ISSN 1070-3632, Russian Journal of General Chemistry, 2010, Vol. 80, No. 11, pp. 2263–2273. © Pleiades Publishing, Ltd., 2010.
Original Russian Text © V.M. Uvarov, E.S. Borovinskaya, D.A. de Vekki, V.P. Reshetilovskii, 2010, published in Zhurnal Obshchei Khimii, 2010, Vol. 80, No. 11, pp. 1799–1809.

Experimental Study and Simulation of Kinetics of Acetophenone Hydrosilylation with Diphenylsilane in the Presence of Rhodium Complexes in a Microreactor

V. M. Uvarov[a], E. S. Borovinskaya[a], D. A. de Vekki[a], and V. P. Reshetilovskii[b]

[a] *St. Petersburg State Institute of Technology, Moscovskii pr. 26, St. Petersburg, 190013 Russia*
e-mail: hydrosilation@newmail.ru

[b] *Technical University of Dresden, 01062, Dresden, Germany*

Received January 19, 2010

Abstract—The hydrosilylation of acetophenone with diphenylsilane in a microreactor in the presence of complexes $[Rh(cod)Cl]_2$ and $[Rh(CO)_2(\mu\text{-}Cl)]_2$ and (*R*)-(–)-*cis*-mirtanyl- and (*R*)-(+)-bornylamine in situ was studied, the kinetics simulation of the process was performed, and the multicriteria optimization of the process was carried out. The influence of the micro-mixing effect on the reaction rate was revealed. Best results in the microreactor were obtained for the $[Rh(cod)Cl]_2$–$BornylNH_2$ catalytic system. It was established that the formation of 1-phenylethanol and related enol silyl ethers are simultaneous competing reactions.

DOI: 10.1134/S1070363210110071

Microstructural reactors (microreactors) compose an innovative class of reaction equipment with the internal size generally not exceeding 2 mm. They have several advantages over conventional reactor, like higher safety, better control over the flow parameters, short time of diffusion of reactants, high specific surface area of interaction and efficiency of heat transfer [1, 2]. In addition, the research based on the microreactor technique allows the convergence of the conditions of the laboratory experiments to industrial processes and provides more opportunities for the study of chemical reactions and improve their efficiency [2]. These benefits contribute to high potential of microstructural reactors for use in the field of analytical and synthetic chemistry [2–9].

A highly effective method for the synthesis of organosilicon compounds is the catalytic hydrosilylation. At present, importance of this reaction increases due to new fields of application of organosilicon compounds like the synthesis of biologically active substances, flavorings, immobilized catalysts, insec-ticides, etc. Of particular interest is the hydrosilylation of ketones, an alternative to catalytic hydrogenation and reduction of C=O group by metal hydrides [10, 11].

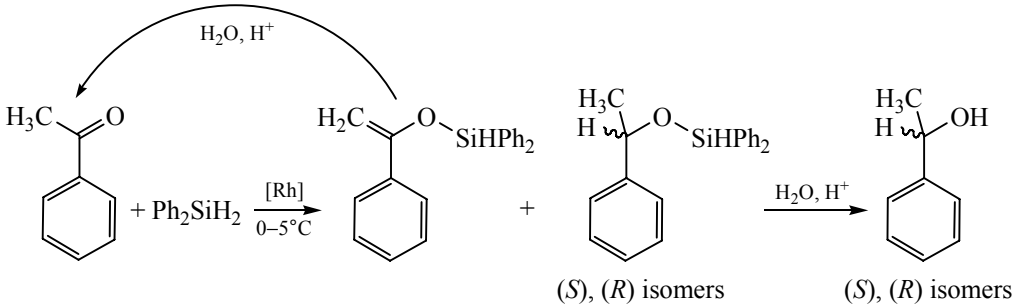
The high chemo- and stereoselectivity of hydrosilylation of C=O group is achieved using catalytic systems based on the rhodium(I) complexes with various nitrogen-containing chiral ligands. A disadvantage of the ligands of this type is relative complexity of their synthesis and the low rate of the hydrosilylation on such catalysts [12, 13].

An approach to solving this problem is to use the nitrogen-containing ligands based on available natural monoterpenes [14–17]. At the same time, hydrosilylation using microreactor technique may result in increased rate and selectivity of the process. Todayit is known that the hydrosilylation of alkenes and alkynes can be successfully carried out in the microstructured reactor [18].

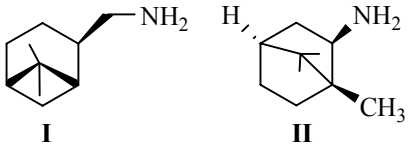
In this regard, we considered it important and interesting to study the reaction of liquid-phase hydrosilylation in the presence of rhodium complexes and chiral nitrogen-containing monoterpenes as ligands in a flow microreactor.

Description of the reaction system. The hydrosilylation of acetophenone with diphenylsilane is used often as a model reaction for estimating effectiveness of rhodium catalysts and studying the effect of various

conditions on the hydrosilylation of ketones [13, 19, 20]. The reaction products are 1-phenylethanol and acetophenone enol silyl ethers. The subsequent hydrolysis of the mixture of products leads to the formation of 1-phenylethanol (*S*)- and (*R*)-isomers and regeneration of the parent ketone.



As a pre-catalysts of the process the complexes $[Rh(cod)Cl]_2$ and $[Rh(CO)_2(\mu\text{-}Cl)]_2$ were selected, which have high catalytic activity in hydrosilylation of ketones and are used traditionally as pre-catalysts for the reactions of this type [13, 15]. The ligands used in this work were the industrially available nitrogen-containing derivatives of mono- and bicyclic terpenes, (*R*)-(–)-*cis*-mirtanylamine ($MyrtNH_2$, **I**) and (*R*)-(+)-bornylamine ($BornylNH_2$, **II**) that differ by the distance between the coordinating nitrogen atom and asymmetric center.



I **II**

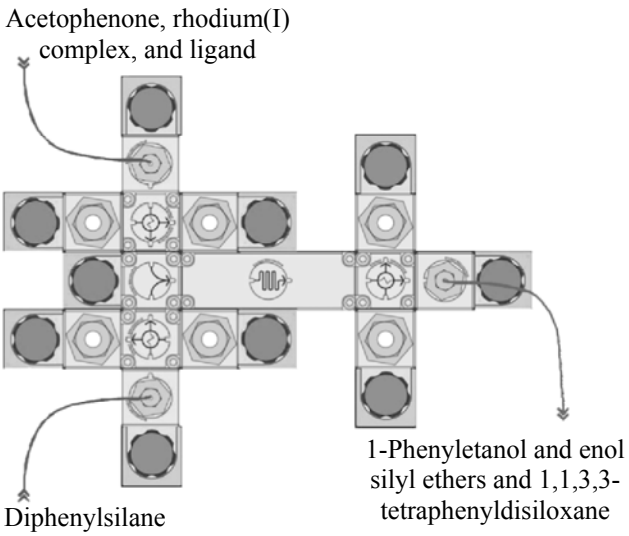


Fig. 1. Scheme of the installation for hydrosilylation of acetophenone with diphenylsilane in a microstructured reactor.

The formation of the catalytic system was performed by adding respective amine in situ, since the interaction of rhodium complex with the amine proceeded rapidly enough [15, 21], and the complex formed was not inferior by its catalytic properties to one synthesized in advance. Technologically this is significantly simpler because it allows avoiding the laborious stage of the synthesis of the complex proper [15]. In our experiments we used the amine in excess from 2.1 to 10-fold with respect to the complex, since it is well known [22–25] that the introduction of 2–13-fold molar excess of chiral ligand in situ can increase asymmetric induction. The acetophenone conversion in a certain time period was taken as a measure of the catalytic activity of the system.

Research installation. The microreactor setup for the hydrosilylation comprises individual modules placed on the assembling plate and having standard interfaces to provide the flexibility of the reactor at its use in the desired reaction conditions (Fig. 1) [3].

The microreactor was filled with anhydrous THF and cooled to 0°C using micro heat exchangers and a thermostat. The reagents are fed into the micro heat exchangers for cooling to 0°C, and then passed in a micromixer, in which each stream is divided into many layers passing the flat channels of 70 μm thickness. Then the layers are directed to mixing. The resulting reaction mixture enters the microreactor, which is a temperature-controlled thin tube of 80 μm inner diameter, the typical residence time of the reaction mixture is 15 min. At the reactor output the product was sampled to determine the acetophenone conversion and the reaction chemoselectivity by means of ^1H NMR spectroscopy. Then the reaction mixture enters the refrigerated container, where the hydrolysis

Hydrosilylation of acetophenone with diphenylsilane in the microreactor and the mixing reactor

Complex	Ligand (L)	L:Rh	Conversion of acetophenone, %				Selectivity, %				Yield,[a] %				Yield,[b] %
			microreactors, 15 min	mixing reactor, min			microreactors, 15 min	mixing reactor, min			microreactors, 15 min	mixing reactor, min			microreactors, 15 min
				15	30	60		15	30	60		15	30	60	
$[Rh(cod)Cl]_2$	–	–	**82**	**65**	84	95	**82**	**86**	81	80	**67**	**56**	68	77	6
	$BornylNH_2$	2.1	65	–	–	92	73	–	–	70	47	–	–	65	13
		5	61	–	–	76	78	–	–	68	48	–	–	52	13
		10	53	–	–	92	71	–	–	71	38	–	–	66	13
	$MyrtNH_2$	2.1	**50**	**42**	–	83	**67**	**68**	–	62	**33**	**29**	–	52	12
		5	**56**	**18**	–	74	**60**	**72**	–	69	**34**	**12**	–	51	12
		10	40	–	–	36	90	–	–	78	36	–	–	28	16
$[Rh(CO)_2(\mu\text{-}Cl)]_2$	–	–	**100**	**80**	80	81	**90**	**73**	73	70	**90**	**58**	58	57	6
	$BornylNH_2$	2.1	60	–	–	74	15	–	–	66	9	–	–	49	20
		5	12	–	–	70	73	–	–	34	9	–	–	23	22
		10	12[c]	–	–	22	75[c]	–	–	57	9[c]	–	–	13	4
	$MyrtNH_2$	2.1	41	–	–	85	21	–	–	27	9	–	–	23	30
		5	9	–	–	80	50	–	–	33	5	–	–	26	5
		10	8	–	–	15	62	–	–	56	5	–	–	8	5

[a] Yield of 1-phenylethanol silyl ether according to ^1H NMR spectrum. [b] Yield of the products of dehydrocondensation (tetraphenyldisiloxane and other siloxanes), according to ^1H NMR spectroscopy. [c] Reaction duration 35 min.

of the formed silyl ether is carried out to determine its enantiomeric composition.

Experimental research. The hydrosilylation of acetophenone with diphenylsilane in the microreactor in the presence of rhodium catalysts proceeds in accordance with the above scheme. Carrying out the reaction in aerobic conditions lead to the additional appearance in the ^1H–^{29}Si 2D NMR spectrum of the signals at δ_H 5.67 ppm and δ_{Si} –19.21 ppm, corresponding to SiH group of 1,1,3,3-tetraphenyldisiloxane. 1,1,3,3-Tetraphenyldisiloxane is a typical product of catalytic conversion of diphenylsilane at the hydrosilylation in a non-inert atmosphere in a traditional mixing reactor [15, 26], and its formation is a result of the reaction competing with the hydrosilylation.

$$Ph_2SiH_2 \xrightarrow{[Rh],\,[O]} HPh_2Si{-}O{-}SiPh_2H \xrightarrow{H^+,\,H_2O} \text{Polysiloxanes.}$$

Yield of tetraphenyldisiloxane in the microreactor depends considerably on the applied catalytic system (see the table). Use of $[Rh(cod)Cl]_2$ or $[Rh(CO)_2(\mu\text{-}Cl)]_2$ in the absence of amines gives disiloxane in only 6% yield, whereas the catalytic system based on $[Rh(cod)Cl]_2$ and amines added in situ leads to a two-fold increase in the yield. Unlike cyclooctadiene catalytic system, the yield of tetraphenyldisiloxane with $[Rh(CO)_2(\mu\text{-}Cl)]_2$ depends on the structure and the amount of added amines and reaches its maximum value (30%) when the $[Rh(CO)_2(\mu\text{-}Cl)]_2$: $MyrtNH_2$ ratio equal 1 : 2.1. The yield of tetraphenyldisiloxane in traditional mixing reactor is by 2–5% higher than in microreactors [15]. Increasing the reaction duration has practically no effect on the siloxane yield.

The catalytic system based on $[Rh(cod)Cl]_2$ exhibits higher activity in hydrosilylation in the microreactor compared with the traditional one. The acetophenone conversion after 15 min in the presence of

$[Rh(cod)Cl]_2$ without amines is 82% in the microreactor and only 65% in the mixing reactor (see the table). In the traditional mixing reactor the ketone conversion reaches 84% only after 30 min, which is close to the conversion in the microreactor in 15 min, and 60 min is required to increase it to 95%.

The reaction chemoselectivity achieved in the microreactor within 15 min is identical numerically with the conversion of acetophenone (see the table), the yield of 1-phenylethanol silyl ether is 67%. In the traditional reactor the chemoselectivity in 15 min is somewhat higher than in the microreactor, but the yield of product is less than 11%. The increase in the reaction duration in the mixing reactor to 60 min leads to an increase in the 1-phenylethanol silyl ether yield to 77%, while chemoselectivity remains virtually unchanged.

Introducing in situ of an amine in the catalytic system based on $[Rh(cod)Cl]_2$ causes a decrease in the reaction activity and selectivity compared to the hydrosilylation without amines both in the microreactor and in the traditional reactor.

The acetophenone conversion achieved in the microreactor in 15 min in the presence of 2.1-fold and 5-fold amount of $MyrtNH_2$ is 50 and 56% respectively against 42 and 18% in the traditional reactor (see the table). That is, the catalytic activity of $[Rh(cod)Cl]_2$–$MyrtNH_2$ system in the microreactor is higher than in a traditional reactor. Increasing the excess to 10-fold leads to further decrease in the acetophenone conversion, which is in the microreactor does not exceed 40%.

Bornylamine inhibites the reaction less than mirtanylamine does (see the table). The conversion of acetophenone in the presence of bornylamine at a $[Rh(cod)Cl]_2$: $BornylNH_2$ ratio equal to 1: 2.1 and 1: 5 is 65 and 61% respectively, and 10-fold excess of $BornylNH_2$ leads to an even greater decrease in the ketone conversion (53%).

Selectivity of the 1-phenylethanol silyl ether forma-tion in the presence of the $[Rh(cod)Cl]_2$ complex and 2.1-fold amount of $MyrtNH_2$ both in microreactor, and in the mixing reactor after 15 min is 67%, that is, it is by 15% less than in the absence of $MyrtNH_2$. The increase in the amount of amine to 10-fold shows a positive effect on the reaction chemoselectivity in the microreactor, extending it to 90%. In the case of conventional reactor, a 10-fold excess of $MyrtNH_2$ also leads to an increase in selectivity, which reaches the value obtained in the reaction without adding amine (78%).

Yield of 1-phenylethanol silyl ether in the microreactor is little dependent on the amount of $MyrtNH_2$ in the catalytic system (see the table), whereas in the traditional reactor at increase in $MyrtNH_2$ concentration the yield decreases.

The hydrosilylation of acetophenone in the presence of $BornylNH_2$ proceeds more selectively than with $MyrtNH_2$. The chemoselectivity in the microreactor at the $[Rh(cod)Cl]_2$: $BornylNH_2$ ratio 1 : 5 is 78%. The use of amine both in higher and lower concentration produces virtually no effect on chemoselectivity, which is 73% and 71% for 2.1- and 10-fold $BornylNH_2$ excess, respectively. The yield of 1-phenylethanol silyl ether in the microreactor decreases only in going from 5-fold to 10-fold amount of $BornylNH_2$ (see the table). It is interesting to note that in the traditional reactor the chemoselectivity after 60 min does not depend on the amount of $BornylNH_2$ (~70%) and is comparable with the selectivity in the microreactor after 15 min. The exception is the ratio of $[Rh(cod)Cl]_2$: $BornylNH_2$ equal to 1:5, at which the selectivity is by 10% less than in the microreactor (see the table). That is, the selectivity of the reaction is almost independent of the content of $BornylNH_2$ both in the microreactor and in the traditional mixing reactor.

In the microreactor the catalytic system based on $[Rh(CO)_2(\mu\text{-}Cl)]_2$ in the absence of amines is more active and selective than the system containing $[Rh(cod)Cl]_2$. The acetophenone conversion in the case of $[Rh(CO)_2(\mu\text{-}Cl)]_2$ is by 18% higher than in the presence of $[Rh(cod)Cl]_2$ (see the table), the selectivity of the reaction with the carbonyl complexes is higher than in the presence of $[Rh(cod)Cl]_2$. In the traditional reactor in the presence of carbonyl complex both conversion (80–81%) and the reaction chemoselectivity (70–73%) are lower than in the microreactor and practically do not depend on the reaction duration (15–60 min), whereas at the hydrosilylation with the cyclooctadiene complex an increase in conversion with time is observed.

The mirtanyl- and bornylamines introduced in situ in the catalytic carbonyl-containing system reduce the activity of the system compared with the activity in the absence of amine, as was in the case when $[Rh(cod)Cl]_2$ was used as a pre-catalyst. However, the activity of the $[Rh(CO)_2(\mu\text{-}Cl)]_2$–amine system was lower than that of

the systems based on $[Rh(cod)Cl]_2$. This occurs at the hydrosilylation both in the microreactor and in the traditional reactor. This probably is connected with the irreversible destruction of the catalytically active carbonyl metallocomplex intermediate (or the true catalyst) as a result of its reduction, which is observed only in this catalytic system.

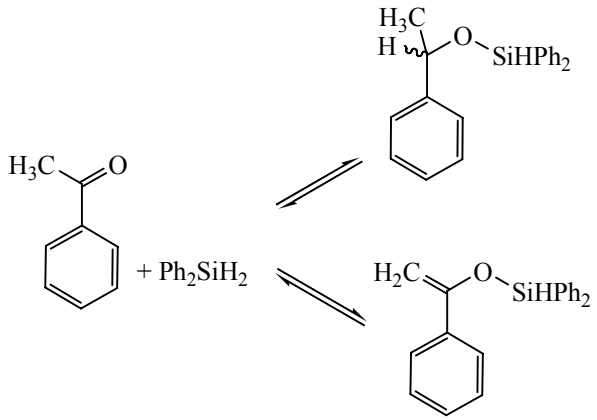
The maximum activity of the catalytic system based on $[Rh(CO)_2(\mu\text{-}Cl)]_2$ at carrying out the reaction in the microreactor is achieved in the presence of $BornylNH_2$ at the complex : amine ratio 1 : 2.1 (60% conversion), but the selectivity is extremely low (15%). Replacing $BornylNH_2$ by $MyrtNH_2$ at the same ratio of complex to amine leads to reduced activity of the catalytic system, but increases selectivity to 21% (see the table). At the same time in the traditional reactor the system $[Rh(CO)_2(\mu\text{-}Cl)]_2$–$MyrtNH_2$ shows higher activity. Conversion of acetophenone in the microreactor at the $[Rh(CO)_2(\mu\text{-}Cl)]_2$: ligand ratio 1 : 5 is ~5 times less than at the ratio 1 : 2.1.

A 10-fold amount of $BornylNH_2$ virtually deactivates catalysts (after 15 min no formation of products is observed), and in the case of $MyrtNH_2$ the acetophenone conversion did not exceed 8%. Thus, the catalytic activity of the systems based on $[Rh(CO)_2(\mu\text{-}Cl)]_2$ and amines is not only lower than that of the systems based on $[Rh(cod)Cl]_2$, but shows greater sensitivity to the content of amine. Apparently, amine increases stability of the catalytic system, preventing the process of reduction.

The selectivity of formation of 1-phenylethyl silyl ether in the microreactor at the use of the catalytic system based on $[Rh(CO)_2(\mu\text{-}Cl)]_2$ and an amine is lower than at the hydrosilylation with the $[Rh(cod)Cl]_2$–amine system. Minimum chemoselectivity corresponds to the catalyst : amine ratio equal to 1 : 2.1 and the maximum, to the ratio 1 : 10. In addition, at low concentration of amine a higher selectivity is observed in the presence of $MyrtNH_2$, but with an increase in the amine quantity the selectivity of hydrosilylation is higher in the presence of the system containing $BornylNH_2$. The hydrosilylation in the traditional reactor in the presence of a catalytic system containing $BornylNH_2$ proceeds more selectively than with the system based on $MyrtNH_2$ although the general trend of increasing chemoselectivity with increasing amine concentration in the mixture is retained. It is noteworthy that in most cases the selectivity of the reaction after 15 min in the microreactor at the use of $[Rh(CO)_2(\mu\text{-}Cl)]_2$ and amines is higher than after 60 min in the traditional reactor. At the same time the yield of 1-phenylethanol silyl ether in the presence of $[Rh(CO)_2(\mu\text{-}Cl)]_2$ and amine depends only slightly on the structure and quantity of the nitrogen-containing compounds (see the table), due both to low acetophenone conversion and reaction selectively.

Asymmetric induction at the acetophenone hydrosilylation with diphenylsilane in the presence of rhodium complexes with chiral amines in the microreactor does not exceed 8% . In all cases mainly 1-(*R*)-phenylethanol is formed, as is the case of hydrosilylation in the traditional mixing reactor [15]. The maximum enantiomeric excess observed in the presence of $[Rh(cod)Cl]_2$ with $BornylNH_2$ in the 1 : 10 ratio. A decrease in amount of $BornylNH_2$ reduces the enantiomeric excess to 5 and 2% *ee* at 5- and 2.1-fold excess of amine relative to the complex respectively. The enantiomeric excess achieved with the catalytic system based on rhodium carbonyl complex is 5% *ee* at carrying out the reaction in either the microreactor or traditional mixing reactor (the ratio $[Rh(CO)_2(\mu\text{-}Cl)]_2$: $BornylNH_2$ = 1: 2.1). Note that the asymmetric induction in the microreactor in 15 min can be achieved only in the presence of $BornylNH_2$, whereas in the traditional mixing reactor both amines are "working" [15]. The difficulty of achieving asymmetric induction in the presence of $MyrtNH_2$ may be due to the presence a methylene hinge in its structure allowing free rotation of the ligand chiral center around the metal atom.

Simulation of the process. The process of hydrosilylation of acetophenone with diphenylsilane is a homogeneous reaction. Its kinetics can be simulated in the framework of the formal mathematic description. In this regard, in the first stage of the simulation we assumed the possible reaction schemes and their formalization. Then the differential equations were generated, the inverse kinetic problem was solved, and the multicriteria optimization of process wasperformed using the Kinetic software package [27] designed to simulate the kinetics of chemical processes. The transformation of diphenylsilane in 1,1,3,3-tetraphenyldisiloxane was not taken into account at the simulation because its rate on the average is 3–15 times lower than the rate of the formation of the desired product. The increase in the rate of this process was observed only at the almost complete absence of the target product, that is, in the conditions, which are not of interest for the hydrosilylation.



The kinetic curves for the reaction of acetophenone with diphenylsilane (Figs. 2–5) usually are characterized by the presence of two steps with different rate. The first section corresponds to the hydrosilylation proceeding with a high rate, therewith in the reaction medium there is a sufficient amount of the reactants and catalytically active particles. The second section corresponds to slowing down of the reaction due to the decrease in the concentration of reactants in the mixture and possible deactivation of the catalyst.

The result of simulation of the process kinetics in the presence of the complexes $[Rh(cod)Cl]_2$ or $[Rh(CO)_2(\mu\text{-}Cl)]_2$ with various amounts of $MyrtNH_2$ or $BornylNH_2$ are plotted in Figs. 2–5 where the kinetic curves are obtained by simulation while the dots correspond to experimental observations. In this case the error of calculations is within the experimental errors, which confirms the authenticity of the calculations. The analysis of the kinetic curves of the process taking into account the published data [28] and comparing the simulation results with the regularities of chemical reactions of various types suggests that in this case the formation of 1-phenylethanol and enol silyl ethers is the result of two parallel competitive reactions.

The results obtained by simulation allow us the estimation of the difference in the rates of hydrosilylation in the traditional mixing reactor and in the microreactor. Owing to the effect of micro mixing, in the microreactor in the absence of amines both the catalytically active complexes show a fairly high rate of the process in the first section of the kinetic curve (Figs. 2–5). The rhodium(I) carbonyl complex by its activity exceeds cyclooctadiene complex both in the traditional reactor, and in the microreacor, the best result is observed in the presence of $[Rh(CO)_2(\mu\text{-}Cl)]_2$ at carrying out the reaction in the microreactor (acetophenone conversion 100%, Figs. 3, 5).

As already noted, the amine addition decreases the catalytic properties of cyclooctadiene complex, even to a greater extent than of the carbonyl complexes. A catalytic system based on $[Rh(CO)_2(\mu\text{-}Cl)]_2$ in this case is not selective, as practically directs the reaction entirely to the formation of enol silyl ether and ceases to "work" towards the formation of the desired product (see the table). This experimental fact agrees with the assumption of parallel competing reactions. Application of microreactor as compared to the traditional reactor, for the hydrosilylation in the presence of both complexes and amines, initially increases the reaction rate. This is more expressed with the catalytic system $[Rh(cod)Cl]_2$–$MyrtNH_2$ (Fig. 2). Increase in the amount of the ligand added in situ in the case of this system accelerates the hydrosilylation in the

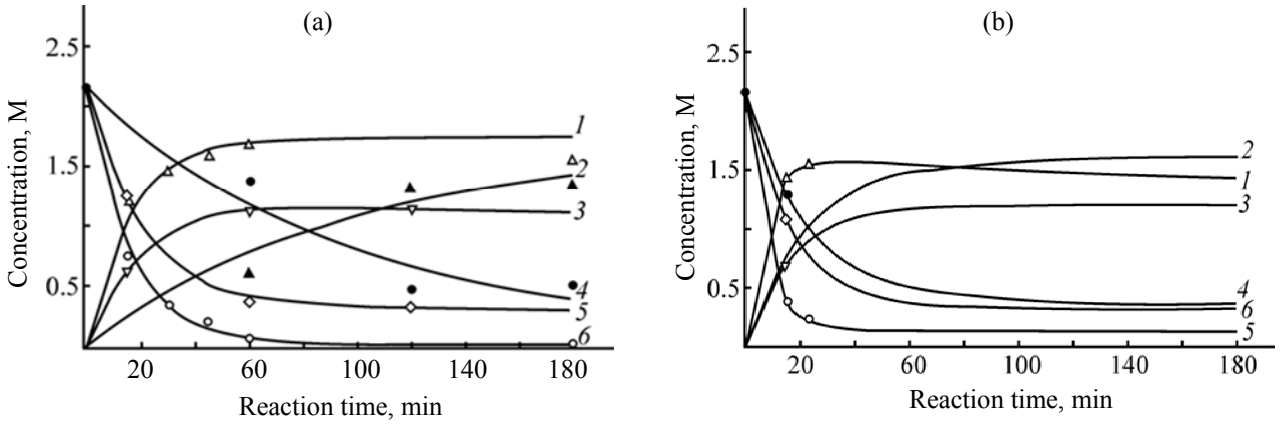


Fig. 2. Kinetic curves of the changes in the concentration of acetophenone and accumulation of 1-phenylethanol silyl ester in the (a) traditional reactor and (b) microreactor at the varied $[Rh(cod)Cl_2]_2$: $MyrtNH_2$ ratio (dots correspond to experimental data, lines are obtained by simulation): (*1, 6*) 1:0, (*2, 4*) 1:10, (*3, 5*) 1:2.1; (*1–3*) silyl ether, (*4–6*) acetophenone.

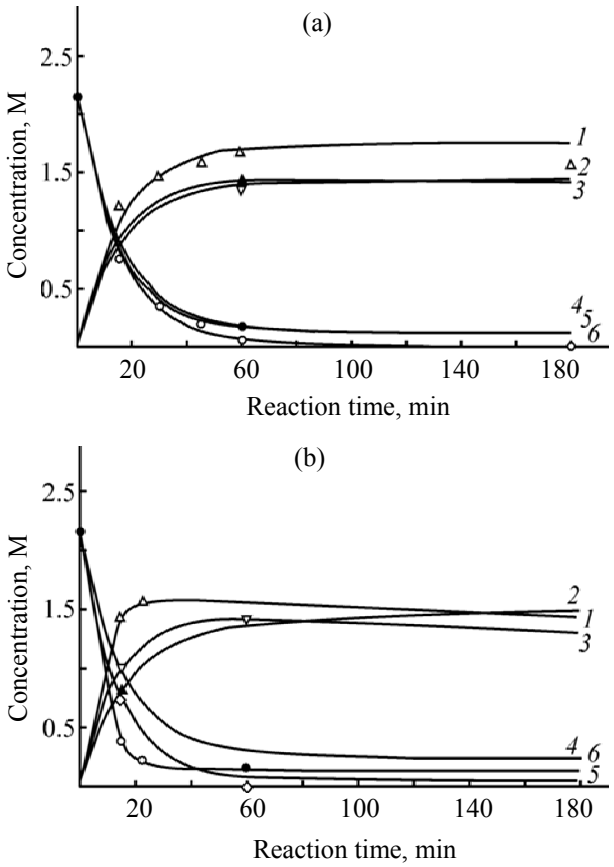


Fig. 3. Kinetic curves of the changes in the concentration of acetophenone and accumulation of 1-phenylethanol silyl ether in the (a) traditional reactor and (b) microreactor at the varied ratio of $[Rh(cod)Cl_2]_2$: $BornylNH_2$ (dots correspond to experimental data, lines are obtained by simulation): (*1, 6*) 1:0, (*2, 4*) 1:10, (*3, 5*) 1:2.1; (*1–3*) silyl ether, (*4–6*) acetophenone.

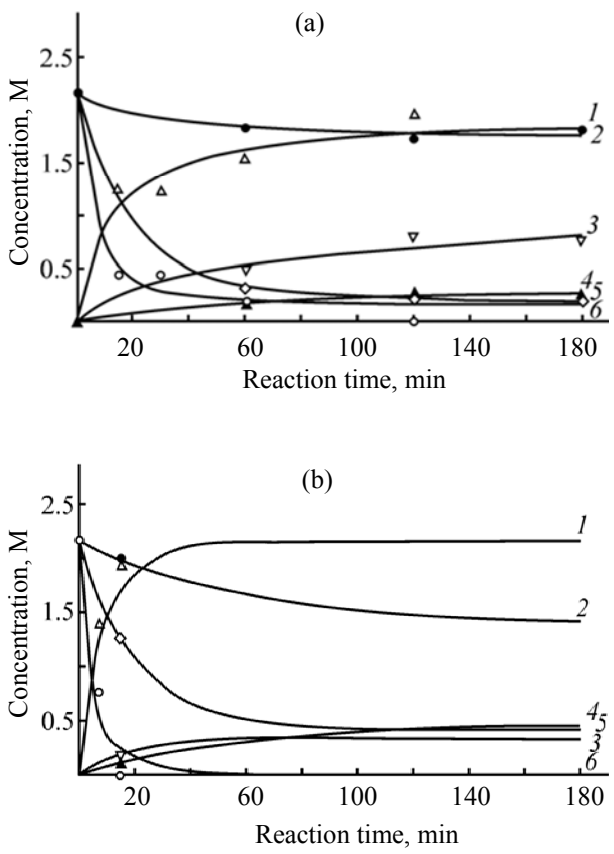


Fig. 4. Kinetic curves of the changes in the concentration of acetophenone and accumulation of 1-phenylethanol silyl ether in the (a) traditional reactor and (b) microreactor at the varied ratio of $[Rh(CO)_2(\mu\text{-}Cl)]_2$: $MyrtNH_2$ (dots correspond to experimental data, lines are obtained by simulation): (*1, 6*) 1:0, (*2, 4*) 1:10, (*3, 5*) 1:2.1; (*1–3*) silyl ether, (*4–6*) acetophenone.

microreactor (Fig. 2), but with other catalytic systems, the reaction rate decreased with increasing concentration of amine both in the microreactor and in the traditional reactor (Figs. 3–5).

The model obtained is quite adequate to allow us the estimation of the optimum conditions of process, including the area where the experimental data are lacking. For this purpose, based on the principles of multicriteria optimization and following the procedure described in [31], we have formulated a generalized criterion for finding the optimal mode of hydrosilylation in the microreactor and the mixing reactor, combining the maximum yield of target product and the minimum yield of silyl enol ether, at a sufficiently high value of acetophenone conversion. We also included in the consideration the duration factor, the structure and the ratio of metallocomplex and amine. Optimal conditions were determined from the analysis of the absolute value of the so-called generalized desirability index *D*.

According to multicriteria optimization, the best complex for carrying the reaction in the presence of amine both in the traditional reactor and in the microreactor is $[Rh(cod)Cl]_2$. The best results are achieved in the microreactor in the presence of $[Rh(cod)Cl]_2$ and 10-fold amount of $MyrtNH_2$, D = 0.733 (Fig. 6), and the same complex with $BornylNH_2$ ranked second in efficiency (the complex : amine ratio is 1 : 5, D = 0.719). On the contrary, in the traditional reactor at the ratio of complex : amine = 1: 2.1 or 1: 10 the effectiveness of this complex in the presence of $BornylNH_2$ is higher (D = 0.646, and 0.658, respectively) than with $MyrtNH_2$ (D = 0.634–0.637).

The optimal conditions of the reaction, obtained from the analysis of simulation (an additional criterion

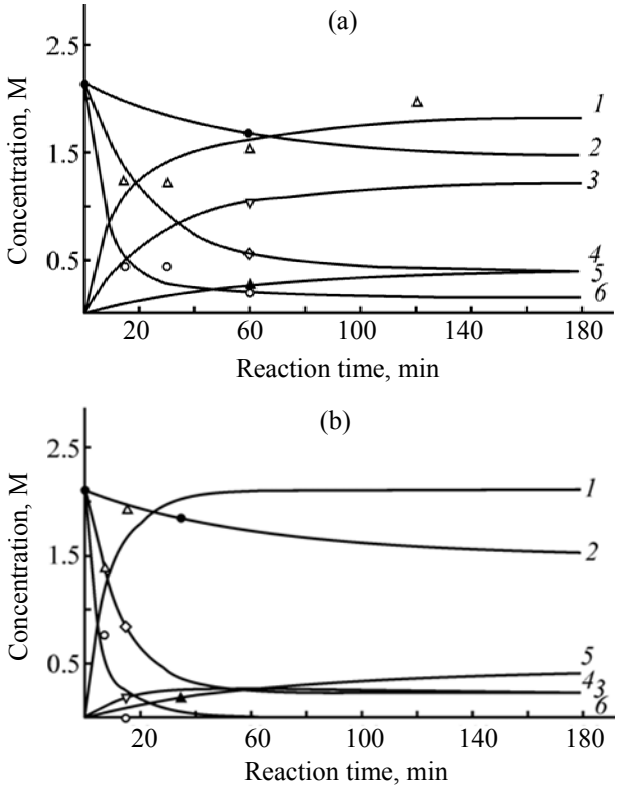


Fig. 5. Kinetic curves of the changes in the concentration of acetophenone and accumulation of 1-phenylethanol silyl ether in the (a) traditional reactor and (b) microreactor at the varied ratio of $[Rh(CO)_2(\mu\text{-}Cl)]_2$: $BornylNH_2$ (points correspond to experimental data, lines are obtained by simulation): (*1, 6*) 1:0, (*2, 4*) 1:10, (*3, 5*) 1:2.1; (*1–3*) silyl ether, (*4–6*) acetophenone.

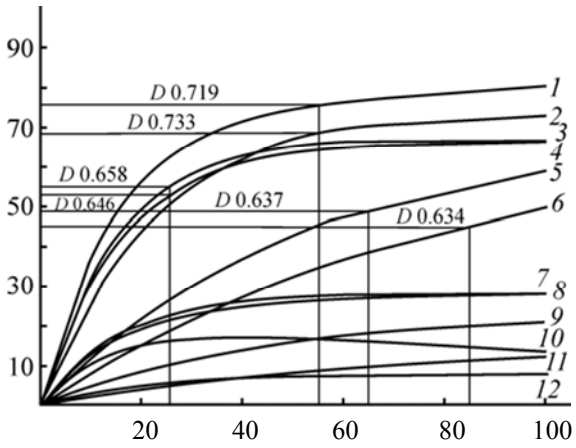


Fig. 6. Optimal regimes of hydrosilylation in the (*1, 2, 10, 12*) microreactor and (*3–9*) mixing reactors at the following catalyst : amine ratio: (*1, 5, 9, 10*) 1:5, (*2, 3, 6, 8, 11, 12*) 1:10, (*4, 7*) 1:2.1; (*1, 3, 4, 7, 8, 10*) $BornylNH_2$, (*2, 5, 6, 9, 11, 12*) $MyrtNH_2$; (*1–6*) yield of 1-phenylethanol silyl ether, (*7–12*) yield of silyl enol ether; *D* is generalized maximum desirability index.

is the maximum reaction rate in the first section of the kinetic curve) depend on the structure of the ligands and the definite technological task. The best results in the microreactor with $MyrtNH_2$ (see the ratio of $[Rh(cod)Cl]_2$: amine = 1 : 10) is achieved at the duration 55 min (Fig. 6): yield of 1-phenylethyl silyl ether is 68%, and of the byproduct, 7%. In turn, use of bornylamine (ratio $[Rh(cod)Cl]_2$: $BornylNH_2$ = 1 : 5), at duration 55 min provides a higher yield 1-phenylethanol silyl ether (75%) with more than 2 times greater amount of by-product (16%), which adversely affects the value of the generalized criterion, lowering it from the $D = 0.733$ to $D = 0.719$.

In the traditional mixing reactor the yield of the desired product with the best catalytic system is 54% after 25 min at a ratio of $[Rh(cod)Cl]_2$: $BornylNH_2$ equal to 1 : 10, 52% after 25 min at a ratio of $[Rh(cod)Cl]_2$: $BornylNH_2$ equal to 1: 2.1, and 49% after 65 min at the ratio of $[Rh(cod)Cl]_2$: $MyrtNH_2$, equal to 1 : 5 (Fig. 6). In the first case, the yield of silyl enol ether reaches 21%, in the second case 22%, while in the third case 18.0%.

Thus, depending on the technological and economic purposes, the application of multicriteria optimization allows the choice between the different optimal modes of hydrosilylation, advancing to the first place one or another criterion.

From the results of multicriteria optimization it can be concluded that the use of microreactors allows reaching higher reaction rates of hydrosilylation and, consequently, higher yields of the desired product, maintaining cost-effective level of selectivity.

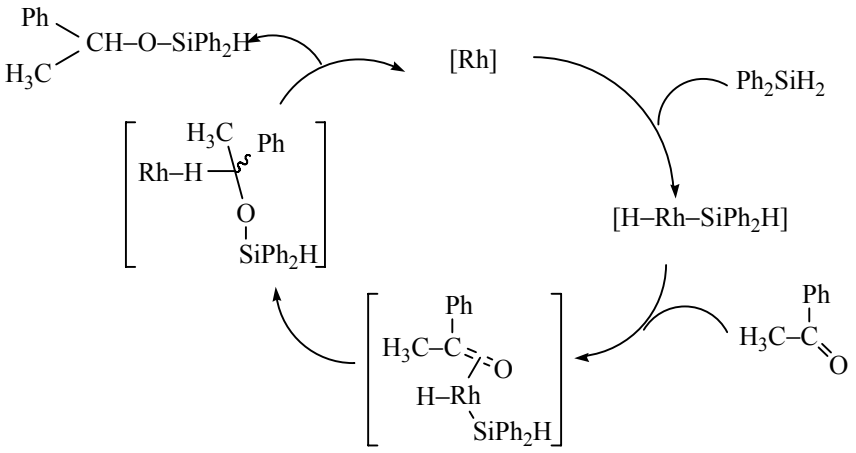
The mechanism of catalytic action of rhodium complexes. To identify the structure of catalysts used for the hydrosilylation, we investigated interaction of rhodium complexes with amines in C_6D_6 using NMR spectroscopy. The interaction of rhodium(I) complexes with amines is very fast, and after 5 min in the ^1H and ^{13}C 2D NMR spectra were observed the characteristic signals of NCH_2 and NCH groups of coordinated amines [δ_H 2.95 and 3.42 ppm, and δ_C 52.2 m (J_{RhC} = 35.2 Hz) and 61.5 m (J_{RhC} = 33.1 Hz) ppm for $MyrtNH_2$ and $BornylNH_2$ respectively]. In addition, the ^{13}C NMR spectrum of the carbonyl complex contains two doublets differing by intensity at δ_C 180–185 ppm (J_{RhC} =65.2 and 73.8 Hz, and J_{RhC} = 65.8 and

74.2 Hz for $MyrtNH_2$ and $BornylNH_2$ respectively), corresponding to two asymmetric CO groups of the new complex, *cis*-$[Rh(CO)_2(RNH_2)Cl]$. This allows us a suggestion that the first macrokinetic stage is the interaction of binuclear rhodium complexes with amine leading to the mononuclear complexes containing the coordinated amine:

$$1/2[Rh(LL')(\mu\text{-}Cl)]_2 + RNH_2 \rightarrow [Rh(LL')(RNH_2)Cl],$$

L = L '= CO; LL' = cod; R = mirtanyl or bornyl.

The modern schemes of the mechanism of Rh-catalyzed hydrosilylation of ketones are based on the mechanism proposed by Ogima [29]. This mechanism involves oxidative addition of diphenylsilane to the Rh(I) complex followed by the coordination of acetophenone and migration of silyl group to the oxygen atom of the coordinated acetophenone, resulting in the formation of a Rh–C bond. The final stage is the reductive elimination of the 1-phenylethanol silyl ether and regeneration of the catalyst.



Our corrections of this scheme relate primarily to the mechanism of formation of the enol silyl ether and establishing existence of the stage of enantiomeric differentiation. For example, Reyes et al. [28] suggest that the key stage of formation of the enol silyl ether is the β-elimination of proton in the siloxyalkyl intermediate. As to the enantiodifferentiation, it was shown in [30] that the ketone interacts with the coordinated silicon hydride, while the coordination of ketone to the rhodium atom does not occur.

The formation 1-phenylethanol silyl ether proceeds concurrently with the competing reaction generating the corresponding enol as a byproduct, which is in good agreement with the results of the kinetic-mathematical simulation. The higher rate of the process in the microreactor compared with the traditional reactor, the decrease in the rate of target reaction upon increase in the concentration of amine in the reaction medium, as well as the prevalence of the rate of enol silyl ether formation over the target reaction in the presence of $[Rh(CO)_2(\mu\text{-}Cl)]_2$ and amines may be partly due to the fact that micro-mixing facilitates the ketone and amine entering into the coordination sphere of rhodium atom and promotes the destruction of less stable intermediates.

The level of the stable activity of the complexes responsible for the formation of the desired product can be estimated from the selectivity. For example, in the case of the catalytic system $[Rh(CO)_2(\mu\text{-}Cl)]_2$–amine (including variation of their ratio in the traditional reactor), the selectivity falls to the range of 25 to 65%. In the microreactor the upper limit of the range can be increased to 73%, but the lower limit falls to 15%. The catalytic system based on $[Rh(cod)Cl]_2$ shows a more narrow range of selectivity both in the microreactor (60–90%), and in the traditional mixing reactor (62–78%). Thus, in the latter case, the selectivity of hydrosilylation in the traditional reactor increases to 78%, while in the microreactor up to 90%. Namely, it seems that in the microreactor the stabilization by the amine of the intermediate responsible for the formation of 1-phenylethanol silyl ether upon increasing the concentration of the amine occurs more effectively.

This all suggests that the coordination of ketone to the rhodium atom does occur, in contrast to the assumptions about the lack of such coordination [30]. Thus, a substantial positive effect at the use of microstructural reactor (as compared with the traditional mixing reactor) for the hydrosilylation in

the presence of rhodium catalyst is due to the acceleration of all stages of the catalytic cycle and the increased selectivity at the stage of transformation of the siloxyalkyl intermediate.

Thus, the experimental study of the reaction of the acetophenone hydrosilylation with diphenylsilane in the presence of rhodium complexes showed that this process in most cases proceeds more efficiently in the microreactor than in the traditional mixing reactor. Maximum catalytic activity and selectivity are observed in the presence of $[Rh(CO)_2(\mu\text{-}Cl)]_2$ without amines. Adding of amine to the complex in situ leads to a decrease in activity of the catalytic system and reaction selectivity, the best results were achieved with the $[Rh(cod)Cl]_2$–$BornylNH_2$ system. Enantioselectivity of hydrosilylation achieved in the microreactor is lower than in the traditional reactor, and the configuration of the formed isomer of 1-phenylethanol remains unchanged.

The mathematical modeling of the process in a microreactor and in traditional reactor at the assumption of two parallel reaction is in good agreement with experimental data and, thus, confirms the generally accepted reaction mechanism of acetophenone hydrosilylation with diphenylsilane. The multicriteria optimization of the process allowed the choice of the most effective catalytic system and optimum conditions for its use depending on the specific technological target.

EXPERIMENTAL

NMR spectra (1D, 2D, COSY, DEPT, HMBC, HSQC) were registered on Bruker WM-400 and DRX 500P instruments from solutions in $CDCl_3$ at the operating frequencies 400.13, 500.13 (^1H), 125.76 (^{13}C), and 99.35 (^{29}Si) MHz. The measurements were performed without additional reference compounds, the frequency was taken relatively to the signal of the deuterium-containing solvent.

The acetophenone hydrosilylation with diphenylsilane was carried out in a mixing reactor as described in [15], and in a microreactor according to the following procedure. The diphenylsilane cooled to 0°C (2.68 mmol) and a solution of 0.0215 mmol of a complex, 0.0–0.215 mmol of amine and 2.15 mmol of acetophenone in 0.25 ml of anhydrous THF cooled and kept at 0°C for 10 min with stirring were fed to the micro mixer at 0–5°C and then to the microreactor. After 15 min, the reaction mixture except the first and the last portions was collected in a receiver cooled to 0°C. From the mixture was taken a sample for the NMR investigation of the product conversion and the reaction selectivity, and then the mixture was hydrolyzed by adding 1 ml of methanol and, 1 h latter, of 5 ml of 1N HCl. The products were extracted with diethyl ether (2×20 ml), dried over Na_2CO_3, and analyzed to estimate the enantiomeric composition as in [15].

In the experiments were used methanol, diethyl ether, acetophenone, and THF of chemically pure grade, (*R*)-(–)-*cis*-mitrylamine from Aldrich, (*S*)-(+)-α-methoxy-α-trifluoromethylphenylacetyl chloride and diphenylsilane from Acros, (*R*)-(+)-borhylamine, $[Rh(cod)Cl]_2$ and $[Rh(CO)_2(\mu\text{-}Cl)]_2$ from Fluka, and silica gel 60 from Merck.

ACKNOWLEDGMENTS

This work was performed at a financial support of Russian Foundation for Basic Research (grant no. 09-03-00341a), St. Petersburg Government (grant MKH/15-05/005/), and the Program of DAAD (Leonard-Euler-Stipendium).

REFERENCES

1. Ehrfeld, W., Hessel, V., and Löwe, H., *Microreactors: New Technology for Modern Chemistry*, Weinheim: Wiley–VCH, 2000.
2. Borovinskaya, E.S. and Reshetilovskii, V.P., *Khim. Prom–t'*, 2008, no. 5, p. 1.
3. Borovinskaya, E.S., Mammitzsch, L., Uvarov, V.M., Schael, F., and Reschetilowski, W., *Chem. Eng. Technol*., 2009, vol. 32, no. 6, p. 919.
4. Hessel, V., Löwe, H., Müller, A., and Kolb, G., *Chemical Micro Process Engineering – Processing and Plants*, Weinheim: Wiley–VCH, 2005.
5. Haswell, S.J., Middleton, R.J., O'Sullivan, B., Skelton, V., Watts, P., and Styring, P., *Chem. Commun*., 2001, no. 5, p. 391.
6. Fletcher, P.D.I., Haswell, S.J., Pombo-Villar, E., Warrington, B H., Watts, P., Wong, S.Y.F., and Zhang, X., *Tetrahedron*, 2002, vol. 58, no. 24, p. 4735.
7. Bellefon, C., Tanchoux, N., Caravieilhes, S., Grenouillet, P., and Hessel, V., *Angew. Chem., Int. Ed*., 2000, vol. 39, no. 19, p. 3442.
8. Jähnisch, K., Hessel, V., Löwe, H., and Baerns, M., *Angew. Chem., Int. Ed*., 2004, vol. 43, no. 4, p. 406.
9. *Microreactors in Organic Synthesis and Catalysis*, Wirth, T., Ed., Weinheim: Wiley–VCH, 2008.

10. Yu, Z.-X., Wender, P.A., and Houk, K.N., *J. Am. Chem. Soc*., 2004, vol. 126, no. 30, p. 9154.
11. Yu, Z.-X., Cheong, P.H.-Y., Liu, P., Legault, C.Y., Wender, P.A., and Houk, K.N., *J. Am. Chem. Soc*., 2008, vol. 130, no. 8, p. 2378.
12. Helmchen, G., Krotz, A., Ganz, K.-T., and Hansen, D., *Synlett.*, 1991, no. 4, p. 257.
13. Marciniec, B., Maciejewski, H., Pietraszuk, C., and Pawluć, P., *Hydrosilylation. A Comprehensive Review on Recent Advances, Advances in Silicon Science*, Marciniec, B., Ed., Springer, 2009, vol. 1.
14. de Vekki, D.A., Uvarov, V.M., Reznikov, A.N., and Skvortsov, N.K., *Izv. Akad. Nauk, Ser. Khim*., 2008, vol. 57, no. 2, p. 594.
15. de Vekki, D.A., Uvarov, V.M., Skvortsov, N.K., and Reshetilovskii, V.P., *Zh. Obshch. Khim*., 2010, vol. 80, no. 1, p. 39.
16. Brunner, H., Störiko, R., and Nuber, B., *Tetrahedron: Asymmetry*, 1998, vol. 9, no. 3, p. 407.
17. Chelucci, G., Gladiali, S., Sanna, M.G., and Brunner, H., *Tetrahedron: Asymmetry*, 2000, vol. 11, no. 16, p. 3419.
18. Odedra, A., Geyer, K., Gustafsson, T., Gilmour, R., and Seeberger, P.H., *Chem. Commun*., 2008, no. 26, p. 3025.
19. Lin, G-Q., Li, Y-M., and, Chan, A.S.C., *Principles and Applications of Asymmetric Synthesis*, New York: Wiley, 2001.
20. Ojima, I. and Hirai, K., *Asymmetric Synthesis*, Morisson, J.D., Ed., New York: Academic Press, 1985, vol. 5.
21. Rollmann, L.D., *Inorg. Chim. Acta*, 1972, vol. 6, no. 1, p. 137.
22. Pavlov, V.A., *Usp. Khim*., 2001, vol. 70, no. 12, p. 1175.
23. Brunner, H., Becker, R., and Riepl, G., *Organometallics*, 1984, vol. 3, no. 9, p. 1354.
24. Brunner, H. and Kürzinger, A., *J. Organomet. Chem*., 1988, vol. 346, no. 3, p. 413.
25. Brunner, H. and Obermann, U., *Chem. Ber*., 1989, vol. 122, p. 499.
26. Brown-Wensley, K.A., *Organometallics*, 1987, vol. 6, no. 7, p. 1590.
27. Borovinskaya, E.S., *Candidate Sci. (Chem.) Dissertation*, St. Petersburg, 2008.
28. Reyes, C., Prock, A., and Giering, W.P., *Organometallics*, 2002, vol. 21, no. 3, p. 546.
29. Ojima, I., Kogure, T., Kumagai, M., and Horiuchi, S., *J. Organomet. Chem*., 1976, vol. 122, no. 1, p. 83.
30. Zheng, G.Z. and Chan, N.H., *Organometallics*, 1995, vol. 14, no. 1, p. 70.