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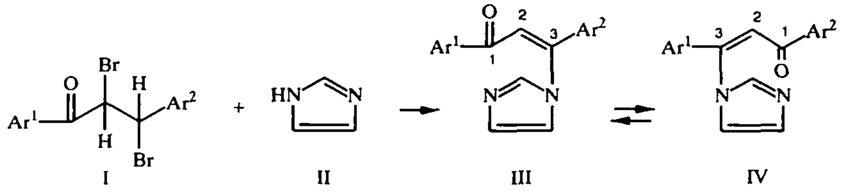
1,3-TRANSAMINATION IN ENAMINES OF β-DIKETONES WITH AN IMIDAZOLE RING AS THE AMINE COMPONENT (ENAMINE–ENAMINE REARRANGEMENT)

B. A. Rekhter and M. A. Rekhter

By condensation of chalcone dibromides with excess 1,2,4-triazole in DMSO at 110-130°C for 3.5-4 h, we obtained 1,3-diaryl(1H-1,2,4-triazol-1-yl)-2-propen-1-ones, which are enamines of β-diketones with a 1,2,4-triazole ring as the amine component [1, 2]. We showed for the example of the reaction of 2,3-dibromo-1-(2,4-dichlorophenyl)-3-(4-nitrophenyl)-1-propanone (I) with 1,2,4-triazole that the low-temperature variant of this condensation is preferable: holding the mixture of reagents at −20°C to +20°C for 24-240 h, making it possible to reduce formation of by-products to a minimum.

In condensation of dibromide I with imidazole II, which occurs faster than the reaction with 1,2,4-triazole, we observed formation of a mixture of isomeric enamines III and IV (Scheme 1).

Scheme 1



$Ar^1 = 2,4\text{-}Cl_2C_6H_3$; $Ar^2 = 4\text{-}O_2NC_6H_4$

The ratio of isomers varies depending on the temperature: in frozen DMSO (−10°C to −15°C, 120 h), the major component of the mixture is the enamine III, while when the reaction is carried out at room temperature (120 h), the major component is enamine IV. If the reaction mixture obtained in frozen DMSO is then held for the same time at ~20°C, then the ratio of enamines in it changes in favor of compound IV. By heating each of the enamines at 140-160°C for 20 min, a mixture is obtained whose major component, as should be expected, is the enamine IV. The ratio III:IV was determined by TLC or weighing after preparative separation of the mixture by crystallization. Due to the similarity of the IR, UV, and ^{13}C NMR spectra for both compounds, no physicochemical method has been developed so far for quantitatively determining each of them in the reaction mixture. So the exact change in the ratio III:IV over the course of the reaction is yet to be determined.

The indicated conversions could not be reproduced by UV irradiation of solid samples of III and IV or their benzene solutions. In analogy with 1,2,4-triazole [1,2], we assume that enamine III is the direct product of condensation of reagents I and II. Enamine IV is formed as a result of isomerization of the latter.

We call interconversions between enamines III and IV "enamine–enamine rearrangement" (its probable mechanism is shown in Scheme 2).

The reaction begins with addition of a water molecule at the activated double bond of enamine III with simultaneous 1,3-migration of the imidazole ring. The intermediate V formed is converted to enamine IV (V → VI → VII → IV). The key step is isomerization of the unsaturated diol VI to the keto alcohol VII, which then is easily dehydrated. As we see from this scheme, enamine–enamine rearrangement is favored by a 6-membered transition state, including $C_{(1)}-C_{(2)}-C_{(3)}$ atoms of

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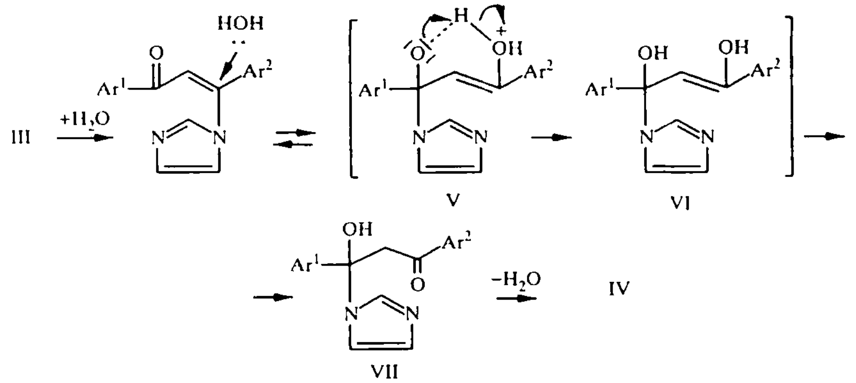
Scheme 2



the β-diketone moiety of enamine III and $N_{(1)}-C_{(2)}-N_{(3)}$ atoms of the imidazole ring; a 1,3-position for its nitrogen atoms, for which the amine $N_{(1)}$ goes to the imine $N_{(3)}$ and vice versa; the effect of the solvent DMSO, increasing the reactivity of the water molecule as a nucleophilic reagent; and possibly the catalytic effect of the imidazole or its HBr salt. In enamines III and IV, as in imidazole, the amine atom $N_{(1)}$ probably carries a partial positive charge while the imine $N_{(3)}$ carries a significant negative charge. So the imidazole may react as an intramolecular nucleophile, attacking the electrophilic carbon atom of the CO group and thus promoting formation of the intermediate V.

3-(4-Nitrophenyl)-3-(1H-imidazol-1-yl)-1-(2,4-dichlorophenyl)-2-propen-1-one (III) and 3-(2,4-dichlorophenyl)-3-(1H-imidazol-1-yl)-1-(4-nitrophenyl)-2-propene-1-one (IV). A. Dibromide I (4.8 g, 10 mmoles) was mixed at 20°C with 6.8 g (100 mmoles) imidazole in 50 ml DMSO. The solution immediately took on an intense orange color. After 30 min, by TLC the enamines III and IV were observed in the reaction mixture, with III predominant (visualizing agent, an aqueous solution of $KMnO_4$). After 72 h, the reaction mixture was poured into 500 ml water, and by extraction with benzene (6 × 100 ml) the enamines III and IV were recovered together with a small amount of imidazole. By washing the benzene extract with water (6 × 100 ml), the imidazole was completely removed from it. The benzene solution was dried with Na_2SO_4 and evaporated to dryness.

The mixture of enamines III, IV (80% yield) was crystallized at 20°C from a 2:1 benzene–hexane mixture. Yellow crystals of enamine III (0.9 g) were separated and dried over P_2O_5. T_{mp} 166-168°C; R_f 0.73 (benzene–acetone, 2:1). Found, %: C 54.99; H 3.36; N 10.28. $C_{18}H_{11}Cl_2N_3O_3 \cdot 0.5H_2O$. Calculated, %: C 54.42; H 3.30; N 10.58. IR spectrum (KBr): 3315, 3214, 3148, 3134, 3110, 3099, 3070, 3043, 3007, 2940, 2856, 2724, 1621, 1599, 1579, 1521, 1470, 1414, 1387, 1348, 1320, 1240, 1188, 1099, 1073, 1016, 902, 846, 815, 761, 717, 694, 656, 614, 593, 576 cm^{-1}. IR spectrum ($CHCl_3$): 1666, 1585, 1553, 1527, 1485, 1467, 1414, 1376, 1340, 1318, 1284, 1189, 1142, 1105, 1066, 1031, 1014, 940, 902, 871, 858, 824 cm^{-1}. UV spectrum (λ, nm (lg ε)): 197.5 (1.150); 300.8 (0.515) (concentration of 0.91 mg of the compound in 10 ml ethanol, d = 0.1 cm).

The mother liquor was held for 2 days at +5°C; a slight precipitate of enamine III (mainly on the walls of the container) was separated, the solvents were evaporated, and the residue was crystallized from a 1:1 benzene–hexane mixture at +5°C. Enamine IV (1.4 g) was isolated, T_{mp} 105-106°C; R_f 0.62 (2:1 benzene–acetone). Found, %: C 54.49; H 3.27; N 10.42. $C_{18}H_{11}C_{12}N_3O_3 \cdot 0.5H_2O$. Calculated, %: C 54.42: H 3.30; N 10.58. IR spectrum (KBr): 3147, 3120, 3109, 3089, 3077, 3066, 3039, 3024, 2851, 1607, 1585, 1550, 1521, 1479, 1406, 1391, 1377, 1345, 1284, 1239, 1206, 1142, 1097, 1081, 1037, 1026, 896, 882, 863, 809, 780, 737, 704, 647 cm^{-1}. IR spectrum ($CHCl_3$): 1672, 1611, 1587, 1552, 1527, 1481, 1396, 1379, 1351, 1303, 1289, 1246, 1106, 1069, 1018, 930, 899, 859, 821 cm^{-1}. UV spectrum (λ, nm (lg ε)): 195.8 (1.09); 272.5 (0.410); 300.8 (0.357) (concentration 0.85 mg of the compound in 10 ml ethanol, d = 0.1 cm).

A total of 0.61 g of the compound was isolated from the mother liquor; according to TLC it is identical to enamine IV. The ratio of enamines II:IV ~ 1:2.

B. A mixture of dibromide I with imidazole in DMSO was rapidly frozen and placed in a freezer (–10°C to –15°C). Periodic withdrawal of samples from the solidified solution showed (TLC) that enamine III predominated in its mixture with enamine IV. After 120 h, the flask was taken out of the freezer and allowed to stand for 120 h more at ~20°C. According to TLC data, the ratio of enamines III and IV changed in favor of IV.

C. Crystals (0.1-0.2 g) of enamine III or IV were heated at 140-160°C for 20 min. After cooling the melt, it was analyzed by TLC in the benzene–acetone system (2:1). In each run, we observed a mixture of enamines III and IV, with IV predominating.

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