

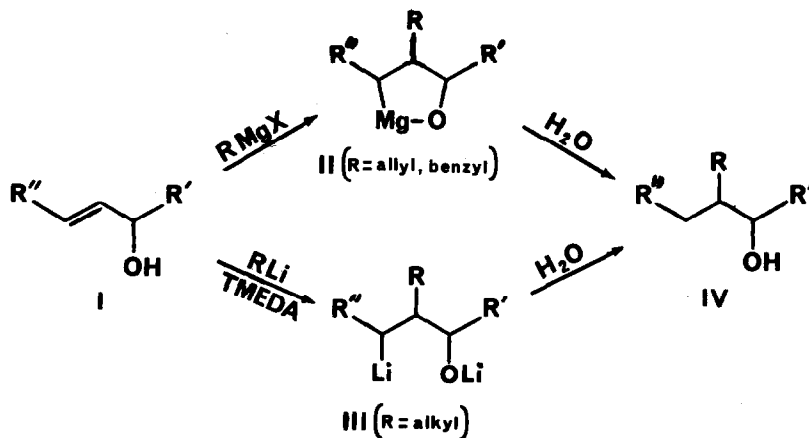
ADDITION OF ORGANOLITHIUM REAGENTS TO THE DOUBLE  
BOND OF ALLYLIC ALCOHOLS

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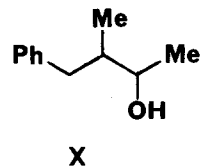
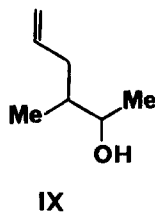
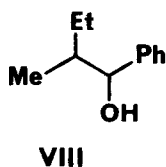
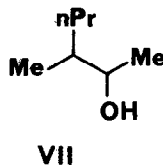
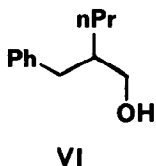
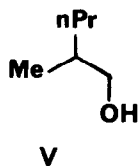
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Reactive (allyl and benzyl) Grignard reagents have been shown to add to the double bond of allylic alcohols (I;  $R'' = H$  or Ar); the intermediates formed in this reaction are probably the cyclic adducts II, which are themselves Grignard reagents and lead to a variety of products when treated with suitable electrophiles (1).



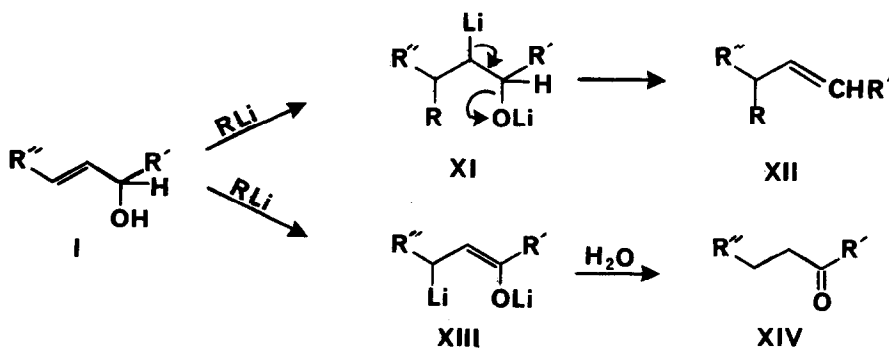
The potential usefulness of this reaction would be considerably enhanced if intermediates such as II could be made with groups (R) other than allyl and benzyl. Our attempts to use ordinary saturated Grignard reagents ( $R = \text{alkyl}$ ) have met with very little success (1b). We have found, however, that primary alkyl-lithium reagents add readily to certain allylic alcohols (I;  $R'' = H$  or Ar) in the presence of NNN'N'-tetramethylethylenediamine (TMEDA) (2, 3); hydrolysis of the intermediates (presumably the open-chain dilithio adducts III) affords the alcohols IV. Thus, the reaction (2.5 hrs at room temperature) between 1 mole of allyl alcohol and 2.3 moles of propyllithium in pentane containing 1 mole of TMEDA, followed by hydrolysis, gave 2-methyl-pentanol (V), isolated in 73 %

yield. Similarly, cinnamyl alcohol and propyllithium gave 70% of VI,  $\alpha$ -methallyl alcohol and propyllithium 65% of VII, and  $\alpha$ -phenylallyl alcohol and ethyl-



lithium 30% of VIII. The alcohols IX and X were obtained from  $\alpha$ -methallyl alcohol and allyllithium in THF-ether (4), and from  $\alpha$ -methyl- $\gamma$ -phenylallyl alcohol and methylithium in ether, respectively; both these reactions were very slow, and it was necessary to add enough TMEDA to combine with all the lithium salts present in solution (5).

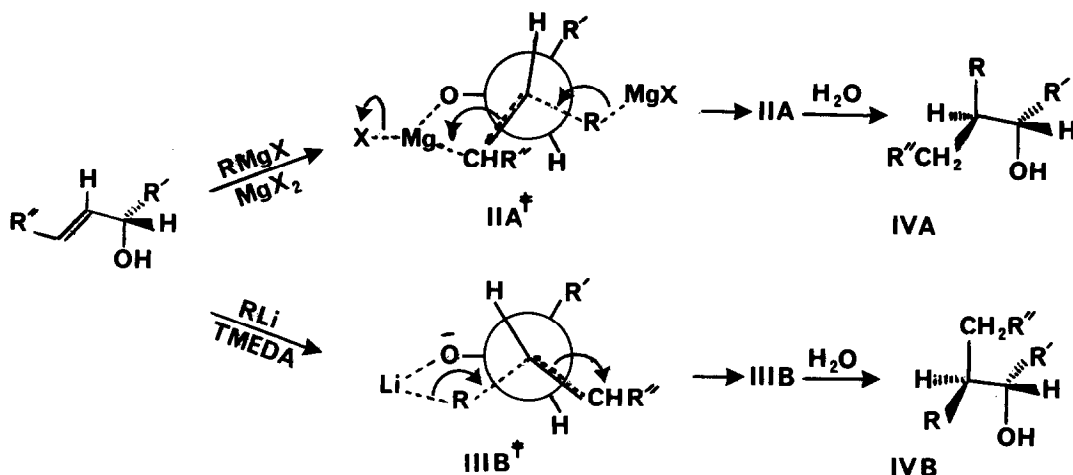
We have observed two side reactions. (a) Olefin formation: in most cases, the addition reaction, leading to III, is accompanied by what is presumably an addition-elimination process (cf. XI) leading to olefin XII (6, 7). (b) Isomerisation: when R' or R'' is a phenyl group, the allylic proton is acidic and carbonyl compounds (XIV) are formed, presumably via the dilithio intermediate XIII (8).



As is the case with the allyl Grignard addition (1), the allyllithium addition reaction is extremely sensitive to the substitution pattern in the allylic

alcohol. Cinnamyl alcohol, which leads to a benzylic lithio adduct (III,  $R'' = \text{Ph}$ ), reacts with propyllithium in pentane even in the absence of TMEDA (9). Allylic alcohols with a terminal double bond, which lead to primary lithio adducts (III;  $R'' = \text{H}$ ), react only in the presence of TMEDA. And allylic alcohols with a non-terminal double bond (e.g., cyclohexenol) appear to give olefin (XII) by the addition-elimination process (6a), rather than a secondary lithio adduct (III;  $R'' = \text{alkyl}$ ).

The addition of allyl Grignard to  $\alpha$ -methallyl alcohol was found previously to be very stereoselective, the diastereoisomer ratio (IVA/IVB) in the product (IX  $\equiv$  IV;  $R = \text{allyl}$ ,  $R' = \text{Me}$ ,  $R'' = \text{H}$ ) being about 8 (1). The allyllithium ad-



dition reaction is also stereoselective (in one case, remarkably so), but in the opposite direction; the predominant isomer in the alcohols VII-X always has configuration IVB, the diastereoisomer ratios (IVB/IVA) being  $>50$  (VII), 6 (VIII), 2 (IX), and 3 (X) (10).

This reversal of steric course suggests that the neighbouring oxygen plays opposite roles in these two reactions. The allyl Grignard addition is strongly catalysed by magnesium halide (1, 11), and it seems likely that the role of the oxygen is to hold the electrophilic catalyst in position (1); this implies a rigid transition state in which the bulky groups ( $R$  and  $R'$ ) are expected to be preferentially trans, as in  $\text{IIA}^\ddagger$ , which leads ultimately to IVA. The allyllithium addition, on the contrary, is catalysed by TMEDA; this catalyst presumably serves, among other things, to free the oxygen from its counter-ion ( $\text{Li}^+$ ), thus allowing it to hold the nucleophilic reagent in position; this again implies a rigid transition state, in which the bulky groups (this time  $R'$  and  $\text{CHR}''$ ) are again expected to be preferentially trans, as in  $\text{IIIB}^\ddagger$ , which leads ultimately to IVB.

**Acknowledgements.**— We are deeply indebted to Dr. J.K.Crandall, who informed us recently of his results in this area, and who very kindly suggested delaying publication of his work (already submitted for publication). See J.K.Crandall and A.C.Clark, *Tetrahedron Letters*, 325 (1969).

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#### Footnotes

1. M.Chérest, H.Felkin, C.Frajerman, C.Lion, G.Roussi, and G.Swierczewski; (a) *Tetrahedron Letters*, 875 (1966); (b) unpublished work.
2. As far as we are aware, no previous example of the addition of a primary alkyllithium reagent to a non-conjugated double bond has been reported. Secondary and tertiary alkyllithium reagents will add in certain cases: P.D.Bartlett, S.Friedman, and M.Stiles, *J.Amer.Chem.Soc.*, 75, 1771 (1953); L.Lardicci, P.Salvadori, P.Pino, and L.Conti, *Atti Acad.Nat.Lincei, Cl.Sci. Fis., Mat., Nat.*, 40, 601 (1966).
3. We are indebted to Dr. B.Castro (Paris) for drawing our attention to the merits of TMEDA. See G.G.Eberhardt and W.A.Butte, *J.Org.Chem.*, 29, 2928 (1964).
4. J.J.Eisch and A.M.Jacobs, *J.Org.Chem.*, 28, 2145 (1963).
5. The alcohols (V-X) were all identified by comparison with authentic samples.
6. (a) J.K.Crandall and L-H.C.Lin, *J.Amer.Chem.Soc.*, 89, 4527 (1967) [footnote p. 4528]. (b) Similar olefin formation also occurs in the reaction between allyl Grignard and allylic alcohols (ref. 1b), and is almost exclusive in the reaction between alkyllithium reagents and allylic ethers in pentane [C.D.Broadbush, *J.Org.Chem.*, 30, 4131 (1965); A.Tambuté, unpublished work].
7. When R' = Ph, the olefin XII reacts further with the alkyllithium (see ref. 9).
8. Even ethanolic potassium hydroxide is basic enough to convert  $\alpha$ -phenylallyl alcohol into propiophenone: M.Tiffeneau, *Bull.Soc.Chim.*, [4], 1, 1205 (1907) [footnote, p. 1209]; see also J.K.Crandall and L-H.C.Lin, *J.Org.Chem.*, 33, 2375 (1968).
9. The addition of organolithium reagents to conjugated double bonds is, of course, a well-known reaction; see, e.g., E.Grovenstein and G.Wentworth, *J.Amer.Chem.Soc.*, 89, 1852 (1967).
10. The NMR analysis of the alcohols VIII was kindly done for us by Dr.J.P. Guetté (Paris) [see J.P.Guetté and A.Horeau, *Bull.Soc.Chim.*, 1747 (1967)]. The other diastereoisomeric pairs (VII, IX and X) were analysed by GC [see Y.Gault and H.Felkin, *Bull.Soc.Chim.*, 742 (1965)].
11. C.Kaeseberg, unpublished work.