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SYNTHESIS OF ISOMERIC 2-OXAZOLIDINONES FROM (1*R*,2*R*)- AND (1*S*,2*S*)-2-AMINO-1-(4-NITROPHENYL)-1,3-PROPANEDIOLS

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A synthesis is reported for (4R,5R)- and (4S,5S)-4-hydroxymethyl-5-(4-nitrophenyl)oxazolidin-2-ones and (1'R,4R)- and (1'S,4S)-4-[hydroxy(4-nitrophenyl)methyl]oxazolidin-2-ones from (1R,2R)- and (1S,2S)-2-amino-1-(4-nitrophenyl)-1,3-propanediols. The effect of the experimental conditions on the formation of these compounds was studied.

Keywords: (1*R*,2*R*)- and (1*S*,2*S*)-2-amino-1-(4-nitrophenyl)-1,3-propanediols, (4*R*,5*R*)- and (4*S*,5*S*)-4-hydroxymethyl-5-(4-nitrophenyl)oxazolidin-2-ones, (1'*R*,4*R*)- and (1'*S*,4*S*)-4-[hydroxy(4-nitrophenyl)-methyl]oxazolidin-2-ones.

2-Oxazolidinones have attracted considerable attention in chemistry. These compounds display a variety of biological activity [1-4] and are used in asymmetric synthesis [5]. Formation of the 2-oxazolidinone ring is used when necessary to protect both the adjacent amino and hydroxy groups [6-8].

In our previous work [9], we synthesized (1*S*,2*S*)-2-ethoxycarbonylamino-1-(4-nitrophenyl)-1,3-propanediol (**2**) from (1*S*,2*S*)-2-amino-1-(4-nitrophenyl)-1,3-propanediole (**1**) with subsequent conversion to isomeric 2-oxazolidinones: (1'*S*,4*S*)-4-[hydroxy(4-nitrophenyl)methyl)oxazolidin-2-one (**4**) and (4*S*,5*S*)-4-hydroxymethyl-5-(4-nitrophenyl)oxazolidin-2-one (**3**) according to Scheme 1.

It is known that the closure of the oxazolidinone ring upon treatment of a suitable methylcarbamate proceeds rather rapidly even at room temperature and in a slightly basic medium (pH 9.5) in only 20 min [8]. But we maintained the reaction mixture under similar conditions for about 120 h, and only a slight amount of oxazolidinone **4** was obtained as a precipitate [9].

In this conection the aim of the present work was the search of the conditions most favorable for formation of the one of the isomeric 2-oxazolidinones, permitting a reduction of the reaction time.

Base is a catalyst in the formation of 2-oxazolidinones but it may lead to undesired racemization. Propanediol **2** is sensitive to the pH value and the solution at pH > 10 turns reddish; the product isolated is less pure. Thus, propanediol **2** is initially [9] treated with a 1:1 mixture of water and saturated methanolic potassium carbonate, which has pH ~9.5.

In a search for optimal reaction conditions, the pH of the reaction solution was raised to 10 by addition solid potassium hydroxide. Furthermore, different amounts of propanediol **2** were treated with equal volumes of the indicated solution. In experiment 5, 20 ml water was added to 50 ml used solution to reduce the solubility of oxazolidinone **4** (Table 1).

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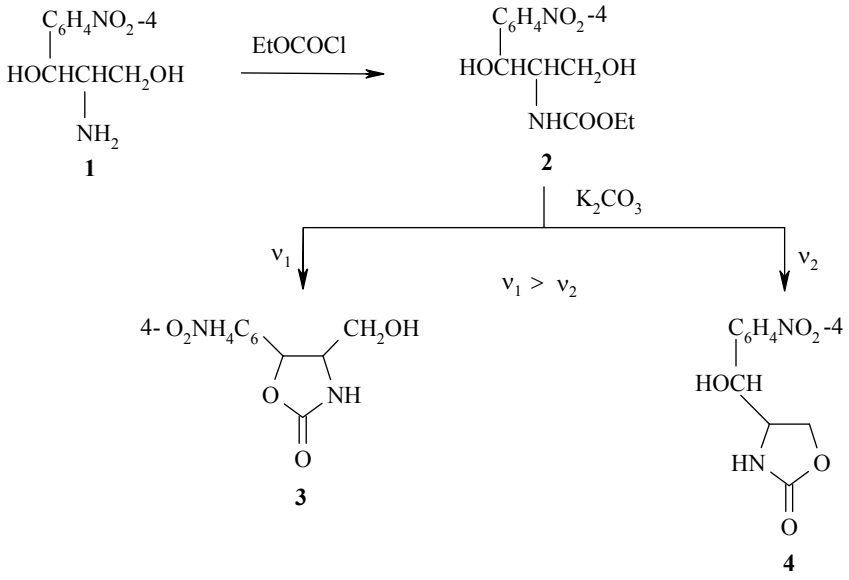
0009-3122/07/4310-1325

Sheme 1



The slight increase in the pH from 9.5 to 10 leads to a significant increase in the reaction rate. The formation of a precipitate of oxazolidinone **4** in experiments 2-5 starts in the first day. In experiment 1, a precipitate of oxazolidinone **4** did not separate out upon completion of the reaction, while in experiment 5, the rapid crystallization of both **3** and **4** occurred after 29 h throughout the entire bulk of the reaction mixture, such that the reaction was not completed. We should note that in all experiments 1-5, the reaction mixture contained a slight amount of propanediol **2** after completion of the reaction, as indicated by thin-layer chromatography.

The solubility of oxazolidinone **4** was found to be higher in alkaline medium and thus the reaction mixtures were subsequently treated as follows. In experiments 1-4, concentrated hydrochloric acid was added dropwise with stirring to bring the solution pH to 7-8 and mixtures were left overnight for the complete crystallization of oxazolidinone **4**. A precipitate of product **4** also formed in the reaction mixture in experiment 1 after standing overnight (Table 1). A sample of the reaction mixture was taken with a pipette upon rapid stirring to insure homogeneity. Methanol and water were removed on a rotary evaporator at room temperature, the residue was dried and the ratio of oxazolidinones **3** and **4** was determined on the basis of the ^{1}H NMR spectra taken in DMSO-d_6 (Table 1). In experiments 1-4, the precipitate of oxazolidinone **4** was filtered off, washed with a small amount of 1:1 water–methanol, dried, and weighed (Table 1).

TABLE 1. Experimental Data on the Conversion of Propanediol **2** Into a Mixture of Oxazolidinones **3** and **4** at pH 10

Experiment	Amount of compound **2**, g	Volume, ml	Precipitate mass, g	Reaction time, h	**3** : **4**, %
1	2	50	0.14	8	69 : 31
2	4	50	0.50	20	68 : 32
3	8	50	2.25	28	57 : 43
4	10	50	4.37	33	35 : 65
5	10	70	5.50	29	55 : 45

In experiment 5, the reaction mixture was treated as follows: a portion of the reaction mixture was removed with a spatula and dried. The ratio of products **3** and **4** was determined by ^{1}H NMR spectroscopy. The reaction mixture in this experiment was filtered under vacuum. The precipitate was washed with 1:1 water-methanol, dried, and weighed. The mother liquor was made acidic and combined with the mother liquors from experiments 1-4. Methanol was then removed on a rotary evaporator at room temperature. The precipitate formed, which was mainly a mixture of oxazolidinones **3** and **4**, was filtered off and dried. This mixture was used directly for the synthesis of the esters or subjected to chromatography on a silica gel column using 15:1 ethyl acetate–methanol or ethyl acetate to give additional amounts of **4** and **3**.

The reaction course was followed by thin-layer chromatography. The thin-layer chromatography data and values given in Table 1 showed that oxazolidinone **3** is the product of kinetic control ($v_1 > v_2$). The concentrations of **2-4** in solution drop after the begining of precipitation of oxazolidinone **4**. A supersaturated solution of **4** apparently forms in the first step of the reaction. Thus, the concentration of this product in solution drops after the begining of crystallization. The decrease in the concentration of propanediol **2** is related to its conversion to oxazolidinones **3** and **4**, while the decrease in the concentration of oxazolidinone **3** is related to its conversion to **4**, which has low solubility and precipitates out. In order to determine whether an equilibrium exists in the reaction mixture between oxazolidinones **3** and **4** and which of these compounds is the product of thermodynamic control, solutions of **3** and **4** in the indicated reaction mixture were maintained for 24 h. Both products with the predominance of oxazolidinone **3** were found after maintenance for 24 h in the solutions, which originally contained pure oxazolidinone **3** or **4**. Thus, oxazolidinone **3** is the product of both kinetic and thermodynamic control in the conversion of propanediol **2** into oxazolidinones **3** and **4**. Equilibrium between products **3** and **4** is also established upon the treatment of **4** with hydrazine hydrate in ethanol at reflux for 1-2 h though propanediol **2** is not converted into a mixture of **3** and **4** under these conditions. This failure may be attributed to the greater acidity of the 2-oxazolidinones and carbamates in comparison with alcohols and permits us to make a conclusion concerning the mechanism of formation of oxazolidinones **3** and **4**, namely, the conversion of propanediol **2** into oxazolidinones **3** and **4** occurs as an intramolecular nucleophilic replacement of the ethoxy group.

An alternative mechanism entails the formation of an isocyanate as the result of the loss of an ethoxy group from the carbamate anion under base catalysis conditions. The alkoxy group is not considered a good leaving group and such mechanism is considered when there is an aryloxy leaving group [10].

Nevertheless, the existence of an equilibrium between oxazolidinones **3** and **4** and the formation of a large amount of **4** as a consequence (Table 1) indicate the formation of (1*S*,2*S*)-1,3-dihydroxy-1-(4-nitrophenyl)-2-propyl isocyanate (isocyanate **5**) (Scheme 2) from oxazolidinones **3** and **4**. Insoluble oxazolidinone **4** ($v_4 > v_3$), which separates as a precipitate and, thereby, becomes the major product of this reaction in the step involving the conversion of isocyanate **5** into a mixture of oxazolidinones **3** and **4**, becomes the product of kinetic control.

We attempted to elucidate whether nascent isocyanate **5** reacts with water and methanol (components of the reaction mixture) to give **1** and **2a**, i.e., whether all the reactions shown in Scheme 2 are possible.

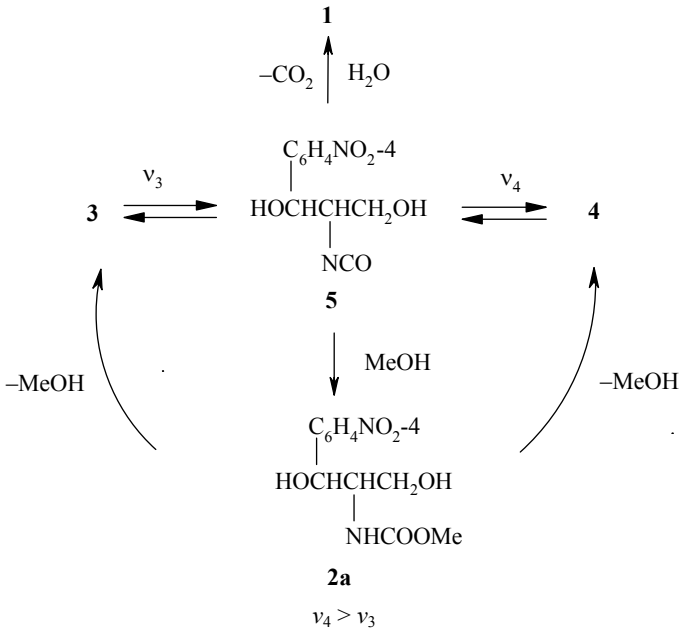
The formation of propanediol **2a**, whose chromatographic mobility should be virtually identical to the mobility of **2**, might account for the finding that the reaction could not initially be brought to completion.

As already noted, both oxazolidinones **3** and **4**, upon suitable treatment, give a mixture of only these products. An experiment was performed, in which **2** was treated with the indicated water-methanol mixture for 103 h. This experiment terminated with the complete conversion of propanediol **2** and formation of only two products, oxazolidinones **3** and **4**.

Hence, the formation of **1** and **2a** is impossible under the reaction conditions.

The experiments carried out both in this work and our previous study [9] indicated that a high yield of **4** is favored by 1) a higher pH value (~10), 2) prolonged treatment of the reaction mixture, which facilitates the conversion of **3** to **4**, and 3) a minimal volume for the reaction mixture (Table 1, experiment 4), which facilitates

Sheme 2

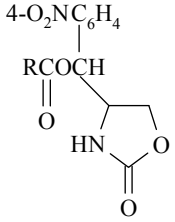


the more complete separation of oxazolidinone **4** as a precipitate. Observing all these conditions permits the isolation of pure **4** in high yield. On the other hand, a lower pH value (9.5) and larger reaction mixture volume (Table 1, experiment 1) are more favorable for the formation of oxazolidinone **3**. The rapid separation of oxazolidinone **4** over the course of 24 h is, in our view, undesirable and indicates a pH value over the optimal value for the preparation of **3**. The increase in the pH value probably increases the rate of conversion of **3** to **4** to a greater extent than the rate of conversion of **2** to the mixture of **3** and **4**.

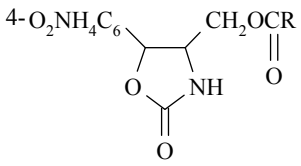
Unfortunately, in contrast to oxazolidinone **4**, oxazolidinone **3** could not be isolated from the reaction mixture as a pure compound.

The pH range from 9.5 to 10 studied in this work is probably close to the limit, below which the reaction does not proceed. A reduction in the pH during the experiment may be related both to the absorption of atmospheric carbon dioxide and the presence of impurities.

In light of the data on the reactivity of propanediol **2**, (1*R*,2*R*)-2-ethoxycarbonylamino-1-(4-nitrophenyl)-1,3-propanediol (**6**) was converted to (1'*R*,4*R*)-4-[hydroxy(4-nitrophenyl)methyl]oxazolidin-2-one (**7**) and (4R,5R)-4-hydroxymethyl-5-(4-nitrophenyl)oxazolidin-2-one (**8**). Stereoisomers display different biological activity and, thus, hold interest for biological testing. Esters **9** and **10**, which are enantiomers described in our previous work [9], were obtained from **7** and **8**, while two new esters **11** were obtained from **4**.



9a-e (1'*R*,4*R*), **11a**, **b** (1'*S*,4*S*)



10a-e (4*R*,5*R*)

9, **10 a** R = Me, **b** R = Et, **c** R= Pr, **d** R = $(CH_2)_3Cl$,**e** R = PhCHCl;
11 a R = Pr, **b** R = $(CH_2)_3Cl$

We have already noted that the acylation of chromatographically-purified **3** and **4** requires two equivalents of acid chloride [9]. In the present work, we carried out the acylation of **4, 7,** and **8,** isolated from the reaction mixtures and dried in the air. In this case, a total of three or four equivalents of acid chloride was required for the acylation of these compounds. All the esters obtained are solids and most of them crystallize readily, especially after purification by column chromatography.

The treatment of oxazolidinones **7** and **8** with the racemic acid chloride of phenylchloroacetic acid gave a mixture of diastereomers. The ^{1}H NMR spectrum in acetone-d_6 showed signals for the protons of the CHCl, CHAr, and NH groups of both diastereomers of **9e**, while the signals of only the protons of the CHCl and CHAr groups are doubled in the spectrum of the diastereomers of **10e**. The diastereomers of **10e** are formed in 1:1 ratio, while the diastereomers of **9e** are formed in unequal amounts. The different stereochemical result is readily attributed to the circumstance that greater steric differences arise in the acylation of the second alcohol group in **7**, which facilitate formation of the diastereomers in unequal amounts, than in the acylation of the first alcohol group in **8**.

EXPERIMENTAL

The ^{1}H NMR spectra were taken on a Bruker Avance 200 spectrometer at 200 MHz in DMSO-d_6 or acetone-d_6 with TMS as the internal standard and treated using the MESTREC program. The melting points were determined on a Koefler block. In the experiments there were used Merck silica plates, silica gel pouwder of SDS grade, the acid chlorides of Acros, while (1*R*,2*R*)- and (1*S*,2*S*)-2-amino-4-(4-nitrophenyl)-1,3-propanediols were supplied by the Akrikhin firm. The chromatographic separation of all the products was carried out on a 3×40 cm silica gel column using different eluents.

(1*S*,2*S*)-2-Ethoxycarbonylamino-1-(4-nitrophenyl)-1,3-propanediol (2). A mixture of **1** (106 g, 0.5 mol), sodium carbonate (106 g, 1 mol), and methylene chloride (600 ml) was added to a 1000-ml round-bottomed flask equipped with a reflux condenser and magnetic stirrer. Ethyl chlorocarbonate (52.5 ml, 0.53 mol) was added with stirring to the mixture cooled with ice to 5-10°C at a rate such that the temperature did not rise over 15°C. The reaction mixture was stirred overnight and filtered on a Buchner filter. The precipitate was washed with methylene chloride. The volume of the filtrate was reduced to 100-150 ml by distilling off methylene chloride on a water bath. The crystalline precipitate of compound **2** was collected on a Buchner filter and washed with methylene chloride. The previously obtained precipitate of compound **2** and inorganic compounds was placed in a beaker and treated with hot ethyl acetate and filtered. This procedure was repeated two or three times. The organic fractions contain pure **2**. These fractions were combined and ethyl acetate was almost entirely distilled off. The crystalline precipitate was filtered off, washed with a small amount of methylene chloride, and dried. The two portions of compound **2** were combined. The yield of compound **2** was 112 g (79%); mp 118°C (mp 118°C [9]).

(1*R*,2*R*)-2-Ethoxycarbonylamino-1-(4-nitrophenyl)-1,3-propanediol (6) was obtained analogously in the reaction of (1*R*,2*R*)-2-amino-1-(4-nitrophenyl)-1,3-propanediol (98 g, 0.46 mol) with ethyl chlorocarbonate (45.5 ml, 0.46 mol) in the presence of sodium carbonate (98 g, 0.92 mol). The yield of **6** was 114 g (87%); mp 118°C (the mp for the (1*S*,2*S*)-stereoisomer was 118°C [9]).

(1'*S*, 4*S*)-4-[Hydroxy(4-nitrophenyl)methyl]oxazolidin-2-one (4). A mixture of compound **2** (10 g, 35 mmol), water (50 ml), and saturated methanolic sodium carbonate (50 ml) was added to a 250-ml round-bottomed flask equipped with a magnetic stirrer. The flask was sealed with a stopper and the reaction mixture was stirred with the magnetic stirrer. After 67 h, the reaction mixture was brought to pH 7-8 by adding concentrated hydrochloric acid and left overnight. The precipitate of almost pure compound **4** was filtered off. The yield of compound **4** was 5.67 g (68%); mp 205-206 (mp 206-207°C [9]).

(4*S*,5*S*)-4-Hydroxymethyl-5-(4-nitrophenyl)oxazolidin-2-one (3). Methanol was removed from the mother liquor obtained in the previous experiment on a rotary evaporator. A crystalline precipitate formed, which was filtered off, washed with water, and dried. The isolated product (2.07 g, 25.7%) was a mixture of **3** and **4** with predominance of the former. Oxazolidinone **3** was purified by chromatography on a silica gel column with 15:1 ethyl acetate–methanol as the eluent and recrystallized from ethyl acetate, mp 136-137°C (mp 137-138°C [9]).

(1'*R*,4*R*)-4-[Hydroxy(4-nitrophenyl)methyl]oxazolidin-2-one (7) was obtained analogously by treating compound **6** (12 g, 42 mmol) with the indicated aqueous methanolic sodium carbonate solution (90 ml) for 54 h. The yield of **7** was 4.4 g (44%); mp 206-207°C (mp for the (1'*S*, 4*S*)-stereoismer 206-207°C [9]).

(4*R*,5*R*)-4-Hydroxymethyl-5-(4-nitrophenyl)oxazolidin-2-one (8). A mixture of **7** and **8** was isolated from the mother liquor obtained in the previous experiment (3.27 g, 33%). Oxazolidinone **8** was purified by column chromatography using 15:1 ethyl acetate–methanol as the eluent and recrystallized from ethyl acetate, mp 136-137°C (mp for the (4*S*,5*S*)-stereoisomer 137-138°C [9]).

(1'*R*,4*R*)-4-[Butanoyloxy(4-nitrophenyl)methyl]oxazolidin-2-one (9c). A mixture of compound **7** (1.5 g, 6.3 mmol), chloroform (25 ml), and pyridine (5.5 ml, 68 mmol) was added to a 100 ml round-bottomed flask equipped with a magnetic stirrer. Then, butanoyl chloride (2.68 g, 25.2 mmol) was slowly added dropwise with stirring. The mixture was stirred for 1 h. Then, water (15 ml) was added and the mixture was stirred for an additional 1 h. The reaction mixture was transferred to a separatory funnel and chloroform (30 ml) was added. The organic layer was separated, washed with dilute hydrohloric acid, aqueous sodium bicarbonate, and water, and dried over sodium sulfate. Chloroform was distilled off and the dry product was purified by chromatography on a silica gel column using 7:3 ethyl acetate-methanol as the eluent. The solvent was distilled off on a rotary evaporator and the crystalline precipitate was washed on the filter with 1:1 ethyl acetate–methanol. The yield of **9c** was 1.50 g (77%); mp 118-119°C. ^{1}H NMR spectrum (acetone-d_6), δ, ppm (*J*, Hz): 7.73-8.30 (4H, H arom); 7.09 (1H, br. s, NH), 5.97 (1H, d, *J* = 5.4, CH–O); 4.22-4.45 (3H, m, CH–N and CH_2–O); 2.47 (2H, t, *J* = 6.5, CH_2–CO); 1.65 (2H, m, CH_2); 0.92 (3H, t, *J* = 7.3, CH_3). Found, %: C 55.03; H 5.26; N 9.30. $C_{14}H_{16}N_2O_6$. Calculated, %: C 54.54; H 5.23; N 9.09.

(1'*S*,4*S*)-4-[Butanoyloxy(4-nitrophenyl)methyl]oxazolidin-2-one (11a) was obtained analogously by the reaction of compound **4** (3 g, 12.6 mmol) and butanoyl chloride (4.02 g, 37.8 mmol). The yield of **11a** was 2.8 g (72%); mp 118-119°C.

(1'*R*,4*R*)-4-[4-Chlorobutanoyloxymethyl-(4-nitrophenyl)]oxazolidin-2-one (9d) was obtained analogously by the reaction of compound **7** (1.5 g, 6.3 mmol) and 4-chlorobutanoyl chloride (3.55 g, 25.2 mmol). The crude product was purified chromatographically using 5:2 ethyl acetate–cyclohexane as the eluent. The yield of **9d** was 1.84 g (77%); mp 122-123°C. ^{1}H NMR spectrum in acetone-d_6, δ, ppm (*J*, Hz): 7.76-8.30 (4H, H arom); 7.14 (1H, br. s, NH); 5.98 (1H, d, *J* = 5.8, CH–O); 4.23-4.44 (3H, m, CH–N and CH_2–O); 3.66 (2H, t, *J* = 6.4, CH_2Cl); 2.66-2.74 (2H, m, CH_2); 2.04-2.16 (2H, CH_2CO; overlaps with the signal for acetone-d_6), Found, %: C 49.54; H 4.47; Cl 10.34; N 8.21. $C_{14}H_{15}ClN_2O_6$. Calculated, %: C 49.06; H 4.41; Cl 10.34; N 8.17.

(1'*S*,4*S*)-4-[4-Chlorobutanoyloxymethyl-(4-nitrophenyl)]oxazolidin-2-one (11b) was obtained analogously by the reaction of compound **4** (3 g, 12.6 mmol) and 4-chlorobutanoyl chloride (5.33 g, 37.8 mmol). The yield of **11b** was 2.77 g (64%); mp 122-123°C.

(1'*R*,4*R*)-4-[Acetoxy(4-nitrophenyl)methyl]oxazolidin-2-one (9a) was obtained analogously by the reaction of compound **7** (2 g, 8.4 mmol) and) acetyl chloride (2.64 g, 33.6 mmol). The crude product was purified chromatographically using 5:2 ethyl acetate–cyclohexane as the eluent. The yield of **9a** was 1.92 g (82%); mp 175-176°C (mp for the (1'*S*,4*S*)-stereoisomer was 156°C [9]).

(1'*R*,4*R*)-4-[(4-Nitrophenyl)propionyloxymethyl]oxazolidin-2-one (9b) was obtained analogously by the reaction of compound **7b** (1.5 g, 6.3 mmol) and propionyl chloride (2.33 g, 25.2 mmol). The crude product was purified chromatographically using 5:2 ethyl acetate–cyclohexane as the eluent. The yield of **9b** was 1.47 g (79%); mp 147-148°C (mp for the (1'*S*,4*S*)-stereoisomer 149-150°C [9]).

(1'*R*,4*R*)-4-[(4-Nitrophenyl)-(*R,S*)-phenylchloroacetoxymethyl]oxazolidin-2-one (9e) was obtained analogously by the reaction of compound **7** (1.5 g, 6.3 mmol) and propionyl chloride (3.6 g, 19.0 mmol). The crude product was purified chromatographically using 5:2 ethyl acetate–cyclohexane as the eluent. The yield of **9e** was 1.43 g (58%); mp 72-73°C (mp for the (1'*S*,4*S*)-stereoisomer 72-73°C [9]).

(4*R*,5*R*)-4-Acetoxymethyl-5-(4-nitrophenyl)oxazolidin-2-one (10a) was obtained analogously by the reaction of mixture of the compounds **7** and **8** (2.1 g, 8.8 mmol) and acetyl chloride (2.08 g, 26.5 mmol). The crude product was purified by chromatography using 5:2 ethyl acetate–cyclohexane as the eluent. The yield of **10a** was 1.45 g (59%); mp 68°C (mp for the (4*S*,5*S*)-stereoisomer 68°C [9]).

(4*R*,5*R*)-5-(4-Nitrophenyl)-4-propionyloxymethyl-2-oxazolidinone (10b) was obtained analogously by the reaction of mixture of the compounds **7** and **8** (2 g, 8.4 mmol) and propionyl chloride (2.33 g, 25.2 mmol). The crude product was purified chromatographically using 7:3 ethyl acetate-cyclohexane as the eluent. The yield of **10b** was 1.47 g (60%); mp 105°C (mp for the (4*S*,5*S*)-stereoisomer 105°C [9]).

(4*R*,5*R*)-4-Butanoyloxymethyl-5-(4-nitrophenyl)oxazolidin-2-one (10c) was obtained analogously by the reaction of mixture of the compounds **7** and **8** (2 g, 8.4 mmol) and butanoyl chloride (2.68 g, 25.2 mmol). The crude product was purified chromatographically using 6:4 ethyl acetate–cyclohexane as the eluent. The yield of **10c** was 1.65 g (57%); mp 101-102°C (mp for the (4*S*,5*S*)-stereoisomer 100-101°C [9]).

(4*R*,5*R*)-4-(Chlorobutanoyloxymethyl)-5-(4-nitrophenyl)oxazolidin-2-one (10d) was obtained analogously by the reaction of mixture of the compounds **7** and **8** (2 g, 8.4 mmol) and 4-chlorobutanoyl chloride (3.55 g, 25.2 mmol). The crude product was purified chromatographically using 6:4 ethyl acetate–cyclohexane as the eluent. The yield of **10d** was 0.91 g (57.1%); mp 128-129°C (mp for the (4*R*,5*R*)-stereoisomer 129-130°C [9]).

(4*R*,5*R*)-5-(4-Nitrophenyl)-(*R,S*)-4-(phenylchloroacetoxymethyl)oxazolidin-2-one (10e) was obtained analogously by the reaction of mixture of the compounds **7** and **8** (2 g, 8.4 mmol) and racemic phenylchloroacetyl chloride (4.76 g, 25.2 mmol). The crude product was purified chromatographically using 1:1 ethyl acetate–cyclohexane as the eluent. The yield of **10e** was 1.88 g (57%); mp 132-133°C (mp for the (4*S*,5*S*)-stereoisomer 132-133°C [9]).

Experiments on the Isomerization of 2-Oxazolidinones 3 and 4.

1. A sample of chromatographically pure compound **4** (0.15 g) and 1:1 mixture of distilled water and saturated methanolic potassium carbonate (15 ml) were added to a 50-ml round-bottomed flask equipped with a magnetic stirrer. The flask was sealed and left over night. Thin-layer chromatography using ethyl acetate as the eluent showed presence of **3** and **4** with the predominance of **3**.

2. A sample of chromatographically pure compound **4** (0.238 g, 1 mmol) and hydrazine hydrate (0.5 g, 10 mmol) in ethanol (15 ml) were added to a 50-ml round-bottomed flask. The mixture was heated at reflux for 2 h. Thin-layer chromatography with ethyl acetate as the eluent showed the presence of **3** and **4** with the predominance of **3**.

Similar results were obtained in the isomerization of oxazolidinone **3**.

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