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Synthesis and Applications of (-)-(*S*)-3-Amino-quinuclidine-Derived Thiourea

Evija Rolava[1], Māris Turks[2],
[1–2] *Riga Technical University*

Abstract **− A synthesis of enantiopure thiourea organocatalyst based on (-)-(*S*)-3-aminoquinuclidine dihydrochloride was developed with quantitative product yield. The catalyst was tested in different reactions: asymmetric Michael addition of ketones and malonates to nitroalkenes, nitromethane 1,4-addition to *trans*-chalcone, and Friedel-Crafts alkylation of indoles with *trans*-β-nitrostyrene. The novel thiourea proved to catalyze the aforementioned reactions and expected products were obtained in mediocre yields and low enantioselectivities.**

Keywords **− aminoquinuclidine, bifunctional thiourea organocatalysts, asymmetric synthesis, Chiralpak IA.**

I. Introduction

The use of small, environmentally friendly organic molecules to catalyse enantioselective transformations in a simple and metal-free manner, named organocatalysis, is a challenge for synthetic chemistry [1]. In the last decade the double hydrogen-bonding motif is becoming a powerful tool in organocatalysis for the activation of carbonyl groups and nitroalkenes through weak hydrogen-bond interactions [2]. The resulting nitroalkanes are versatile synthetic building blocks as they can be easily transformed into variety of different functional groups – amines, ketones, carboxylic acids and nitrile oxides [3].

Various molecular scaffolds have proved themselves as bifunctional thiourea organocatalysts – catalysts consisting of thiourea as a hydrogen-bond donor and basic amine functioning as a hydrogen-bond acceptor in a single molecular scaffold. A typical catalyst from this family is the cinchona-alkaloid-derived catalyst **1** (Soós catalyst), which contains the thiourea moiety [4] (Fig. 1).

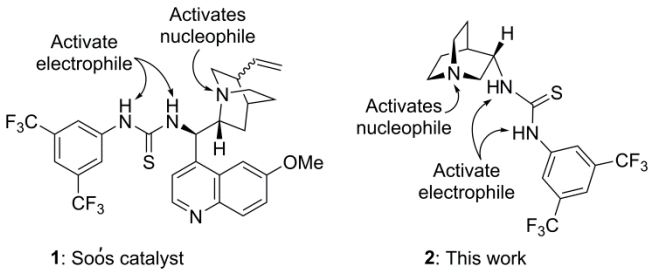
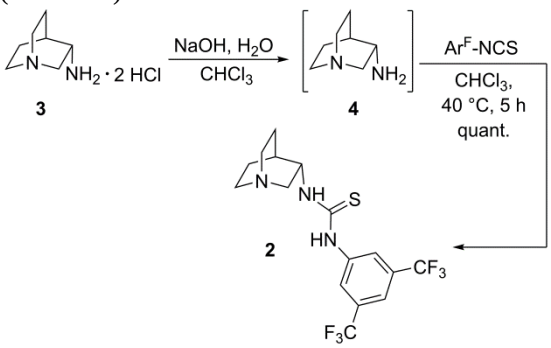


Fig. 1. Examples of bifunctional thiourea organocatalysts.

Moreover, quinuclidine bicyclic structure has a significant role in organic synthesis as a chemical building block, which is present in many chiral catalysts. This fact attracted our attention to synthesis of aryl(thio)urea organocatalyst **2 (Fig. 1)** using (-)-(*S*)-3-aminoquinuclidine dihydrochloride as a scaffold. Previously compound **2** was obtained as a racemate and applied as a catalyst only in the Baylis-Hillman reaction between methyl acrylate and *o*-chlorobenzaldehyde [5].

II. Results and Discussion

General procedure based on literature data about the synthesis of similar ureas is a one-step reaction starting from the corresponding amine [6]. The optimized reaction conditions for producing compound **2** were as follows: 1) dihydrochloride (compound **3**) was handled with sodium hydroxide and the free base (compound **4**) was extracted from the solid phase in $CHCl_3$; 2) bis(3,5-trifluoromethyl)phenylthio-isocyanate was added to the latter chloroform solution in the absence of any additives and the resulting reaction mixture was gently warmed to 40 °C. In these transformations product **2** was obtained in quantitative yield (Scheme 1).



Scheme 1. Synthesis of bifunctional tertiary amine-thiourea organocatalyst **2** based on quinuclidine platform.

With the product **2** ready, we have started an application of it as a bifunctional organocatalyst. Different types of asymmetric reactions were tested (Table I).

Thus, thiourea **2** showed a catalytic activity in:

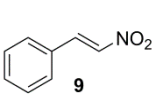
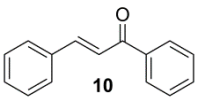
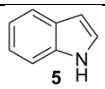
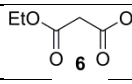
- Friedel-Crafts alkylation of indole **5** with *trans*-β-nitrostyrene **9**;
- Michael reaction between diethylmalonate **6** and *trans*-β-nitrostyrene **9**;
- Nitromethane **8** 1,4-addition to *trans*-chalcone **10**.

Target products were not obtained in the following reactions:

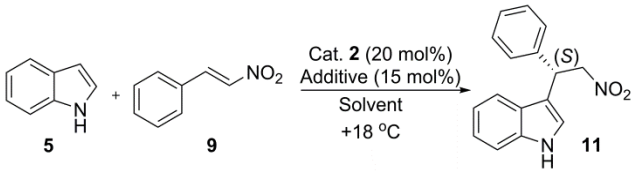
- Michael reaction between acetone **7** and *trans*-β-nitrostyrene **9**;
- Michael reaction between diethylmalonate **6** and *trans*-chalcone **10**.

TABLE I

SUMMARY OF CATALYTIC ACTIVITY OF THE POTENTIAL CATALYST **2** IN DIFFERENT ASYMMETRIC REACTIONS

	 **9**	 **10**
 **5**	reaction proceeds	exp. not performed
 **6**	reaction proceeds	no reaction
 **7**	no reaction	exp. not performed
$MeNO_2$ (**8**)	exp. not performed	reaction proceeds

*A. Friedel-Crafts Alkylation of Indole with Trans-β-nitrostyrene*The addition of indole to *trans*-β-nitrostyrene was used as a test reaction to explore the feasibility of the enantioselective Friedel-Crafts alkylation catalyzed by compound **2** (Scheme 2, Table II). Thiourea-based organocatalyst **2** was able to increase the reactivity of *trans*-β-nitrostyrene **9** in the Friedel-Crafts alkylation reaction with indole **5**, performed at room temperature (Table II, entries 2, 5 and 6), with respect to the non-catalyzed reaction (entry 1).



Scheme 2. Catalytic enantioselective Friedel-Crafts alkylation of indole **5** with *trans*-β-nitrostyrene **9**.

TABLE II.

RESULTS OF CATALYTIC ENANTIOSELECTIVE FRIEDEL-CRAFTS ALKYLATION OF INDOLE **5** WITH *TRANS*-β-NITROSTYRENE **9** WITH ADDITIVES ACCORDING TO SCHEME 2[A]

Entry	Cata-lyst	Additive	Solvent	*t*, h	Yield of product **11**, %	*ee*, % (*S*)
1	-	-	CH_2Cl_2/ toluene	360	-	-
2	**2**	-	tolulene	360	22	8[b]
3	**2**	-	$CHCl_3$	144	-	-
4	**2**	-	CH_2Cl_2	360	-	-
5	**2**	(1*R*)-(-)-10-camphorsulfonic acid	CH_2Cl_2	168	42	7[c]
6	**2**	(1*R*,3*S*)-(+)-camphoric acid	CH_2Cl_2	168	44	7[c]

[a] Reaction conditions: **5** (0.134 mmol), **9** (1-2 equiv) **2** (20 mol-%), solvent (0.15-0.3 mL) and additive (20 mol-%). Yield of the product isolated after flash chromatography.

[b] The absolute configuration of the product **11** was determined by comparing the specific rotation (at 23 °C) of **11** with that of literature data [7].

[c] Determined by HPLC analysis using *Chiralpak IA* column (0.46 cm × 25 cm) (Isocratic method: 5 % isopropanol/hexanes; 40 min; injection 5 µl (0.70 mg/ml hexanes + 30 % isopropanol); flow rate 1 ml/min; detector wavelenght 254 nm).

Solvent choice has a large effect on the catalytic activity of a bifunctional catalyst [8]. The target compound **11** was not obtained by using CH_2Cl_2 and $CHCl_3$ as solvents in the absence of additives (entries 3 and 4). Whereas, the use of toluene gave desired product **11** with 22 % yield (entry 2). It was a rather slow reaction which resulted in 8 % *ee*. In the presence of additives (1*R*)-(-)-10-camphorsulfonic acid and (1*R*,3*S*)-(+)-camphoric acid, we improved the yield to 44 %, but the obtained product was still almost racemic – 7 % *ee* (entries 5 and 6).

The ability of thiourea **2** to promote the Friedel-Crafts additions of indoles **5** to nitroalkenes **9** might be interpreted on the basis of a reversible formation of a complex **12** involving a double hydrogen bond between the thiourea hydrogen atoms and two oxygen atoms of nitroalkene (Fig. 2) [9]. Also quinuclidine amine function is expected to interact with the indolic proton through a weak hydrogen bond, helping it to direct the attack from one side.

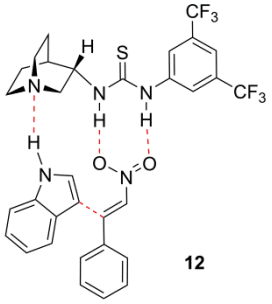
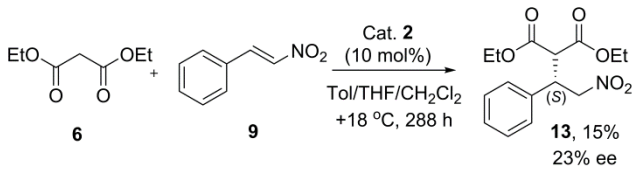


Fig. 2. Possible transition state model in the thiourea-catalyzed Friedel-Crafts alkylation of indole **5** with *trans*-β-nitrostyrene **9**.

B. Michael Reaction Between Diethylmalonate and Trans-β-nitrostyrene

Catalyst **2** has displayed organocatalytic activity in asymmetric Michael addition between diethylmalonate and *trans*-β-nitrostyrene (Scheme 3). In a non-catalyzed reaction of *trans-β*-nitrostyrene **9** with diethylmalonate **6** no product traces were detected by GC-MS analyses. The reaction **6** + **9** → **13** in the presence of 10 mol-% of **2** in solvent mixture toluenetetrahydrofuran/CH_2Cl_2 afforded the desired Michael adduct (17 % conversion by gas chromatography-mass spectrometry (GC-MS)) with (*S*)-isomer being the major enantiomer (23 % ee). The absolute configuration of the isolated product **13** was determined by comparing the specific rotation ($[\alpha]_D^{23}$ = 1.7 (c = 0.6, $CHCl_3$) with that of literature data [10].



Scheme 3. Catalytic Michael reaction of diethylmalonate to trans-β-nitrostyrene.

C. Catalytic Michael 1,4-Addition of Nitromethane to Trans-chalcone

Thiourea catalyst **2** slightly promotes the Michael reaction between nitromethane and *trans*-chalcone with 15 % isolated yield (Scheme 4). The enantiomeric composition of the product was not determined due to the low yield.

Scheme 4. Catalytic Michael reaction of nitromethane to *trans-chalcone.*

III. Conclusion

An optimized protocol for enantiomerically pure (-)-(*S*)-3-aminoquinuclidine-derived thiourea derivative was developed to give the desired product in quantitative yield. Thiourea **2** has shown an organocatalytic properties in Friedel-Crafts alkylation reaction between indole and *trans*-β-nitrostyrene. So far, it has displayed also promising organocatalytic activity in asymmetric Michael addition between diethylmalonate and *trans*-β-nitrostyrene. Further elaboration of reaction solvents and additives might help to increase the reaction yields and enantioselectivities. Due to the ease of access this catalyst might to be useful in other organocatalytic transformations which still wait to be uncovered.

IV. Experimental section

Commercial reagents were used without purification. Solvents were distilled prior to use. Flash chromatography was performed on *Rocc* silica gel (*SI 1721*, 40 μm − 63 μm, pores 60±5 Å). ^{1}H-NMR and ^{13}C-NMR spectra (nuclear magnetic resonance spectroscopy) were recorded at 300 MHz and at 75.5 MHz, respectively. Proton signals for residual non-deuterated solvents (δ 7.26 for $CDCl_3$ and δ 2.50 for $DMSO_{d6}$) and carbon signals (δ 77.1 for $CDCl_3$ and δ 39.5 for $DMSO_{d6}$) were used as an internal references for ^{1}H-NMR and ^{13}C-NMR spectra, respectively. Chemical shift (δ) values are reported in ppm and coupling constants *J* in Hz. Furier-transform infrared (FT-IR) spectra were recorded in thin films on KBr plates using *Perkin Elmer Spectrum BX*. Optical rotations were measured at 23 °C on a *Anton Paar MCP 500* polarimeter using a sodium lamp as the light source (589 nm); the length of the cell was 1 dm. Enantiomeric excess was determined by high-performance liquid chromatography (HPLC) analysis using *Chiralpak IA* column 0.46 cm × 25 cm (isocratic method: 5 % isopropanol/hexanes; 40 min; injection volume 5 μl (0.70 mg/ml hexanes with 30 % isopropanol); flow rate 1 ml/min; detector wavelength 254 nm. Yields refer to chromatographically and spectroscopically homogeneous materials.

The following conditions for gas chromatography analysis were used: *Agilent Technologies 6890* gas chromatograph with mass selective detector, Agilent *19091J-433 HP-5* 5 % phenylmethylsiloxane capillary column 30 m × 0.25 mm, film thickness – 0.25 μm, injector temperature – 250 °C, detector temperature – 250 °C, carrier gas – helium, flow rate – 1 ml/min, injection volume (splitless injection) 5 μl. Temperature conditions were: 80 °C for 3 min, rise at 50 °C/min to 310 °C and upkeep in 310 °C for 10 min.

A. 1-(3,5-bis(Trifluoromethyl)Pphenyl)-3-((3S)-quinuclidin-3-yl)thiourea (2)

To a solution of (-)-(*S*)-3-aminoquinuclidine dihydrochloride **3** (0.150 g, 0.753 mmol, 1 equiv) in $CHCl_3$ (15 mL) was added NaOH (0.060 g, 1.51 mmol, 2 equiv) and H_2O (0.7 mL). The resulting mixture was stirred until substrate **3** was dissolved. Then anhydrous Na_2SO_4 was added, stirred for 30 min and filtered. To the filtrate of the free base **4** bis(3,5-trifluoromethyl)phenylisothiocyanate (0.138 ml, 0.75 mmol, 1 equiv) was added in 40 ºC. After stirring with reflux in 40 ºC for 30 min, the solvent evaporation under reduced pressure provided **2** (0.290 g, quant. yield). The NMR data and other characteristics of products **2** fully correspond to those reported earlier [5]. $[\alpha]_D^{23} = 0.64$ (c = 1.2, $CHCl_3$); FT-IR: 3270 cm^{-1}, 3047 cm^{-1}, 2951 cm^{-1}, 2879 cm^{-1}, 1538 cm^{-1}, 1473 cm^{-1}, 1386 cm^{-1}, 1278 cm^{-1}, 1174 cm^{-1}, 1132 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ: 7.83 (s, 2H), 7.69 (s, 1H), 6.91 − 6.48 (br s, 1H), 4.50 − 4.32 (br s, 1H), 3.49 (dd, AB syst., 1H, ^{2}J = 14.1 Hz, ^{3}J = 9.4 Hz), 2.88 − 2.76 (m, 4H), 2.60 (dd, AB syst., 1H, ^{2}J = 14.1 Hz, ^{3}J = 4.5 Hz), 2.16 − 2.08 (m, 1H), 1.76 − 1.66 (m, 2H), 1.60 − 1.49 (m, 2H).

B. General Procedure for Synthesis of 3-((S)-2-Nitro-1-phenylethyl)-1H-indole

Reaction conditions and results are summarized in Table III. A mixture of indole **5**, t*rans*-β-nitrostyrene **9**, catalyst **2** and additives were dissolved in respective solvent. The resulting reaction mixture was held at respective temperature and controlled by GC-MS. Sample preparation for analysis of the reaction mixture: ~10 μl aliquot was taken with Pasteur pipette, diluted with 2 mL CH_2Cl_2 and injected in GC-MS. For isolation of the product solvents were removed under reduced pressure. Purification by column chromatography (ethyl acetate/hexanes 3 %) yielded the product. NMR data and other characteristics of products **11** fully correspond to those reported earlier [7]. The enantiomeric excess and the absolute configuration of the product were determined by comparing the specific rotation of **11** with that of literature data [7]. Enantiomeric excess was determined also by HPLC analysis of **11** using *Chiralpak IA* column. ^{1}H-NMR ($CDCl_3$, 300 MHz) δ: 8.10 (br s, 1H, H-N(1)), 7.46 (d, 1H, ^{3} = 8.1 Hz, H-C(c)), 7.37 − 7.25 (m, 6H, H-C(e), H-C(g), H-C(4), H-C(5), H-C(6), H-C(7)), 7.21 (td, 1H, ^{3}J = 8.3 Hz, ^{4}J = 0.9 Hz, H-C(d)), 7.09 (td, 1H, ^{3} =8.1 Hz, ^{4}J = 0.9 Hz, H-C(f)), 7.03 (d, 1H, ^{3}J = 2.5 Hz, H-C(2)), 5.20 (dd, 1H, ^{3}J = 7.7 Hz, ^{3}J = 8.1 Hz, H-C(a)), 5.08 (dd, AB syst., 1H, ^{2}J = 12.4 Hz, ^{3}J =7.5 Hz, H_a-C(b)), 4.95 (dd, AB syst., 1H, ^{2}J = 12.4 Hz, ^{3}J = 8.3 Hz, H_a-C(b)); ^{13}C-NMR ($CDCl_3$), 75 MHz) δ: 139.2, 136.6, 129.0, 127.8, 127.6, 122.8, 121.7, 120.1, 119.0, 114.5, 111.4, 79.6, 41.6; in GC-MS t_R (retention time) was 8.62 min; specific rotation for 85 % *ee* (*R*)) product [7]: $[\alpha]_D^{r.t.} = -8$ (c = 0.65, $CHCl_3$)

TABLE III
REACTION CONDITIONS AND RESULTS OF ASYMMETRIC FRIEDEL-CRAFTS ALKYLATION (**5** + **9** → **11**)

Entry	Solvent: volume, mL	Catalyst **2**: mass, mg; amount of subst., mmol; equiv	Indole: mass, mg; amount of subst., mmol; equiv	*Trans*-β-nitrostyrene: mass, mg; amount of subst., mmol; equiv	Additive: mass, mg; amount of subst., mmol; equiv	T, °C	*t*, h	Σ *t*, h	Yield, %	*ee*, %, config.
1	CH_2Cl_2 (0.3) toluene (0.2)	-	59.0 0.503 1.5	50.0 0.335 1	-	-20 +4	48 18	66	-	-
2	toluene (0.2)	11.0 0.027 0.2	16.0 0.134 1	20.0 0.134 1	-	+19	360		22	8[a] (*S*)
3	$CHCl_3$ (0.2)	5.5 0.013 0.2	8.0 0.067 1	20.0 0.134 2	-	+19	144			-
4	CH_2Cl_2 (0.3)	43.0 0.107 0.2	63.0 0.535 1	80.0 0.535 1	-	+19	360		-	-
5	CH_2Cl_2 (0.15)	11.0 0.029 0.2	16.0 0.134 1	20.0 0.134 1	(1*R*)-(-)-10-camphorsulfonic acid 5.00 0.020 0.15	+19	168		42	7[b] (*S*)
6	CH_2Cl_2 (0.15)	11.0 0.029 0.2	16.0 0.134 1	20.0 0.134 1	(1*R*,3*S*)-(+)-camphoric acid 4.00 0.020 0.15	+19	168		44	7[b] (*S*)

[a] The absolute configuration of the product **11** was determined by comparing the specific rotation (at 23 °C) of **11** with that of literature data [7].
[b] Determined by HPLC analysis using *Chiralpak IA* column.

C. General Procedure for Synthesis of (R)-Ethyl-2-carbethoxy-4-nitro-3-phenylbutyrate

The reaction conditions and results are summarized in Table IV**.** To a solution of *trans*-β-nitrostyrene **9** and catalyst **2** in toluene (0.2 mL) diethylmalonate **6** was added. The resulting reaction mixture was held at ambient temperature for 5 days and tetrahydrofuran (0.1 mL) and CH_2Cl_2 (0.1 mL) was added. Sample preparation for analysis of the reaction mixture: ~10 µl aliquot was taken with Pasteur pipette, diluted with 2 mL CH_2Cl_2 and injected into GC-MS. After 12 days solvents were removed under reduced pressure. The residue was purified by column chromatography (ethyl acetate/hexanes 4 %) and yielded product **13**. The NMR data and other characteristics of products **13** fully correspond to those reported earlier [10]. The enantiomeric excess and the absolute configuration of the product was determined by comparing the specific rotation of **13** with that of literature data [10]. ^{1}H-NMR ($CDCl_3$, 300 MHz) δ: δ 7.35 − 7.15 (m, 5H, H-C(Ar)), 4.86 (dd, 1H, ^2J = 12.9, ^3J = 4.7 Hz, H_a-C(4)), 4.79 (dd, 1H, ^2J = 12.9, ^3J = 9.2 Hz, H_b-C(4)), 4.20 − 4.12 (m, 3H, H-C(3), H-C(3`)), 3.94 (q, 2H, $^3J$ = 7.0 Hz, H-C(1`)), 3.75 (d, 1H, ^3J = 9.8 Hz, H-C(2)), 1.20 (t, 3H, ^3J = 7.0 Hz, H-C(4`)), 0.97 (t, 3H, $^3J$ = 7.0 Hz, H-C(2`)); in GC-MS t_R (retention time) was 7.17 min; specific rotation for 95 % *ee* (*S*)) product [10]: $[\alpha]_D^{23}$ = 7.3 (c = 1.07, $CHCl_3$).

TABLE IV
REACTION CONDITIONS AND RESULTS OF CATALYTIC MICHAEL REACTION OF DIETHYLMALONATE TO TRANS-β-NITROSTYRENE (6 + 9 → 13)

Entry	Catalyst **2**: mass, mg; amount of subst., mmol; equiv.	Diethylmalonate: volume, µl; amount of subst., mmol; equiv.	*Trans*-β-nitrostyrene: mass, mg; amount of subst., mmol; equiv.	*t*, h	Yield of comp. **13**, %	$[\alpha]_D^{23}$ of comp. **13**	*ee*, %, config. of comp. **13**
1	-	62.0 0.403 1	60.0 0.403 1	144	-	-	-
2	16.0 0.040 0.1	62.0 0.403 1	120.0 0.806 2	288	15	1.73 (c 0.6, $CHCl_3$)	23 (*S*)

D. 3-Nitro Methyl-1,3-diphenyl-2-propen-1-one (14)

To a solution of 1,3-diphenyl-2-propen-1-one **10** (60.0 mg, 0.289 mmol, 1.0 equiv) and catalyst **2** (12.0 mg, 0.029 mmol, 0.1 equiv) in toluene (0.2 ml) nitromethane **8** (46.0 µl, 0.85 mmol, 3 equiv) was added. Reaction mixture was stirred for 336 h and controlled by GC-MS. Sample preparation for analysis of the reaction mixture: ~10 µl aliquot was taken with Pasteur pipette, diluted with 2 mL CH_2Cl_2 and injected in GC-MS. For isolation of the product solvents were removed under

reduced pressure. Purification by column chromatography (ethyl acetate/hexanes 2 %) yielded product **14** (15 %). The NMR data and other characteristics of products **14** fully correspond to those reported earlier [10]. ^{1}H-NMR ($CDCl_3$, 300 MHz) δ: 7.92 (d, 3H, ^3J = 7.3 Hz, H-C(2``), H-C(6``)), 7.58 (t, 1H, ^3J = 7.3 Hz, H-C(4``)), 7.46 (t, 2H, $^3J$ = 7.5 Hz, H-C(3``), H-C(5``)), 7.38 − 7.24 (m, 5H, H-C(Ar)), 4.84 (dd, AB syst., 1H, ^2J = 12.4 Hz, ^3J = 6.8 Hz, H_a-C(3`)), 4.69 (dd, AB syst.,1H, $^2J$ = 12.4 Hz, $^3J$ = 7.9 Hz, $H_b$-C(3`)), 4.23 (quintet, 1H, ^3J = 7.2 Hz, H-C(3)), 3.53 − 3.37 (m, 2H, H-C(2)); in GC-MS t_R (retention time) was 7.67 min.

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Evija Rolava obtained her *Bc. chem.* degree (2012) and *Mg. sc. ing.* (in Chemical Engineering) degree at Riga Technical University (2014).
E. Rolava has worked as a senior laboratory assistant (2011–2012) and a research assistant (2012–2014) at the Faculty of Materials Science and Applied Chemistry, Riga Technical University. Her research was focused on the synthesis and application of novel urea and thiourea organocatalysts based on carbohydrate β-amino alcohols and (-)-(*S*)-3-aminoquinuclidine dihydrochloride. Furthermore, her previous research included synthesis of carbohydrate based *N*-acyl-spirooxazolidinone derivatives (Turks, M. *et al.*, A practical access to glucose- and allose-based (5+5) 3-spiropseudonucleosides from a common intermediate. *Carbohydr. Res.* 2013, vol. 375, 5–15.) and its application as chiral auxiliaries in diastereoselective alkylation reactions.
E-mail: rolavaevija@gmail.com

Māris Turks obtained his *Bc. chem.* Degree at the University of Latvia in 1998 and *Mg. chem.* degree at Riga Technical University in 2000. Further, he was a doctoral student at the Swiss Federal Institute of Technology, Lausanne under the guidance of Professor Pierre Vogel, where he earned his *Dr. ès. sc.* degree in Synthetic Organic Chemistry in 2005. M. Turks has worked as a postdoctoral associate at the Swiss Federal Institute of Technology, Lausanne in 2005 followed by appointment as SNSF postdoctoral fellow at Stanford University under the guidance of Professor Barry M. Trost in 2006. In 2007 he accepted an academic position at the Faculty of Materials Science and Applied Chemistry, Riga Technical University, where currently he is a professor and the head of the Institute of Technology of Organic Chemistry. Dr. Turks' current research interests deal with carbohydrate chemistry, functionalized heterocycles, and applications of liquid sulfur dioxide in organic synthesis.
E-mail: maris_turks@ktf.rtu.lv

Evija Rolava, Māris Turks. No (-)-(*S*)-3-aminohinuklidīna atvasinātas tiourīnvielas sintēze un pielietojums

Šajā darbā izstrādāta enantiomēri tīra, uz (-)-(*S*)-3-aminohinuklidīna platformas veidota tiourīnvielas atvasinājuma iegūšana ar kvantitatīvu iznākumu. Pēc dihidrohlorīda nošķelšanas (-)-(*S*)-3-aminohinuklidīnu iesaistīja reakcijā ar bis(3,5-trifluormetil)fenilizotiocianātu, tādējādi iegūstot vēlamo produktu, ar iespēju to izmantot enantioselektīvas *C-C* saites veidošanā. Potenciālo organokatalītisko spēju enantioselektīvi katalizēt pārbauda vispārīgos piemēros.

Pierādīta enantiomēri tīrās 1-(3,5-bis(trifluormetil)fenil)-3-((3*S*)-hinuklidīn-3-il)tiourīnvielas organokatalītiskā daba: tā spēja katalizēt Frīdela-Kraftsa reakciju, alkilējot indolu ar *trans*-β-nitrostirolu. Reakcijā, kā šķīdinātāju lietojot toluolu, iegūst produktu ar 22 % iznākumu un nelielu *S*-izomēra pārsvaru. Absolūto konfigurāciju nosaka gan pēc īpatnējās optiskās griešanas datiem, gan lietojot augstas efektivitātes šķidruma hromatogrāfiju ar *Chiralpak IA* kolonnu. Izmantojot dihlormetānu, produktu ar iznākumu 42 % − 44 % iegūst reakcijai pievienojot skābes piedevas – (*1R*)-(-)-10-kamparsulfoskābi un (1*R*, 3*S*)-(+)-kamparskābi, tomēr tiourīnvielas atvasinājuma katalizētspēja ir neselektīva – *ee* 7 %. 1-(3,5-bis(trifluormetil)fenil)-3-((3*S*)-hinuklidīn-3-il)tiourīnviela izrāda organokatalītisko spēju asimetriskā Maikla pievienošanās reakcijā starp dietilmalonātu un *trans*-β-nitrostirolu, dodot produktu ar 23 % *ee*, kā arī nitrometāna 1,4-pievienošanās reakcijā *trans*-halkonam.

Эвия Ролава, Марис Туркс. Синтез и применение тиомочевины на основе 3-аминохинуклидина.

В данной статье разработан метод получения энантиомерно чистого производного тиомочевины на основе (-)-(*S*)-3-амино-хинуклидина, с количественным выходом. После выделения в свободной форме, (-)-(*S*)-3-амино-хинуклидин подвергается реакции с 3,5-бис(трифторметил)фенилизотиоцианатом, образуя желаемый продукт, который можно использовать для энантиоселективного формирования С-С связи.

Доказаны органокаталитические свойства чистой 1-(3,5-бис(трифторметил)фенил)-3((3*S*)-хинуклидин-3-ил)тиомочевины. Алкилирование индола 2-*транс*-нитростиролом по Фриделю-Крафтсу в толуоле проходит с выходом 22 % и небольшим энантиомерным избытком *S*-изомера. Абсюлютная конфигурация определена как по величине удельного вращения продукта, так и при помощи ВЭЖХ на хиральной стационарной фазе, используя колонну *Chiralpak IA*. Реакция в дихлорметане проходит только при добавлении (*1R*)-(-)-10-камфорсульфоновой кислоты или (1*R*,3*S*)-(+)-камфорной кислоты, но реакция не стереоселективна – *ee* = 7 %. 1-(3,5-Бис(трифторметил)фенил)-3-((3*S*)-хинуклидин-3-ил)тиомочевина органокаталитически активна в энантиоселективной реакции присоединения диэтилмалоната к 2-*транс*-нитростиролу (*ee* = 23 %), а также в реакции конъюгированного присоединения нитрометана к *транс*-халкону.