A new scheme for the mechanism of Fischer indolization of arylhydrazones

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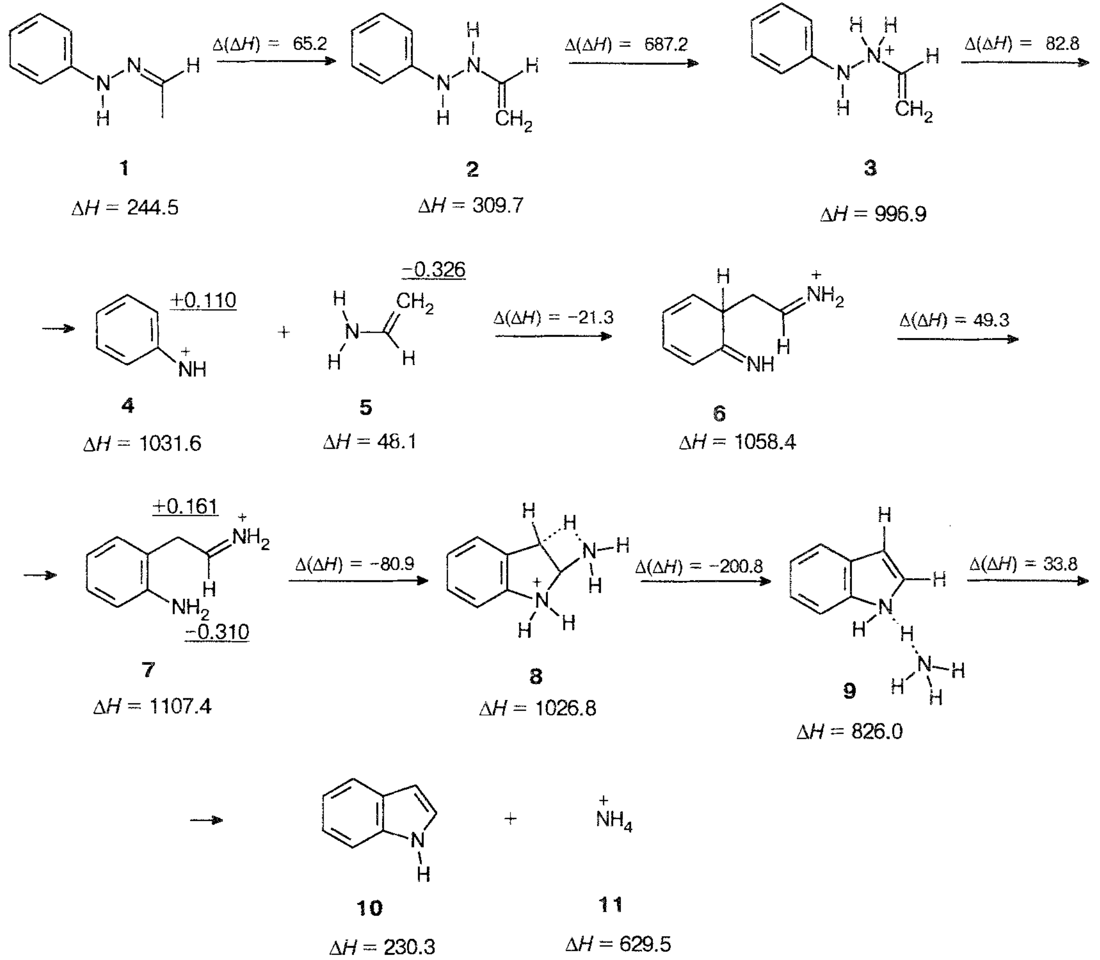
A new scheme for the mechanism of Fischer indolization of arylhydrazones has been suggested based on quantum-chemical calculations by the MNDO AM1 method.

Key words: arylhydrazones, Fischer indolization.

A scheme for the mechanism of acid-catalyzed Fischer indolization of arylhydrazones was proposed for the first time in the 1920's[1] and was later completed and refined.[2,3] However, the character of the transformations of several intermediates still remains unclear. In particular, the cleavage of the N—N bond and the formation of a new C—C bond (Scheme 1) was considered to be an intramolecular synchronous [3,3]-sigmatropic shift type process.[4] However, using isotopic labelling we demonstrated[5] that the N—N bond in

Scheme 1



Translated from *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 5, pp. 961—962, May, 1994.

1066-5285/94/4305-0907 $12.50 © 1995 Plenum Publishing Corporation

phenylhydrazones can be cleaved without the formation of a new C—C bond under conditions of the Fischer reaction. This fact disagrees with the synchronous mechanism of the considered reaction and indicates the possibility that this process is intramolecular.

Based on quantum-chemical calculations by the MNDO AM1 method[6] we suggested an expanded scheme of the reaction mechanism. In Scheme 1 the enthalpy (ΔH/kJ mol^{-1}), its changes ($\Delta(\Delta H)$/kJ mol^{-1}), and the atomic charge values (q) are presented.

As can be seen from Scheme 1, the absorption of energy during tautomerization of hydrazone **1** to enehydrazine **2** is 65.2 kJ mol^{-1}, and that during protonation of enehydrazine **2** is 687.2 kJ mol^{-1}, which is characteristic of nitrogen-containing compounds. It is assumed that in protonated enehydrazine **3** the N—N bond undergoes heterolytic cleavage to form of the aniline cation **4** and enamine **5**. Here the C atom in the *ortho*-position of **4** has a positive charge, and the terminal C atom of enamine **5** has a rather high negative charge. Under favorable steric conditions, these atoms can form a new C—C bond by the mechanism of intermolecular nucleophilic addition to afford the diimine intermediate **6**. The transformation of **6** to aminoimine **7** is accompanied by the absorption of energy (49.3 kJ mol^{-1}). Aminoimine **7**, formed as a result of the difficult process of intramolecular proton transfer with the highest value of enthalpy (ΔH = 1107.7 kJ mol^{-1}), must be the transition complex of the Fischer reaction. The positive charge is concentrated on the C atom of the imino group of compound **7**, and the high negative charge is concentrated on the N atom of the amino group, thus favoring pyrrole ring closure. In this process intermediate **8** is formed with the liberation of energy (80.9 kJ mol^{-1}). Ammonia, which is eliminated from compound **8**, attacks the proton of the amino group, resulting in the elimination of the proton and the formation of unsubstituted indole **10** and ammonium ion **11**.

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Received February 2, 1994;
in revised form February 28, 1994