(b) **19** (83%), and (c) **12** (26%), **13** (7%), **19** (9%), and **22** (33%), respectively. These results confirmed the similarity of reactivity of the borane complex and the free base toward acid treatment.

(18) M. Shamma and W. A. Slusarchyk, *Tetrahedron*, **23**, 2563 (1967).
(19) Treatment of **22** or **21** with diazomethane gave (±)-2,3,9,10-tetramethoxyaporphine [**23**, mp 115.5–116 °C (lit.[20] mp 115.5–116.5 °C)].
(20) R. K. Callow, J. M. Gulland, and R. D. Haworth, *J. Chem. Soc.*, 658 (1929).
(21) The methoxonium ions in which the methyl groups are attached to the carbonyl oxygens of **11** or **17** are represented by [**11**$^{+}$·CH_3] or [**17**$^{+}$·CH_3], respectively.

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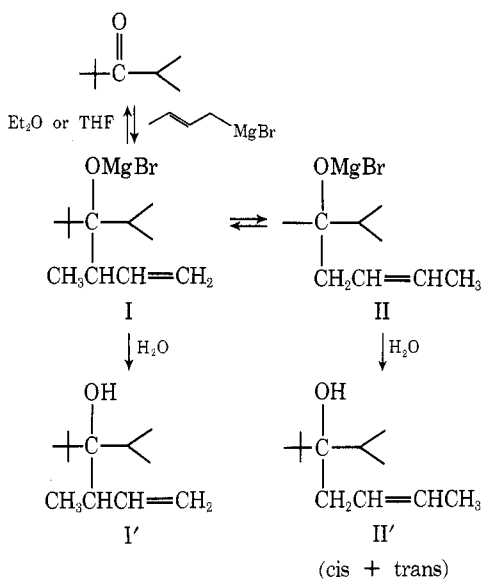
The First Documented Reversible Addition of Allylmagnesium Bromide to a Ketone

Summary: It has been shown for the first time that an *unsubstituted* allylic-type organometallic, allylmagnesium bromide, undergoes reversible additions to ketones forming magnesium salts of allylcarbinols and in the reverse step it is the allyl group which departs cleanly.

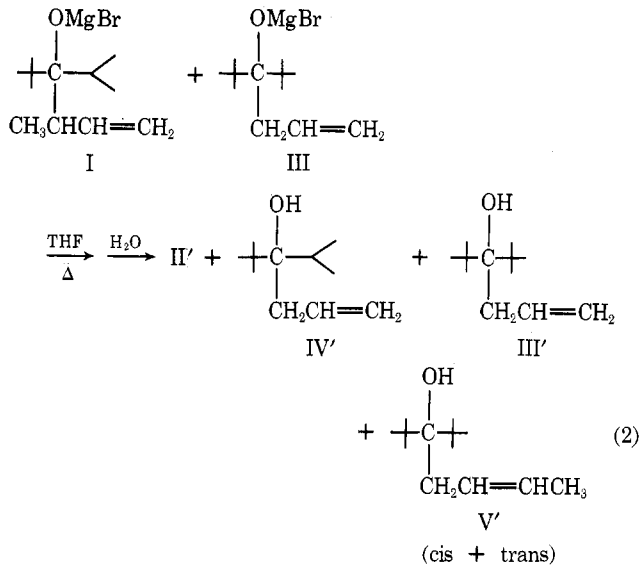
Sir: Previously we[1] reported that crotylmagnesium bromide reacts with *tert*-butyl isopropyl ketone to produce first α-methallylisopropyl-*tert*-butylcarbinol (kinetic product, I′) which then rearranges because of steric crowding to a cis–trans mixture of crotylisopropyl-*tert*-butylcarbinols (thermodynamic products, II′) (eq 1).



(1)

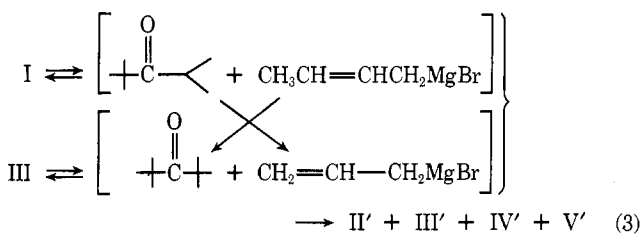
In recent years there have been several disclosures[2–6] of similar reversible additions to carbonyl-containing compounds by *substituted* allylic organometallics, but no one has reported that the parent allyl organometallic (e.g., allylmagnesium bromide) themselves undergo similar reversible additions. This is understandable since such reversibilities would lead to products identical with starting material and hence the reversibilities would go unnoticed.

We are hereby reporting the first documented reversibility of an unsubstituted *allyl* system derived from di-*tert*-butylallylcarbinol. The probe employed for detection of this otherwise disguised reaction was a crossover experiment in conjunction with a protonation reaction to trap the intermediates. The crossover experiment is illustrated by eq 2. The products



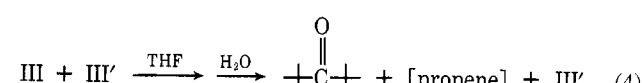
(2)

of the crossover experiment are very illuminating. It is clear that the allyl and butenyl groups have interchanged positions and that the alkoxide (I) rearranged at least in part to the crotyl system (II′). Likewise carbinol III′ but not I′ was detected in the products. The mechanism whereby alkoxides such as I are converted to isomers such as II has never been firmly established although several proposals have been put forth. Whatever the mechanism of these isomerizations might be, one can best accommodate the experimental facts depicted in eq 2 by concluding that *both* starting magnesium salts "come apart" during the course of the transformation. This regenerates the allyl and crotyl Grignard reagents as well as isopropyl *tert*-butyl ketone and di-*tert*-butyl ketone. These four entities then recombine to form the "scrambled" carbinols (eq 3).



(3)

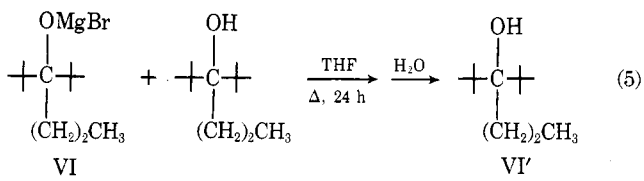
In order to provide further proof that compound III does indeed dissociate as depicted in eq 3, it was refluxed in THF in the presence of an equivalent amount of III′ which can act as a protonating agent. Equation 4 shows the results. The ratio



(4)

of di-*tert*-butyl ketone to recovered carbinol (III′) was 43:57 which is very close to the theoretical 50:50.

When the experiment shown in eq 4 was repeated under identical conditions except that *n*-propyl-di-*tert*-butylcarbinol and its corresponding bromomagnesium salt were used, only recovered carbinol and *no* di-*tert*-butyl ketone were produced (eq 5). The results of these protonation studies



(5)

confirm that, under the mild conditions used, allylic reversal is occurring and that this reversal *requires* a homoallylic species.

In earlier,[7] but related, work, some alkali metal salts of highly branched tertiary alcohols were cleaved thermally, but temperatures in the range of 200–300 °C were required. Significantly in none of these cases did the tertiary alcoholates contain an alkenyl group as in our examples. It is also noteworthy that the rate of *addition* of allylic-type organometallics to ketones is rapid[8] compared with that of other alkyl groups. Since it is now obvious that such additions are reversible, it is not surprising that in the reverse step it is the allylic group which is cleanly removed. Implications of these and related findings will be published later.

Acknowledgment. We wish to thank the National Science Foundation for its financial support of this work.

Supplementary Materials Available. The procedure for the preparation of all starting materials and the experimental details of the crossover study (total, 3 pages). Ordering information is given on any current masthead page.

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(2) P. Miginiac, *Bull. Soc. Chim. Fr.*, 1077 (1970).
(3) F. Barbot and P. Miginiac, *C. R. Hebd. Seances, Ser. C*, **272**, 1682 (1971).
(4) F. Gérard and P. Miginiac, *C. R. Hebd. Seances, Ser. C*, **273**, 674 (1971).
(5) F. Gérard and P. Miginiac, *C. R. Hebd. Seances, Ser. C*, **275**, 1129 (1972).
(6) F. Gérard and P. Miginiac, *Bull. Soc. Chim. Fr.*, 1924 (1974).
(7) H. D. Zook, J. March and D. F. Smith, *J. Am. Chem. Soc.*, **81**, 1617 (1959).
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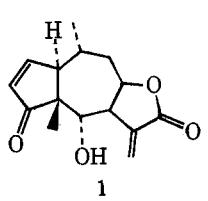
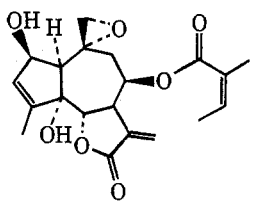
The Stereospecific Synthesis of α-Methylene-γ-butyrolactones of *trans*-1,3-Dihydroxycycloalkanes

Summary: The reactions of 1,1-diethoxy-2-propenyl cuprates with 3,4-epoxycycloalkenes have been found to be largely regiospecific and stereospecific; the product from 1,2 opening of 1,3-cycloheptadiene monoepoxide has been converted to the *trans*-hydroxy-*cis*-butyrolactone of cycloheptane.

Sir: Despite the plurality of synthetic methods[1] for the preparation of α-methylene-γ-butyrolactones fused to cycloalkanes, there is a scarcity of regiospecific and stereospecific methods for construction of α-methylene lactones of 1,3-diols.[2] We wish to report an efficient synthetic scheme for the conversion of cyclic allylic epoxides into the *trans*-hydroxy-*cis*-α-methylene-γ-butyrolactone system found in the antitumor natural product, helenalin (1). The related *cis*-hydroxy-*trans*-α-methylene-γ-butyrolactone found in euparotin (2) is also potentially accessible from the reactions described herein.

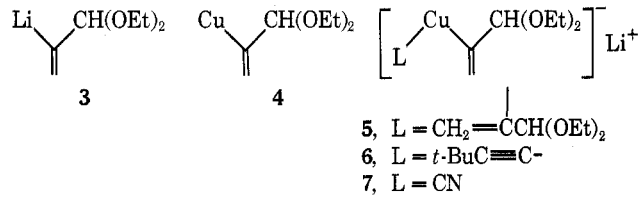


1



2

As part of our general interest in the synthesis of naturally occurring antitumor agents possessing the α-methylene lactone unit, we have investigated the reactions of various epoxides with organometallic synthons of an acrylate unit. In this paper we report the reactivity of several organocopper reagents (**4–7**)[3] and the corresponding lithio species (**3**),[4] de-



3 **4**

5, L = $CH_2{=}C(CH(OEt)_2)$–
6, L = *t*-Bu$C{\equiv}C$–
7, L = CN

rived from 2-bromo-3,3-diethoxypropene, with several simple epoxides and three activated epoxycycloalkenes.

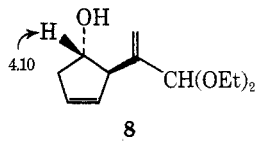
All of the organocopper reagents listed above were prepared from the isopropenyllithium derivative **3**. Copper reagents **5** and **6** have been previously described;[3] the reagent **4** was prepared from the reaction of **3** with 1 equiv of cuprous iodide in THF at −55 °C, while reagent **7** (L = CN) was prepared from cuprous cyanide and **3** in THF at −40 °C.[5]

When reagent **3** was treated with cyclohexene epoxide, propylene oxide, and styrene epoxide under a variety of reaction conditions, including the presence of salts such as anhydrous magnesium bromide, no detectable amounts of alcohol products were found. In the case of the reactive 1,3-cyclohexadiene monoepoxide and 1,3-cycloheptadiene monoepoxide, reagent **3** was once again ineffective, at temperatures up to −40 °C in THF or ether, in opening the epoxide ring.[6]

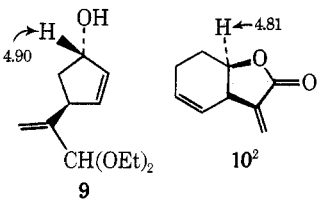
Previous studies involving the reactions of organocuprates with epoxides have largely focused on the reactions of dialkyl cuprates with simple epoxides and in some cases acyclic vinyl epoxides.[7] The most relevant work to this paper comes from investigations of Rickborn[8] and Weiland and Johnson[9] of 1,3-cyclohexadiene monoepoxide and dialkylcuprates. These workers found that both 1,2 and 1,4 additions of the cuprates occurred to about equal extent and that the stereochemistry of the products with dimethylcopper lithium was exclusively trans.

We have found that the organocopper reagents (**4–7**) undergo the expected 1,2 and 1,4 additions to the monoepoxides of cyclopentadiene, 1,3-cyclohexadiene, and 1,3-cycloheptadiene. More significantly from a synthetic standpoint, the regiospecificity of the addition can be altered to maximize the 1,2 product with trans stereochemistry. Maximum yields of total adducts from the cuprates (**5–7**) were obtained at −40 °C with 1.5–2 equiv of reagent. The effect of ether as the reaction solvent was significant in optimizing the ratio of 1,2 to 1,4 products. Furthermore, the mixed cyanocuprate **7** consistently gave the lowest yields of the adducts with the various unsaturated epoxides. The neutral copper(I) reagent **4** also seemed to be less reactive than reagents **5** and **6** and gave predominately the 1,4 regioisomer from 3,4-epoxycyclohexene. The yields and isomer ratios of the reaction products are summarized in Table I.

The structural assignments of the respective regioisomers were made on the basis of the diagnostic chemical shifts of the protons on carbons bearing the hydroxyl group in key compounds.[10] The regioisomers **8** and **9** from 3,4-epoxycyclo-



8



9 **10**[2]