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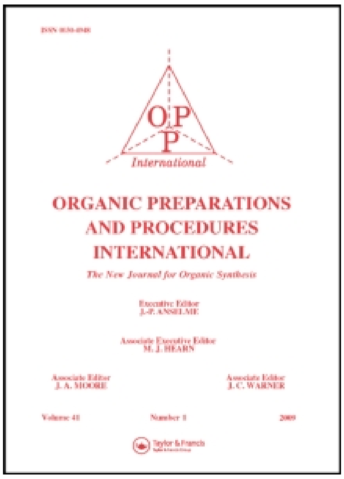

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THE EFFECT OF SOLVENTS AND CHELATING AGENTS ON THE REACTION ALKYNYL LITHIUM REAGENTS WITH OXIRANES†

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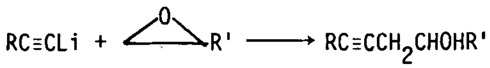
The reaction of alkynyl lithium reagents with oxiranes to produce homoopropargylic alcohols is well known.[1] The reaction is usually carried out



in liquid ammonia or in mixtures of ammonia and other co-solvents such as dioxane, tetrahydrofuran and dimethyl sulfoxide. However, substituted oxiranes react sluggishly to give the acetylenic alcohols in poor yields even at elevated temperatures.[2] Because solvents such as hexamethylphosphorictriamide (HMPT) readily enhance the rate of alkylation of alkynyl lithium reagents,[3] the effect this solvent on the rate of reaction of these reagents with ethylene oxide and substituted oxiranes was investigated.

Tetrahydrofuran was chosen as the primary solvent because of its convenience and its superior solubility for the longer chain alkynes and oxiranes. The effect of HMPT as a co-solvent in the reaction of ethylene oxide with several lithium alkynes is tabulated in Table 1. First the minimum amount that would influence the rate and yield of this reaction was determined because HMPT is considered to be carcinogenic. It was found that 1:1 molecular equivalents was sufficient to maintain the rate and yield of the alkylation. The reaction is easily carried out in ordinary glass equipment at ice bath temperatures (see Experimental). Apparently the HMPT complexed the lithium cation and thus increased the nucleophilicity of the alkynyl anion. This complex is strong and is considered to be responsible for the high proportions of <u>cis</u>-olefins that result from the reactions of non-stabilized ylides with aldehydes when HMPT is used as a co-solvent in the Wittig reaction.[4] Indeed the complex between HMPT and lithium bromide has been isolated and characterized.[5]

TABLE 1. Influence of Solvents on the Reaction of 1-Alkynes with Oxirane

1-Alkyne[a]	ml THF	ml HMPT	% Yield
Decyne	120	60	91
Hexadecyne	175	75	90
Dodecyne	120	60	93
Dodecyne	120	30	94
Dodecyne	120	18[b]	92
Dodecyne	120	15	77
Dodecyne	120	7.5	68
Dodecyne	120	0	19
Dodecyne[c]	60	(b[d])	84
Dodecyne[c]	60	(b[e])	41
Dodecyne[c]	60	(b[f])	40

a. Reactions were run on a 0.1 molar scale. b. One molar equivalent plus 10%. c. Reactions run on a 0.05 molar scale. d. 8.3 ml tetramethylethylenediamine in place of HMPT. e. 6.17 g diazabicyclo[2.2.2]octane (DABCO) in place of HMPT. f. 4 ml ethylenediamine (EDA) in place of HMPT.

Other additives that would be expected to exert the same effect on this reaction as HMPT were investigated in consideration of the potential carcinogenicity of HMPT. Diazabicyclo[2.2.2]octane (DABCO)[6], N,N,N',N',- tetramethylethylenediamine (TMEDA),[7,8] and ethylenediamine (EDA)[9] which are reported to increase the nucleophilicity of organolithium reagents, were substituted for HMPT (last 2 entries in Table 1). The results indicate that TMEDA is equivalent to HMPT and is more effective than DABCO or EDA. Thus TMEDA can be substituted for HMPT in this reaction, and this substitution may be possible for other applications in which the carcinogenic properties of HMPT might be a problem.

The results of the reaction of 1-dodecynyllithium with substituted oxiranes in the presence of HMPT are recorded in Table 2. Despite earlier reports[2], the yields were generally good though it was sometimes necessary to warm the reaction mixture gently, and the very sterically hindered cis and trans-2,3-dimethyloxirane failed to react with 1-dodecynyllithium, even under forcing conditions. In the case of unsymmetrically substituted oxiranes that are capable of forming isomeric homoallylic alcohols (entries 1, 2, and 6 in Table 2), the sole formation of the secondary alcohol was indicated by gas chromatographic analysis[10] and by the proton NMR spectrum that had an absorbtion pattern characteristic of the secondary alcohol.

TABLE 2. Reaction of Substituted Epoxides with 1-Dodecynyllithium

Epoxide[a]	ml THF	ml HMPT	% Yield
2-Methyloxirane	60	9	82
2-Ethyloxirane	60	9	54
cis- and trans-2,3-dimethyloxirane	60	9	0[b]
Cyclohexene oxide	60	9	0[c]
Cyclohexene oxide	60	9	55[d]
2-Hexyloxirane	60	9	31,53[d]

a. Reactions run on a 0.05 molar scale. b. Twelve hrs at room temperature or 50° for 20 hrs. c. Forty-eight hrs at room temperature. d. Reaction heated at 50° for 20 hrs.

This procedure emphasizes the marked effect chelating agents can have on alkylation reactions. However, it is much more important that in nucleophilic alkylation procedures utilizing HMPT, the amount of this potentially carcinogenic solvent can be limited without any adverse effect on the yield of the reaction. In some cases it may be possible to replace HMPT with less toxic materials.

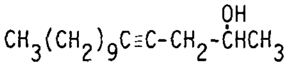
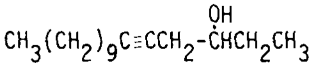
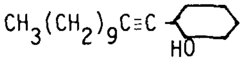
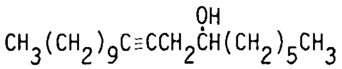
EXPERIMENTAL

Elemental analyses and mass spectra of the product alcohols were in agreement with the assigned structures. Gas chromatographic analyses were performed with a Varian Model 2100 gas chromatograph with glass columns (2 m X 2 mm i.d.) packed with 5% Carbowax 20M and 5% OV-101 on 100/120 mesh AW and

DMCS-treated Chromosorb W. The columns were operated at a N_2 flow rate of 20 ml/min. THF and HMPT were distilled from calcium hydride and stored over 4A° molecular sieves. The DABCO was dried over P_2O_5, the TMEDA and EDA were dried over 4A° molecular sieves.

Reaction of 1-Alkynyllithium Reagents with Ethylene Oxide. General Procedure.-Under a nitrogen atmosphere and with vigorous mechanical stirring, *n*-butyllithium (0.12 mol, 71 ml of a 1.55 molar soln.) was added slowly to a soltion of 0.1 mol of alkyne in 120 ml of tetrahydrofuran (THF) at or below 5°. The reaction mixture was held at 0° for 1 hr. and then chilled to about -50°; HMPT (0.11 mol, 18 ml) was then added followed by rapid addition of the oxirane (0.15 mol 7.45 ml) that had been collected in a second dropping funnel with the aid of dry ice Dewar condenser. The dry ice reaction bath was replaced with an ordinary ice bath and the reaction mixture was allowed to come to room temperature overnight as the bath melted and worked up by dilution with water and extraction with ether. The ethereal extracts were washed with water and dried over sodium sulfate. The products were isolated and purified by distillation or recrystallization (Table 3). The procedure for substituted oxiranes differed from that for ethylene oxide in that in some cases the reaction mixture was heated to 50° with a water bath for up to 20 hrs, the molar ratio of epoxide to alkynyllithium was reduced to approximately 1:1, and it was not necessary to collect the substituted oxiranes with the dry ice Dewar condenser.

TABLE 3. Homopropargylic Alcohols from 1-Alkynes with Oxiranes[a]

Alcohol	Analyses Calc'd(Found) C	 H	IR (cm^{-1})	Mass Spectrum
$CH_3(CH_2)_7C\equiv C(CH_2)_2OH$ bp.85°/.07mm, n_n^{27}1.4576	79.06 (79.25)	12.16 (11.98)	3590,2850, 2870,2930, 2960,1050	193(P+1),192(P),191 (P-1),165(P+1-18), 164(P-18),163(P-19)
$CH_3(CH_2)_9C\equiv C(CH_2)_2OH$ bp. 95°/.05mm, n_D^{27}1.4589	79.94 (79.80)	12.46 (12.61)	3590,2860, 2880,2930, 2960,1050	211(P+1),210(P), 209(P-1),193(P+1-18), 192(P-18),191(P-19)
$CH_3(CH_2)_{13}C\equiv C(CH_2)_2OH$ bp. 140°/.05[c] mm[b]	81.13 (81.55)	12.86 (13.18)	3590,2850, 2870,2930, 2960,1050	267(P+1),266(P), 265(P-1),249(P+1-18), 248(P-18),247(P-19)
 $CH_3(CH_2)_9C\equiv C\text{-}CH_2\text{-}\overset{OH}{C}HCH_3$ bp. 100°/.05 mm, n_D^{27}1.4560	80.29 (80.09)	12.58 (12.43)	3570,2850, 2870,2930, 2960,1015, 1040	225(P+1),224(P), 223(P-1),207(P+1-18), 206(P-18),205(P-19)
 $CH_3(CH_2)_9C\equiv CCH_2\text{-}\overset{OH}{C}HCH_2CH_3$ bp. 110°/.05 mm, n_D^{27}1.4574	80.60 (80.43)	12.68 (12.51)	3580,2860, 2860,2870, 2930,2960, 1025,1060	239(P+1),238(P),23 237(P-1),221(P+1-18), 220(P-18),219(P-19)
 bp. 150°/.05 mm, n_D^{27}1.4741	81.75 (81.90)	12.20 (12.10)	3580,2855, 2930,1040, 1070	265(P+1),264(P), 263(P-1),247(P+1-18), 245(P-19)
 $CH_3(CH_2)_9C\equiv CCH_2\overset{OH}{C}H(CH_2)_5CH_3$ bp. 153°/.02 mm, n_D^{27}1.4595	81.56 (81.25)	13.00 (13.21)	3570,2850, 2870,2910[c] 1040,1070	295(P+1),294(P), 2930(P-1),277(P+1-18), 275(P-19)

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[a] Infrared spectra were recorded in CCl_4 on a Nicolet 7199 Fourier transform infrared spectrometer; mass spectra were determined on a Finnegan model 1015 S/L with methane as the ionizing gas. [b] mp. 49-50° after recrystallization from hexane. [c] Broad unresolved cluster of peaks.

REFERENCES

† Mention of a commercial or proprietary product in this paper does not constitute an endorsement of that product by the U. S. Department of Agriculture.

1. a) H. G. Viehe (ed.), "Chemistry of Acetylenes", p. 241, Marcel Dekker, New York, 1969; b) L. Brandsma, "Preparative Acetylenic Chemistry," pp. 50-61, Elsevier Publishing Co., New York, 1971.
2. a) R. T. Arnold, G. Smolinski, J. Am. Chem. Soc., 81, 6443 (1959); b) W. J. Gensler, C. B. Abrahams, ibid, 80, 4595 (1958); c) J. Fried, C. H. Linn, and S. H. Ford, Tetrahedron Lett., 1379 (1969).
3. a) M. Schwartz and R. M. Waters, Synthesis, 614 (1974); b) H. Normant, Angew. Chem. Int. Engl. Ed., 6, 1046 (1967).
4. P. E. Sonnet, Org. Prep. Proced. Int., 6, 269 (1974).
5. A. Magnusson, Tetrahedron Lett., 2713 (1977).
6. E. J. Corey and D. Seebach, J. Org. Chem., 31, 4097 (1966).
7. S. Bhann and F. Scheinmann, Chem. Comm. 817 (1975).
8. H. Normant, T. Cuvigny and P. Savignac, Synthesis, 805 (1975).
9. O. F. Beumel, Jr., and R. F. Harris, J. Org. Chem., 28, 2775 (1963); 29, 1972 (1964). F. L. M. Pattison and R. E. A. Dear, Can. J. Chem., 41, 2600 (1963).
10. The product from reaction 2 in Table 2 gave a single sharp peak upon gas chromatographic analysis on both the Carbowax 20M and OV-101 columns.

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