$/TMS)[b] δ [ppm]	^{13}C-N.M.R. (CDCl$_3$/TMS)[c] δ [ppm]
8b[d]		106–108°/15	$C_9H_{16}O$ (140.2)	3320 (OH), 1670 (C=C), 1655	5.40 [m, H(c), H(f), H(g)]; 4.05 [s, *E*-H(a)]; 3.88 [s, *Z*-H(a)]; 2.10 [m, 2H(d), 2H(e)]; 1.65 [m, 3H(b), 3H(h)]	68.2 [*Z*-C(a)]; 60.2 [*E*-C(a)]
7c		108–114°/0.05	$C_{13}H_{24}O$ (196.3)	3300 (OH), 1665 (C=C)	5.57 [m, H(b), H(c)]; 5.06 [m, H(d)]; 4.12 [d, *E*-H(a)]; 3.98 [d, *Z*-H(a)]	63.2 [*Z*-C(a)]; 58.2 [*E*-C(a)]
10[e]		72–76°/0.01[e]	$C_{10}H_{16}O$ (152.2)	3310 (OH), 1945 (C=C=C), 1675 (C=C), 1655, 1625	6.00 [dq, H(e)]; 5.52 [d, H(f)]; 3.96 [d, 2H(a)]; 1.72 [s + d, 3H(b), 3H(g)]	204.0 [C(d)]; 101.1 [C(c)]; 91.7 [C(e)]; 64.4 [C(a)]
11		37–38°/0.05	$C_8H_{12}O$ (124.2)	3310 (OH), 1965 (C=C=C), 1640 (C=C)	5.68 [m, H(g)]; 4.96 [m, H(e), 2H(h)]; 3.86 [d, 2H(a)]; 2.68 [m, 2H(f)]; 1.68 [d, 3H(b)]	201.2 [C(d)]; 100.8 [C(c)]; 91.0 [C(e)]; 64.3 [C(a)]

[a] All products gave satisfactory microanalyses (C ±0.39%, H ±0.27%).

[b] Measured with a JEOL MH 100 spectrometer.

[c] Measured with a JEOL FX 60 Q spectrometer.

[d] G.L.C. and ^{13}C-N.M.R. data indicate a 60:40 *Z*/*E*-ratio for double bond C(g)—C(f).

[e] Partial decomposition occurs during distillation, physical data given for crude product.

lithium reagents a competitive metallation reaction occurs. Also reduction to non-alkylated allenols[5] is not observed in the present case.

The dienol and en-allenol products are useful synthons for the preparation of pheromones as the alcohol function can be simply used for chain lengthening reactions. The ready availability of the starting epoxides[6], the simplicity of the experimental procedures, and the catalytic aspects render this method attractive. Syntheses of the insect pheromones of *Pectinophora Gosypiella* and *Phthorimaea Operculella* via this method are in progress.

General Procedures for Dienols and En-allenols:

Method A, Stoichiometric Reaction: Under a nitrogen atmosphere the epoxide (25 mmol) is added at −20° to a stirred solution of the lithium dialkenylcuprate or alkenylcopper (30 mmol) in ether (100 ml). The reaction mixture is stirred for 1.5 h at −20° and is then hydrolysed at −20° with saturated ammonium chloride solution (50 ml). The aqueous layer is extracted twice with ether (250 ml). The extracts and organic layer are washed with 17% ammonium hydroxide solution (50 ml), water (50 ml), and dried with magnesium sulfate. The product is isolated by distillation.

Method B, Catalytic Reaction: Under a nitrogen atmosphere a solution of the organometallic reagent (30 mmol) is slowly added at −25° to a mixture of the epoxide (25 mmol) and copper(I) iodide or bromide (1.25 mmol) in ether (100 ml; tetrahydrofuran is used for allylic organometallic reagents). After 30 min the mixture is hydrolysed and treated as described for Method A.

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[1] For a review on organocopper reagents, see: G. H. Posner, *Org. React.* **22**, 253 (1975).

[2] R. J. Anderson, *J. Am. Chem. Soc.* **92**, 4978 (1970).

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

[4] P. Vermeer, J. Meijer, C. de Graaf, H. Schreurs, *Recl. Trav. Chim. Pays-Bas* **93**, 46 (1974).

[5] P. R. Ortiz de Montellano, *J. Chem. Soc. Chem. Commun.* **1973**, 709.

[6] For isoprene oxide see: E. J. Reist, I. G. Junga, B. R. Baker, *J. Org. Chem.* **25**, 1673 (1970). For butadiene oxide the same method was applied, using 10% lithium chloride solution instead of pure water.

[7] A. Alexakis, J. F. Normant, J. Villieras, *Tetrahedron Lett.* **1976**, 3461.

[8] J. F. Normant, G. Cahiez, M. Bourgain, C. Chuit, J. Villieras, *Bull. Soc. Chim. Fr.* **1974**, 1656.

0039-7881/78/0732-0530 $ 03.00