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DUALITY OF MECHANISM IN THE ADDITION OF ALLYLIC GRIGNARD REAGENTS TO CARBON-CARBON DOUBLE BONDS. THE STEREOSELECTIVE CYCLISATION OF 2,7-OCTADIENYLMAGNESIUM BROMIDE TO CIS-(2-VINYLCYCLOPENTYL)-METHYLMAGNESIUM BROMIDE

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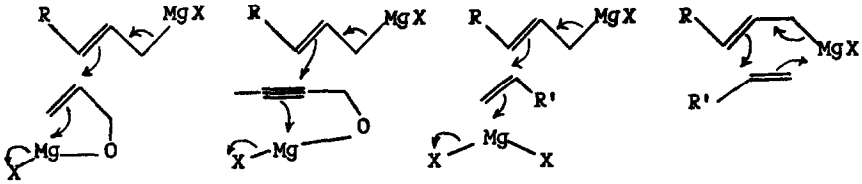
In recent years, a number of examples have been reported of the addition of allylic Grignard reagents to isolated, non-activated, carbon-carbon multiple bonds. These additions are promoted by the presence of a hydroxyl[1,2] or an amine[3] group near the multiple bond, and, in the case of allylic[2,4,5] and propargylic[6] alcohols, evidence has been presented in favour of a mechanism involving intramolecular electrophilic assistance by the magnesium bound to the oxygen, as shown in A and B. Nothing, however, is known about the mechanism of addition to simple, non-functional, olefins.[7]

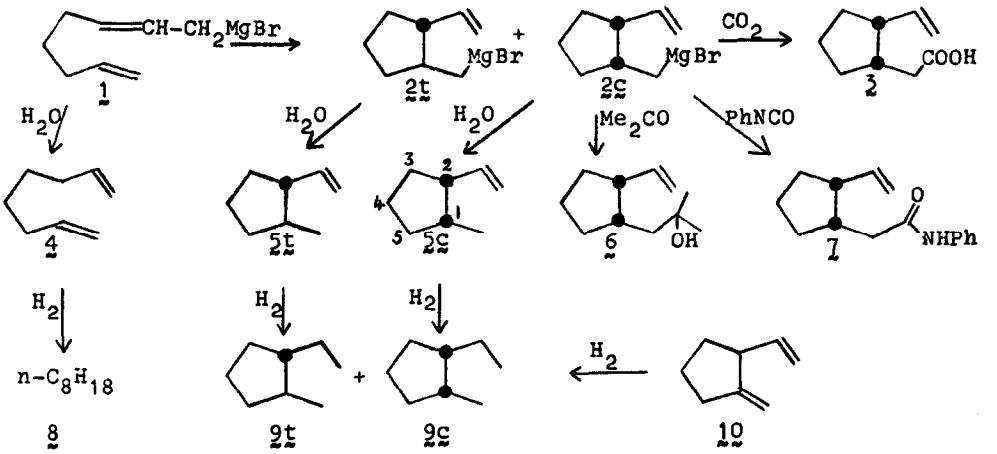


A B C D

Here we report the cyclisation of the Grignard reagent 1, the stereochemical course of which indicates that this intramolecular addition of an allylic Grignard reagent to a simple olefin does not take place by the mechanism shown in C (similar to A and B), but rather by a mechanism involving a cyclic transition state, as shown in D [RR' = $(CH_2)_3$].

An ethereal solution (0.4M) of the reagent 1 was prepared at 0° from the corresponding bromide.[8] Immediate hydrolysis of this solution afforded a mix-

ture of octadienes (mostly 4), containing only 3% of cyclised products (5c



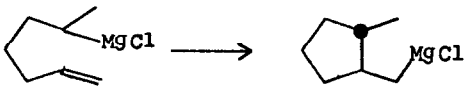
and/or 5t). When the solution was refluxed, however, smooth cyclisation took place; the reaction appeared to be first order, with a half-life of about two hours. Hydrolysis of the reaction mixture, followed by hydrogenation, gave a compound which had the retention time of cis-1-ethyl-2-methylcyclopentane 9c,[9] and which contained at most 3% of the trans isomer 9t and about 7% of n-octane 8.[10] Other reactions of the cyclised Grignard reagent 2c, leading to 3, 6 and 7, are shown in the Scheme.[11]

The structure and configuration of the major hydrolysis product 5c were confirmed by ^{13}C nmr spectroscopy.[12] Cmr spectra of the hydrocarbon showed the presence of methyl (176.8 ppm) and vinyl (methylene - 78.8, methine - 52.5) groups as well as two methine and three methylene units. The low field of the methines due to each sidechain exerting a deshielding effect on the neighbouring ring carbon revealed their vicinal relationship and limited the structure of the compound to 5c or 5t. Assignment of the chemical shifts of the ring carbons depended on the signal of the methylene unit (C-4) without proximate substituents appearing at high field (169.4) and the olefinic methylene group shifting C-3 upfield (162.2) of C-5 (159.3) and C-2 downfield (144.4) with respect to C-1 (154.1).

Determination of the stereochemistry was based firstly on comparison of the δ values of C-4 and C-5 of the hydrocarbon with those of cis- and trans-1,2-dimethylcyclopentane.[13] While the C-4 shift is identical in all three substances, that of C-5 differs (159.5 in cis-dimethylcyclopentane and 157.7 in the trans-isomer). In face of a similar disposition of the vinyl group to C-4 and C-5, the models reflect a cis configuration (5c) for the olefinic hydrocarbon. A similar conclusion can be drawn from C-2 shifts. The olefinic methylene function is expected to deshield C-2 of 5 by 10.1 ± 0.7 ppm [τ 9.4 (effect of an

ethyl group on C-2)[14] + 0.5 to 1.8 (extra effect of a trigonal centre)[15]] from C-2 of the models (155.1 for the cis and 150.0 for the trans models). If the found value is corrected for this effect, it agrees with that of the cis model. Finally, the shift of the methyl group of the olefinic hydrocarbon fits more closely that of the cis (177.6) than trans model (174.0). The lowered value indicates probably the smaller size of the vinyl methine moiety than that of a methyl group.

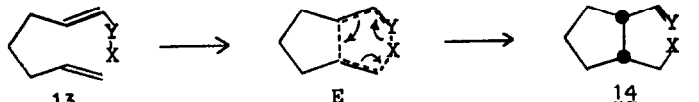
The cyclisation of 1 is therefore highly stereoselective and leads predominantly (> 30:1) to the cis isomer 2c. This stereochemical outcome indicates that the reaction cannot have taken place by the mechanism shown in C, since this would be expected to afford predominantly the trans isomer 2t, just as the cyclisation of the non-allylic Grignard reagent 11 leads predominantly (> 10:1) to the trans isomer 12t.[16] Furthermore, cyclisation occurring by



11 12t

this mechanism (C) should be catalysed by magnesium bromide, as is the reaction with allylic alcohols (A);[5] in fact the addition of magnesium bromide to 1 appeared to have very little effect on the rate of cyclisation, whereas its removal (by precipitation with dioxane) increased the rate significantly.

The fact that the cyclisation of the reagent 1 (≡ 13c) occurs very rapidly[17] and leads preferentially to the cis isomer 2c (≡ 14c) strongly suggests a mechanism involving a six-membered cyclic transition state. Such a cyclic transition state E (X = MgBr, Y = CH_2) [≡ D, RR' = $(CH_2)_3$] would present analogies with the transition state E (X = H, Y = CH_2) and E (X = H, Y = O) invoked in the thermal cyclisations of 1,6-dienes 13a[18] and ε-ethylenic ketones (cf. 13b),[19] both of which also lead preferentially to cis-substituted cyclopentanes (14a and 14b, respectively).



13 E 14

a X = H, Y = CH_2
b X = H, Y = O
c X = MgBr, Y = CH_2

Thus there appear to be two distinct mechanisms for the addition of allylic Grignard reagents to non-activated double bonds:

(1) a cyclic mechanism, shown in D, in the case of simple, non-functional, olefins;

(2) a non-cyclic mechanism, shown in A, involving intramolecular electrophilic assistance, in the case of olefins having a hydroxyl or an amine group

near the double bond.

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Footnotes and references

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8. Prepared from 4 and NBS, bp_{28} 98°, n_D^{25} 1.4898.

9. A 2:1 mixture of 9c and 9t was obtained by hydrogenation of 10 over PtO_2 in AcOH [W.D.Huntsman and R.P.Hall, J.Org.Chem., 27, 1988 (1962)].

10. This probably arose, at least in part, from adventitious hydrolysis of 1.

11. The microanalyses and spectra (ir and nmr) of these three compounds were consistent with the structures 3, 6 and 7 assigned to them.

12. Noise resonance decoupled and single frequency off-resonance decoupled spectra were run on the neat liquid with 20% v/v of dioxane added as internal standard ($\delta = \delta_{dioxane} + 125.5$ ppm).

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16. W.C.Kossa, T.C.Rees and H.G.Richey, Tetrahedron Letters, 3455 (1971). Cf. also: 7-bromohept-5-enal in the presence of magnesium cyclises preferentially to trans-2-vinylcyclopentanol [H.Felkin,Y.Gault and G.Roussi, Tetrahedron, 26, 3761 (1970)].

17. The half-life (2 h at 35° in Et_2O) for the cyclisation of 1 may be compared with those for (a) the cyclisation of the non-allylic reagent 11 (30 min. at 100° in THF; ref. 12), and (b) the intermolecular addition of allylmagnesium chloride to 1-octene (about 4 days at 85° in THF; ref. 7a).

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