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# Conformational Analysis, Spectral and Catalytic Properties of 1,3-Thiazolidines, Ligands for Acetophenone Hydrosilylation with Diphenylsilane

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**Abstract—**2-Aryl- and 2-furyl-4-carboxy-1,3-thiazolidines were synthesized. Their spectral properties were studied, and conformational analysis was performed. It was shown that they exist in solution as an equilibrium of neutral and zwitter-ion forms. The influence of the nature of substitutents and of their location in a benzene ring of thiazolidines as ligands of rhodium complexes on acetophenone hydrosilylation with diphenylsilane was examined. Thiazolidines containing donor substituents in the *para*-position of the benzene ring were found to be the most effective; maximal asymmetrical induction (55% *ee*) was reached in the presence of 2-(4-methoxyphenyl)-4-carboxy-1,3-thiazolidine.

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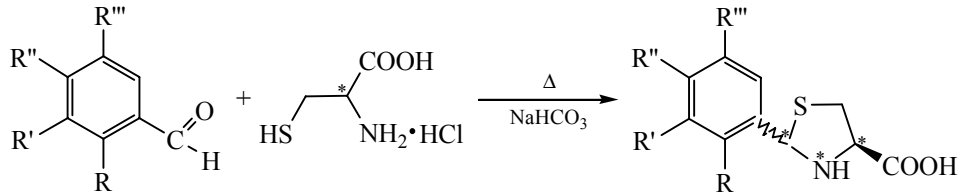
It was reported earlier [1–5] that asymmetrical hydrosilylation of acetophenone with diphenylsilane proceeds under nitrogen or argon atmosphere in the presence of $[Rh(COD)Cl]_2$ and monodentate thiazolidines *in situ* reaching maximal asymmetrical induction of 18.6%. On the other hand, it is known [6] that the presence of water traces at ketone hydrosilylation in the presence of $[Rh(COD)Cl]_2$ and diphosphines accelerates the reaction.

In this connection the study of acetophenone hydrosilylation with diphenylsilane in the presence of $[Rh(COD)Cl]_2$ and some 2-substituted 1,3-thiazolidines *in situ* under not inert atmosphere is of undoubtful interest. On the other hand, the extension of the series of thiazolidine compounds is of separate interest due to their chemo- and radioprotective properties and low toxicity [7–10].

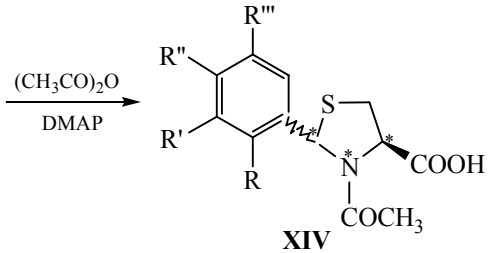
**Synthesis, conformational analysis, and spectral parameters of thiazolidines.** Synthesis of 2-aryl-(hetaryl)-4-carboxy-1,3-thiazolidines **I–XIII** and **XV** was carried out by condensation of *L*-cysteine hydrochloride and the corresponding aldehydes in aqueous alcohol in the presence of sodium hydrogen carbonate [11–14] by the protocols mentioned below; *N*-acetyl-2-phenyl-4-carboxy-1,3-thiazolidine **XIV** was obtained by acylating thiazolidine **I** with acetic anhydride in the presence of dimethylaminopyridine (DMAP).

Thiazolidines **I–XIII** and **XV** are white crystalline substances, soluble in DMF and DMSO, poorly soluble in alcohols and tetrahydrofuran and virtually insoluble in water, diethyl ether, chloroform, acetone, hexane, toluene etc. The esterification with methanol or ethanol in the presence of thionyl chloride gives the corresponding esters, which are well soluble in nonpolar organic solvents.

All the obtained thiazolidines have (*R*)-amino acid chirality ($C^4$-ring). During the process of thiazolidine ring formation the additional asymmetrical center at $C^2$-atom appears. After one crystallization from methanol (ethanol) (2*R*, 4*R*)- and (2*S*, 4*R*)-diastereomers were obtained, whose ratio for compounds **I–XIII** and **XV** can be determined by means of $^1$H NMR spectroscopy from the relationship between the areas of signals at $C^2$-atom: The proton signal of the (2*R*, 4*R*)-isomer is upfield relative to the signal of (2*S*, 4*R*)-isomer. The identification of thiazolidine **XIV** diastereomers by the NMR method is more difficult and will be discussed below. The ratio of (2*R*, 4*R*)- and (2*S*, 4*R*)-diastereomers in thiazolidines **I–IV** and **VI–XII** is ~7:8, in thiazolidines **V**, **XIII** and **XV**) ~5:9, and in thiazolidine **XIV** ~3:2.

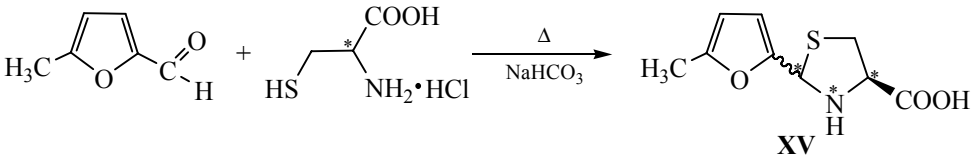


**I–XIII**



**XIV**

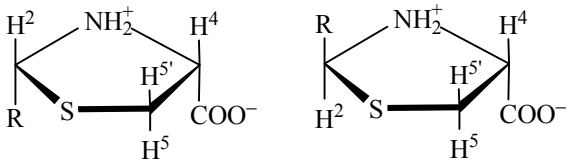
**I, XIV**, R = R' = R'' = R''' = H; **II**, R = OH, R' = R'' = R''' = H; **III**, R = R'' = R''' = H, R' = OH; **IV**, R = R' = R''' = H, R'' = $OCH_3$; **V**, R = R''' = $OCH_3$, R' = R'' = H; **VI**, R = H, R' = R'' = R''' = $OCH_3$; **VII**, R = OH, R' = $OCH_3$, R'' = R''' = H; **VIII**, R = R''' = H, R' = $OCH_3$, R'' = OH; **IX**, R = R' = R''' = H, R'' = $CH_3$; **X**, R = R' = R''' = H, R'' = $C_2H_5$; **XI**, R = R' = R''' = H, R'' = *i*-Pr; **XII**, R = R' = R''' = H, R'' = F; **XIII**, R = R'' = R''' = H, R' = $NO_2$.



**XV**

In the $^1$H NMR spectrum of compounds **I–XIII** and **XV** there are signals of two nonequivalent protons at thiazolidine $C^5$-atom at $\delta_H$ 2.8–3.4 ppm, proton $H^4$ signal is observed at $\delta_H$ 3.7–4.3 ppm, proton $H^2$ signal, at $\delta_H$ 5.3–5.9 ppm. The proton signals of aryl substituent are registered in the range of $\delta_H$ 6.7–7.6 ppm (except for thiazolidine **XIII**, where they appear at $\delta_H$ 7.6–8.2 ppm), and furan ring protons, at $\delta_H$ 5.9–6.4 ppm. Summary signal of the exchanging imine and carboxy protons appears before the use of a narrowing filter as a very broad band of half-width 1 ppm at 3.3–3.6 ppm. The band location, its strong broadening, the absence of the separate signals of NH- and COOH-groups and the absence of proton $H^2$ splitting or significant broadening allow an assumption that similar to the majority of amino acids the thiazolidines exist as an equilibrium of neutral and zwitter-ion forms, being in dynamic exchange conditions. The spectra of compounds **II**, **III**, **VII** and **VIII** contain the band of analogous large half-width in the range of 9.4–10.3 ppm corresponding to phenol OH-proton, also exchanging protons with carboxy and imino-groups.

Screening and spin-spin proton coupling constants in the studied compounds depend strongly on absolute



(2*R*,4*R*)-isomer (2*S*,4*R*)-isomer

R = aryl, furyl.

configuration of $C^2$-atom, which on the one hand allows a conclusion about the conformation of thiazolidine ring, and on the other hand, to assign signals of two protons at $C^5$-atom. In (2*R*, 4*R*)-diastereomer aryl/furyl substituent and carboxy group are located on one side of the ring and suffer a sufficient steric interaction. As a result, the thiazolidine ring is predominantly in the conformation, which provides maximum reciprocal removal of these groups. Then protons $H^2$, $H^4$, and $H^5$ occupy axial position relative to thiazolidine ring, and the aryl substituent and the carboxy group, equatorial positions. In (2*S*, 4*R*)-diastereomer the substituents are on different sides of the ring, the steric interaction is absent. There are no additional limitations for the conformational mobility of the thiazolidine ring; the

corresponding protons can dynamically exchange axial and equatorial positions.

It is known [15] that in the axial position the screening is greater than in the equatorial. Consequently, in (2*R*, 4*R*)-diastereomer the chemical shifts $H^2$, $H^4$ and $H^5$ must be less, and the chemical shifts $H^{5'}$ and of aryl/furyl groups protons should be greater than in the conformationally free (2*S*, 4*R*)-diastereomer. It makes possible to assign proton signal in the range of 3.00-3.15 ppm to the proton $H^5$ (in *trans*-position relative to $H^4$), and signal at 3.2–3.4 ppm, to (2*R*, 4*R*)-isomer proton $H^{5'}$ (in *cis*-position relative to $H^4$). The proton $H^5$ in (2*R*, 4*R*)-diastereomer is shifted upfield relative to (2*S*, 4*R*)-diastereomer similarly to the signals $H^2$ and $H^4$, and the proton $H^{5'}$ signal is shifted to the same side as aryl/furyl group protons.

The thiazolidine ring conformation can be analyzed by means of two vicinal coupling constants $^3J_{cis}$ and $^3J_{trans}$ between the proton $H^4$ (that corresponds to cysteine α-proton) and the protons $H^{5'}$ and $H^5$ (β-protons). The value of the coupling constant depends on the dihedral angles $H^4$–$C^4$–$C^5$–$H^{5'}$ (*cis*-angle) and $H^4$–$C^4$–$C^5$–$H^5$ (*trans*-angle) values, whose difference modulus in all the conformations remains approximately equal to 120°. The typical range of changes of the angle $H^4$–$C^4$–$C^5$–$H^{5'}$ in 4*R*-carboxythiazolidines is from –30° ($H^4$ and $H^5$ in the maximal axial position) to 30° ($H^4$ and $H^5$ in the maximal equatorial position). Taking into account characteristic angular dependences for the vicinal constants in cyclopentanes [15], in this range $^3J_{cis}$ has maximum 9 Hz at 0° (2-*endo*-conformation) and decreases to 6.5 Hz at the extreme angle value. The angle $H^4$–$C^4$–$C^5$–$H^5$ changes from –150° to –90°, respectively, and in this case the constant $^3J_{trans}$ decreases steadily from 8.6 to ~0 Hz. In thiazolidines the constants are somewhat less owing to the effect of the electronegative sulfur atom, but their angular dependence and mutual relationships remain the same. If one assumes that thiazolidine ring is conformationally nonrigid, the *cis*- and *trans*-angle may dynamically take all allowed values from –30° to 30° and from –150° to –90°, respectively. In this case the averaged values of the constants $^3J_{cis}$ and $^3J_{trans}$ will be approximately 7 and 4 Hz. An increase in the constant $^3J_{trans}$ will indicate the preferred existence of conformation with the negative *cis*-angle and the equatorial carboxy group, and the decrease in $^3J_{trans}$ value, the conformation with axial carboxy group. An increase in the constant $^3J_{cis}$ at $^3J_{trans}$ ~4 Hz will correspond to 2-*endo*-conformation with the zero *cis*-angle.

In the spectra of the (2*R*, 4*R*)-diastereomers of the 2-substituted 1,3-thiazolidines the value of the coupling constants $^3J_{cis}$ and $^3J_{trans}$ comprise on the average 7 and 9 Hz, the scatter of values for different compounds is small. Such values indicate the sufficiently rigid fixation of the thiazolidine ring in the conformation with the large negative *cis*-angle and the equatorial carboxy group in complete agreement with the postulated above steric interaction of carboxy and aryl/furyl groups. In the spectra of (2*S*, 4*R*)-diastereomers the values $^3J_{cis}$ and $^3J_{trans}$ are close to 7 and 4 Hz in accordance with the conformational mobility of thiazolidine ring. The values of constants observed for diastereomers confirm the validity of the assignment of the signals of the protons $H^{5'}$ and $H^5$. The value $^3J_{trans}$ is on the average more than 4 Hz. This is consistent with the general rule: In the case of nonrigid ring the conformation with the equatorial substituent is somewhat more advantageous.

The geminal coupling constant $^2J(H^5H^{5'})$ changes little and comprises for all compounds approximately 10 Hz; its value in (2*S*, 4*R*)-diastereomer is more on the average by 0.3 Hz, which agrees well with the higher conformational mobility. It should be noted that $^3J_{trans}$ is the most sensitive to the nature of the aryl substituent in (2*S*, 4*R*)-diastereomer among all observed constants. The introduction of substituents into the *ortho*-position of the benzene ring leads to its increase (the greatest value 6.0 Hz is observed for compounds **V** and **XIII**, the smallest, 3.8 Hz, for **VIII**), i.e. the substituent makes more preferable the conformation of (2*S*, 4*R*)-diastereomer with the equatorial carboxy group. These regularities are observed in all spectra of compounds **I–XIII**, **XV** and make it possible to unambiguously identify all diastereomers signals even at their equal concentrations. The conformational strain of (2*R*, 4*R*)-diastereomers is most probably the reason for the fact that they are formed in the synthesis in smaller quantities.

The signals of aromatic protons of both diastereomers of 2-aryl-4-carboxy-1,3-thiazolidines are two typical AA'XX' spectra with a “large” AX constant (9 Hz, *ortho*-constant) and a “small” constant (about 2.5 Hz, total effect of $^4J_{AA'}$, $^4J_{XX'}$, $^5J_{AX'}$, *meta*- and *para*-constants).

The spectrum of the *N*-acylated derivative **XIV** deserves a separate examination. At room temperature its $^1$H NMR spectrum contains four sets of signals (the best distinguishable in the regions of signals of $H^4$ and $COCH_3$), each corresponding to the initial formula of

the compound. The reason for this is the hindered rotation of the acetyl group around the amide bond, as a result of which each diastereomer is represented by a pair of conformers. The NMR spectra of these conformers are distinguished also strongly as the spectra of diastereomers (Fig. 1). The signals assignment in this case is performed both using the published data on the NMR spectroscopy of purified diastereomers of related compounds and on the basis of the analysis of NMR spectra at 100°C (at this temperature the sufficiently fast rotation of acyl group occurs, and the signals of two conformers are merged) [11, 13, 16].

The identification of *N*-acylthiazolidine diastereomers is the most easily performed through the signals of protons $H^4$, which are well resolved. The signals of (2*S*, 4*R*)-diastereomer conformers have the coupling constants $^3J_{trans}$ 4–9 Hz, for (2*S*, 4*R*)-diastereomer signals $^3J_{trans}$ are no more than 1.6 Hz (Fig. 1). (2*R*, 4*R*)-Diastereomer **A** (41%) is prevailing in the mixture of conformers, and the content of the second conformer **B** is practically 2 times less (20%). A quantity of (2*S*, 4*R*)-diastereomer conformers comprises 21 and 18% for **C** and **D** respectively. Thus, in thiazolidine **XIV** (2*R*, 4*R*)-diastereomer prevails. It should be noted that the chemical shifts of the protons $H^2$ and $COCH_3$ for different diastereomers **A** and **C**, or **B** and **D** are more similar to each other, than in the spectra of the conformers of one diastereomer. It is obvious that **A** and **C** are the conformers with identical orientation of acyl group relative to carboxy group, and the presence of acyl group strongly affects the conformation of thiazolidine. First, zwitter-ion form becomes impossible and in the $^1$H NMR spectrum of thiazolidine **XIV** the broadened signal of carboxy group at 13.07 ppm is observed. Secondly, due to the conjugation of the lone electron pair of nitrogen and π-orbitals of CO-group the thiazolidine aminoacyl fragment is flat [16]: The atoms $C^2$, N, $C^4$ and acyl group approach the arrangement in the one plane; as a result the acyl group occupies strictly equatorial position and it interacts sterically with COOH and aryl group. The strong overlapping of the $H^5$ and $H^{5'}$ signals prevents the complete signals assignment for conformers **B–D**, but the coupling constants $^3J_{cis}$ and $^3J_{trans}$ can be reliably determined from the analysis of $H^4$ signals. The value of the coupling constants $^3J_{cis}$ and $^3J_{trans}$ of conformer **A** are close to (2*R*, 4*R*)-diastereomers of compounds **I–XIII** (rigid ring, equatorial carboxy group), and the conformer **B** constants have values, which correspond to free ring with the preferred axial position of COOH

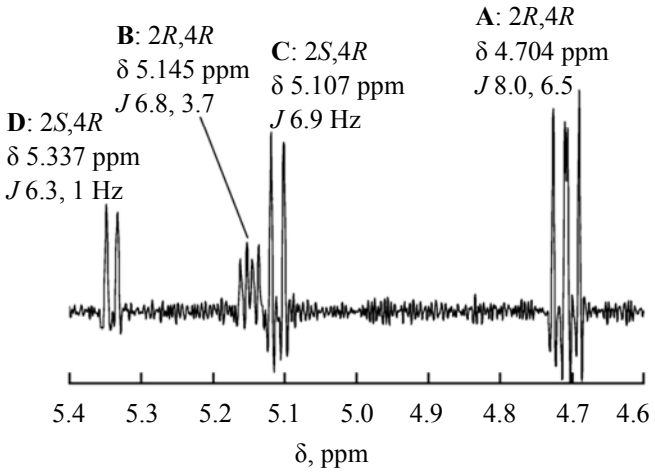



**Fig. 1.** The fragment of $^1$H NMR spectrum of thiazolidine **XIV** at room temperature corresponding to the signals of proton $H^4$ after applying the narrowing digital filter [**A, B** are conformers of (2*R*, 4*R*)-diasteromer; **C, D** are conformers of (2*S*, 4*R*)-diasteromer].

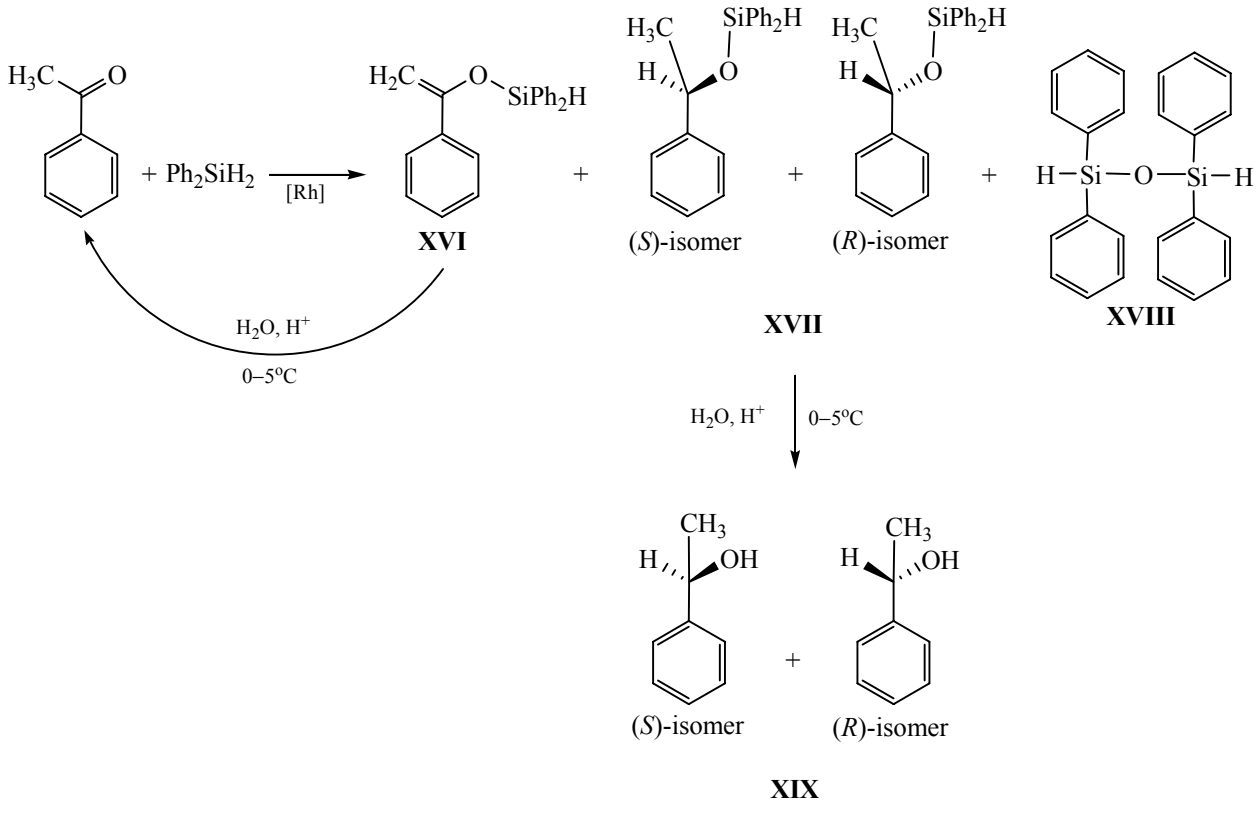
group. In contrast to (2*S*, 4*R*)-diastereomers of compounds **I–XIII**, the values of $^3J_{trans}$ for conformers **C** and **D** are close to zero, indicating that the *cis*-angle is rigidly fixed near 30°, and the carboxy group is located in the maximally axial position. The geminal coupling constant of conformer **A** increases in the module to 12 Hz. All protons of thiazolidine **XIV** conformers are strongly deshielded in comparison with the protons of compounds **I–XIII**, the $H^2$ proton signal falls into the region 6.1–6.4 ppm, and $H^4$, to 4.7–5.4 ppm. The smallest deshielding of thiazolidine protons is observed in the conformer **A**, and deshielding of the phenyl *ortho*-protons in this conformer is, on the contrary, maximal. The analysis of chemical shifts and the construction of the simplest molecular models makes it possible to conclude that in the conformer **A** as before exists the typical for (2*R*, 4*R*)-diastereomer conformation with the greatest reciprocal distance between the carboxy and phenyl groups. In this case the protons $H^2$, $H^4$, and $H^5$ occupy axial positions, and the phenyl group and $H^{5'}$, equatorial positions. One of the fragments of acyl group (C=O or $CH_3$) is approached to COOH group. When C=O fragment approaches the COOH group, the repulsion can be theoretically relieved due to the formation of intramolecular hydrogen bond, and all three lateral groups will prove to be in the advantageous equatorial position. The turn of acyl group by 180° will lead to unfavorable steric interaction of COOH and $CH_3$ groups and will force them to displace to the axial position (with the observed decrease in the $^3J_{trans}$

value). In (2*S*, 4*R*)-diastereomer there is no conformations, where the groups R and COOH could simultaneously occupy equatorial positions not destroying the coplanarity of thiazolidine aminoacyl fragment; therefore COOH group is rigidly fixed in the axial position ($^3J_{trans}$ is close to zero). Apparently, *N*-acylation makes the ring of (2*S*, 4*R*)-diastereomer more strained than that of (2*R*, 4*R*)-diastereomer, in contrast to the isomers of initial thiazolidine **I**. On the basis of the above stated and also taking into account the relative values of the chemical shifts of $H^2$, $H^4$ and $COCH_3$ in the pair of the conformers, it is possible to assume with the confidence that in the conformers **A** and **C** the acyl group is oriented to the carboxy group side by C=O fragment, and in the conformers **B** and **D,** by the $CH_3$ group.

The $^{13}C$ NMR spectra of investigated thiazolidines are identical to the spectra of related compounds, given in the literature [11, 12, 17]. In (2*S*, 4*R*)-diastereomer the chemical shifts of all the $^{13}C$ nuclei of thiazolidine are somewhat less than in (2*R*, 4*R*)-diastereomer. The carboxy carbon nucleus is, on the contrary, more screened in (2*R*, 4*R*)-diastereomer. The greater chemical shifts values of the carbon atoms $C^2$ and $C^4$ in (2*R*, 4*R*)-diastereomer confirm the above discussed effect, according to which the substituents at these atoms (aryl/furyl and carboxy group) in (2*R*, 4*R*)-diastereomer occupy preferably equatorial position.

The IR spectra of thiazolidines contain characteristic stretching vibrations of the groups N–H and O–H (3410–3450 $cm^{-1}$), C–H (2590–3070 $cm^{-1}$), C=O and C=C (1550–1725 $cm^{-1}$).

**Hydrosilylation.** The acetophenone hydrosilylation with diphenylsilane followed by hydrolysis of the formed mixture of silyl ethers isomers **XVII** is one of the synthetic approaches to 1-phenylethanol (*S*)- or (*R*)-isomers **XIX** and is widely used as a model reaction to evaluate the catalyst efficiency and the influence of different conditions on the hydrosilylation of prochiral compounds [18–20]. The main side reaction of the diphenylsilane addition, which occurs during the hydrosilylation in the presence of rhodium complexes, is the formation of enol silyl ether **XVI**, which with the subsequent hydrolysis of the reaction mixture is easily converted into the initial acetophenone.



The reaction carried out under not inert atmosphere (aerobic conditions) leads additionally to 1,1,3,3-tetraphenyldisiloxane **XVIII** formation. In this case the ligand structure in the rhodium complex has the decisive effect on its yield [21].

The acetophenone hydrosilylation with diphenylsilane under not inert atmosphere in the presence of $[Rh(COD)Cl]_2$ and of the introduced *in situ* thiazolidines **I–XV** occurs sufficiently slowly, and in all cases enol silyl ether **XVI** and siloxane **XVIII** are formed along with the main product **XVII** (see the table). The acetophenone conversion (the ratio complex : thiazolidine is 1:10) depends on the structure of thiazolidine used, but the target product yield does not exceed 42% after 24 h. At the same time the yield of compound **XVII** attains 93–99% after 38–65 h, when bidentate pyridine-thiazolines were used [2]. If the reaction is carried out in the presence of pyridine-oxazolines, the yield reaches 62% after only 18 h [22]. The reaction under aerobic condition has certain positive effect on the desired product yield. For example, the yield of ether **XVII** in the presence of **I** under the air atmosphere is equal to 39% vs. 35% with the reaction under nitrogen atmosphere [2].

The maximal acetophenone conversion is observed with the use of *N*-acetyl-2-phenyl-4-carboxy-1,3-thiazolidine (73%); however, the ether **XVII** yield (40%) is comparable with that in the presence of 2-phenyl-, 2(3-[hydroxyphenyl])- or 2(3-tolyl)-4-carboxy-1,3-thiazolidines (see the table) and it is by 7% higher than enol silyl ether yield and by 17% higher than the by-product, tetraphenyldisiloxane, yield. Therefore the presence of acyl protection in thiazolidine affects favorably the hydrosilylation rate (probably, because of the formation of low-active zwitter-ion form), but has a negative effect on the process selectivity. The decrease in the target product yield occurs also at the use of the acylated bidentate pyridinethiazolidines, which is connected with the decrease in the donor ability of the thiazolidine nitrogen atom [2].

The variation in the substituents location and nature in the benzene ring of thiazolidines **I–XIII** provides a possibility to affect the hydrosilylation activity and chemoselectivity. The presence of only one donor substituent in *ortho*-, *meta*- or *para*-positions of the benzene ring (compounds **II–IV**, **IX–XI**) or total absence of substituents makes it possible to reach 48–65% acetophenone conversion in 24 h, and the yield of ether **XVII** reaches 30–42% (see the table). At the same time in the first reaction stage in the presence of thiazolidines with electron-donor group the yield of ether **XVII** is higher than in the case of ligand containing unsubstituted phenyl ring (for example, after 1 h the yield of ether **XVII** is equal to 20 and 26% in the presence of compounds **IV** and **III,** respectively, vs. 7% with thiazolidine **I**). The hydrosilylation selectivity in the presence of *meta*-substituted phenylthiazolidine is found to be somewhat lower (60%), than in the presence of a donor group in *ortho*- (~100%) or *para*-positions (67%).

The concurrent reaction, the tetraphenyldisiloxane formation, depends on the donor substituent location, but otherwise than depends the hydrosilylation: The yield of compound **XVIII** is greater when the benzene ring donor group is closely located to the thiazolidine core. For example, the presence of OH-group in *ortho*- or *meta*-positions leads to 40 and 13% yield of siloxane, respectively. The presence of donor substituents in *para*-position leads to a decrease in the yield of siloxane **XVIII** (see the table). In this case the increase in the electron-donor properties of these substituents

Reaction of acetophenone with diphenylsilane in the presence of $[Rh(COD)Cl]_2$ and thiazolidines (24 h, $C_c$ 1 mol %, complex:thiazolidine, 1:10)

| Thiazolidine | | **I** | **II** | **III** | **IV** | **V**[a] | **VI**[a] | **VII** | **VIII**[a] | **IX** | **X** | **XI** | **XII** | **XIII** | **XIV** | **XV** |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Acetophenone conversion, % | | 60 | 31 | 65 | 48 | 45 | 62 | 30 | 72 | 53 | 49 | 60 | 3 | 28 | 73 | 1 |
| Yield, % | **XVI** | 21 | traces | 26 | 16 | 14 | 25 | traces | 37 | 11 | 19 | 24 | 0 | traces | 33 | 0 |
| | **XVII** | 39 | 31 | 39 | 32 | 31 | 36 | 30 | 35 | 42 | 30 | 36 | 3 | 28 | 40 | 1 |
| | **XVIII** | 3 | 40 | 13 | 8 | 18 | 11 | 66 | 12 | 12 | 11 | 8 | 6 | 27 | 19 | 8 |

[a] Reaction time 48 h.

leads to a gradual decrease in the tetraphenyldisiloxane yield (for example, to 12 and 8% in the case of methyl and methoxy groups, respectively).

The fluorine in *para*-position having strong *–I* and weak *+M* effects causes considerable inhibition both of the hydrosilylation (conversion 3%) and dehydrocondensation of diphenylsilane (yield of siloxane **XVIII** is 6%). A 4-fold increase in the reaction time in the presence of thiazolidine **XII** makes it possible to reach 29% conversion of acetophenone, but in this case in the reaction products 1-phenylethanol is present, and the unreacted diphenylsilane is completely converted into siloxane **XVIII** (77%).

The acetophenone conversion in the presence of thiazolidine containing a strong acceptor substituent in the *meta*-position, nitro group, proves to be close to its conversion in the presence of thiazolidine with the donor substituent, *meta*-hydroxy group, while the addition selectivity with the use of nitrophenylthiazolidine is almost 100% (see the table). The yield of siloxane **XVIII** in the presence of ligand **XIII** attains 27%, which is greater by 14% than at the use of hydroxythiazolidine **III**. This shows that the use of thiazolidines with the donor substituents in the benzene ring is more preferable in comparison with the use of thiazolidines, which contain electron-acceptor groups.

Uncoordinated influence of donor substituents in the benzene ring, i.e., the combination of two methoxy-groups in *ortho*- and *meta*-position or of methoxy-group in *meta*-position and of hydroxy-group in *ortho*- or *para*-position relative to the thiazolidine ring in certain cases leads to an increase in acetophenone conversion in comparison with compounds **II** and **IV**, which contain only one substituent. However, the yield of the desired reaction product in these cases proves to be similar (31–35%), and only hydrosilylation selectivity is considerably distinguished. After 24 h the acetophenone conversion in the presence of ligands **II** and **VII** virtually coincided (see the table). The yields attain 34, 45, and 72% respectively after 48 h with the use of thiazolidines **II**, **V** and **VIII**. At the same time within 1 h after the beginning of the reaction the ketone conversion and ether **XVII** yield coincided (for example, 26% in the presence of ligand **II** and 34% in the presence of ligand **VIII**). However, for instance, in the presence of thiazolidine **V** the transformation of acetophenone does not occur. After 48 h the yield of siloxane **XVIII** in the presence of compounds **V** and **VIII** is equal to 18 and 12%, respectively, whereas in the presence of ligand **VII** it reaches 66% after 24 h. The high yield of tetraphenyldisiloxane in the presence of two donor groups, one of which is located in the *ortho*-position relative to the thiazolidine ring, correlates with its yield in the case of only one *ortho*-located substituents. Therefore, even with the uncoordinated influence of substituents the presence of one of them in *ortho*-position of the benzene ring contributes to tetraphenyldisiloxane formation.

The introduction of three methoxy-groups simultaneously into *ortho*-, *meta*-, and *para*-positions, probably, proves to be superfluous despite the fact that acetophenone conversion after 48 h reaches 62% (in 1 h 16%), yield of ether **XVII,** 36% (in 1 h, 12%), and of siloxane **XVIII,** 11% (in 1 h, 6%). Thus, the catalysts with thiazolidines containing two and more substituents in the benzene ring, located in *meta*- or *para*-position, are more effective for hydrosilylation, than in the dehydrocondensation reactions, in contrast to thiazolidines, which have at least one group in *ortho*-position of the benzene ring.

Replacement of aryl substituent in the thiazolidine ring by methylfuryl group affects negatively both the hydrosilylation (acetophenone conversion after 150 h does not exceed 3%) and the dehydrocondensation of diphenylsilane (siloxane yield is 8%). Thus, an increase in the electron-acceptor properties of the substituent in position 2 of thiazolidine ring affects negatively the hydrosilylation.

The twofold decrease in the thiazolidine concentration, as a rule, affects negatively the reaction rate and ether **XVII** yield. For example, after 24 h the yield of 1-phenylethanol silyl ether in the case of the ratio $[Rh(COD)Cl]_2$:thiazolidine (**I**, **III**, **IX** and **X**), 1:5, is by 15, 17, 3, and 9% less than for the ratio 1:10, respectively. An increase in the reaction time is, as a rule, accompanied by 1-phenylethanol appearance in the reaction medium. It leads to the significant yields growth of enol **XVI** and tetraphenyldisiloxane and to only small change in ether **XVII** yield.

As a result of the electronic nature variation of the benzene ring substituents in 2-aryl-4-carboxy-1,3-thiazolidines, it becomes possible to control the hydrosilylation enantioselectivity to a greater extent than the reaction chemoselectivity. The use of a diastereomers mixture of thiazolidines **I–XV** to reach asymmetrical induction during the hydrosilylation is based on [2], where it has been shown that one diastereomer participates in the reaction catalyzed by

rhodium, but the second is not coordinated at all. Consequently, the presence of the uncoordinating diasteromer will have a negligible effect on the optical yield of 1-phenylethanol isomers, since the asymmetrical induction is underlain by the formation of a chiral transition state. Furthermore, in the reaction medium the thiazolidines epimerization on the $C^2$-atom occurs, and the catalysis occurs with the participation of epimeric ligand form [2].

Introduction of the donor substituents into the benzene ring in the *ortho*- or *para*-positions leads to the preferred formation of (*R*)-phenylethanol. Also an increase in the optical yield occurs, the maximum value of which is observed in the presence of thiazolidine **IV** (55% *ee*). The replacement of methoxy-group in *para*-position by the weaker electron-donor substituent (alkyl group) decreases the optical yield of alcohol **XIX**, which, for example, in the presence of ethylphenylthiazolidine **X** attains 30% *ee*. The presence of donor group in *ortho*-position (hydroxy-group) proves to be less effective (16% *ee*), and its *meta*-position (OH group in *meta*-position reduces the electron density on the benzene carbon atom bonded directly to the thiazolidine frame) makes it possible to obtain alcohol **XIX** with the opposite configuration in low optical yield (12% *ee*).

The uncoordinated influence of donor substituents (OH and $OCH_3$) affects negatively the asymmetrical induction, which in this case does not exceed 3% *ee*. It is necessary to note that the configuration of the alcohol obtained at the uncoordinated influence of the substituents depends on their strength. For example, two identical by the strength donor groups (methoxy-groups) in *ortho*- and *meta*-position favor the formation, insignificant as it is, of (*S*)-phenylethanol (1% *ee*). At the same time the strong donor (methoxy group) in *para*-position and the less strong donor (hydroxy-group) in *meta*-position act as one donor substituent in *para*-position to give (*R*)-phenylethanol.

Thus, the presence of the donor group in benzene ring (with the uncoordinated influence of substituents where one of them must be strong electron donor), which increases the electron density on the benzene carbon atom bonded directly the thiazolidine frame, is optimum for the asymmetrical induction and affords (*R*)-isomer of 1-phenylethanol. The opposite configuration of alcohol is predominantly formed in the presence of substituents, which reduce the electron density on the mentioned carbon atom.

**Factor analysis.** The introduction of substituents into thiazolidines benzyl moiety was shown above to influence the equilibrium between thiazolidine ring conformations, the hydrosilylation rate, and selectivity. For revealing possible concealed interrelation between the catalytic activity and structural characteristics of examined thiazolidines the factor analysis was performed by the main components method [23]. The chemical shifts of thiazolidine ring protons and vicinal coupling constants $^3J$ were taken as the active structural variables, participating in the construction of main constituents, while geminal coupling constants $^2J$ were not considered since their dispersion in the studied compounds was comparable with the error in the coupling constant determination and it was considerably random. In view of different dimensionality and substantially distinguished dispersions value, the selected variables were autoscaled. The diasteremers ratio, geminal coupling constants $^2J$, and catalytic properties were analyzed as additional passive variables; they were also autoscaled and projected on the main components formed by the structural variables.

The combined analysis of (2*R*, 4*R*)- and (2*S*, 4*R*)-isomers of thiazolidines **I–XIII** and **XV** showed that the first main component (MC-1) describes 56% of dispersion, and the sum of two high-order main components (MC-1 + MC-2) is equal to 89%. In this case MC-1 reproduces the difference between diastereomers, since its counts (value of the main components contribution) for (2*R*, 4*R*)- and (2*S*, 4*R*)-isomers have different sign. Changes in the structural parameters coincide with those examined by means of conformational analysis: going from (2*S*)- to (2*R*)-configuration is accompanied by the growth of $\delta_{H^5}$, $\delta_{H^{5'}}$, and $^3J_{trans}$ and by the decrease in the values $\delta_{H^4}$ and $\delta_{H^2}$, which is caused by the steric repulsion of aryl and carboxy groups in the (*R*)-isomer. The counts of the second main component for diastereomers with the identical aryl substituent are distinguished substantially, i.e., aryl group substituents have different effect on the diastereomers conformation. Therefore (2*R*, 4*R*)- and (2*S*, 4*R*)-isomers were separately analyzed (Fig. 2).

Each variable (active or additional) is mapped onto the loading plot as a vector (Figs. 2a, 2b); the identical direction of vectors indicates the strong positive correlation of variables, and opposite direction, the strong inverse correlation. The perpendicular vectors position shows the absence of correlation. The loads (projection of vectors on axis, Figs. 2a, 2b) reflect the

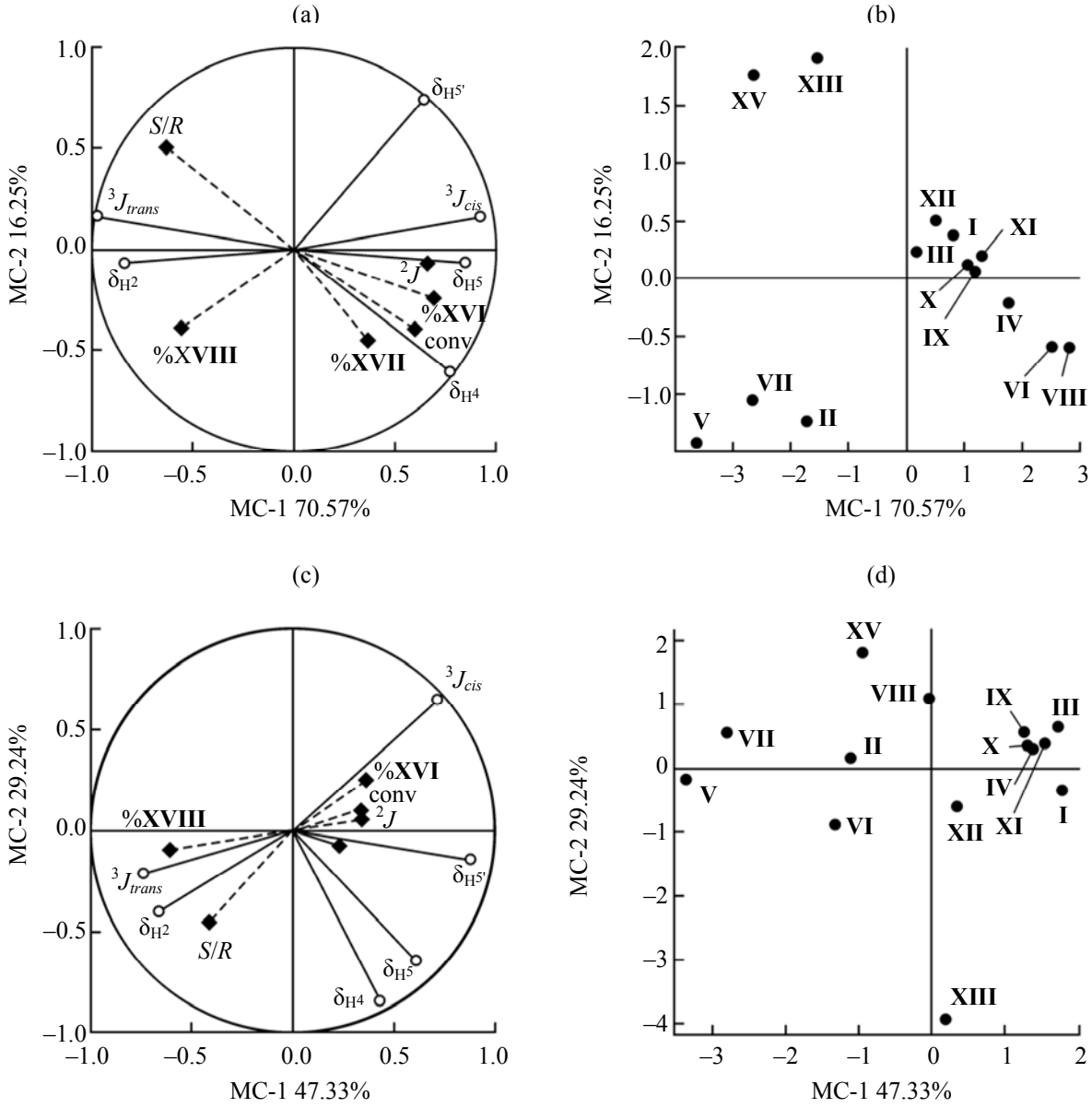



**Fig. 2.** Plots of (a, b) loads and (c, d) of counts of (a, b) (2*S*, 4*R*)-diastereomers and (c, d) (2*R*, 4*R*)-diastereomers of thiazolidines **I–XIII**. Active variables (bright circles): $\delta_{H2}$, $\delta_{H4}$, $\delta_{H5}$, $\delta_{H5'}$ are chemical shifts of protons; $J_{trans}$ and $J_{cis}$ are vicinal coupling constants. Additional variables (dark rhombs): $^2J$ are coupling constants $^2J_{H5\text{-}H5'}$; *S*/*R* is the concentrations ratio for (2*S*, 4*R*)- and (2*R*, 4*R*)-isomers; (conv) is the conversion of acetophenone; %**XVI**–%**XVIII** is the yield of compounds **XVI–XVIII**.

contribution of MC-1 and MC-2 into the dispersion of the corresponding variables, and their lengths, the dispersion portion of variables, described by these main components.

It is easy to note that for (2*S*, 4*R*)-isomers (Figs. 2a, 2b) MC-1 and MC-2 describe 87% of dispersion of experimental matrix. The third main component (it is not shown in Fig. 2) describes an additional 9% of dispersion, but its contribution is essential only from thiazolidines **XIII** and **XV**, due to the special feature of their NMR spectra, caused by an essential difference in the properties of substituents in thiazolidines **XIII** and **XV** from the remaining group of compounds. To the remaining main components correspond 4% of dispersion, that is within the range of the experimental error. All the investigated compounds on the calculation plot are divided into three clear groups. The first group is formed by compounds **III**, **V** and **VII**, which contain substituents

in the *ortho*-position of the benzene ring of thiazolidine. The second group includes thiazolidines **XIII** and **XV**, and the third group includes all the remaining compounds. All counts with exception of the first group compounds are approximately located along one line (main sequence), direction of which is governed by the variable $\delta_{H^4}$. The motion along this line from the furyl and nitrophenyl thiazolidine derivatives to the *meta*- and *para*-disubstituted derivatives of thiazolidines is accompanied by an increase in MC-1 count and by a decrease in MC-2 count, and also by an increase in the values $\delta_{H^4}$, $\delta_{H^5}$ and decrease in $\delta_{H^2}$ and $^3J_{trans}$ values.

Taking into account the discussed above dependences of these parameters on thiazolidine ring structure, it is possible to say that the passage from the preferred conformation with axial aryl and equatorial carboxyl groups to the conformation with equatorial aryl and axial carboxyl groups occurs. Simultaneously content of (2*S*, 4*R*)-configuration in the diastereomers mixture decreases (variable *S*/*R* in Fig. 2a) and catalytic properties are strengthened: acetophenone conversion and yields of ethers **XVI** and **XVII** grow. The correlation of catalytic properties with the structural characteristics of thiazolidines reaches ~0.7.

The introduction of substituents into the benzene ring *ortho*-position of (2*S*, 4*R*)-isomers leads to the negative counts of MC-1 and MC-2 that corresponds to a strong decrease in $\delta_{H^{5'}}$, and also to an increase in $\delta_{H^2}$ and to decrease in $\delta_{H^5}$ and $^3J_{cis}$. Changes in the structural variables in comparison with the compounds located on the main sequence, indicate significant interaction of substituents in the *ortho*-position of the benzene fragment with thiazolidine ring. This, in principle, agrees well with the formation of the hydrogen bond between the imine group of thiazolidine and the hydroxy or methoxy group oxygen in the aryl fragment, for whose formation a complete steric freedom exists in (2*S*, 4*R*)-isomers. Furthermore, for compounds **III**, **V,** and **VII** the correlation between the structural parameters and side tetraphenyldisiloxane is additionally observed (vector, which corresponds to an increase in tetraphenyldisiloxane yield is clearly directed to the described group side).

The factor analysis for (2*R*, 4*R*)-isomers (Figs. 2b, 2d) shows that two high-order main components describe only 77% of dispersion of set, but in this case the complete dispersion of active structural variables for (2*R*, 4*R*)-isomers proves to be 2.5 times less than for (2*S*, 4*R*)-isomers. MC-1 and MC-2 satisfactorily describe active variables, but the load on MC-2 and subsequent MC for some compounds have sufficiently random nature. This is possible, when the steric repulsion of aryl and carboxy groups has decisive importance for the dynamic structure of (2*R*, 4*R*)-isomers, and the influence of substituents on the conformational mobility is substantially less. Apparently, a change in the chemical shifts in this case stronger depends on inductive and other effects, than on the displacement of the conformational equilibrium. The described thiazolidines as a whole are lined up along MC-1 direction. Only nitro-derivative **XIII** is separately located. Thiazolidines with the *para*-substituted benzene ring form very compact group; compounds with the large number of the benzene ring substituents (**V**, **VI**, **VII**) deviate from this group into the range of negative MC-1 counts, and the unsubstituted phenyl- (**I**) and *meta*-hydroxylphenylthiazolidines, into the range of positive MC-2 counts. Structural parameters of (2*R*, 4*R*)-isomers, corresponding to MC-1, indicate the insignificant competition between aryl and carboxy groups for equatorial position, in contrast to (2*S*, 4*R*)-isomers. More negative values of MC-1 correspond to the conformation with the equatorial aryl group; however, the load of active variables on the main components is sufficiently low. There are no expressed correlation between the structural parameters and catalytic properties of (2*R*, 4*R*)-isomers, since the corresponding correlation coefficients do not exceed 0.4.

The sum of the obtained data allows an assumption that in the catalytic cycle (2*S*, 4*R*)-isomers participate, since the correlation between their structural parameters and catalytic properties is expressed to a greater extent than for (2*R*, 4*R*)-isomers. According to the factor analysis, the catalysis is more effective as the number of donor substituents in *meta*- and *para*-positions of benzene ring increases, and the introduction of substituents into *ortho*-position or the presence of *meta*-nitro group produces a negative effect.

Simultaneously, it is experimentally shown that the catalysts on the basis of $[Rh(COD)Cl]_2$, in whose coordination sphere 2-aryl-4-carboxy-1,3-thiazolidines with an aryl fragment, benzene ring containing donor substituent in *para*-position, are included, manifest the greatest effectiveness for acetophenone hydrosilylation by diphenylsilane.

## EXPERIMENTAL

The $^1H$ and $^{13}C$ NMR spectra were registered on Bruker AC-200 and WM-400 instruments with

accumulation at operating frequencies 400 ($^1$H) and 50 ($^{13}$C) MHz in $CDCl_3$ and $(CD_3)_2SO$ without additional references and the frequency stabilization on the deuterium signal of the solvent. The Lorentz–Gauss window function was applied to the free induction decay for refining chemical shifts and the deter-mination of the spin–spin coupling constants (initial characteristic lines width in the spectra was 2 Hz), which made it possible to attain the half-width of the lines of aliphatic protons of 0.4 Hz with the retention of high signal/noise ratio. The IR spectra were recorded on a Shimadzu FTIR-8400S spectrometer (4000–500 $cm^{-1}$) from KBr pellets. Melting points were measured in capillaries with the heating rate 2 deg $min^{-1}$.

The factor analysis was performed using chemometrics.xla plug-in to MS Excel, which was kindly supplied by Prof. A.L. Pomerantsev (Institute of Chemical Physic of Russian Academy of Sciences).

The acetophenone hydrosilylation with diphenylsilane was carried out in THF solution; molar ratio acetophenone:$Ph_2SiH_2$:catalyst:THF equaled 1:1.25:0.01:1.4. Into a reactor were charged 0.0215 mmol of [Rh(COD)Cl]$_2$, THF, and acetophenone ($C_c$ 1 mol %), 5- or 10-fold excess of ligand relative to complex. The mixture was kept for 5–15 min at room temperature and cooled to 0°C. To this mixture was added diphenylsilane in two equal portions. The reaction mixture was kept at 0°C for 2–3 h, after that the temperature was gradually increased to ambient. The reaction progress was monitored by $^1$H NMR method. In order to isolate the hydrolysis product to the reaction mixture was added 1 ml of methanol and after 1 h 5 ml of 1 M HCl solution, then the mixture was extracted with diethyl ether, dried over $MgSO_4$, passed through short column with silica gel, and concentrated. The analysis of enantiomeric composition was made by the $^1$H NMR method after the reaction of the obtained 1-phenylethanol with (*S*)-(+)-α-methoxy-α-trifluoro-methylphenylacetyl chloride by procedure [24]. The enantiomeric excess was determined by the ratio of methyl groups doublets of the obtained diastereomers at $\delta_H$ 1.64 [*J* 6.6 Hz, (*S*,*S*)-isomer] and 1.57 ppm [*J* 6.6 Hz, (*S*,*R*)-isomer], that corresponds to (*S*)- and (*R*)-isomers of 1-phenylethanol.

In the experiments commercially available methanol (Merk), diphenylsilane (Acros), chemically pure acetophenone, THF, diethyl ether, *L*-cysteine and hydrochloric acid were used. [Rh(COD)Cl]$_2$ was obtained as reported in [25].

2-Aryl(hetaryl)-4-carboxy-1,3-thiazolidines **I–XV** were prepared by procedures [7, 11–14, 17] and used in catalysis without additional purification.

**2-Phenyl-4-carboxy-1,3-thiazolidine (I)**. Yield 78%, mp 140–142°C (decomp.) (154–155°C [17, 26], 157–159°C [27], 158-159°C [28, 29], 159–160°C [12, 30–32], 163–165°C [33], 166–171°C [13]). *R*/*S* ratio equals 46/54. IR spectrum, $cm^{-1}$: (OH, NH) 3430 br; ν (CH) 2962, 2928, 2877, 2745, 2704, 2659, 2605, 2558; 2469; ν(C=O, C=C) 1622, 1575; δ(NH) 1494; ν(C=C) 1475; δ(CH) 1450; 1436; 1425; 1381; 1307; ν(CN) 1237, 1210, 1138, 1078; 1014; δ(OH) 921, 914; 857; 808; 767; δ(CH) 715; 695; 649; 620, 618; 583; 527; 502; 457.

(2*R*, 4*R*)-isomer. $^1$H NMR [$(CD_3)_2SO$], δ, ppm: 3.063 d.d (1H, $H^5$, *J* 10.3, 8.8 Hz), 3.368 d.d (1H, $H^{5'}$, *J* 10.3, 7.2 Hz), 3.876 d.d (1H, $H^4$, *J* 8.8, 7.2 Hz), 5.487 s (1H, $H^2$), 7.360 m (2H, $H^{3,5}$, Ph, *J* 7.5, 1.5 Hz), 7.501 m (2H, $H^{2,6}$, Ph, *J* 7.5, 1.5 Hz), 7.316 m (1H, $H^4$, Ph, *J* 7.5, 1.5 Hz).

(2*S*, 4*R*)-isomer. $^1$H NMR spectrum [$(CD_3)_2SO$], δ, ppm: 3.127 d.d (1H, $H^5$, *J* 10.4, 4.7 Hz), 3.289 d.d (1H, $H^{5'}$, *J* 10.4, 7.1 Hz), 4.216 d.d (1H, $H^4$, *J* 4.7, 7.1 Hz), 5.670 s (1H, $H^2$), 7.316 m (2H, $H^{3,5}$, Ph, *J* 7.5, 1.5 Hz), 7.425 m (2H, $H^{2,6}$, Ph, *J* 7.5, 1.5 Hz), 7.250 m (1H, $H^4$, Ph, *J* 7.5, 1.5 Hz).

**2-(2-Hydroxyphenyl)-4-carboxy-1,3-thiazolidine (II)**. Yield 96 %, mp 151–154°C (decomp.) (164–166°C [11], 171°C [34], 174–175°C [35]). *R*/*S* ratio equals 46/54. IR spectrum, $cm^{-1}$: ν(OH, NH) 3450–3400; ν(CH) 3100, 2983, 2956, 2925, 2850, 2689, 2563; 2468; ν(C=O, C=C) 1629, 1625, 1619, 1600, 1599, 1578, 1572, 1566, 1562; δ(NH) 1501; ν(C=C) 1471; δ(CH) 1460, 1454; 1390; 1383; 1332; ν(CN) 1238; 1152; 1097; 1063; 1039; δ(OH) 937; 862; 783, 768, 758; 679; 489; 420.

(2*R*, 4*R*)-isomer. $^1$H NMR spectrum [$(CD_3)_2SO$], δ, ppm: 3.057 d.d (1H, $H^5$, *J* 10.1, 8.9 Hz), 3.327 d.d (1H, $H^{5'}$, *J* 10.1, 6.6 Hz), 3.818 d.d (1H, $H^4$, *J* 8.9, 7.0 Hz), 5.631 s (1H, $H^2$), 6.782 d.t (1H, $H^5$, Ph, *J* 7.7, 1.0 Hz), 6.833 d.d (1H, $H^3$, Ph, *J* 7.7, 1.0 Hz), 7.112 d.t (1H, $H^4$, Ph, *J* 7.7, 1.8 Hz), 7.324 d.d (1H, $H^6$, Ph, *J* 7.7, 1.8 Hz).

(2*S*, 4*R*)-isomer. $^1$H NMR spectrum [$(CD_3)_2SO$], δ, ppm: 3.144 d.d (1H, $H^5$, *J* 10.1, 5.2 Hz), 3.191 d.d (1H, $H^{5'}$, *J* 10.1, 6.6 Hz), 4.199 d.d (1H, $H^4$, *J* 6.6, 5.2 Hz), 5.824 s (1H, $H^2$), 6.741 d.t (1H, $H^5$, Ph, *J* 7.7, 1.0 Hz), 7.782 d.d (1H, $H^3$, Ph, *J* 7.7, 1.0 Hz), 7.041 d.t (1H,

$H^4$, Ph, *J* 7.7, 1.8 Hz) 7.282 d.d (1H, $H^6$, Ph, *J* 7.7, 1.8 Hz).

**2-(3-Hydroxyphenyl)-4-carboxy-1,3-thiazolidine (III)**. Yield 83%, mp 165–167°C (decomp.) (178–179°C [7]). *R*/*S*-ratio equals 45/55. IR spectrum, $cm^{-1}$: ν(OH, NH) 3424 br; ν(CH) 3087, 3014, 2933, 2840, 2741, 2695, 2622, 2583, 2488; ν(C=O, C=C) 1629, 1626, 1620, 1595, 1591; δ(NH) 1503; ν(C=C) 1490; δ(CH) 1461; 1420; 1392; 1349; 1324, 1317; 1290; ν(CN) 1242; 1197; 1163; 1063; 1009; 995; 971; δ(OH) 923; 866, 859; 818; 766; 733; 696; 627; 617; 598; 585; 541; 528; 501; 457; 442.

(2*R*, 4*R*)-isomer. $^1$H NMR spectrum [$(CD_3)_2SO$], δ, ppm: 3.039 d.d (1H, $H^5$, *J* 10.3, 8.6 Hz), 3.348 d.d (1H, $H^{5'}$, *J* 10.3, 7.2 Hz), 3.865 d.d (1H, $H^4$, *J* 8.6, 7.2 Hz), 5.401 s (1H, $H^2$), 6.705 d.t (1H, $H^4$, Ph, *J* 8.2, 1.0 Hz), 6.893 m (1H, $H^6$, Ph, *J* 7.6, 2.0 Hz), 6.900 m (1H, $H^2$, Ph, *J* 1.0, 2.0 Hz), 7.141 m (1H, $H^5$, Ph, *J* 8.2, 7.6 Hz).

(2*S*, 4*R*)-isomer. $^1$H NMR spectrum [$(CD_3)_2SO$], δ, ppm: 3.097 d.d (1H, $H^5$, *J* 10.3, 4.6 Hz), 3.257 d.d (1H, $H^{5'}$, *J* 10.3, 6.9 Hz), 4.181 d.d (1H, $H^4$, *J* 4.6, 6.9 Hz), 5.571 s (1H, $H^2$), 6.642 m (1H, $H^4$, Ph, *J* 8.2, 1.0 Hz), 6.824 m (1H, $H^6$, Ph, *J* 7.6, 2.0 Hz), 6.834 m (1H, $H^2$, Ph, *J* 1.0, 2.0 Hz), 7.094 m (1H, $H^5$, Ph, *J* 8.2, 7.6 Hz).

**2-(4-Methoxyphenyl)-4-carboxy-1,3-thiazolidine (IV)**. Yield 95%, mp 146–148°C (decomp.) (156–158°C [11], 161–162°C [7], 163–164°C [29], 207–208°C [36]). *R*/*S* ratio equals 47/53. IR spectrum, $cm^{-1}$: ν(OH, NH) 3440 br; ν(CH) 2960, 2915, 2839, 2757, 2668, 2605, 2478; ν(C=O, C=C) 1609, 1578; δ(NH) 1512; ν(C=C) 1463; δ(CH) 1440; 1422; 1379; 1307; 1295; 1258, 1247; ν(CN) 1236; 1210; ν(C–O) 1174; 1135; 1028, 1026; δ(OH) 922; 862; 836; 809; 733; 697; 644; 610; 567; 523; 493.

(2*R*, 4*R*)-isomer. $^1$H NMR spectrum [$(CD_3)_2SO$], δ, ppm: 3.057 d.d (1H, $H^5$, *J* 10.0, 8.5 Hz), 3.347 d.d (1H, $H^{5'}$, *J* 10.0, 7.2 Hz), 3.739 s (3H, $OCH_3$), 3.856 d.d (1H, $H^4$, *J* 8.5, 7.2 Hz), 5.438 s (1H, $H^2$), 6.910 m (2H, $H^{3,5}$, Ph, *J* 9.0, 2.0 Hz), 7.428 m (2H, $H^{2,6}$, Ph, *J* 9.0, 2.0 Hz).

(2*S*, 4*R*)-isomer. $^1$H NMR spectrum [$(CD_3)_2SO$], δ, ppm: 3.144 d.d (1H, $H^5$, *J* 10.2, 4.0 Hz), 3.275 d.d (1H, $H^{5'}$, *J* 10.2, 7.2 Hz), 3.726 s (3H, $OCH_3$), 4.240 d.d (1H, $H^4$, *J* 7.2, 4.0 Hz), 5.583 s (1H, $H^2$), 6.875 m (2H, $H^{3,5}$, Ph, *J* 9.0, 2.0 Hz), 7.358 m (2H, $H^{2,6}$, Ph, *J* 9.0, 2.0 Hz).

**2-(2,5-Dimethoxyphenyl)-4-carboxy-1,3-thiazolidine (V)**. Yield 35%, mp 120–125°C (decomp.). *R*/*S* ratio equals 37/63. IR spectrum, $cm^{-1}$: ν(OH, NH) 3450–3400; ν(CH) 3010, 2967, 2937–2920, 2853, 2833; 1735; ν(C=O) 1630; ν(C=C) and δ(NH) 1590, 1576, 1567; δ(NH) 1495; ν(C=C) 1460; 1430; 1384; 1347; 1308; 1281; ν(CN) 1240; 1211; ν(C–O) 1178; 1052; 1027; 949; 880; 862; 824; 800; 746; 700; 628; 442.

(2*R*, 4*R*)-isomer. $^1$H NMR spectrum [$(CD_3)_2SO$], δ, ppm: 2.971 d.d (1H, $H^5$, *J* 10.0, 9.0 Hz), 3.295 d.d (1H, $H^{5'}$, *J* 10.0, 6.7 Hz), 3.699 s (3H, $OCH_3$, $C^2$, Ph), 3.735 s (3H, $OCH_3$, $C^5$, Ph), 3.844 d.d (1H, $H^4$, *J* 9.0, 6.7 Hz), 5.640 s (1H, $H^2$), 6.840 d.d (1H, $H^4$, Ph, *J* 8.8, 3.3 Hz), 6.934 d (1H, $H^3$, Ph, *J* 8.8 Hz), 7.122 d (1H, $H^6$, Ph, *J* 3.3 Hz).

(2*S*, 4*R*)-isomer. $^1$H NMR spectrum [$(CD_3)_2SO$], δ, ppm: 2.967 d.d (1H, $H^5$, *J* 10.2, 6.0 Hz), 3.127 d.d (1H, $H^{5'}$, *J* 10.2, 6.7 Hz), 3.681 s (3H, $OCH_3$, $C^2$, Ph), 3.724 s (3H, $OCH_3$, $C^5$, Ph), 4.172 d.d (1H, $H^4$, *J* 6.0, 6.7 Hz), 5.794 s (1H, $H^2$), 6.767 d.d (1H, $H^4$, Ph, *J* 8.9, 3.3 Hz), 6.877 d (1H, $H^3$, Ph, *J* 8.9 Hz), 6.976 d (1H, $H^6$, Ph, *J* 3.3 Hz).

**2-(3,4,5-Trimethoxyphenyl)-4-carboxy-1,3-thiazolidine (VI)**. Yield 80%, mp 146–148°C (decomp.). *R*/*S* ratio 43/57. IR spectrum, $cm^{-1}$: ν(OH, NH) 3434 br; ν(CH) 3070, 2954, 2930, 2854, 2837; 1741; ν(C=O) 1641; ν(C=C) 1593; δ(NH) 1512; ν(C=C) 1461; 1427; 1377; 1332; 1306; 1256; ν(CN) 1248; 1193; 1161; ν(C–O) and δ(C–O) 1132 s; 1010; 998; 993; 946; 838; 821; 657; 620; 499.

(2*R*, 4*R*)-isomer. $^1$H NMR spectrum [$(CD_3)_2SO$], δ, ppm: 3.071 d.d (1H, $H^5$, *J* 9.8, 9.3 Hz), 3.321 d.d (1H, $H^{5'}$, *J* 9.8, 6.8 Hz), 3.633 s (3H, $OCH_3$, $C^4$, Ph), 3.763 s (6H, $OCH_3$, $C^{3,5}$, Ph), 3.853 d.d (1H, $H^4$, *J* 9.3, 6.8 Hz), 5.419 s (1H, $H^2$), 6.849 s (2H, $H^{2,6}$, Ph).

(2*S*, 4*R*)-isomer. $^1$H NMR spectrum [$(CD_3)_2SO$], δ, ppm: 3.154 d.d (1H, $H^5$, *J* 10.3, 4.0 Hz), 3.283 d.d (1H, $H^{5'}$, *J* 10.3, 7.2 Hz), 3.623 s (3H, $OCH_3$, $C^4$, Ph), 3.751 s (6H, $OCH_3$, $C^{3,5}$, Ph), 4.290 d.d (1H, $H^4$, *J* 7.2, 4.0 Hz), 5.561 s (1H, $H^2$), 6.759 s (2H, $H^{2,6}$, Ph).

**2-(2-Hydroxy-3-methoxyphenyl)-4-carboxy-1,3-thiazolidine VII**. Yield 86%, mp 147–149°C (decomp.) (142–143°C [37]). *R*/*S* ratio equals 47/53. IR spectrum, $cm^{-1}$: ν(OH, NH) 3250 br; ν(CH) 3107, 3025, 2987, 2975, 2959, 2944, 2840; ν(C=O, C=C) 1639, 1632; 1605; δ(NH) 1485; 1441; 1345; 1282; ν(CN) 1237; 1183; 1159; ν(C–O) and δ(C–O) 1078, 1059; 983; 938; δ(OH) 926; 838; 807; 768; 737; 699; 636; 489.

(2*R*, 4*R*)-isomer. $^1$H NMR spectrum [$(CD_3)_2SO$], δ, ppm: 2.952 d.d (1H, $H^5$, *J* 10.0, 9.2 Hz), 3.329 d.d (1H, $H^{5'}$, *J* 10.0, 6.9 Hz), 3.773 s (3H, $OCH_3$, $C^3$, Ph), 3.824 d.d (1H, $H^4$, *J* 9.2, 6.9 Hz), 5.658 s (1H, $H^2$), 6.756 d.d (1H, $H^5$, Ph, *J* 8.1, 7.7 Hz), 6.897 d.d (1H, $H^4$, Ph, *J* 8.1, 1.4 Hz), 6.942 d.d (1H, $H^6$, Ph, *J* 7.7, 1.4 Hz).

(2*S*, 4*R*)-isomer. $^1$H NMR spectrum [$(CD_3)_2SO$], δ, ppm: 3.005 d.d (1H, $H^5$, *J* 10.2, 5.4 Hz), 3.186 d.d (1H, $H^{5'}$, *J* 10.2, 6.7 Hz), 3.761 s (3H, $OCH_3$, $C^3$, Ph), 4.198 d.d (1H, $H^4$, *J* 5.4, 6.7 Hz), 5.853 s (1H, $H^2$), 6.718 d.d (1H, $H^5$, Ph, *J* 8.2, 7.7 Hz), 6.831 d.d (1H, $H^4$, Ph, *J* 8.2, 1.5 Hz), 6.912 d.d (1H, $H^6$, Ph, *J* 7.7, 1.5 Hz).

**2-(4-Hydroxy-3-methoxyphenyl)-4-carboxy-1,3-thiazolidine (VIII)**. Yield 97%, mp 141–144°C (decomp.) (164–166°C [11]). *R*/*S* ratio equals 48/52. IR spectrum, $cm^{-1}$: ν(OH, NH) 3430–3400; ν(CH) 3053, 3006, 2972, 2925, 2853; 1741; ν(C=O, C=C) 1625, 1622, 1609, 1596; δ(NH) 1519; ν(C=C) 1467; 1452, 1440; 1380; 1334; 1292; 1277; ν(CN) 1248; 1216; 1160; ν и δ(C–O) 1135; 1049; 1028; 1001; 964; δ(OH) 919; 862; 847; 820; 797; 762; 652; 618; 561; 496.

(2*R*, 4*R*)-isomer. $^1$H NMR spectrum [$(CD_3)_2SO$], δ, ppm: 3.045 d.d (1H, $H^5$, *J* 9.8, 8.9 Hz), 3.323 d.d (1H, $H^{5'}$, *J* 9.8, 7.1 Hz), 3.755 s (3H, $OCH_3$, $C^3$, Ph), 3.828 d.d (1H, $H^4$, *J* 8.9, 7.1 Hz), 5.383 s (1H, $H^2$), 6.717 d (1H, $H^5$, Ph, *J* 8.1 Hz), 6.875 d.d (1H, $H^6$, Ph, *J* 8.1, 2.1 Hz), 7.100 d (1H, $H^2$, Ph, *J* 2.1 Hz).

(2*S*, 4*R*)-isomer. $^1$H NMR spectrum [$(CD_3)_2SO$], δ, ppm: 3.153 d.d (1H, $H^5$, *J* 10.4, 3.8 Hz), 3.267 d.d (1H, $H^{5'}$, *J* 10.4, 7.3 Hz), 3.743 s (3H, $OCH_3$, $C^3$, Ph), 4.276 d.d (1H, $H^4$, *J* 3.8, 7.3 Hz), 5.513 s (1H, $H^2$), 6.828 d (1H, $H^6$, Ph, *J* 8.1 Hz), 6.688 d.d (1H, $H^5$, Ph, *J* 8.1, 2.3 Hz), 7.009 d (1H, $H^2$, Ph, *J* 2.3 Hz).

**2-(4-Tolyl)-4-carboxy-1,3-thiazolidine (IX)**. Yield 90%, mp 154–155°C (decomp.) (144–145°C [32], 185°C [38]). *R*/*S* ratio equals 47/53. IR spectrum, $cm^{-1}$: ν(OH, NH) 3440 br; ν(CH) 3025, 2961, 2924, 2872, 2715, 2674, 2614, 2478; ν(C=O, C=C) and δ(NH) 1628, 1579, 1572; ν(C=C) and δ(CH) 1434; 1383; 1309; ν(CN) 1237; 1212; 1184; 1140; 1014; δ(OH) 921; 861; 815; 785; 724; 641; 606; 561; 476; 409.

(2*R*, 4*R*)-isomer. $^1$H NMR spectrum [$(CD_3)_2SO$], δ, ppm: 2.287 s (3H, $CH_3$), 3.045 d.d (1H, $H^5$, *J* 10.1, 8.8 Hz), 3.353 d.d (1H, $H^{5'}$, *J* 10.1, 7.2 Hz), 3.853 d.d (1H, $H^4$, *J* 8.8, 7.2 Hz), 5.433 s (1H, $H^2$), 7.161 m (2H, $H^{3,5}$, Ph, *J* 8.0, 2.0 Hz), 7.377 m (2H, $H^{2,6}$, Ph, *J* 8.0, 2.0 Hz). $^{13}$C NMR spectrum [$(CD_3)_2SO$] δ, ppm: 20.60 (1C, $CH_3$), 38.2 (1C, $C^5$), 65.80 (1C, $C^4$), 71.77 (1C, $C^2$), 127.06 (2C, $C^{3,5}$, Ph), 128.95 (2C, $C^{2,6}$, Ph), 137.52 (1C, $C^4$, Ph), 136.68 (1C, $C^1$, Ph), 172.48 (1C, COO).

(2*S*, 4*R*)-isomer. $^1$H NMR spectrum [$(CD_3)_2SO$], δ, ppm: 2.264 s (3H, $CH_3$), 3.127 d.d (1H, $H^5$, *J* 10.3, 4.3 Hz), 3.273 d.d (1H, $H^{5'}$, *J* 10.3, 7.1 Hz), 4.219 d.d (1H, $H^4$, *J* 4.3, 7.1 Hz), 5.614 s (1H, $H^2$), 7.118 m (2H, $H^{3,5}$, Ph, *J* 8.0, 2.0 Hz), 7.307 m (2H, $H^{2,6}$, Ph, *J* 8.0, 2.0 Hz). $^{13}$C NMR spectrum [$(CD_3)_2SO$] δ, ppm: 20.63 (1C, $CH_3$), 37.94 (1C, $C^5$), 64.97 (1C, $C^4$), 71.01 (1C, $C^2$), 126.77 (2C, $C^{3,5}$, Ph), 128.67 (2C, $C^{2,6}$, Ph). 135.95 (1C, $C^4$, Ph), 138.25 (1C, $C^1$, Ph), 173.02 (1C, COO).

**2-(4-Ethylphenyl)-4-carboxy-1,3-thiazolidine (X)**. Yield 61%, mp 146°C (decomp.). *R*/*S* ratio equals 46/54. IR spectrum, $cm^{-1}$: ν(OH, NH) 3450–3350; ν(CH) 2962, 2929, 2867, 2760, 2614, 2473; ν(C=O, C=C) and δ(NH) 1621, 1574; ν(C=C) 1475; ν(C=C) and δ(CH) 1434; 1380; 1311; ν(CN) 1237; 1211; 1185; 1140; 1064; 1016; δ(OH) 922; 860; 829; 771; 643; 610; 486.

(2*R*, 4*R*)-isomer. $^1$H NMR spectrum [$(CD_3)_2SO$], δ, ppm: 1.157 t (3H, $CH_3$, *J* 7.5 Hz), 2.583 m (2H, $CH_2CH_3$, *J* 7.5 Hz), 3.050 d.d (1H, $H^5$, *J* 10.0, 8.8 Hz), 3.355 d.d (1H, $H^{5'}$, *J* 10.0, 7.2 Hz), 3.858 d.d (1H, $H^4$, *J* 8.8, 7.2 Hz), 5.452 s (1H, $H^2$), 7.193 m (2H, $H^{3,5}$, Ph, *J* 8.0, 2.0 Hz), 7.402 m (2H, $H^{2,6}$, Ph, *J* 8.0, 2.0 Hz).

(2*S*, 4*R*)-isomer. $^1$H NMR spectrum [$(CD_3)_2SO$], δ, ppm: 1.149 t (3H, $CH_3$, *J* 7.5 Hz), 2.565 m (2H, $CH_2CH_3$, *J* 7.5 Hz), 3.126 d.d (1H, $H^5$, *J* 10.2, 4.5 Hz), 3.275 d.d (1H, $H^{5'}$, *J* 10.2, 7.1 Hz), 4.220 d.d (1H, $H^4$, *J* 4.5, 7.1 Hz), 5.620 s (1H, $H^2$), 7.150 m (2H, $H^{3,5}$, Ph, *J* 8.0, 2.0 Hz), 7.332 m (2H, $H^{2,6}$, Ph, *J* 8.0, 2.0 Hz).

**2-(4-Isopropylphenyl-4-carboxy-1,3-thiazolidine (XI)**. Yield 66%, mp 128–130°C (decomp.). *R*/*S* ratio equals 46/54. IR spectrum, $cm^{-1}$: ν(OH, NH) 3400 br; ν(CH) 2963, 2925, 2888, 2874, 2713, 2596; 2473; 1708; ν(C=O, C=C) and δ(NH) 1580, 1572; ν(C=C) and δ(CH) 1467, 1425; 1382; 1301; ν(CN) 1235; 1210; 1137; 1063; 1015; δ(OH) 921; 860; 829; 809; 753; 692; 638; 607; 562; 548; 491; 419.

(2*R*, 4*R*)-isomer. $^1$H NMR spectrum [$(CD_3)_2SO$], δ, ppm: 1.170 t (6H, $CH_3$, *J* 7.0 Hz), 2.866 m (1H, $CHCH_3$, *J* 7.0 Hz), 3.050 d.d (1H, $H^5$, *J* 9.9, 8.7 Hz), 3.355 d.d (1H, $H^{5'}$, *J* 9.9, 7.2 Hz), 3.860 d.d (1H, $H^4$, *J* 8.7, 7.2 Hz), 5.451 s (1H, $H^2$), 7.224 m (2H, $H^{3,5}$, Ph, *J* 8.0, 2.0 Hz), 7.408 m (2H, $H^{2,6}$, Ph, *J* 8.0, 2.0 Hz).

(2*S*, 4*R*)-isomer. $^1$H NMR spectrum [$(CD_3)_2SO$], δ, ppm: 1.179 t (6H, $CH_3$, *J* 7.0 Hz), 2.848 m (1H, C*H*$CH_3$, *J* 7.0 Hz), 3.125 d.d (1H, $H^5$, *J* 10.4, 4.4 Hz), 3.275 d.d (1H, $H^{5'}$, *J* 10.4, 7.2 Hz), 4.218 d.d (1H, $H^4$, *J* 4.4, 7.2 Hz), 5.621 s (1H, $H^2$), 7.180 m (2H, $H^{3,5}$, Ph, *J* 8.0, 2.0 Hz), 7.338 m (2H, $H^{2,6}$, Ph, *J* 8.0, 2.0 Hz).

**2-(4-Fluorophenyl)-4-carboxy-1,3-thiazolidine (XII)**. Yield 85%, mp 160°C (decomp.) (166°C [7]). *R*/*S* ratio equals 44/56. IR spectrum, $cm^{-1}$: ν(OH, NH) 3500–3400; ν(CH) 3025, 2942; ν(C=O, C=C) and δ(NH) 1639, 1635, 1630, 1619, 1611, 1605; ν(C=C) and δ(CH) 1513, 1510; 1438; 1381; 1334; 1313, 1311; 1270; ν(CN) 1231; 1167; 1102; 1052; ν(CF) 1003; 878; 864; 846; 832; 815; 792; 608; 547; 529; 507, 419.

(2*R*, 4*R*)-isomer. $^1$H NMR spectrum [$(CD_3)_2SO$], δ, ppm: 3.066 d.d (1H, $H^5$, *J* 9.9, 9.1 Hz), 3.349 d.d (1H, $H^{5'}$, *J* 9.9, 7.1 Hz), 3.868 d.d (1H, $H^4$, *J* 9.1, 7.1 Hz), 5.490 s (1H, $H^2$), 7.178 m (2H, $H^{3,5}$, Ph, *J* 8.6, 3.2; $J_{HF}$ 8.8 Hz), 7.561 m (2H, $H^{2,6}$, Ph, *J* 8.6, 3.2; $J_{HF}$ 5.6 Hz).

(2*S*, 4*R*)-isomer. $^1$H NMR spectrum [$(CD_3)_2SO$], δ, ppm: 3.118 d.d (1H, $H^5$, *J* 10.2, 4.5 Hz), 3.285 d.d (1H, $H^{5'}$, *J* 10.2, 7.0 Hz), 4.191 d.d (1H, $H^4$, *J* 4.5, 7.0 Hz), 5.658 s (1H, $H^2$), 7.136 m (2H, $H^{3,5}$, Ph, *J* 8.6, 3.2; $J_{HF}$ 8.8 Hz), 7.467 m (2H, $H^{2,6}$, Ph, *J* 8.6, 3.2; $J_{HF}$ 5.6 Hz).

**2-(3-Nitrophenyl)-4-carboxy-1,3-thiazolidine (XIII)**. Yield 20%, mp 150–152°C (decomp.) (151–153°C [37], 154–156°C [14]). *R*/*S* ratio equals 36/64. IR spectrum, $cm^{-1}$: ν(OH, NH) 3460–3410; ν(CH) 3098, 3056, 3006, 2923; ν(C=O, C=C) and δ(NH) 1631, 1625, 1621; ν(NO, C=C) and δ(CH) 1537, 1530; 1395; 1370, 1362; ν($NO_2$) 1350; 1327; 1298; ν(CN) 1253; 1197; 1138; 1000; 959; 909; ν(CN) 848, 841; 807, 805; 748; 697; 628; 419.

(2*R*, 4*R*)-isomer. $^1$H NMR spectrum [$(CD_3)_2SO$], δ, ppm: 3.116 d.d (1H, $H^5$, *J* 10.0, 8.9 Hz), 3.348 d.d (1H, $H^{5'}$, *J* 10.0, 6.7 Hz), 3.936 d.d (1H, $H^4$, *J* 8.9, 6.7 Hz), 5.656 s (1H, $H^2$), 7.633 d.d (1H, $H^5$, Ph, *J* 8.1, 6.7 Hz), 7.947 m (1H, $H^6$, Ph, *J* 6.7, 2.0, 0.8 Hz), 8.151 m (1H, $H^4$, Ph, *J* 8.1, 2.4, 0.8 Hz), 8.431 d.d (1H, $H^2$, Ph, *J* 2.4, 2.0 Hz).

(2*S*, 4*R*)-isomer. $^1$H NMR spectrum [$(CD_3)_2SO$], δ, ppm: 3.092 d.d (1H, $H^5$, *J* 10.2, 5.5 Hz), 3.317 d.d (1H, $H^{5'}$, *J* 10.2, 6.9 Hz), 4.114 d.d (1H, $H^4$, *J* 5.5, 6.9 Hz), 5.853 s (1H, $H^2$), 7.603 d.d (1H, $H^5$, Ph, *J* 7.9, 6.6 Hz), 7.853 m (1H, $H^6$, Ph, *J* 6.6, 2.0, 1.0 Hz), 8.097 m (1H, $H^4$, Ph, *J* 7.9, 2.2, 1.0 Hz), 8.270 d.d (1H, $H^2$, Ph, *J* 2.2, 2.0 Hz).

***N*-Acetyl-2-phenyl-4-carboxy-1,3-thiazolidine (XIV)**. Yield 69%, mp 123–126°C (decomp.) (151–152°C [33]). *R*/*S* ratio equals 61/39. IR spectrum, $cm^{-1}$: ν(OH, NH) 3440 br; ν(CH) 3059, 3027, 2969, 2922, 2841, 2585; ν(C=O) 1725, 1721, 1708; ν(C=O, C=C), δ(NH) 1604, 1598; δ(CH) 1420, 1408; 1352; ν(CN) 1239, 1200, 1172; 1129; 940; 890; 833; 796; 734, 727, 700; 683; 600; 436; 419.

(2*R*, 4*R*)-isomer. $^1$H NMR spectrum [$(CD_3)_2SO$], δ, ppm: conformer **A** (41%) 1.783 s (3H, $CH_3$), 3.071 d.d (1H, $H^5$, *J* 12.0, 7.9 Hz), 3.38–3.46 (1H, $H^{5'}$), 4.704 d.d (1H, $H^4$, *J* 7.9, 6.5 Hz), 6.367 s (1H, $H^2$), 7.17–7.39 (3H, Ph), m 7.685 (2H, $H^{2,6}$, Ph, *J* 7.5 Hz); conformer **B** (20%) 2.045 s (3H, $CH_3$), 3.30–3.46 (2H, $H^{5,5'}$), 5.145 d.d (1H, $H^4$, *J* 6.8, 3.7 Hz), 6.153 s (1H, $H^2$), 7.17–7.39 (3H, Ph), m 7.488 (2H, $H^{2,6}$, Ph, *J* 7.5 Hz).

(2*S*, 4*R*)-isomer. $^1$H NMR spectrum [$(CD_3)_2SO$], δ, ppm: conformer **C** (21%) 1.744 s (3H, $CH_3$), 3.14–3.19 (1H, $H^5$), 3.30–3.46 (1H, $H^{5'}$), 5.107 d (1H, $H^4$, *J* 6.9 Hz), 6.367 s (1H, $H^2$), 7.17–7.39 (5H, Ph); conformer **D** (18%) 1.783 s (3H, $CH_3$), 3.14–3.19 (1H, $H^5$), 3.30–3.46 (1H, $H^{5'}$), 5.337 d.d (1H, $H^4$, *J* 6.3, 1.0 Hz), 6.137 s (1H, $H^2$), 7.17–7.39 (5H, Ph).

**2-(5'-Methyl-2'-furyl)-4-carboxy-1,3-thiazolidine (XV)**. Yield 52%, mp 111°C (decomp.). *R*/*S* ratio equals 36/64. IR spectrum, $cm^{-1}$: ν(OH, NH) 3434 br; $\nu_{asym}$(CH) 2978, 2944, 2917; $\nu_{sym}$(CH) 2861; ν(CH) 2748, 2590; 1731; 1618, 1615; ν(C=O, C=C) and δ(NH) 1572, 1568, 1553; δ(CH) 1437; 1380; 1360; 1318; 1290; ν(CN) 1237; 1221; 1166; 1138; 1058; 1021; 1004; 956; 856; 835; 835; 797; 789; 627; 595; 514; 477.

(2*R*, 4*R*)-isomer. $^1$H NMR spectrum [$(CD_3)_2SO$], δ, ppm: 2.239 s (3H, $CH_3$), 2.960 d.d (1H, $H^5$, *J* 10.0, 8.9 Hz), 3.327 d.d (1H, $H^{5'}$, *J* 10.0, 7.2 Hz), 3.827 d.d (1H, $H^4$, *J* 8.9, 7.2 Hz), 5.528 s (1H, $H^2$), 6.017 d (2H, $H^5$, furyl, *J* 3.2 Hz), 6.341 d (1H, $H^4$, furyl, *J* 3.2 Hz). $^{13}$C NMR spectrum [$(CD_3)_2SO$] δ, ppm: 13.19 (1C, $CH_3$), 38.0 (1C, $C^5$), 64.31 (1C, $C^4$), 65.00 (1C, $C^2$), 106.51 (1C, $C^4$, furyl), 108.32 (1C, $C^3$, furyl), 149.19 (1C, $C^5$, furyl), 151.61 (1C, $C^2$, furyl), 172.07 (1C, COO).

(2*S*, 4*R*)-isomer. $^1$H NMR spectrum [$(CD_3)_2SO$], δ, ppm: 2.209 s (3H, $CH_3$), 2.970 d.d (1H, $H^5$, *J* 10.1, 6.0 Hz), 3.268 d.d (1H, $H^{5'}$, *J* 10.1, 6.8 Hz), 4.088 d.d (1H, $H^4$, *J* 6.0, 6.8 Hz), 5.659 s (1H, $H^2$), 5.955 d (2H, $H^5$, furyl, *J* 3.1 Hz), 6.193 d (1H, $H^4$, furyl, *J* 3.1 Hz). $^{13}$C NMR spectrum [$(CD_3)_2SO$] δ, ppm: 13.19 (1C, $CH_3$), 37.62 (1C, $C^5$), 63.99 (1C, $C^4$), 64.49 (1C, $C^2$),

106.21 (1C, $C^4$, furyl), 107.21 (1C, $C^3$, furyl), 151.06 (1C, $C^5$, furyl), 152.25 (1C, $C^2$, furyl), 172.44 (1C, COO).

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