

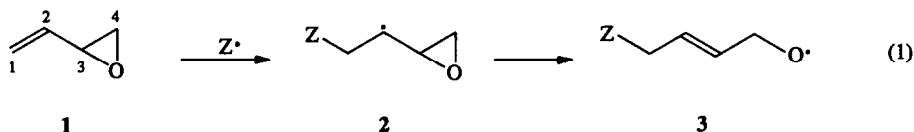
Radical Chain Addition to Vinyl Epoxides Catalysed by Amine-Boranes: Synthesis of Allylic Alcohols

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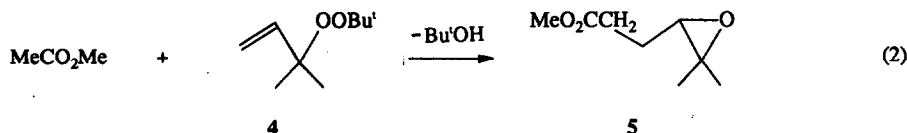
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Abstract: *In the presence of an amine-borane polarity reversal catalyst, vinyl epoxides react at the α -C-H group of an ester to give allylic alcohols. A free radical chain mechanism is followed, involving ring opening of an intermediate oxiranylcarbiny radical to give an allyloxy radical.*

Vinyl epoxides **1** are versatile and readily accessible building blocks for organic synthesis.¹ Oxiranylcarbiny radicals **2**, formed by homolytic addition to C-1 of **1**, are known to undergo rapid ring opening with C-O cleavage to give allyloxy radicals **3** when the C-4 substituent is H or an alkyl group.^{2,3} However, when a vinyl, aryl or acyl group is attached to C-4 of **1**, C-C bond cleavage competes or is seen exclusively.⁴



We have reported recently that allylic t-butyl peroxides react with esters exclusively at an α -C-H group in the presence of an amine-borane catalyst.⁵ For example, in the presence of quinuclidine-borane and under the influence of UV light, methyl acetate reacts with the allylic peroxide **4** according to eqn. (2). This reaction follows a radical

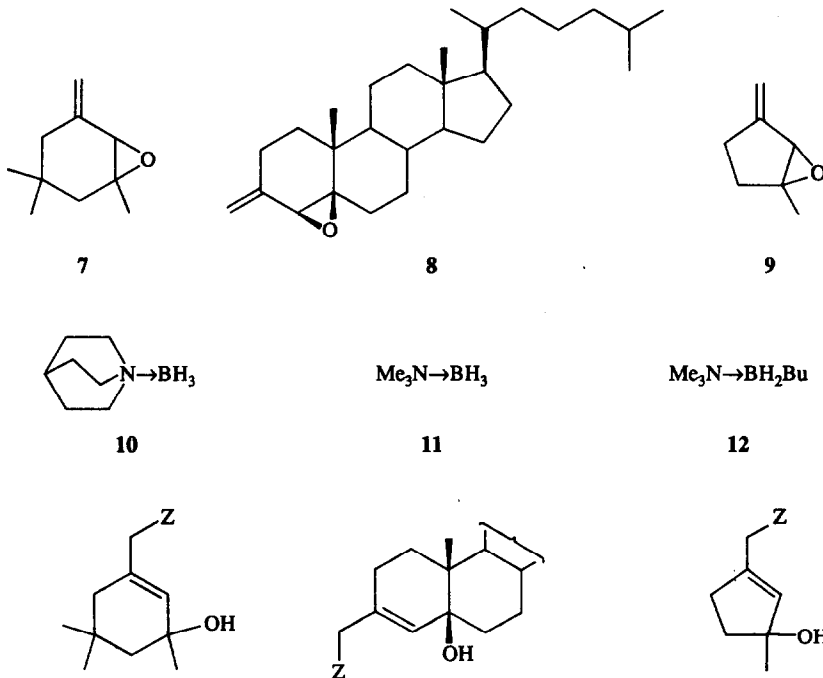


chain pathway in which the function of the amine-borane is to act as a polarity reversal catalyst⁶ to promote and to control the regioselectivity of the overall reaction of t-butoxyl radicals with the ester, by way of the cycle of reactions (3) and (4) ($\text{XO}^\bullet = \text{Bu}^\bullet\text{O}$, $\text{Z} = \text{CH}_2\text{CO}_2\text{Me}$). The nucleophilic amine-boranyl radical **6** abstracts hydrogen exclusively from an electron-deficient α -C-H group in the ester.⁶



We now report that vinyl epoxides react in an analogous way with esters (HZ) in the presence of amine-boranes to yield allylic alcohols. The propagation stage of the radical chain mechanism evidently involves the sequence shown in eqn. (1), together with the catalytic cycle of reactions (3) and (4) ($\text{XO}^\bullet = 3$).

For our preliminary work, we have used the vinyl epoxides 7-9, which were prepared by Wittig reactions of $\text{Ph}_3\text{P}=\text{CH}_2$ with the corresponding α,β -epoxyketones.^{7,8} A solution of 7 (1.5 mmol), quinuclidine-borane 10 (0.75 mmol), methyl acetate (0.5 cm^3), and di-*t*-butyl peroxide (DTBP, 1.5 mmol, as photochemical initiator) in benzene (1.0 cm^3) was irradiated under argon for 2-3 h at 30 °C with light from a 125 W medium-pressure mercury discharge lamp. The yield of (13a) determined by ^1H NMR spectroscopy was 65%; no reaction was evident in the absence of the amine-borane or without UV irradiation. Under the same conditions, similar reactions of methyl acetate with 8 and 9 gave the allylic alcohols 14a and 15a, respectively, in the yields indicated alongside the formulae. Dimethyl malonate (1.5 mmol) or dimethyl methylmalonate (1.5 mmol) reacted in the same way with each vinyl epoxide (1.3 mmol), together with 10 (0.65 mmol) and DTBP (1.5 mmol), in benzene (1.5 cm^3) to give the appropriate allylic alcohol in the yield shown. All nine products were isolated in good yields by column chromatography.



Z = $\text{CH}_2\text{CO}_2\text{Me}$ 13a (65%)

Z = $\text{CH}(\text{CO}_2\text{Me})_2$ 13b (82%)

Z = $\text{CMe}(\text{CO}_2\text{Me})_2$ 13c (74%)

14a (62%)

14b (85%)

14c (74%)

15a (45%)

15b (62%)

15c (72%)

In our previous work with allylic *t*-butyl peroxides,⁵ dimethyl methylmalonate did not give good yields of epoxypropanation products analogous to **5**, but this ester reacts efficiently with the vinyl epoxides. Dimethyl methylmalonate was chosen to study the effect on yield of changing the nature and concentration of the amine-borane catalyst, and the results are summarised in the Table.

TABLE: Yields of allylic alcohol **13c** obtained from the photo-induced reaction of dimethyl methylmalonate with **7** in the presence of an amine-borane catalyst^a

Catalyst	10			11			12		
	10	50	100	10	50	100	10	50	100
Mol% catalyst ^b	10	50	100	10	50	100	10	50	100
Yield of 13c (%) ^c	15	70	87	12	47	70	23	65	75

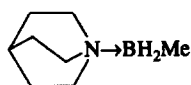
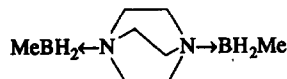
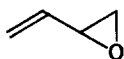
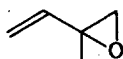
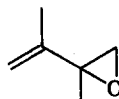
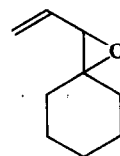
a The vinyl epoxide (0.08 mmol), dimethyl methylmalonate (0.12 mmol), DTBP (0.09 mmol), 1,3,5-tri-*t*-butylbenzene (*ca.* 0.02 mmol) and the amine-borane in C₆D₆ (0.5 cm³) contained in a quartz NMR tube under argon was irradiated for 2.5 h at 30 °C. The yield was estimated using the tri-*t*-butylbenzene as an internal standard.

b Based on vinyl epoxide.

c Essentially all the vinyl epoxide was consumed. With low amine-borane concentrations the intermediate allyloxy radical may react with **7** or **13c** or could fragment, resulting in a reduction in the yield.

Under the same conditions, experiments using the very stable methylborane complexes¹² **16** and **17** as catalysts (50 mol%) gave **13c** in yields of 63 and 82%, respectively.

For reasons which are not entirely clear at present, the yields of allylic alcohols obtained from the more flexible vinyl epoxides **18-21** have so far been very poor. This may be related to the ability of the intermediate allyloxy radicals to undergo 1,5-hydrogen-atom transfer,³ or radical addition to the rigid cyclic vinyl epoxides **7-9** may be more rapid than addition to **18-21**, because of ring strain and/or stereoelectronic factors. An oxiranyl substituent attached to a C=C group is probably weakly electron withdrawing¹⁴ and this would disfavour the addition to vinyl epoxides of species such as HC(CO₂Me)₂ in comparison with less electrophilic carbon-centred radicals.

**16****17****18****19****20****21**

Typical Procedure:— A solution of **7** (0.20 g, 1.3 mmol), dimethyl malonate (0.20 g, 1.5 mmol), **10** (0.08 g, 0.65 mmol) and DTBP (0.22 g, 1.5 mmol) in dry benzene (1.5 cm³), contained in a stoppered quartz tube under argon, was irradiated with light from 125 W medium-pressure mercury discharge lamp for 3 h. The reaction tube was positioned ca. 8 cm from the lamp and was immersed in water maintained at 30 °C. Volatile material was removed by rotary evaporation at room temperature and the residue was subjected to flash chromatography on silica gel, eluting with petroleum spirit (b.p. 30–40 °C)-diethyl ether (7:3 v/v) to give **13b** (0.30 g, 81%) as a viscous oil. NMR (CDCl₃, TMS): δ₁ 0.95 (3H, s), 1.00 (3H, s), 1.22 (3H, s), 1.43 (1H, br.s, OH), 1.47 (1H, d, *J* 14.2 Hz), 1.61 (1H, d, *J* 14.2 Hz), 1.71(1), 1.75(5) (2H, AB quartet, *J* 17.0 Hz), 2.56 (2H, d, *J* 7.9 Hz), 3.57 (1H t, *J* 7.9 Hz), 3.72 (3H, s, MeO), 3.73 (3H, s, MeO) and 5.38 (1H, br.s). δ_c 27.6, 30.2, 30.8, 31.2, 36.5, 42.2, 49.9, 50.2, 52.5, 69.1, 129.4, 134.1 and 169.3. IR (liq. film): ν_{max}/cm⁻¹ 3519, 3446, 2945, 1752, 1735, 734. Found: C, 63.52; H, 8.55. C₁₅H₂₄O₅ requires C, 63.36, H, 8.51%.

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- The *trans*-configuration shown about the double bond in **3** is arbitrary. The possible intramolecular 1,5-hydrogen-atom transfer reactions open to acyclic allyloxy radicals of the type **3** will clearly depend on the geometry about this bond.
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- Compound **7** was prepared according to a literature procedure,⁹ **8** and **9** were prepared by the same method from 4β,5β-epoxycholestan-3-one¹⁰ and 2,3-epoxy-3-methylcyclopentanone,¹¹ respectively.
- All new compounds were fully characterised by ¹H and ¹³C spectroscopy (Varian VXR-400) and IR spectroscopy, together with elemental analysis and/or accurate mass measurement.
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- Compounds **16** and **17** were prepared by displacement of trimethylamine from Me₃N→BH₂Me by treatment with quinuclidine or 1,4-diazabicyclo[2.2.2]octane, respectively, in refluxing benzene.¹³ Complex **17** has two active borane residues per molecule.
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