DIRECT PROOF OF THE FISCHER SYNTHESIS OF INDOLES VIA A SCHEME INVOLVING A SIGMATROPIC [3,3]-SHIFT

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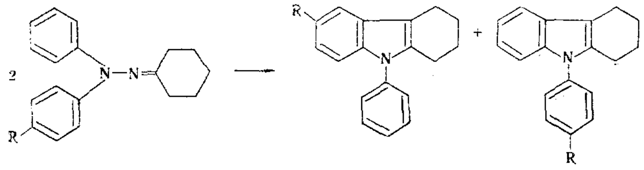
Previously [1] one of us formulated a concept according to which the step involving formation of the C–C bond in the Fischer indole synthesis takes place via a scheme involving sigmatropic [3,3]-rearrangement. In order to experimentally confirm this concept, we investigated the cyclization of p-substituted α,α-diphenylhydrazones of cyclohexanone under Fischer conditions.



I a,b II a,b III a,b

I-III a $R = OCH_3$; b $R = Cl$

According to the generally accepted scheme, in which the step involving formation of the C–C bond is considered to be electrophilic attack on the aromatic ring, we should have observed a pronounced effect of the substituents leading, for donor substituents, to structures of the II type and to structures of the III type for acceptor substituents. This has been demonstrated for electrophilic intramolecular acylation [2]. It is well known (for example, for the Claisen rearrangement) that this effect is small for sigmatropic processes [1]. We have found that both isomeric indoles II and III are formed in similar ratios in all cases under various conditions. Thus the IIa/IIIa isomer ratios are 80/20 (HCl), 77/23 (H_2SO_4), and 62/38 (thermally). The IIb/IIIb isomer ratios are 34/66, 32/68, and 32/68, respectively. Data on the quantitative isomer ratios were obtained by three independent methods – gas–liquid chromatography, IR spectroscopy, and mass spectrometry. All three methods gave results that coincided. Isomeric indoles IIa, IIb, IIIa, and IIIb were obtained for the comparative identification by alternative methods. Thus the results obtained unambiguously confirm that the formation of a C–C bond in the Fischer indole synthesis proceeds via a scheme involving a sigmatropic [3,3]-shift.

LITERATURE CITED

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2. G. Braun, G. Manz, and E. Reinsch, Ann., 468, 277 (1929).

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