formers[7] and consequently yields about a 1:1 mixture of hotrienol **3** and compound **11** on reaction with methyl vinyl ketone. Hotrienol can be isolated by chromatography in 35% yield.[9] This one-step synthesis of hotrienol (**3**) compares favorably with the published[12] synthesis.

Acknowledgment. We gratefully acknowledge the generous support of the Indiana University Department of Chemistry. S.R.W. thanks the Indiana University Research Fund for a Summer Faculty Fellowship.

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(9) All new substances possessed spectral data in accord with the assigned structures. Synthetic **2** and **3** had spectral properties identical with those reported.[4,5]
(10) Compound **9** was never observed in the uncatalyzed reaction, and compound **2** was not detected in the catalyzed reaction. In the presence of $CuBr \cdot S(CH_3)_2$ only the normal 1,4 adduct **8** is obtained; thus, the origin of compound **9** may involve a RCu species.
(11) Temperature has been shown to affect the degree of ionization of pentadienyl anion and thus the ratio of kinetic C-1 or C-3 addition. We have also determined that adduct **6** can isomerize to **5** under the reaction conditions.
(12) O. P. Vig, J. Chander, and B. Ram, *J. Indian Chem. Soc.*, **49**, 793 (1972)

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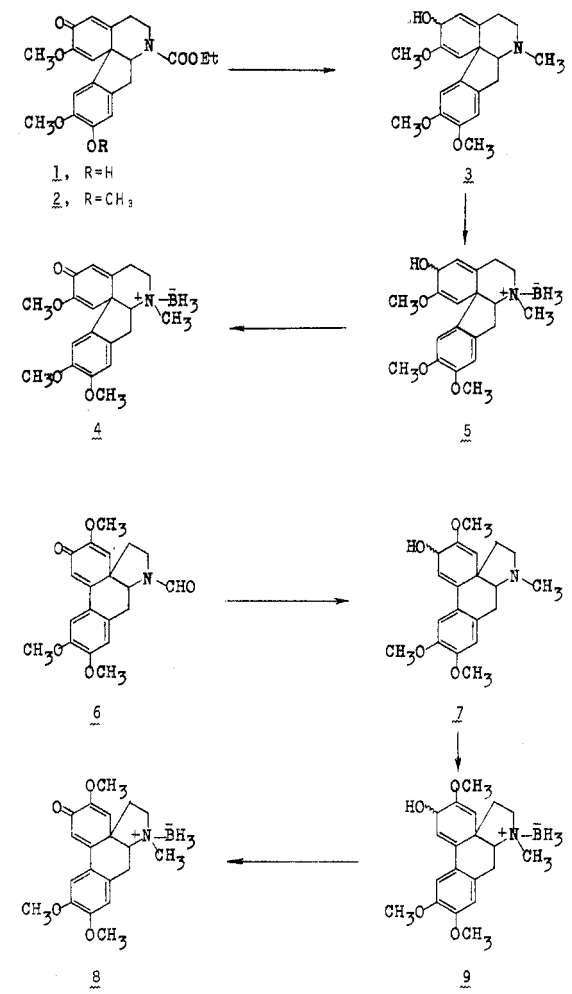
The Synthesis and Chemistry of Elusive Spirodienone Alkaloid Precursors[1]

Summary: *N*-Methylproerythrinadienone and *N*-methylneospirinedienone derivatives, elusive spirodienone intermediates, have been synthesized as borane complexes and shown to be genuine precursors of aporphine and dibenzazonine alkaloids.

Sir: In earlier studies we have shown that spirodienones derived from benzylisoquinolines play important roles in biomimetic syntheses of alkaloids.[2-6] Thus morphinandienones are effective in vitro precursors of aporphine and dibenzazonine alkaloids, and acid-catalyzed rearrangement of morphinandienones to aporphines and dibenzazonines may proceed via the intermediacy of proerythrinadienones and neospirinedienones, respectively.[4,5] The proerythrinadienones have also been proposed as biosynthetic precursors of aporphine[7] and *Erythrina* alkaloids.[8] Attempts to synthesize such spirodienones have failed when the nitrogen atoms were unprotected[8,9] and attempted transformation of *N*-acylproerythrinadienones to aporphines and dibenzazonines has also been unsuccessful.[10] We describe herein the synthesis of the borane complexes[11] of *N*-methylproerythrinadienone (**4**) and *N*-methylneospirinedienone (**8**) derivatives and the first reported laboratory transformation of a proerythrinadienone to an aporphine. In addition, the temperature dependence of rearrangements of these spirodienones is described.

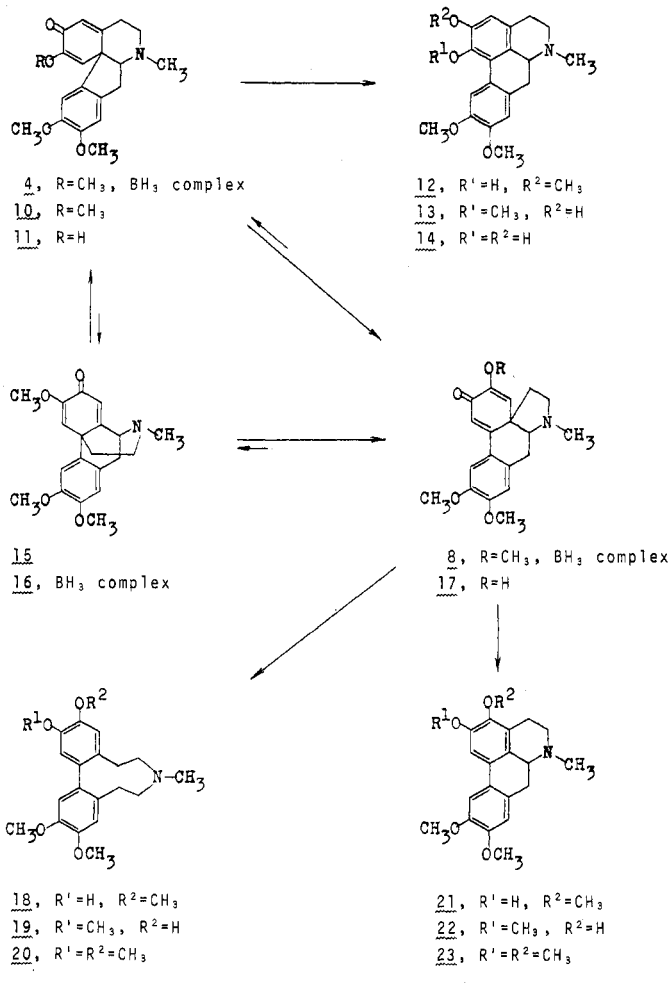
Methylation of (±)-*N*-ethoxycarbonylproerythrinadienone (**1**)[12] with CH_3I–K_2CO_3 in acetone gave **2** (84%, mp 87–89 °C).[13] Reduction of **2** with $LiAlH_4$ in THF gave a mixture of the epimeric dienols (**3**, 73%) which, upon treatment with BH_3–THF followed by MnO_2 oxidation, yielded the (±)-*N*-methylproerythrinadienone–borane complex (**4**, 51% from **3**): mp 135–137 °C ($CHCl_3$–Et_2O); uv λ_{max}^{EtOH}(log ϵ) 286 (3.87), 244 (4.27) nm; ir ($CHCl_3$) 4.21 (B–H), 6.01, 6.11, 6.21 (cyclohexadienone C=O) μ; NMR ($CDCl_3$) δ 6.78, 6.41, 6.16, 5.82 (each s, 4 H, aromatic and olefinic H), 3.88, 3.73, 3.67 (each s, 9 H, 3-OCH_3), 2.71 (s, 3 H, $-NCH_3$); mass spectrum *m/e* (rel %) 355 (6, M^+), 341 (100), 311 (15). Similarly, (±)-*N*-methylneospirinedienone–borane complex (**8**) was prepared by reduction of (±)-*N*-formylneospirinedienone (**6**)[2] with $LiAlH_4$ to the epimeric dienols (**7**, 72%), treatment of **7** with BH_3–THF to give **9**, and oxidation of **9** with MnO_2 to **8** (47% from **7**): mp



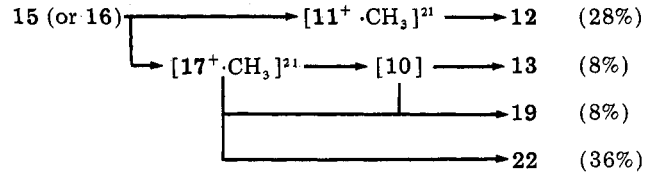
156–158 °C ($CHCl_3$–Et_2O); uv λ_{max}^{EtOH} (log ϵ) 356 (3.92), 290 (4.09), 262 (4.15), 234 (sh, 4.29) nm; ir ($CHCl_3$) 4.20 (B–H), 6.01, 6.10, 6.22 (cyclohexadienone C=O) μ; NMR ($CDCl_3$) δ 6.96, 6.74, 6.34, 6.30 (each s, 4 H, aromatic and olefinic H), 3.92 (s, 6 H, 2-OCH_3), 3.76 (s, 3 H, 1-OCH_3), 2.54 (s, 3 H, $-NCH_3$); mass spectrum *m/e* (rel %) 355 (7, M^+), 341 (100), 326 (70), 310 (28), 298 (59). Thus the spirodienones postulated earlier[4] as intermediates in the acid-catalyzed rearrangements of morphinandienones to aporphines and dibenzazonines were isolated as borane complexes.

Heating the (±)-*N*-methylproerythrinadienone–borane complex (**4**) in concentrated hydrochloric acid on a steam bath

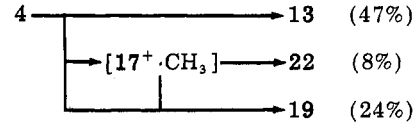
for 1 h gave (±)-predicentrine (**13**) as the hydrochloride (mp 215–217 °C dec[14]) in 75% yield, whereas treatment of **4** with BF_3–Et_2O at room temperature followed by hydrogenation over Pt in methanol afforded (±)-predicentrine (**13**) and erybidine [**19**, mp 176–177 °C (lit.[15] 178–180 °C)] in 44 and 35% yield, respectively. These results represent the first reported laboratory conversions of a proerythrinadienone to an aporphine and support the proposed intermediacy of proerythrinadienones in the acid-catalyzed rearrangement of morphinandienones to aporphines (cf. **15** → [**11**] → **14**)[4] and in the biosynthesis of aporphines in *Dicentra eximia*.[7] When **4** was treated with 1 N NaOH in MeOH followed by $NaBH_4$ reduction, erybidine (**19**) was again obtained (76%). This conversion parallels the biomimetic synthesis of a key *Erythrina* alkaloid precursor[6] and supports the intermediacy of proerythrinadienones in the biosynthesis of *Erythrina* alkaloids in *Erythrina crista galli*.[8] Treatment of **8** with either BF_3–Et_2O at room temperature followed by hydrogenation over Pt in methanol or 1 *N* NaOH in methanol followed by $NaBH_4$ reduction gave **18**[16] (75%, mp 140–142 °C), an isomer of erybidine (**19**). This result supports the proposed intermediacy of *N*-methylneospirinedienones in the acid-catalyzed rearrangement of morphinadienones to dibenzazonines[4,5] and in the $LiAlH_4$ reduction of *N*-formylneospirinedienone dimethyl ketal to *O*-methylerybidine (**20**).[2]



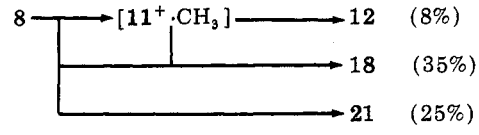
To investigate the temperature dependence of rearrangements of these spirodienones, (±)-*O*-methylflavinantine (**15**)[4,17] was treated with BF_3–Et_2O in benzene under reflux, followed by hydrogenation over Pt in methanol, whereupon four products were obtained: (±)-thalicmidine [**12**, 28%, mp 192–193 °C dec (lit.[18] 192–194 °C dec)], (±)-predicentrine (**13**, 8%), erybidine (**19**, 8%), and an unnatural aporphine, (±)-3-hydroxy-2,9,10-trimethoxyaporphine[19] (**22**, 36%, mp 214–215 °C). At elevated temperature the reaction may thus proceed as shown in the following scheme:



Treatment of (±)-*N*-methylproerythrinadienone–borane complex (**4**) under the same conditions gave (±)-predicentrine (**13**, 47%), erybidine (**19**, 24%), and (±)-3-hydroxy-2,9,10-trimethoxyaporphine (**22**, 8%), presumably via the following scheme:



Finally, the (±)-*N*-methylneospirinedienone–borane complex (**8**), when subjected to the same conditions, yielded (±)-thalicmidine (**12**, 8%), erybidine isomer **18** (35%), and another unnatural aporphine, (±)-2-hydroxy-3,9,10-trimethoxyaporphine[19] (**21**, 25%, mp 210–212 °C dec), presumably via the following scheme:



These observations suggest that the three spirodienones may exist in equilibrium in acidic medium at elevated temperature. It is noteworthy that the conversions from morphinandienones and neospirinedienones to proerythrinadienones and from neospirinedienones to unnatural aporphines have been observed to occur solely at elevated temperature.

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(13) All new compounds were characterized by concordant analytical and spectral data. The structural formulas containing asymmetric atoms refer to racemic mixtures.
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(16) The structure of **18** was confirmed by methylation with diazomethane. Mixture melting point, TLC, and uv, NMR, and mass spectra of the methylated product were identical with those of an authentic sample of *O*-methylerybidine (**20**).[2]
(17) To test whether borane complexes react in the same way as the corresponding free base, rearrangements of morphinandienone–borane complex **16**, prepared by treatment of **15** with BH_3–THF, were examined. Thus treatment of **16** with (a) concentrated hydrochloric acid on the steam bath for 90 min, (b) BF_3–Et_2O at room temperature for 26 h followed by hydrogenation over Pt in methanol, and (c) BF_3–Et_2O in benzene under reflux for 1 h followed by hydrogenation over Pt in methanol gave (a) **14** (78%),

(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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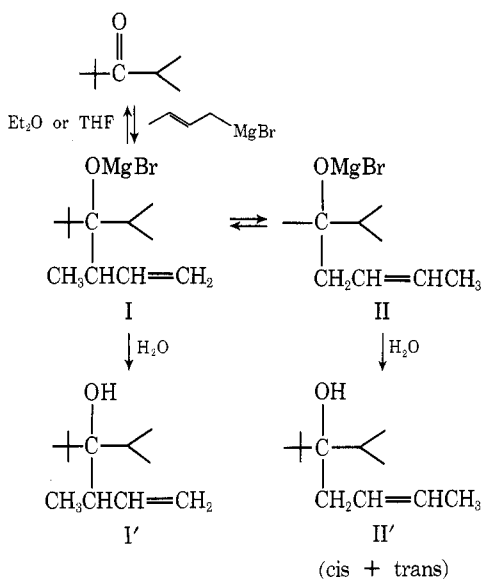
The First Documented Reversible Addition of Allylmagnesium Bromide to a Ketone

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.

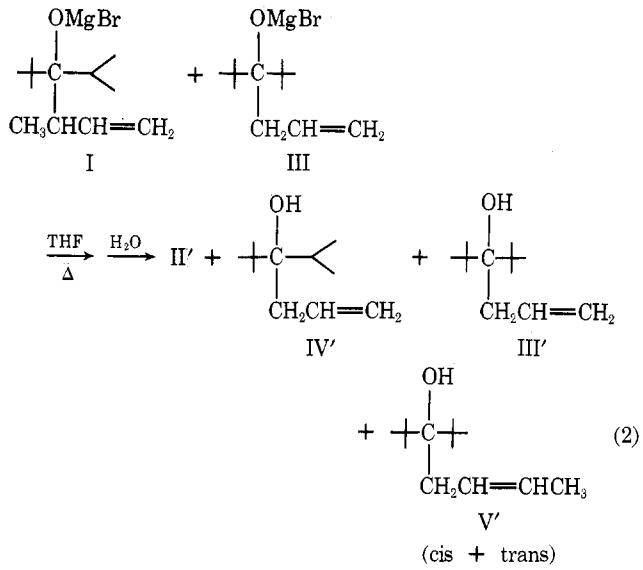
Sir: Previously we[1] reported that crotylmagnesium bromide reacts with *tert*-butyl isopropyl ketone to produce first α-methallylisopropyl-*tert*-butylcarbinol (kinetic product, I′) which then rearranges because of steric crowding to a cis–trans mixture of crotylisopropyl-*tert*-butylcarbinols (thermodynamic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



(1)

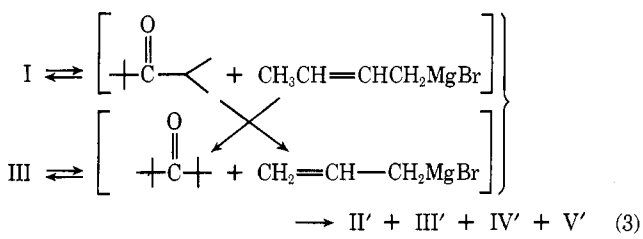
In recent years there have been several disclosures[2–6] of similar reversible additions to carbonyl-containing compounds by *substituted* allylic organometallics, but no one has reported that the parent allyl organometallic (e.g., allylmagnesium bromide) themselves undergo similar reversible additions. 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



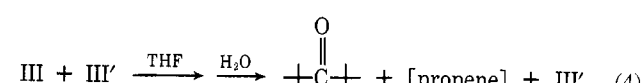
(2)

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)

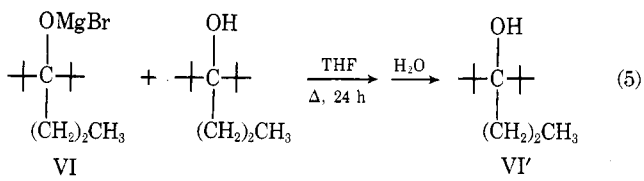
In order to provide further proof that compound III does indeed dissociate as depicted in eq 3, it was refluxed in THF in the presence of an equivalent amount of III′ which can act as a protonating agent. Equation 4 shows the results. The ratio



(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)