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AZACYCLOBUTENIUM ION AS AN INTERMEDIATE IN THE BECKMANN REARRANGEMENT. CYCLIZATION OF 4-/4'-CHLOROPHENYL/-3-PHENYLBUT-3-EN-2-ONE OXIME BENZOATE TO 1-/4'-CHLOROPHENYL/-3-METHYLISOQUINOLINE

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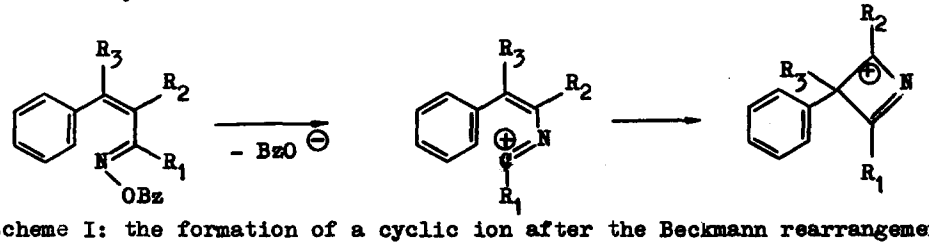
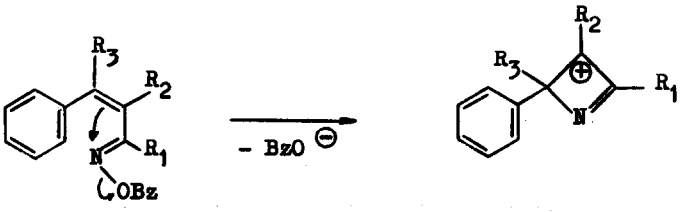
The cyclization of β-phenyl-α,β-unsaturated ketoxime esters may lead to the formation of either quinoline or isoquinoline nucleus. The cyclization of 3,4-diphenylbut-3-en-2-one oxime benzoate to 1-phenyl-3-methylisoquinoline has shown that a specific rearrangement of a intermediate carbonium ion may take place and a mechanism rationalizing this unusual course of reaction has been proposed[1]. The formation of an azacyclobutenium ion has been accepted as an essential intermediate.

Our present investigations were aimed at the confirmation of this hypothesis all the more because the formation of the cyclic ion is possible not only after the Beckmann rearrangement but also as a result of an attack of electron deficient nitrogen on the ethylenic double bond:

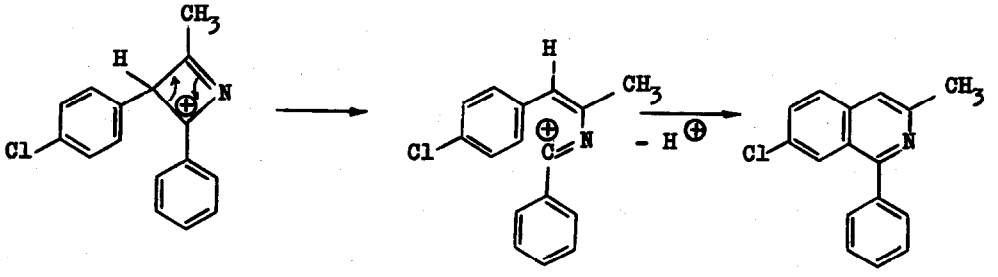


Reaction scheme I: the formation of a cyclic ion after the Beckmann rearrangement

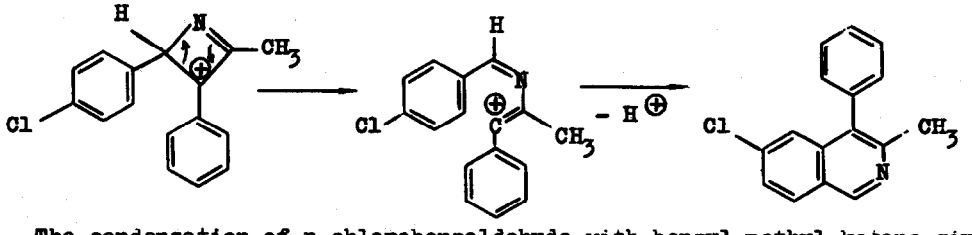


Reaction scheme II: the direct formation of a cyclic ion

The decisive experiment was designed by way of synthesis of a derivative of 3,4-diphenylbut-3-en-2-one oxime benzoate marked in one of the benzene rings by chlorine. The cyclization of 4-/4'-chlorophenyl/-3-phenylbut-3-en-2-one oxime benzoate /R_1=CH_3, R_2=C_6H_5, R_3=H/ should lead to 1-phenyl-3-methyl-7-chloroisoquinoline if the reaction course I is right:



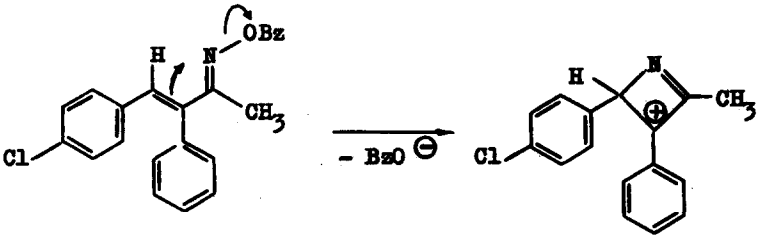
On the other hand, the acceptance of the reaction scheme II allows the expectation of the formation of 3-methyl-4-phenyl-6-chloroisoquinoline:



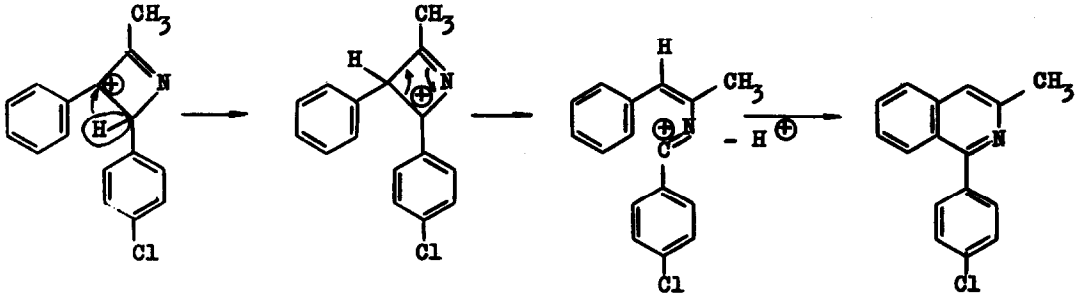
The condensation of p-chlorobenzaldehyde with benzyl methyl ketone gives 4-/4'-chlorophenyl/-3-phenylbut-3-en-2-one, m.p. 125-126°C. The treatment of this ketone with hydroxylamine formate furnishes an oxime, m.p. 191-192°C, and its benzoylation with benzoyl chloride in ether solution leads to oxime benzoate, m.p. 142-143°C. This oxime ester was heated in boiling nitrobenzene for four hours and then the cooled solution was extracted several times with 5 % hydrochloric acid. The combined aqueous layers were made alkaline with dilute sodium hydroxide

solution and a pale yellow precipitate was obtained, m.p. 119-120°C /36 % yield/. The crude product was crystallized from methanol to give white needles, m.p. 121--122°C. The UV and IR spectra confirm the isoquinoline structure, but the cyclization product is neither 1-phenyl-3-methyl-7-chloroisoquinoline /m.p. 89-90°C[2]/, nor 3-methyl-4-phenyl-6-chloroisoquinoline /a lack of a H_1 signal at low field in the NMR spectrum[3]/. The determined m.p. is very close to that reported for 1-/4'-chlorophenyl/-3-methylisoquinoline[4]/. To confirm the identity of our cyclization product with 1-/4'-chlorophenyl/-3-methylisoquinoline we have synthesised this compound from 2-/4'-chlorobenzamido/-1-phenyl-1-hydroxypropane according to the Pictet-Gams method[5]/. The UV, IR and NMR spectra were identical for the cyclization product of oxime benzoate and that obtained from the Pictet-Gams synthesis. There was also no m.p. depression for the mixture of both specimens.

In order to rationalize the formation of the final product of cyclization we propose the following reaction path. The azacyclobutenium ion is formed as a result of heterolysis of the oxygen-nitrogen bond in oxime benzoate:



This carbonium ion stabilizes itself by migration of the hydride ion and then attacks the benzene ring giving rise to the formation of 1-/4'-chlorophenyl/--3-methylisoquinoline:



The interpretation accepts and confirms the reaction scheme II, since the migration of the hydride ion within the azacyclobutenium ion formed after the Beckmann rearrangement, according to reaction scheme I, should furnish 3-methyl--4-/4'-chlorophenyl/-isoquinoline. The final conclusion of our present research work lies therefore in the acceptance of azacyclobutenium ion as an intermediate in the Beckmann rearrangement.

The investigations modify in some way our earlier hypothesis of a new type of carbonium ion rearrangement during the formation of isoquinoline nucleus from β-phenyl-α,β-unsaturated oxime esters[1], but on the other hand they confirm the existence of azacyclobutenium ion. The results give evidence that in the Beckmann rearrangement not only the azacyclopropene ring[6], but also other azacyclalkene rings may be considered as intermediates.

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