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SOME SELECTED SCHIFF-BASE EXCHANGE REACTIONS*

James V. Crivello, T. Kurosaki** and G. F. D'Alelio

Department of Chemistry

University of Notre Dame

Exchange reactions involving Schiff-bases have been known for some time. Reddelien and Danilof[1] in 1921 described an exchange involving the amine moiety in an aromatic ketonanil. When β-naphthalamine was added to diphenylketonanil in a melt, partial replacement of aniline occurred giving rise to an equilibrium mixture of products.

$$(C_6H_5)_2C{=}NC_6H_5 + C_{10}H_7NH_2 \rightleftharpoons \underset{(I)}{(C_6H_5)_2C{=}NC_{10}H_7} + C_6H_5NH_2 \qquad \text{(eq. 1)}$$

Further, they found that when aniline was distilled out of the reaction mixture the equilibrium was shifted and a quantitative yield of the new Schiff base (I) was obtained.

These workers list three conditions upon which the reaction depends:

1. The volatility of the amine;
2. The chemical affinity of the amine for the ketone moiety in the Schiff base;
3. The concentration of the amine.

A reinvestigation of this amine exchange reaction was initiated in our

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** Present address: National Aeronautics and Space Administration, Langley Field, Virginia laboratories to determine the scope of the reaction for its possible applicability in polymerizations. Of the three conditions listed by Reddelien and Danilof, the first was found for our purposes to be the most important. When the volatility of the replacing amine is low in comparison with the volatility of the amine to be replaced, then very high yields of product can be obtained by preferential distillation of the replaced amine. Table 1 shows that in those cases studied, even where polyfunctional amines or Schiff-bases were used, quantitative yields were obtained. Our experiments also show that the amine exchange reaction is not restricted only to ketonanils, but was used successfully for the first time[2,3] with Schiff bases obtained from aldehydes as well.

Table 1

Synthesis of Some Schiff Bases by Amine Exchange

Reagents	Yield Crude Product	Product	M.P. °C		Catalyst
			Found	Lit.	
p-$CH_3OC_6H_4NH_2$ + $C_6H_5CH{=}NC_6H_5$	Quant.	$C_6H_5CH{=}NC_6H_4OCH_3$	72	72	none
p-$H_2NC_6H_4NH_2$ + 2 $C_6H_5CH{=}NC_6H_5$	Quant.	$C_6H_5CH{=}NC_6H_4N{=}CHC_6H_5$	140	140	$ZnCl_2$
m-$CH_3OC_6H_4NH_2$ + $C_6H_5N{=}CHC_6H_5CH{=}NC_6H_5$	Quant.	$CH_3OC_6H_4N{=}CHC_6H_4CH{=}NC_6H_4OCH_3$	219	220	none

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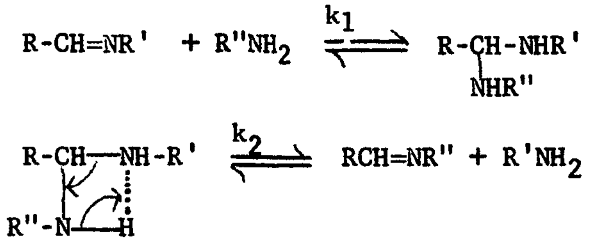
The reaction mechanism as proposed by Reddelien and Danilof and subsequently by ourselves involves the reversible formation of an intermediate by addition of the amine to the carbon-nitrogen double bond of the Schiff base. Under the conditions of the reaction the intermediate then breaks down to give the exchange products, thus:



$$\mathrm{R\text{-}CH{=}NR'} + \mathrm{R''NH_2} \underset{}{\overset{k_1}{\rightleftharpoons}} \mathrm{R\text{-}\underset{NHR''}{CH}\text{-}NHR'}$$

$$\mathrm{R\text{-}CH\text{-}NH\text{-}R'}\ (\mathrm{R''\text{-}N\text{-}H}) \overset{k_2}{\rightleftharpoons} \mathrm{RCH{=}NR''} + \mathrm{R'NH_2}$$

(eq. 2)

another exchange reaction in which carbonyl functions are exchanged in Schiff-bases was described by C. K. Ingold.[4]

$$\mathrm{R\text{-}CH{=}N\text{-}R'} + \mathrm{R''\text{-}CHO} \rightleftharpoons \mathrm{R''\text{-}CH{=}NR'} + \mathrm{R\text{-}CHO} \qquad \text{Eq. 3)}$$

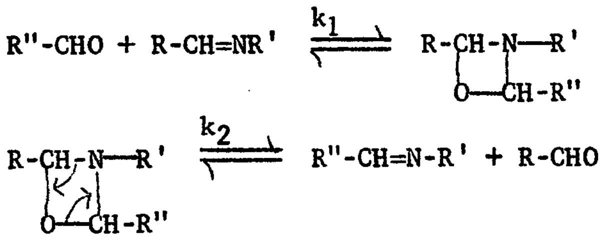
Using a number of Schiff bases and aldehydes in suitable solvents he was able to achieve equilibrium mixtures of products at room temperature in a few days. On reinvestigating this reaction, we found[2,3] that when the reaction was run as a melt and the replaced aldehyde was removed under reduced pressure, high yields could similarly be obtained for this reaction. Table 2 gives the experimental data obtained in these investigations. The last reaction shown in Table 2 was run at room temperature and the yield listed refers to the recrystallized product. The results of these experiments show that the carbonyl exchange is equally as facile as the amine exchange giving high yields of products even when a variety of substituents are used and the reagents are difunctional.

A mechanism for this reaction has been advanced by Ingold involving the intermediacy of a four-membered oxazetidine ring. Subsequent cleavage of the ring produces the exchange products, thus:

Table 2.

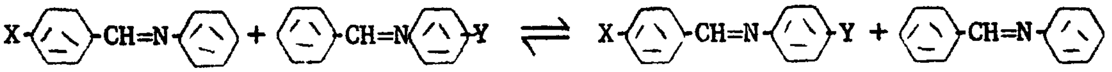
Synthesis of Some Schiff Bases by Carbonyl Exchange

Reagents	Yield Crude Product	Product	M.P. °C		Catalyst
			Found	Lit.	
p-$O_2NC_6H_4CHO$ + $C_6H_5CH{=}NC_6H_5$	Quant.	p-$O_2NC_6H_4CH{=}NC_6H_5$	91	93	none
p-$OCHC_6H_4CHO$ + 2 $C_6H_5CH{=}NC_6H_5$	Quant.	$C_6H_5N{=}CHC_6H_4CH{=}NC_6H_5$	159	159	$ZnCl_2$
p-$O_2NC_6H_4CHO$ + $C_6H_5CH{=}NC_6H_4N{=}CHC_6H_5$	Quant.	$O_2NC_6H_4CH{=}NC_6H_4N{=}CHC_6H_4NO_2$	245	249	none
$(C_2H_5)_2C{=}NC_6H_4N{=}C(C_2H_5)_2$ + 2 C_6H_5CHO	47.2	$C_6H_5CH{=}NC_6H_4N{=}CHC_6H_5$	140	140	none



(eq. 4)

Another mode of exchange can take place between two Schiff-bases. C. K. Ingold and H. A. Piggot[3] report that if two simple Schiff-bases are mixed together in solution, an equilibrium mixture of reagents and products arising from exchange between the two azomethines results.



(eq. 5)

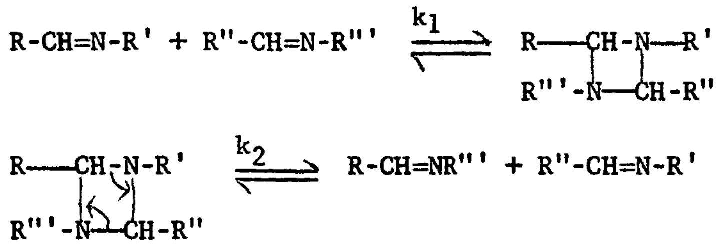
This reaction we have termed a "bis exchange" reaction was also investigated in this research. Applying the techniques used in the preceeding exchange reactions, namely, the use of a melt system and by distilling out one of the Schiff-base products, good yields may be obtained of the desired Schiff-base. Table 3 gives two examples of this reaction.

Table 3

Synthesis of Some Schiff Bases by Bis Exchange Reactions

Reagents	% Yield (Rescrys.)	Product	M.P. °C		Catalyst
			Found	Lit.	
$p\text{-}O_2NC_6H_4CH{=}NC_6H_5$ + $C_6H_5CH{=}NC_6H_4OCH_3\text{-}p$	78.9	$p\text{-}O_2NC_6H_4CH{=}NC_6H_4OCH_3$	135	132	none
$C_6H_5CH{=}NC_6H_4Cl\text{-}p$ + $C_6H_5N{=}CHC_6H_4CH{=}NC_6H_5$	70.0	$p\text{-}ClC_6H_4N{=}CHC_6H_4CH{=}NC_6H_4Cl\text{-}p$	180	---	$ZnCl_2$

The previous investigators also report the isolation in several cases of a diazetidine intermediate from Schiff bases which undergoes decomposition to give two new Schiff bases. A mechanism which may be written for this exchange reaction is the following:



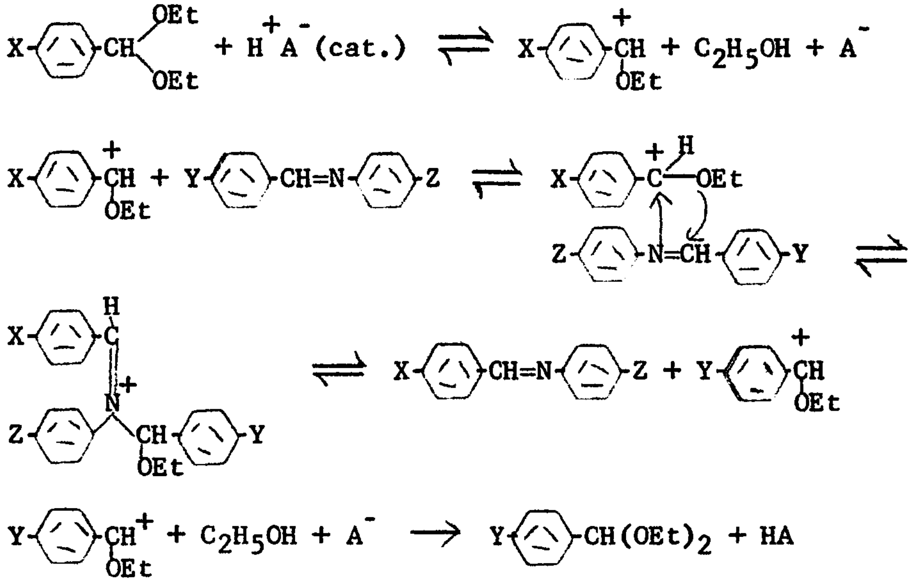
(eq. 6)

An entirely new Schiff base exchange reaction was discovered and extensively investigated in this laboratory. Aromatic acetals were observed to react with azomethines in a fashion similar to the carbonyl exchange.

$$R\text{-}CH{=}N\text{-}R' + R''CH(OR''')_2 \rightleftharpoons R''\text{-}CH{=}N\text{-}R' + RCH(OR''')_2 \qquad \text{(eq. 7)}$$

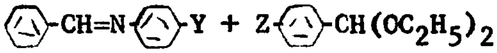
This reaction was found to proceed readily in the presence of Lewis acid catalysts at temperatures above 150°C, whereas in the absence of catalyst reaction failed to occur.

In Table 4 are contained the experimental data for the simple acetal exchange and in Table 5 data obtained using the polyacetal p-xylylidenetetraethylether in the exchange reaction. A mechanism which may be written for the reaction is the following:



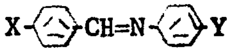
(Eq. 8)

Table 4

Acetal Exchange Between 

Substituents		Catalyst	Temp. °C	Pressure mm Hg	Distillate	Product
Y	Z					
H	p-NO_2	none	150-250	760	$C_6H_5CH(OC_2H_5)_2$ and $C_6H_5CH=NC_6H_5$	none
H	p-NO_2	none	170-195	15	$C_6H_5CH=NC_6H_5$	none
H	p-NO_2	TsOH	160-165	30-50	$C_6H_5CH(OC_2H_5)_2$ 30%	$O_2NC_6H_4N=CHC_6H_5$ 30%
p-NO_2	p-NO_2	TsOH	170-180	760-1.5	$C_6H_5CH(OC_2H_5)_2$ 40%	$O_2NC_6H_4N=CHC_6H_4NO_2$ 25%
p-NO_2	p-NO_2	TsOH	180	25	$C_6H_5CH(OC_2H_5)_2$ 20%	$O_2NC_6H_4N=CHC_6H_4NO_2$ 43%
H	p-Cl	TsOH	170	10-40	$C_6H_5CH(OC_2H_5)_2$ 87%	$ClC_6H_4CH=NC_6H_5$

Table 5

Acetal Exchange Between  and 

Substituents		Cata-lyst	Temp. °C	Pressure mm Hg	Distillate	Product
X	Y					
H	H	TsOH	200-220	760	$C_6H_5CH(OC_2H_5)_2$ 52%	$C_6H_5N{=}CHC_6H_4CH{=}NC_6H_5$ 60% crude
H	H	none	150	15	--------------	No reaction
H	H	TsOH	170	15-35	$C_6H_5CH(OC_2H_5)_2$ 52%	$C_6H_5N{=}CHC_6H_4CH{=}NC_6H_5$ 50%
H	H	TsOH	170	22	$C_6H_5CH(OC_2H_5)_2$ 53%	$C_6H_5N{=}CHC_6H_4CH{=}NC_6H_5$ 85%
H	p-NO_2	None	150-300	760	$C_6H_5CH(OC_2H_5)_2$ 60%	black residue
H	p-NO_2	TsOH	170	15-30	$C_6H_5CH(OC_2H_5)_2$ 30%	$O_2NC_6H_4N{=}CHC_6H_4CH{=}NC_6H_4NO_2$ 20%
H	p-NO_2	TsOH	170	20	$C_6H_5CH(OC_2H_5)_2$ 35%	$O_2NC_6H_4N{=}CHC_6H_4CH{=}NC_6H_4NO_2$ 30%
H	p-Cl	TsOH	170-180	17-27	$C_6H_5CH(OC_2H_5)_2$ 38%	$ClC_6H_4N{=}CHC_6H_4CH{=}NC_6H_4Cl$ 20%
H	p-Cl	TsOH	170-200	15	$C_6H_5CH(OC_2H_5)_2$ 80%	$ClC_6H_4N{=}CHC_6H_4CH{=}NC_6H_4Cl$ 42%
p-Cl	H	TsOH	175	15	$ClC_6H_4(OC_2H_5)_2$ 75%	$C_6H_5N{=}CHC_6H_4CH{=}NC_6H_5$ 35%

__Acknowledgment__.

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