Organometallic Chemistry

Solid-state reactions of organometallic aldehydes with optically active primary β-hydroxyamines

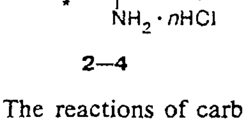
N. S. Khruscheva, N. M. Loim, and V. I. Sokolov*

A. N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences,
28 ul. Vavilova, 117813 Moscow, Russian Federation.
Fax: 007 (095) 135 5085

The solid-state reactions of crystalline ferrocenyl- and ruthenocenylaldehydes with optically active primary β-hydroxyamines were studied at −20 °C. The yield of the products increases substantially in the presence of K_2CO_3. The tautomeric equilibrium between imines and diastereomeric oxazolidines with the predominant formation of one of them is established in solutions of the products in $CDCl_3$.

Key words: aldehydes, primary β-hydroxyamines, solid-state interaction, tautomeric equilibrium, stereoselectivity.

We have previously established that the solid-state reactions of aldehydes with primary amines and secondary β-hydroxyamines are an efficient method for preparing Schiff's bases[1] and oxazolidines,[2,3] respectively. In the latter case, when chiral alcohols are used, the solid-state reaction occurs, as a rule, stereoselectively. In this work, we studied the solid-state reactions of crystalline ferrocenylaldehydes (**1a**) and ruthenocenylaldehyde (**1b**) with optically active primary β-hydroxyamines (**2—4**).



$$\mathrm{Ph{-}}\overset{R}{\underset{*}{\mathrm{C}}}\mathrm{H{-}}\overset{*}{\underset{NH_2\cdot nHCl}{\mathrm{C}}}\mathrm{H{-}}\overset{R^1}{\mathrm{C}}\mathrm{H_2}$$

2—4

2: $R = H, R^1 = OH, n = 0$
3: $R = OH, R^1 = OH, n = 0$
4: $R = OH, R^1 = H, n = 1$

The reactions of carbonyl compounds with primary amines containing the β-hydroxyl group are well studied and usually lead to the formation of imines, oxazolidines, or their mixtures.[4] Previously they were carried out only in solutions. We have established that the solid-state reactions of aldehydes **1a,b** with optically active (*S*)-(−)-2-amino-3-phenylpropan-1-ol (**2**) and (1*S*,2*S*)-2-amino-1-phenylpropane-1,3-diol (**3**) proceed at −20 °C; the time of complete conversion of the reagents depends substantially on their nature. For example, in the reactions of ferrocenylaldehyde and ruthenocenylaldehyde with compound **2**, the conversion of the reagent is more than 90% over 3 days. When these aldehydes react with **3** during the same time, the conversion is not greater than 10—20%, and the yield of the products remains almost unchanged during the further exposure of the reaction mixtures over 2 months. In these cases, the most probable reason for the low yield of the products is their hydrolysis with water, which is formed during the reaction and retained in the reaction mixture due to the reaction with hydroxyl groups of the reagents. The reactions of **1a,b** with **3** in the presence of anhydrous K_2CO_3 occur with the complete conversion of the starting compounds over 3 days in the case of **1a** and over 2 weeks in the case of **1b**. Thus, as already mentioned,[1] the rate of the solid-state reaction of

Translated from *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 12, pp. 2240—2243, December, 1997.

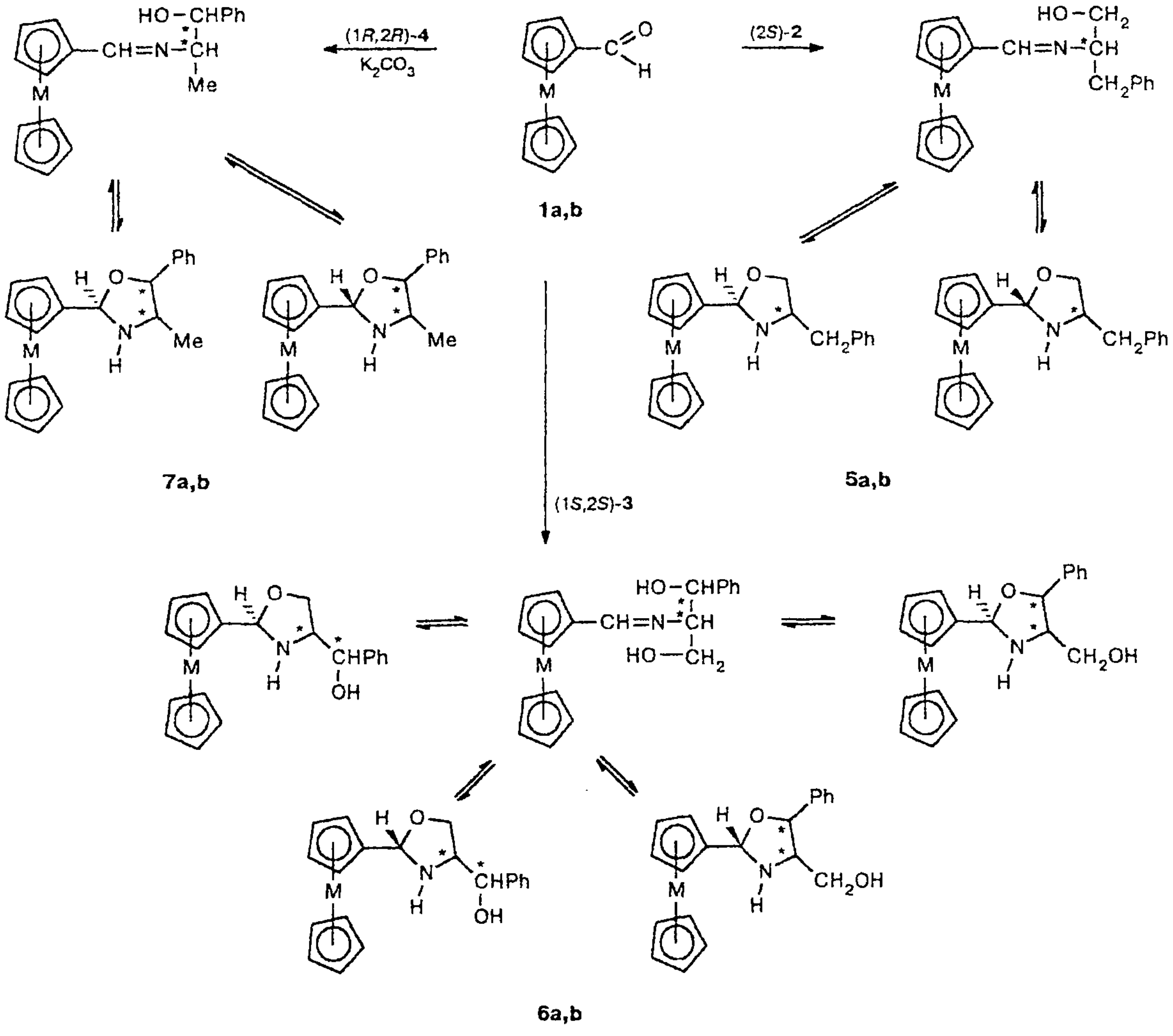
1066-5285/97/4612-2124$18.00

formylruthenocene with **3** is less than that for its ferrocenyl analog.

We have previously shown[1] that both free amines and their salts in the presence of anhydrous K_2CO_3 can be used in the solid-state synthesis of Schiff's bases. We supplemented these data with the solid-state reactions of (1*R*,2*R*)-norpseudoephedrine hydrochloride (**4**) with organometallic aldehydes **1a,b** in the presence of K_2CO_3. In this case, ferrocenylaldehyde also reacts substantially more rapidly than its ruthenium analog: in the case of the reaction of **1a** with **4** at ~20 °C, the complete conversion of the reagents is achieved over 3—4 days, while in the case of the reaction of compound **1b** with **4**, it achieves for 2 weeks.

It is known that in solutions of the products of the reactions between aldehydes and amino alcohols, the tautomeric equilibrium between open-chain and cyclic compounds (*i.e.*, between Schiff's bases and oxazolidines) is established, whose position depends on the time, temperature, and the type of the solvent.[5—7] Based on this fact, it should be expected that the solid-state reactions of chiral compounds **2**—**4** containing the β-hydroxyl group with aldehydes **1a,b** result in the formation of a mixture of the corresponding imines and stereoisomeric oxazolidines. In fact, the ^{1}H NMR spectra of solutions of the solid products of these reactions in both $CDCl_3$ and C_6D_6 showed the formation of three- (for amines **2** and **4**) and five-component (for **3**) mixtures consisting, in each case, of imine and diastereomers of the corresponding oxazolidines (Scheme 1). The ratio of components of the mixtures was determined from the integral intensities of the well-resolved signals of the ring H(2) atoms of oxazolidines (5—5.5 ppm) and the aldiminic proton (~8 ppm). The ^{1}H NMR spectra of the mixtures of products **5**—**7** in $CDCl_3$ show that the overall fraction of oxazolidines in the solution in-

Scheme 1



M = Fe (**a**), Ru (**b**)

Table 1. Relative content of imine and oxazolidines in solutions of compounds 5—7 in $CDCl_3$

Compound	Content of imines (%)[a] [δ][b]	Content of oxazolidines (%)[a] [δ][c]
5a	92 [7.94]	3 [5.36] : 5 [5.20]
5b	80 [7.84]	7 [5.17] : 13 [5.08]
6a	45 [8.18]	17 [5.68] : 27 [5.39] : 10 [5.28] :1[d]
6b	21 [8.10]	25 [5.53] : 41 [5.18] : 12 [5.11] :1[d]
7a	53 [8.20]	34 [5.65] : 13 [5.58]
7b	27 [8.16]	54 [5.49] : 19 [5.33]

[a] Determined from the ratio of integral intensities of the aldiminic proton and H(2) of diastereomeric oxazolidines. [b] Chemical shift of the aldiminic proton. [c] Chemical shift of H(2) of the oxazolidinic cycle. [d] Signals of the fourth diastereomer were not assigned because of its low quantities.

Table 2. Melting points and microanalysis data for compounds 5—7

Compound	M.p. /°C	Found/Calculated (%)			Molecular formula
		C	H	N	
5a	110—113	67.70 67.43	6.23 6.22	3.88 3.93	$C_{20}H_{21}FeNO \cdot 0.5H_2O$
6a	134—136[a]	57.03 56.90	5.04 5.01	3.23 3.22	$C_{20}H_{21}FeNO_2 \cdot 0.6CHCl_3$
7a	127—129	65.63 65.77	6.29 6.35	3.74 3.83	$C_{20}H_{21}FeNO \cdot H_2O$
5b	133—134	60.69 60.51	5.27 5.46	3.68 3.53	$C_{20}H_{21}NORu \cdot 0.25H_2O$
6b	143—144[a]	56.68 56.76	4.99 5.00	3.54 3.29	$C_{20}H_{21}NO_2Ru \cdot 0.15CHCl_3$
7b	88—91	60.38 60.51	4.97 5.46	3.66 3.53	$C_{20}H_{21}NORu \cdot 0.25H_2O$

[a] Recrystallized from the hexane—chloroform mixture.

creases on going from the ferrocene derivatives to the corresponding ruthenocene derivatives, and the maximum content of imine is observed in solutions of products **5a** and **5b** (Table 1). It also follows from the results of the spectral study that the tautomeric equilibrium in the solution is established stereoselectively with respect to the formation of diastereomeric oxazolidines.

However, the data on compounds 5—7 in solutions are insufficient to speculate about the structure of these compounds in the crystalline form. Previously, it has been shown using many examples[8,9] that in solutions the products of condensation of aldehydes with 1,2-amino alcohols are in cyclic-chain tautomeric equilibrium, while only one of these two types of compounds exists in the crystalline form. The narrow intervals of melting points of all six compounds 5—7 (Table 2) is evidence that the individual substances do exist in the cases studied in this work. The IR spectra of these compounds recorded in KBr contain, along with the absorption of OH groups in the 3000—3700 cm^{-1} region, an intense band of the C=N bond at 1655 cm^{-1}, which suggests that the solid products are Schiff's bases. However, the qualitative character of the IR spectra does not allow one to draw final conclusions on the structure of the products of the reactions of aldehydes with primary β-hydroxyamines.

Experimental

^1H NMR spectra were recorded on a Bruker-AMX-400 instrument. The optical rotation was measured on a Perkin—Elmer 141 polarimeter.

Ferrocenylaldehyde[10] and ruthenocenylaldehyde[11] were synthesized according to previously published procedures.

Solid-state reactions of aldehydes 1a,b with amines 2—4 (general procedure). Crystalline aldehyde (1 mmol) was mixed with amine or amine salt (1 mmol) and anhydrous K_2CO_3 (2 mmol for **3** and **4**), and the mixture was let to stand in the dark with stirring from time to time. The reaction run was monitored by ^1H NMR spectra. When the reaction ceased, hexane (hexane—$CHCl_3$ for **6a,b**) and K_2CO_3 were added to the mixture, the mixture was filtered off, and the solution was concentrated *in vacuo*. The yields of compounds 5—7 are quantitative, and their physicochemical parameters are presented in Tables 1 and 2.

This work was financially supported by the Russian Foundation for Basic Research (Project No. 97-03-93033a).

References

1. N. S. Khruscheva, N. M. Loim, and V. I. Sokolov, *Izv. Akad. Nauk, Ser. Khim.*, 1997, 2056 [*Russ. Chem. Bull.*, 1997, **46**, 1952 (Engl. Transl.)].
2. N. S. Khruscheva, N. M. Loim, E. V. Vorontsov, and V. I. Sokolov, *Izv. Akad. Nauk, Ser. Khim.*, 1994, 2250 [*Russ. Chem. Bull.*, 1994, **43**, 2130 (Engl. Transl.)].
3. N. S. Khruscheva, N. M. Loim, V. I. Sokolov, and V. D. Makhaev, *J. Chem. Soc., Perkin Trans. I*, 1997, 2425.
4. E. D. Bergmann, *Chem. Rev.*, 1953, **53**, 309.
5. F. Fulop, K. Pihlaja, J. Mattinen, and G. Bernath, *J. Org. Chem.*, 1987, **52**, 3821.
6. F. Fulop, G. Bernath, J. Mattinen, and K. Pihlaja, *Tetrahedron*, 1989, **45**, 4317.
7. F. Fulop, L. Lazar, G. Bernath, and F. G. Riddel, *Abstr. of 15th Intern. Congress on Heterocyclic Chemistry*, August 6—11, Taipei, PO1-062, 1995.
8. A. F. McDonah and H. E. Smith, *J. Org. Chem.*, 1968, **33**, 1.
9. M. E. A. Astudillo, N. C. J. Chokotho, T. C. Jarris, C. D. Johnson, C. C. Lewis, and P. D. McDonnel, *Tetrahedron*, 1985, **41**, 5919.
10. M. Sato, H. Kono, M. Shiga, I. Motoyama, and K. Hata, *Bull. Chem. Soc. Jpn.*, 1968, **41**, 252.
11. O. Hofer and K. Schlogl, *J. Organometal. Chem.*, 1968, **13**, 443.

Received June 18, 1997