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ON THE STEREOCHEMISTRY OF THE PRINS REACTION

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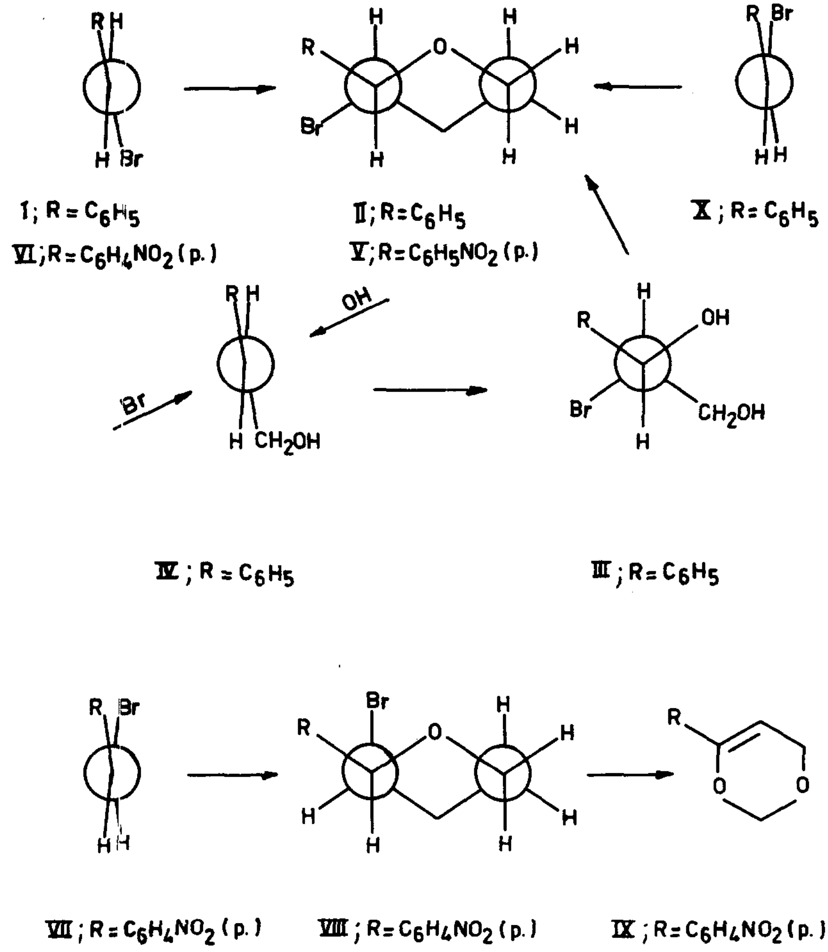
A large amount of work has already been done on the mechanism of the Prins reaction (1-5) and a great deal of emphasis has been placed on the stereochemical aspects of this problem. A mechanism involving a trans addition of a protonated formaldehyde and a neutral formaldehyde molecule to an olefin is generally accepted (6).

We had been studying for some time the stereochemistry of the Prins reaction as applied to β-bromostyrene and to p-nitro-β-bromostyrene and we had arrived to the conclusion that in these cases the addition was cis. While we were completing our studies we became aware through the Chemical Abstracts of the work of Terada (7,8) on the same problem: we wish here to summarize the common results and to report the additional facts and evidence we have collected.

Pure trans-β-bromostyrene (9) (I) gave with paraformaldehyde and sulfuric acid in dioxane the expected 4-phenyl-5-bromo-1,3-dioxane (7)(b.p. 120°/2 mm) (II). The formal of the bromohydrin (III) of trans-cinnamyl alcohol (IV) (10), a known substance (11), was shown to be identi-

Scheme 1



I; R = C_6H_5

VI; R = $C_6H_4NO_2$ (p.)

II; R = C_6H_5

V; R = $C_6H_5NO_2$ (p.)

X; R = C_6H_5

IV; R = C_6H_5

III; R = C_6H_5

VII; R = $C_6H_4NO_2$ (p.)

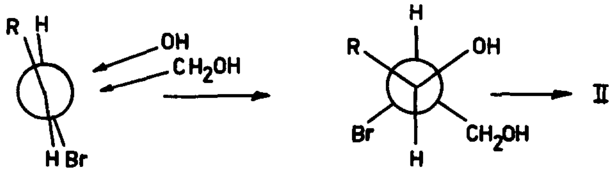
VIII; R = $C_6H_4NO_2$ (p.)

IX; R = $C_6H_4NO_2$ (p.)

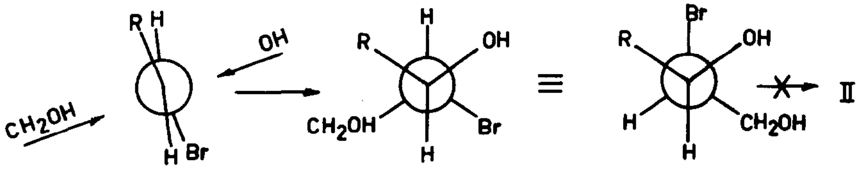
cal to II since, beside having the same IR spectrum and the same retention time in GLC, both gave, by ammonolysis, the same 4-phenyl-5-amino-1;3-dioxane (b.p. 113°/3 mm. - Acetate m.p. 104°) and by nitration the same nitro-derivative (V) (m.p. 132-135° (7). λ_{max} =236 mμ ; ε =10000) later shown to be a p-nitro-derivative.

Therefore the configuration of C_4 and C_5 in II and III (a product of trans addition of Br-OH on trans-cinnamyl alcohol) are the same and this implies that the Prins reaction follows a cis addition mechanism. This can be best visualized if we imagine (in a purely abstract way) the Prins reaction as an addition of CH_2OH-OH on the double bond followed by an acetalization (see fig. 1).

F I G. 1



cis addition



trans addition

We next studied the Prins reaction with *cis* and *trans* p-nitro-β-bromostyrene which have been prepared and to which configurations have been assigned (12). Despite the deactivating influence of the nitro-group the desired m-dioxanes were obtained, after some lengthy trials, in over 80% yield by slow addition of the p-nitrostyrenes into a solution of paraformaldehyde in concentrated sulfuric acid at room temperature. (Note 1). From *trans*-p-nitro-β-bromostyrene (12)(VI), there was obtained exclusively a 4-p-nitrophenyl-5-bromo-1,3-dioxane, (m.p. 132-135°) identical with V. These results show that with *trans*-β-bromostyrene and with *trans*-p-nitro-β-bromostyrene the Prins reaction follows the same stereochemical course, e.g. in both cases there is a *cis* addition. From *cis*-p-nitro-β-bromostyrene (12)(VII) we obtained in addition to a small amount of V (5% ca.) (whose origin from some VI present in the starting material cannot be excluded) a different and therefore diastereomeric 4-p-nitrophenyl-5-bromo-1,3-dioxane (m.p. 163-165°; λ_{max}=269 mμ, ε =10000) formulated as VIII.

The configuration of this compound was fortuitously demonstrated by attempting the ammonolysis of V and VIII with alcoholic ammonia at 150°.

Note 1. Terada (7) has reported an unsuccessful attempt to carry out a Prins reaction with p-nitro-β-bromostyrene; most of the starting material was recovered unchanged.

From V only starting material was recovered and the residue thereof consisted of intractable tars. On the other hand, from VIII we obtained in 70% yield an unsaturated compound, m.p. 132-135° formulated as IX on the base of analysis, IR spectrum (medium band at 1650 cm^{-1}) and UV spectrum (λ_{max}=320 mμ, ε =9500).

Since the elimination reaction would require that the benzylic hydrogen (activated by the p-nitro group) be trans to the bromine, the formation of IX from VIII confirms the configuration previously assigned to VIII. However VIII can be obtained from cis-p-nitro-β-bromostyrene only through a cis addition.

We shall now add that, while the Prins reaction with the p-nitro-β-bromostyrenes is, as shown, largely or totally stereospecific, we found that the Prins reaction with cis-β-bromostyrene (9) (X) afforded the same compound II previously obtained from trans-β-bromostyrene. This fact, in our opinion, gives support to the previous hypothesis of a carbonium-ion or oxygen-coordinated carbonium-ion intermediate (6) since such intermediate would allow in the case of X a strain-relieving inversion followed by a normal cis addition. However when an electron-withdrawing group is present, as in VI and VII, such a carbonium-ion is unlikely to be found and consequently the reaction is stereospecific.

In summary unless we challenge the previous assignements of configuration to the β-bromostyrenes and their p-nitro-derivatives, we feel that we have convincingly demonstrated that in certain cases the Prins reaction involves a stereospecific cis addition.

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