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MECHANISM OF THE EXCHANGE REACTION OF AROMATIC SCHIFF BASES

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The recognition of the exchange reaction of aromatic Schiff bases has led Ingold and Piggott /1, 2/ to the assumption of a one-step formation of a dimeric intermediate with 1,3-diazetidine structure. As this assumption contradicts the principle of conservation of orbital symmetry and the methyleneanils isolated by the authors were later shown /3/ to have a trimeric rather than a dimeric structure, an investigation of the mechanism became necessary.

Reproduction of the preparative experiments has shown that the substituted benzylideneanilines described by the authors /1, 2/ as 1,3-diazetidines are, in fact, mixtures containing the starting and resulting Schiff bases in various ratios. This result is supported by the NMR spectra which reveal no signal in the expected δ = 5.0 - 6.0 ppm region for ring protons.

The kinetics of the exchange reaction were studied by NMR spectroscopy /VARIAN-A-60D/, following the intensity of the azomethine proton signal / δ = 8.2 - 8.6 ppm/ and, in the case of the methoxy substituted derivatives, that of the methoxy proton singlet / δ = 3.6 - 3.9 ppm/.

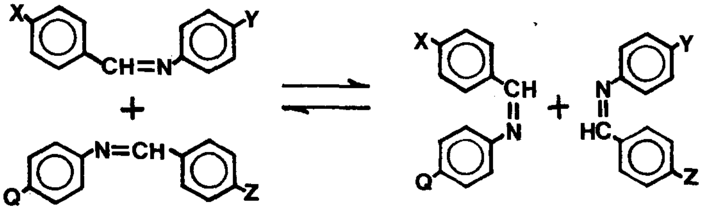


Table 1

Rate and equilibrium constants of the exchange reaction of aromatic Schiff bases in tetrachloroethylene at 110°C

X	Y		Z	Q		kx10^4 $dm^3mol^{-1}s^{-1}$	K
O_2N-	-H	I	H-	$-OCH_3$	II	13.4	1.18
O_2N-	$-OCH_3$	III	H-	-H	IV	11.4	
CH_3O-	-H	V	H-	$-NO_2$	VI	3.16	1.22
CH_3O-	$-NO_2$	VII	H-	-H	IV	2.59^{*}	
CH_3O-	-H	V	H-	-Br	VIII	10.2	0.93
CH_3O-	-Br	IX	H-	-H	IV	11.0^{*}	

*Value calculated from the reverse reaction on the basis of the equilibrium constant.

The experimental data permit the following conclusions:

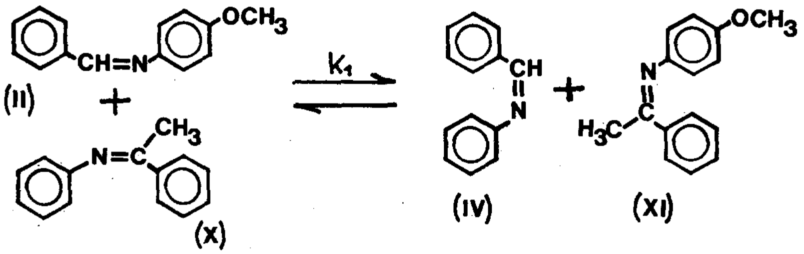
(i) The process leads to an equilibrium, in all cases, independent of the X and Y substituents;

(ii) The process follows a second order rate law: calculations based on the integrated rate equation for a reversible second order reaction /4/ yield fairly good rate constants /± 5 %/;

(iii) The value of the equilibrium constant is close to unity.

The rate constant and position of the equilibrium are not altered significantly on changing the N-substituent from an aryl to an alkyl group: the exchange occurs also with benzylidenemethylamine.

It is remarkable that the exchange takes place also with Schiff bases of aryl ketones as reaction partners



The equilibrium between acetophenone anil /X/ and benzylidene-p-anisidine /II/ is reached more rapidly /k_1 = 4.58x10^{-3} $dm^3mol^{-1}s^{-1}$ in tetrachloroethylene at 110°C/ than that between two aldimines. Also in the latter case, the rate constants depend only slightly on the substituents of the aldimine partners, while the equilibrium constants differ significantly: in the case of benzylidene-p-anisidine /II/ K=0.6 as opposed to $K < 0.2$ for the p-nitraniline derivative /VI/.

The rate constants of the exchange reaction in solvents with different polarities differ by several orders of magnitude /Table 2/ suggesting an ionic intermediate rather than a concerted process.

Table 2

Rate constants of the reaction of p-nitrobenzylideneaniline /I/ with benzylidene-p-anisidine /II/ in various solvents

Solvent	$k \times 10^3$ /$dm^3 mol^{-1} s^{-1}$/	
	36°C	110°C
Benzonitrile	21.30	>100
Acetonitrile	17.30	>100
Nitrobenzene	1.32	>100
o-Dichlorobenzene	-	4.87
Tetrachloroethylene	-	1.34
Chlorobenzene	-	0.85
Pyridine	-	0.06

The low rate constant observed in the polar, but also basic, pyridine suggests proton catalysis in the reaction. Indeed, in the presence of 0.01 mol dm^{-3} of trifluoroacetic acid, the equilibrium is reached instanteneously*.

The proton catalysis was studied in the presence of collidine regarded as a "proton sponge". The apparent second order rate constant for the reaction of p-nitrobenzylideneaniline /I/ with benzylidene-p-anisidine /II/, measured at 36°C in the presence of 2 mol dm^{-3} collidine at various concentrations of trifluoroacetic acid /$(4\text{-}10) \times 10^{-3}$ mol dm^{-3}/, shows a linear dependence on the proton concentration.

Thus, the reaction in either direction obeys the rate law $v = k' [H^+] [Schiff_1] [Schiff_2]$ for low proton concentrations /at constant proton concentration a simple second order rate equation is obtained/.

At high proton concentrations, e.g. in trifluoroacetic acid, no exchange reaction occurs, i.e. two protonated azomethines do not react with each other. Similarly, the exchange does not take place in the absence of protons, a situation observed in the proton acceptor collidine. The reaction does not stop completely, probably because a very low equilibrium proton concentration prevails even in the presence of collidine.

It follows from the above that the first step of the exchange reaction is the interaction of a neutral /XII/ and a protonated /XIII/ Schiff base molecule. The intermediate formed in this way reacts further, according to the following pattern:

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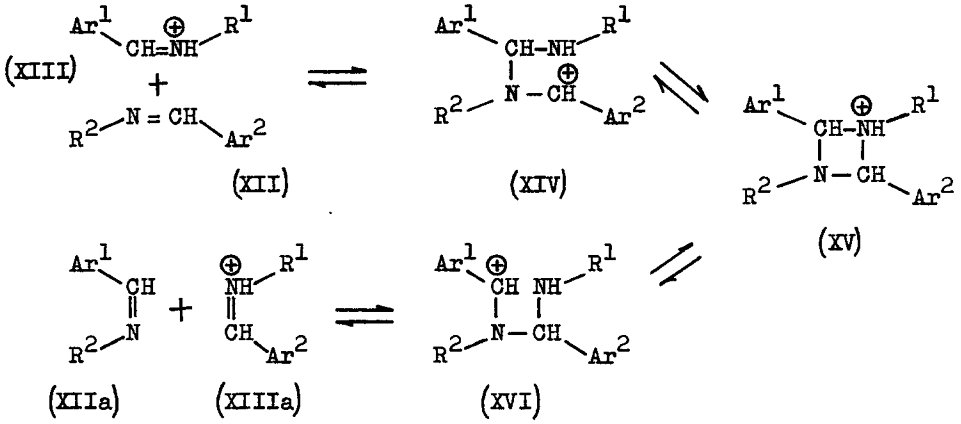
*For this reason the measurements were carried out under strictly standardized conditions, after freeing the solvents and equipment from protons as much as possible.



The suggested cyclic 1,3-diazetidinium intermediate /XV/ must be present only at very low concentrations, as the signal corresponding to this structure cannot be observed in the NMR spectrum.

According to this mechanism, the position of the catalyst proton remains unchanged during the reaction, thus, no kinetic isotope effect should be expected. Indeed, the rate does not change when deuterated trifluoroacetic acid is used as catalyst.

The intramolecular rearrangement described recently by Goldmann et al. /5/ can be considered as a special case of the mechanism proposed above.

On the basis of the above mechanism it can be expected that the process is catalyzed not only by protons, but also by other cations capable of quaternizing the azomethine N-atom. Accordingly, bromine and iodine were found to accelerate the exchange reaction owing to the formation of Schiff base iminium salts /6/ with halogens.

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