

## RING-CHAIN TAUTOMERISM OF IMIDAZOLIDINE SYSTEM

Stanisław Witek, Alicja Bielawska and Jacek Bielawski

Institute of Organic and Polymer Technology  
 Technical University of Wrocław  
 50-370 Wrocław, Poland

The existence of the tautomeric equilibrium of imidazolidine system  $\underline{3} \rightleftharpoons \underline{4}$  has been established. Due to a higher reactivity of NH group in  $\underline{4}$ , the reaction of the system  $\underline{3} \rightleftharpoons \underline{4}$  with PhNCO unbalances the tautomeric equilibrium, and causes an increase in the content of the open-chain urea derivative  $\underline{6}$  in the reaction mixture. The use of isocyanates or other similar reagents, e.g., isothiocyanates, seems to be a convenient method for studies of the tautomerism in similar systems.

N-Monosubstituted ethylenediamine derivatives can react with aldehyde  $\underline{2}$  giving a mixture of imidazolidine  $\underline{3}$  and corresponding Schiff's base  $\underline{4}$ . The composition of this mixture is largely dependent on the structure of the reacting substrates. Chapuis *et al.* [1] suggested the existence of such an equilibrium but did not confirm it experimentally.

The existence of tautomeric equilibrium in oxazolidines has been established by  $^1\text{H}$ -nmr spectra recorded in different solvents [2]. The influence of a solvent on the equilibrium of imidazolidines has not, however, been observed [1]. This would suggest either similar properties of both NH groups or that the tautomeric equilibrium does not exist in this system. Any attempts at establishing the tautomerism of both these systems by chemical reactions /e.g., by acylation/ were unsuccessful [1,3]. Thus, in order to avoid destruction of the system, it seems to us possible to elucidate the tautomeric equilibrium of imidazolidines by means of their reaction with a weaker reagent, such as isocyanate.

A series of imidazolidines were obtained in the reaction of N-methylethylenediamine  $\underline{1}$  with 4-substituted benzaldehydes  $\underline{2a-e}$  [4] using the standard procedure [5]. The composition of the reaction product was determined from its  $^1\text{H}$ -nmr spectra [6,7] via integration of the signals of the H<sup>(a)</sup> and H<sup>(b)</sup> protons according to Chapuis *et al.* [1].

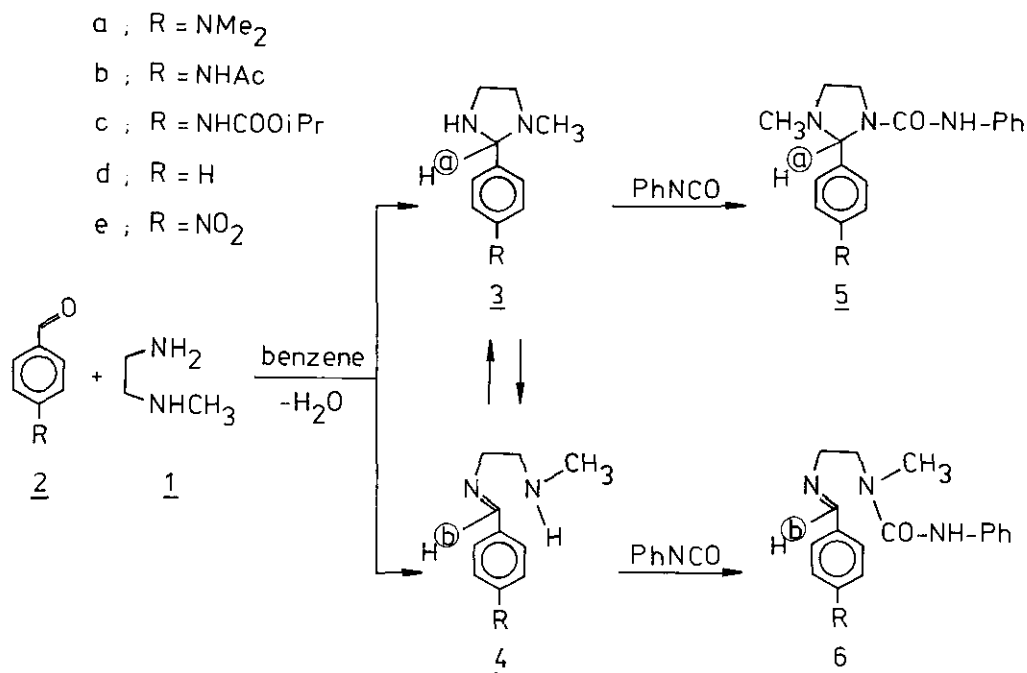


Table 1. Products of reaction of N-methylethylenediamine **1** with aldehydes **2**

Products <b>3</b> + <b>4</b>	Product yield %	mp, °C or bp, °C/mm Hg	$\delta$ , [ ppm ]		%	
			H (a)	H (b)	<b>3</b>	<b>4</b>
a	82.3	202-204/53	4.00	8.33	50	50
b	97.8	82-86.5	4.02	8.40	62	38
c	98.0	72-76	4.00	8.37	65	35
d	75.4	102/3	4.00	8.47	80	20
e	96.6	39-40	4.00	-	100	-

From Table 1 it can be seen that the nature of the substituent R has a marked effect on the composition of the reaction product; an analogous effect has been reported for oxazolidines [8]. The <sup>1</sup>H-nmr spectra recorded in different solvents /CCl<sub>4</sub> → DMSO/ at ambient temperature did not reveal any marked changes in the composition of mixture **3** + **4**.

Table 2. Products of reaction of imidazolidines 3 + 4 with PhNCO

Products <u>5</u> + <u>6</u>	A			B			C		
	Reaction yield, %	Product com- position %		Reaction yield, %	Product com- position, %		Reaction yield, %	Product com- position, %	
		<u>5</u>	<u>6</u>		<u>5</u>	<u>6</u>		<u>5</u>	<u>6</u>
a	95.3	-	100	99.5	-	100	99.8	-	100
b	97.0	30	70	97.0	20	80	98.1	10	90
c	87.2	40	60	88.2	26	74	94.2	15	85
d	81.1	70	30	85.5	57	43	88.3	30	70
e	96.9	100	-	92.3	90	10	94.0	65	35

A - ethyl ether, room temperature, B - benzene, room temperature, C - boiling benzene

Imidazolidines characterized in Table 1 were reacted with phenyl isocyanate at room temperature in benzene. After 24 hr the solvent was evaporated and the so obtained products were analyzed by  $^1\text{H}$ -nmr by integrating signals of the H<sup>(a)</sup> and H<sup>(b)</sup> protons. The so determined ratios of both urea derivatives 5+6 in the reaction product are given in Table 2. Only a small degree of decomposition of the starting imidazolidines 3 + 4 was observed during their reaction with PhNCO. The reaction of 3 + 4 with PhNCO in diethyl ether was carried out similarly. After evaporation of the solvent a crystalline A and oily B fractions were separated. The composition of both fractions was determined again by  $^1\text{H}$ -nmr and, thus, the total content of both products 5 and 6 could be found. Several pure uréa derivatives of 5 and 6 were isolated from both the A and B fractions after recrystallization or after solvent extraction and recrystallization /Table 3/.

By comparing data contained in Tables 1 and 2, it can be seen that the products of reaction of 3 + 4 with PhNCO contain more open-form urea derivatives 6 than the determined content of 4 in the starting imidazolidine. Moreover, the composition of the urea derivatives depends on the kind of solvent. Similarly, an increase in temperature of the reaction brings about an increase in the content of the open form 6 in the reaction mixture /the yield of 6e in boiling benzene was ca. 35%/. The presented results prove the existence of the mobile tautomeric equilibrium in the imidazolidine system.

Table 3. Characteristics of products 5 and 6

Compound	m.p. °C	<sup>1</sup> H-NMR data /CDCl <sub>3</sub> , δ ppm/
<u>6a</u>	101.5 - 103	8.62 /s, 1H, CONH/; 8.37 /s, 1H, H <sup>(b)</sup> /; 7.87 /d, 2H, C <sub>6</sub> H <sub>2</sub> /; 8.87 /d, 2H, C <sub>6</sub> H <sub>2</sub> /; 7.75 - 7.12 /m, 5H, C <sub>6</sub> H <sub>5</sub> /; 3.90 /br.s, 4H, CH <sub>2</sub> -CH <sub>2</sub> /; 3.25 /br.s, 9H, NCH <sub>3</sub> , N(CH <sub>3</sub> ) <sub>2</sub> /;
<u>6b</u>	185 - 187.5	9.56 /s, 1H, NHCOME/; 8.55 /s, 1H, CONHPh/; 8.41 /s, 1H, H <sup>(b)</sup> /; 7.20 - 8.06 /m, 9H, C <sub>6</sub> H <sub>4</sub> , C <sub>6</sub> H <sub>5</sub> /; 4.15 /br.s, 4H, CH <sub>2</sub> -CH <sub>2</sub> /; 3.37 /s, 3H, COCH <sub>3</sub> /; 2.43 /s, 3H, NCH <sub>3</sub> /
<u>6c</u>	135.5 - 137	8.62 /s, 1H, NH/; 8.37 /s, 1H, H <sup>(b)</sup> /; 7.15 - 8.10 /m, 10H, C <sub>6</sub> H <sub>4</sub> , C <sub>6</sub> H <sub>5</sub> , NH/; 5.35 /sept, 1H, CHMe <sub>2</sub> /; 4.05 /br.s, 4H, CH <sub>2</sub> -CH <sub>2</sub> /; 3.35 /s, 3H, NCH <sub>3</sub> /; 1.65 /d, 6H, CH <sub>3</sub> 2/
<u>5c</u>	155.5 - 157	7.25 - 8.00 /m, 10H, C <sub>6</sub> H <sub>4</sub> , C <sub>6</sub> H <sub>5</sub> , NH/; 6.55 /s, 1H, CONHPh/; 5.35 /sept, 1H, CHMe <sub>2</sub> /; 4.87 /s, 1H, H <sup>(a)</sup> /; 2.70 - 4.50 /m, 4H, CH <sub>2</sub> -CH <sub>2</sub> /; 2.65 /s, 3H, NCH <sub>3</sub> /; 1.65 /d, 6H, CH(CH <sub>3</sub> ) <sub>2</sub> /
<u>5d</u>	110.5 - 112	7.75 - 7.00 /m, 10H, C <sub>6</sub> H <sub>5</sub> , C <sub>6</sub> H <sub>5</sub> /; 6.94 /s, 1H, CONHPh/; 4.87 /s, 1H, H <sup>(a)</sup> /; 2.50 - 4.00 /m, 4H, CH <sub>2</sub> -CH <sub>2</sub> /; 2.44 /s, 3H, NCH <sub>3</sub> /
<u>5e</u>	132 - 135	8.54 /d, 2H, C <sub>6</sub> H <sub>2</sub> /; 7.92 /d, 2H, C <sub>6</sub> H <sub>2</sub> /; 7.25 - 7.60 /m, 5H, C <sub>6</sub> H <sub>5</sub> /; 6.75 /s, 1H, CONHPh/; 5.25 /s, 1H, H <sup>(a)</sup> /; 2.87 - 4.25 /m, 4H, CH <sub>2</sub> -CH <sub>2</sub> /; 2.65 /s, 3H, NCH <sub>3</sub> /

Compounds 6a, 5c and 5d were crystallized from benzene; 5e and 6b from 95% ethanol, and 6a from 50% ethanol

Tautomers 3 + 4 react with isocyanate at different rates resulting from the unequal reactivity of both NH groups. It is evident that the open form reacts faster; and, as a result, to preserve the tautomeric equilibrium 3 ⇌ 4 in the solution, there occurs the transformation of 3 into its imine form 4. The influence of temperature and the kind of solvent on a change of ratio 5:6 can be explained by assuming a change in the relative reaction rates of 3 and 4 with PhNCO.

In conclusion, the presented studies furnished a reasonable proof of the existence of ring-chain tautomerism in the imidazolidine system. We believe that our technique, i.e., the use of an isocyanate not causing the destruction of the system or the use of similar reagents, e.g. isothiocyanates, may find application in studies on the tautomerism of similar heterocyclic systems.

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4. Commercial products pure /for preparation of 2c see J. prakt. Chem., 1979, 312, 804; for 2b see J. Chem. Soc., 1944, 4.
5. Refluxing in benzene, water removed by Dean-Stark trap and solvent evaporated
6. All products gave satisfactory elemental analysis data
7. 80 MHz, HMDS ext.,  $\text{CDCl}_3$  or  $\text{CCl}_4$ ,  $\delta$ , ppm, 3c + 4c: 8.97 /br, s, 0.65H,  $\text{NHCOO}/$ , 8.87 /br. s, 0.35H,  $\text{NHCOO}/$ ; 8.37 /s, 0.35H,  $\text{H}^{\text{(b)}}$  /; 7.40 - 7.50 /m, 4H,  $\text{C}_6\text{H}_4/$ ; 5.25 /Sept, 1H,  $\text{CHMe}_2/$ ; 4.00 /s, 0.65H,  $\text{H}^{\text{(a)}}$  /; 3.90 - 2.10 /m, 8H,  $\text{CH}_2\text{-CH}_2$ ,  $\text{NH}$ ,  $\text{NCH}_3$ ,  $\text{N} \begin{array}{l} \text{H} \\ \text{CH}_3 \end{array} /$ ; 1.58 /d, 6H,  $\text{CH CH}_3$  2/, 3e: 8.52 /d, 2H,  $\text{C}_6\text{H}_2/$ ; 8.00 /d, 2H,  $\text{C}_6\text{H}_2/$ ; 4.37 /s, 1H,  $\text{H}^{\text{(a)}}$  /; 3.75 - 2.75 /m, 4H,  $\text{CH}_2\text{-CH}_2/$ ; 2.60 /s, 3H,  $\text{NCH}_3/$ ; 2.50 /s, 1H,  $\text{NH}/$ .
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