Tetrahedron Letters No. 10, pp 723 - 726, 1976. Pergamon Press. Printed in Great Britain.

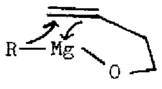
THE STEREOCHEMISTRY OF ADDITION OF THE ALLYL GRIGNARD REAGENT TO ALKENOLS[1]

Herman G. Richey, Jr., Cletus W. Wilkins, Jr., Barry S. Brown, and Robert E. Moore

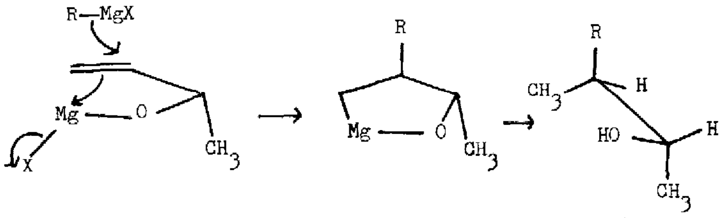
Department of Chemistry, The Pennsylvania State University
University Park, Pennsylvania 16802

(Received in USA 30 December 1975; received in UK for publication 27 January 1976)

Since the original reports by Eisch[2] and by Felkin[3] that additions of Grignard reagents to alkenes are promoted by the presence in the alkene of a hydroxyl group, promoted additions to a variety of alkenols, alkynols, and allenols have been reported.[4-8] Functions such as OMgX or OMgR must be responsible for the promotion. Eisch suggested[2] that, as shown in **1**, addition of R is facilitated by its attachment to OMg. Felkin proposed[3,4] that, as illustrated in **2**, R adds from an external molecule of an organomagnesium compound while OMgX acts simultaneously as an internal electrophile.

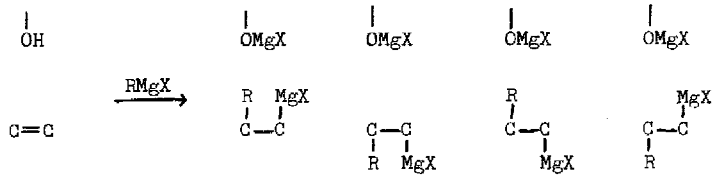


1



2 **3** erythro (major product)

At the time of addition, what relationships exist between the R and Mg that are added and between R and the metallated hydroxyl function? For example, R and Mg might add in a syn or anti fashion, and R and OMgX might be on the same or on opposite sides of the plane of the alkene function. Stereochemistries of addition products (**4**-**7**) that result from these possibilities are shown schematically.[9] Definitive determination of the stereochemical relationships at the time of addition is crucial to unraveling the role of the metallated hydroxyl function in

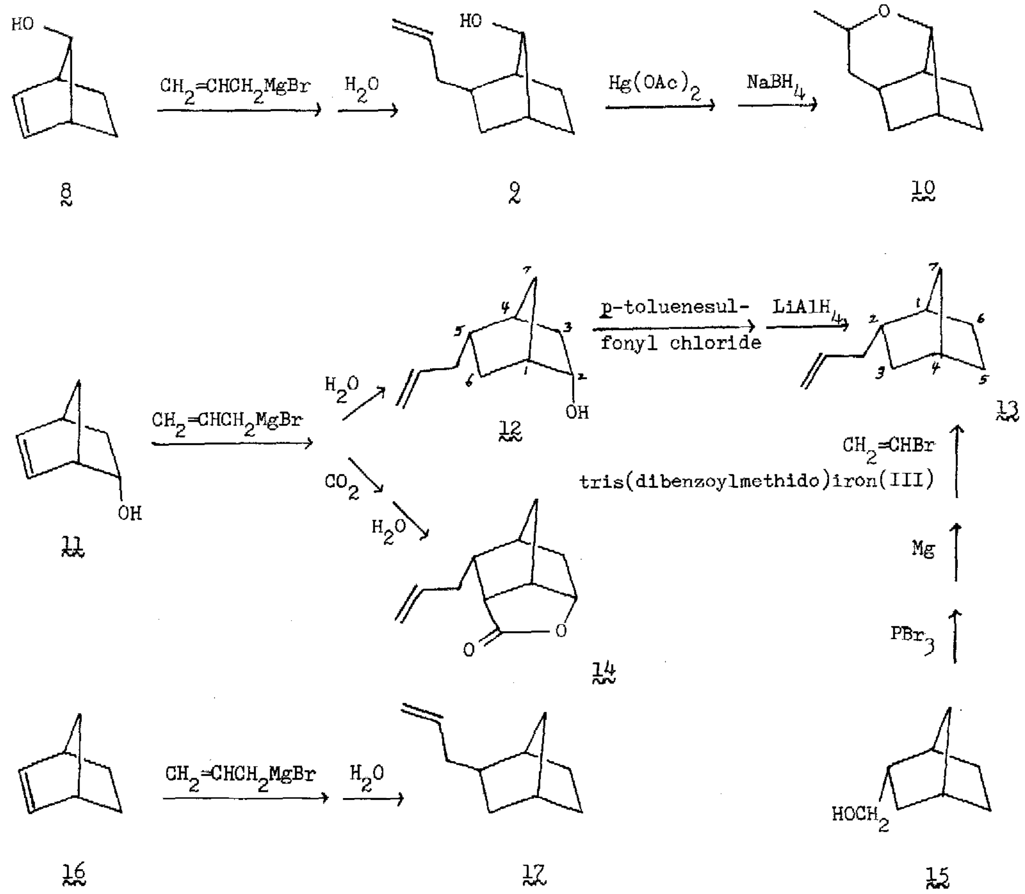


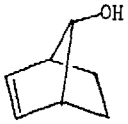
4 5 6 7

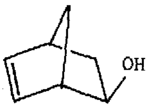
promoting addition.

In this communication we report the results of an investigation of the stereochemical relationship between R and OMgX. On the basis of the erythro:threo ratio of 8:1 observed for the product of addition of allylmagnesium chloride to 3-buten-1-ol, it was proposed that the allyl and metallated hydroxyl groups are preferentially on the same side of the double bond during the addition process.[5] However, due to the ready rotation around the C-C bond linking these functional groups, the spatial relationship that existed between them during addition does not persist in the products. The interpretation of the stereochemical result was based on assuming a reaction process (2→3) and then adding the reasonable assumption that the stereochemistry that kept CH_3 and R as far apart as possible in the transition state would be preferred. However, alternate sets of assumptions could be consistent with the observed stereochemistry.

For our study, we chose systems in which the relationship between R and OMgX is preserved in the products. Additions of allylmagnesium bromide in ether to 8 and to 11 are promoted by the hydroxyl functions. At 100°, addition to 8 is approximately one hundred-fold faster and addition to 11 several-fold faster than to the parent hydrocarbon (16). Moreover, under similar reaction conditions, no addition is observed to epimers 18 and 19. Only single mono-addition products were detected in the reactions of 8, 11, and 16. The stereochemistry of 9 was established by its conversion to cyclic ether 10. The location in 12 of the allyl group at C-5 rather than at C-6 was shown by formation upon carbonation of a cyclic lactone with the spectral properties expected for 14. The *endo* configuration of the allyl group was established by reduction of 12 to 13. An authentic sample of 13 was synthesized from 15 using a procedure developed by Kochi.[10] The hydrocarbon formed from addition to 16 was not identical to 13 and


HO
CH$_2$=CHCH$_2$MgBr
H$_2$O
HO
Hg(OAc)$_2$
NaBH$_4$
O
8
9
10
7
4
5
3
6
1
2
OH
p-toluenesulfonyl chloride
LiAlH$_4$
7
1
2
6
3
4
5
13
CH$_2$=CHCH$_2$MgBr
H$_2$O
12
CO$_2$
H$_2$O
OH
11
CH$_2$=CHBr
tris(dibenzoylmethido)iron(III)
Mg
PBr$_3$
O
O
14
CH$_2$=CHCH$_2$MgBr
H$_2$O
HOCH$_2$
16
17
15


18


19

therefore must have the *exo* configuration **17**.[11] For steric reasons, *exo* approach of reagents to norbornene is preferred. Therefore, the *exo* configuration of the allyl group in **9** and in **17** is unexceptional. However, the *endo* attachment of the allyl group in **12** must result from a strong stereochemical preference dictated by the role played by the metallated hydroxyl group in the addition mechanism. Therefore, at least for the allyl Grignard reagent, addition of R from the side of the alkene function at which hydroxyl is located appears to be greatly preferred.

Acknowledgements: We are grateful to the National Science Foundation for partial support of this research and for aiding in the purchase of the nmr spectrometers that were used. C. W. would like to thank the National Fellowships Fund for a fellowship.

REFERENCES AND FOOTNOTES

(1) Preliminary work is described in B. S. Brown, Senior Thesis, the Pennsylvania State University, 1971; R. E. Moore, *ibid.*, 1972.

(2) J. J. Eisch and G. R. Husk, *J. Am. Chem. Soc.*, **87**, 4194 (1965).

(3) M. Chérest, H. Felkin, C. Frajerman, C. Lion, G. Roussi, and G. Swierczewski, *Tetrahedron Lett.*, 875 (1966).

(4) H. Felkin and C. Kaeseberg, *Tetrahedron Lett.*, 4587 (1970).

(5) H. Felkin, G. Swierczewski, and A. Tambuté, *Tetrahedron Lett.*, 707 (1969).

(6) J. J. Eisch and J. H. Merkley, *J. Organometal. Chem.*, **20**, P27 (1969).

(7) H. G. Richey, Jr., and F. W. Von Rein, *J. Organometal. Chem.*, **20**, P32 (1969); H. G. Richey, Jr., and F. W. Von Rein, *Tetrahedron Lett.*, 3777 (1971); F. W. Von Rein and H. G. Richey, Jr., *Tetrahedron Lett.*, 3781 (1971); S. S. Szucs, unpublished work.

(8) H. G. Richey, Jr., and S. S. Szucs, *Tetrahedron Lett.*, 3785 (1971).

(9) In **4** and **7**, the same Mg could be bonded both to O and to C. Although -OMgX is indicated here and in other places in this paper, -OMgR and -OMgO- are other possibilities. When the hydroxyl function is located unsymmetrically with respect to the double bond, then addition can proceed with two orientations, and stereochemical possibilities corresponding to **4**-**7** will exist for each orientation.

(10) S. M. Neumann and J. K. Kochi, *J. Org. Chem.*, **40**, 599 (1975).

(11) The ^{13}C nmr spectra of **13** and **17** are in accord with the stereochemical assignments. Particularly revealing is the absorption of **13** at 22.4 ppm (downfield from tetramethylsilane) that is assigned to C-6; the highest-field absorption of **17** is at 28.8 ppm.