CHEMIJA. 2012. Vol. 23. No. 3. P. 239–243

AgI nanoparticles as heterogeneous catalysts in one-pot alkylation reaction of chiral amines (L-valine methyl ester) in water-alcohol media

Javad Safaei-Ghomi[1]*,

Abdolrazzagh Gaderi-Zefre[1],

Mohammad Ali Ghasemzadeh[1],

Ahmad Kakavand-Ghalenoei[1],

Masoud Salavati-Niasari[2]

[1] *Department of Organic Chemistry, Faculty of Chemistry, University of Kashan, Kashan, P. O. Box 87317-51167, I. R. Iran*

[2] *Institute of Nano Science and Nano Technology, University of Kashan, Kashan, P. O. Box 87317-51167, I. R. Iran*

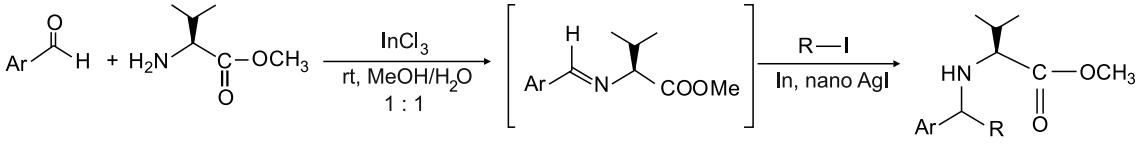
An efficient eco-friendly method for the alkylation reaction of various chiral amines is described by a simple one-pot reaction of aldehydes, amines and alkyl iodides in the presence of AgI nanoparticles in water-alcohol media. Silver iodide nanoparticles mediated the enhanced rate and facility of reaction and showed high influence in the green synthesis of some amine derivatives. Moreover, this nanoparticle increased the yields of products, decreased the reaction times in all cases and did not affect the reaction diastereoselectivity. The heterogeneous mediator was fully characterized by scanning electron microscopy (SEM), X-ray diffraction (XRD) and FT-IR experimental techniques.

Key words: alkylation, silver nanoparticles, chiral amine, water-alcohol media, heterogeneous mediator, one-pot reaction, diastereoselectivity

INTRODUCTION

Amines are important building blocks for the pharmaceutical and chemical industry [1–4]. In recent years, there has been a great interest in the development of organic reactions in water-alcohol media [5, 6]. The use of water-alcohol as a solvent in organic synthesis has many advantages from both economic and environmental aspects [7]. Preparation of alkylated amines from imines was reported by several methods, in which the imines were prepared in situ by aldehydes and amines. In one method aldhydes and amines reacted in the prescence of L-proline as an organocatalyst [8]. The synthesis of secondary amine derivatives under the condensation of diethyl phosphonate, amine and aldhyde with lanthanide triflate catalysis is the other method [9]. Chiral propargylamines can also be prepared by one-pot three-component reaction between alkyne, aldehyde and a secondary amine at room temperature in the presence of CuBr and (R)-quinap as a catalyst [10]. Recently, Barbier type alkylation reactions have been extensively studied with aldehydes, ketones, amines, acetals, and nitriles [11, 12]. The Barbier-Grignard reaction using metallic mediators and alkyl halides in water is one of the most useful and convenient method for performing alkylation reaction. Most of the metal-mediated alkylation reactions of amines were reported using indium [13, 14]. Recently, it was reported that the combination In/AgI/$InCl_3$ was an efficient system for alkylation reaction of amines using unactivated alkyl iodides in water-alcohol [15]. Thus far, there has been no report of the Grignard-Barbier-type

* Corresponding author. E-mail: safaei@kashanu.ac.ir



Scheme. Silver iodide nanoparticles as an effiecient mediator for the preparation of chiral imines

alkylation of amines using nanometals as mediators in aqueous media. The higher efficiency of nanoparticles as mediators in organic reactions under mild conditions, in comparison with traditional solid state catalysts, has been demonstrated [16]. Nowadays, application of nanostructures is an important versatile method for the preparation of organic compounds. Recently, nanoparticles are attracting a great attention since they display homogeneous-like activities due to their large surface areas relative to their bulk forms [17–19]. It has been demonstrated to be efficient on nano-scale materials for various useful chemical transformations for the synthesis of diverse organic compounds, such as preparations of propargylamines [20, 21], triazole derivatives [22], quinoxalines compounds [23], C-N cross coupling reactions [24], alkyne-azide aycloadditions [25], β-acetamido ketones / esters [26], synthesis of diaryl sulphides [27] and other reactions.

Herein, we wish to report a novel and efficient aqueous Barbier-Grignard-type alkylation of amines with alkyl iodides in an indium-nanosilveriodide-indium chloride system. A series of experiments were carried out in an effort to develop an improved procedure for the synthesis of secondary chiral amines by three-component coupling between aldehydes, chiral amino ester and alkyl iodides in water-alcohol media (Scheme).

RESULTS AND DISCUSSION

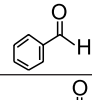
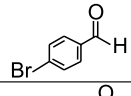
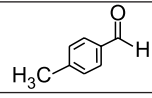
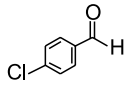
Among the different metals investigated, indium was observed to be an effective metal for the alkylation reactions of L-valine methyl ester in water-alcohol media [15]. We carried out the one-pot Barbier–Grignard-type alkylation reaction of L-valine methyl ester by using In/AgI(np)/$InCl_3$ in water-methanol. The scope and versatility of the present reaction were investigated by using various aldehydes and alkyl iodides. This reaction is an efficient method for alkylation of L-valine methyl ester so that yield gives rise up to 90%, as shown in Table. Utilization of AgI nanoparticles increased the yield of reaction and also decreased the time of reaction impressively. L-valine methyl ester has an asymmetric carbon so there are two possibilities for the attack of alkyl radical to the imine in the second step. Thus, two diastereomeres with different amounts will be produced. We expect that nano silver iodide would not affect the reaction diastereoselectivity. The ratio of two isomers which was determined by ^{1}H NMR integration was not different using bulk or nanoparticle catalysts as shown in the Table.

The results are shown in the Table: the usage of nanoparticles as mediators shows a very remarkable effect on the reaction so we can reach even 90% yield in 18 h (entry 3, 5, Table). Nanoparticles are well dispersed in the solvent so that the reactant reaches the active site by diffusion. The comparison between the time of reaction in the presence of AgI nanoparticles and bulk AgI is shown in the Table.

In order to investigate the morphology and particle size of AgI nanoparticles, a SEM image of AgI nanoparticles was recorded and presented in Fig. 1. These results show that spherical AgI nanoparticles were obtained from $AgNO_3$ and KI with the particle size 45–50 nm under ultrasound power.

Fig. 2 shows the FT-IR spectrum of AgI nanoparticles. The broad peak at 3 436 and 1 628 cm^{-1} can be attributed to

Table. **Indium-silver iodide mediated alkylation reaction of L-Valine methyl ester in water- methanol**

dr[a, b]	Time, h / Yield[b], %	Time, h / Yield[a], %	RI	ArCHO	Entry
89 : 11	28/72	18/85			1
88 : 12	28/53	17/68			2
89 : 11	28/86	18/97			3
89 : 11	28/66	17/79			4
92 : 8	28/82	18/95			5

[a] in presence of AgI nanoparticles.

[b] in presence of bulk AgI.

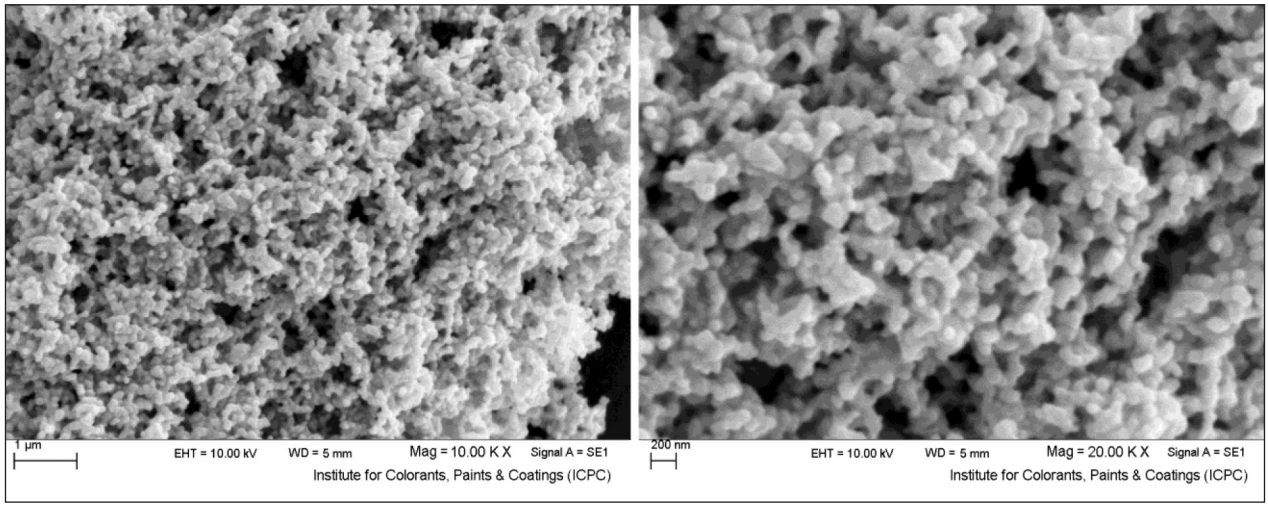


Fig. 1. SEM images of AgI nanoparticles

the ν (OH) stretching and bending vibrations, respectively. Thus, these peaks indicate the presence of physisorbed water linked to nanoparticles. As shown in Fig. 2, the peak corresponding to the CH_2 stretching vibration of SDS (sodium dodecyl sulfonate) at 2 923 cm^{-1} can be seen. The appearance of this peak suggests that a trace amount of SDS has been coated on the surface of AgI nanoparticles.

Fig. 3 shows the XRD pattern of AgI nanoparticles. All reflection peaks in Fig. 1 can be readily indexed to the pure cubic phase of AgI with F-43mspace group (JCDPS No. 78-0641).

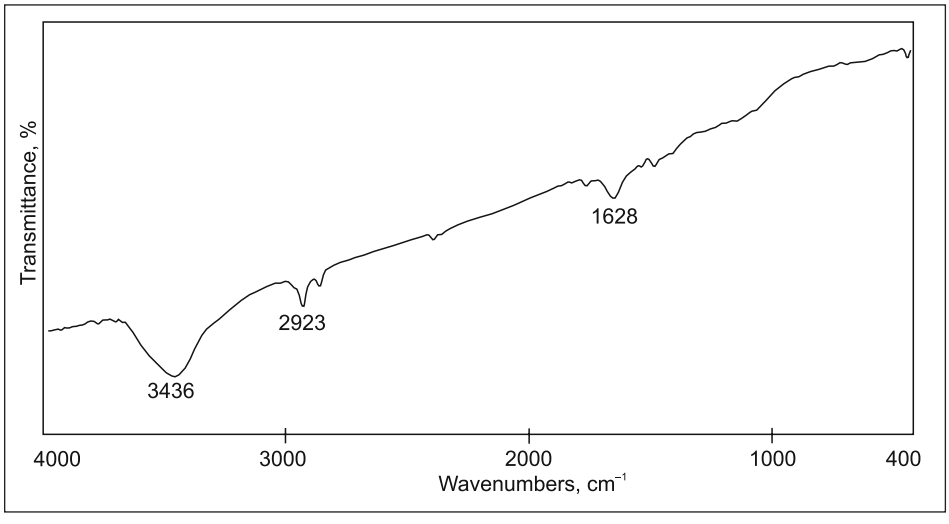


Fig. 2. FT-IR spectrum of AgI nanoparticles

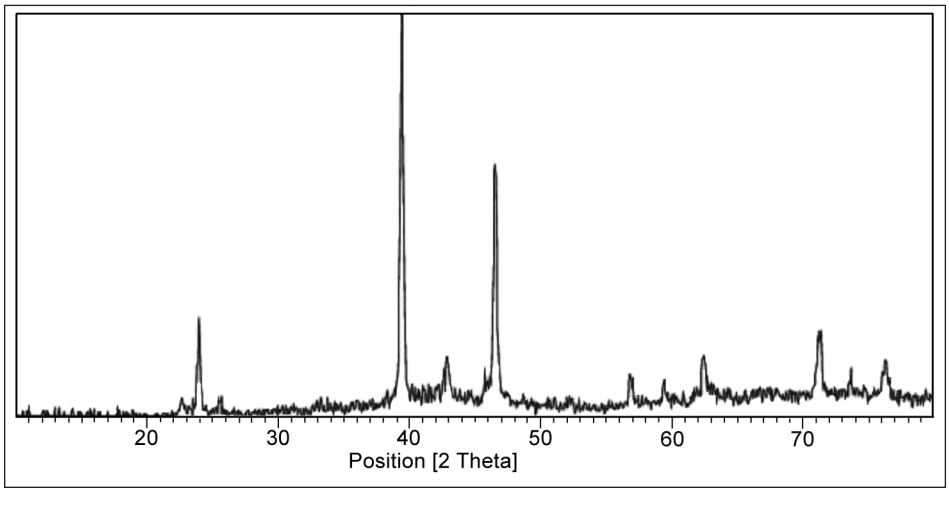


Fig. 3. The XRD pattern of AgI nanoparticles

The crystallite size diameter (D) of the AgI nanoparticles has been calculated by the Debye–Scherrer equation ($D = K\lambda/\beta\cos\theta$), where β FWHM (full-width at half-maximum or half-width) is in radians and θ is the position of the maximum of diffraction peak, K is the so-called shape factor, which usually takes a value of about 0.9, and k is the X-ray wavelength (1.5406 Å for Cu Kα). Crystallite size of AgI has been found to be 48 nm.

EXPERIMENTAL

Chemicals were purchased from Merck in high purity. All of the materials were of commercial reagent grade. Flash-column chromatography was performed by using Merck silica gel 60 with freshly distilled solvents.

The NMR spectra (^{1}H, ^{13}C) were recorded on a Bruker 400 Ultrashield spectrometer by using TMS as an internal standard. The UV–Vis measurements were obtained with a GBC cintra 6 UV–Vis spectrophotometer. The FT-IR spectrum was recorded on a Magna-IR, spectrometer 550 Nicolet in KBr pellets in the range of 400–4 000 cm^{-1}. Powder X-ray diffraction (XRD) was carried out on a Philips diffractometer of X'pert Company with monochromatized Cu Kα radiation (λ = 1.5406 Å). Microscopic morphology of products was visualized by SEM (LEO 1455VP).

Preparation of silver iodide nanoparticle

A solution of 0.415 g KI (25×10^{-4} mol) in 25 ml of distillated water was added dropwise to $AgNO_3$ solution (0.425 g, 25×10^{-4} mol in 25 ml of distillated water) under ultrasound power in the presence of 0.2 g SDS as a surfactant. The yellow as-synthesized precipitate was separated by centrifugation and washed with distillated water and ethanol to remove impurities for several times and then dried.

Typical procedure for indium-(silver iodide nanoparticle) alkylation of L-valine methyl ester

A mixture of water (5 mL), methanol (5 mL), aldehyde (0.5 mmol), amine (1.0 mmol) and $InCl_3$ (0.5 mmol) was stirred well in a round-bottomed flask for 4 h at room temperature. Then, indium (3 mmol), AgI (2 mmol) or AgI nanoparticle (0.5 mmol) and alkyl iodide (2.5 mmol) were added sequentially to the reaction system. The reaction mixture was stirred at room temperature for 24 h (with bulk AgI) and 14 h (with nano AgI). After completion the reaction, it was extracted by using ether, dried over anhydrous sodium sulfate, filtered, and the solvent was evaporated in vacuum to give the crude product. The product was separated using silica-gel column chromatography by using hexane: ethyl acetate (8 : 1) as an eluent.

2-[(1-Cyclohexyl-1-phenylmethyl)amino]-3-methylbutyric acid methyl ester (1)

R_f = 0.65 (EtOAc / hexane 1 : 8). – ^{1}H NMR (400 MHz, $CDCl_3$): 0.85 (d, *J* = 6.7 Hz, 3H), 0.94 (d, *J* = 6.8 Hz, 3H), 1.08–1.37 (m, 13H), 2.73 (d, *J* = 6.3 Hz, 1H), 3.17 (d, *J* = 6.9 Hz, 1H), 3.67 (s, 3H), 7.27–7.36 ppm (m, 5H). – ^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.42 (CO), 142.53 (C), 128.63 (2CH), 127.75 (2CH), 126.82 (CH), 67.36 (CH), 64.52 (CH), 51.22 (CH_3), 44.43 (CH), 31.82 (CH), 29.94 (CH_2), 29.72 (CH_2), 26.52 (CH_2), 26.23 ($2CH_2$), 19.54 (CH_3), 18.63 ppm (CH_3). – IR (KBr, neat): υ = 3 453 (N–H stretching), 2 931 and 2 856 (C–H stretching), 1 729 (C=O stretching), 1 601 and 1 454 cm^{-1} (C=C stretching aromatic).

2-{[1-Cyclohexyl-1-(p-bromophenyl)methyl)]amino}-3-methylbutyric acid methyl ester (2)

R_f = 0.61 (EtOAc / hexane 1 : 8). – ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.82 (d, *J* = 6.8 Hz, 3H), 0.88 (d, *J* = 6.8 Hz, 3H), 1.07–1.85 (m, 13H), 2.65 (d, *J* = 6.3 Hz, 1H), 3.16 (d, *J* = 7.0 Hz, 1H), 3.70 (s, 3H), 7.13–7.46 ppm (m, 4H). – ^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.72 (CO), 141.10 (C), 131.14 (2CH), 130.32 (2CH), 120.76 (CH), 66.93 (CH), 64.62 (CH), 51.42 (CH_3), 44.15 (CH), 31.63 (CH), 29.92 (CH_2), 29.51 (CH_2), 26.42 (CH_2), 26.12 ($2CH_2$), 19.42 (CH_3), 18.61 ppm (CH_3). – IR (KBr, neat): υ = 3 494 (N–H stretching), 2 981 and 2 864 (C–H stretching), 1 738 (C=O stretching), 1 595 and 1 510 cm^{-1} (C=C stretching aromatic).

2-{[1-Cyclohexyl-1-(p-methylphenyl)methyl)]amino}-3-methylbutyric acid methyl ester (3)

R_f = 0.61 (EtOAc / hexane 1 : 8). – ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (d, *J* = 6.7 Hz, 3H), 0.94 (d, *J* = 6.8 Hz, 3H), 1.19–1.75 (m, 13H), 2.32 (s, 3H), 2.72 (d, *J* = 6.4 Hz, 1H), 3.15 (d, *J* = 6.9 Hz, 1H), 3.69 (s, 3H), 7.53–7.73 ppm (m, 4H). – ^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.41 (CO), 139.42 (C), 136.28 (C), 128.46 (4CH), 66.93 (CH), 64.52 (CH), 51.12 (CH_3), 44.53 (CH), 31.83 (CH), 29.94 (CH_2), 29.72 (CH_2), 26.52 (CH_2), 26.23 ($2CH_2$), 21.13 (CH_3) 19.44 (CH_3), 18.63 ppm (CH_3). – IR (KBr, neat): υ = 3 449 (N–H stretching), 2 926 and 2 855 (C–H stretching), 1 728 (C=O stretching), 1 599 and 1 453 cm^{-1} (C=C stretching aromatic).

2-{[1-Cyclohexyl-1-(p-chlorophenyl)methyl)]amino}-3-methylbutyric acid methyl ester (4)

R_f = 0.63 (EtOAc / hexane 1 : 8). – ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.84 (d, *J* = 6.8 Hz, 3H), 0.90 (d, *J* = 6.8 Hz, 3H), 1.40–1.81 (m, 13H), 2.65 (d, *J* = 6.4 Hz, 1H), 3.13 (d, *J* = 6.8 Hz, 1H), 3.71 (s, 3H), 7.27–7.55 ppm (m, 4H). – ^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.23 (CO), 141.12 (C), 132.44 (C), 129.91 (2CH), 127.93 (2CH), 66.71 (CH), 64.65 (CH), 51.32 (CH_3), 44.43 (CH), 31.84 (CH), 29.92 (CH_2), 29.50 (CH_2), 26.43 (CH_2), 26.22 ($2CH_2$), 19.54 (CH_3), 18.52 ppm (CH_3). – IR (KBr, neat): υ = 3 492 (N–H stretching), 2 928 and 2 854 (C–H stretching), 1 731.24 (C=O stretching),1 588 and 1 450 cm^{-1} (C=C stretching aromatic).

2-[(1-Cyclopentyl-1-phenylmethyl)amino]-3-methylbutyric acid methyl ester (5)

R_f = 0.61 (EtOAc / hexane 1 : 8). – ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.85 (d, *J* = 6.8 Hz, 3H), 0.96 (d, *J* = 6.8 Hz, 3H), 1.05–1.43

(m, 11H), 2.60 (d, J = 6.3 Hz, 1H), 3.12 (d, *J* = 8.8 Hz, 1H), 3.71 (s, 3H), 7.03–7.18 ppm (m, 5H). – ^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.32 (CO), 143.53 (C), 128.23 (2CH), 127.85 (2CH), 126.82 (CH), 67.63 (CH), 64.42 (CH), 51.22 (CH_3), 47.63 (CH), 31.72 (CH), 30.14 (CH_2), 30.08 (CH_2), 25.42 (CH_2), 25.13 (CH_2), 19.44 (CH_3), 18.53 ppm (CH_3). – IR (KBr, neat): υ = 3 443 (N–H stretching), 2 939 and 2 866 (C–H stretching), 1 739 (C=O stretching),1 621and 1 434 cm^{-1} (C=C stretching aromatic).

CONCLUSIONS

An efficient, facile and economical method for the alkylation of amines has been developed using AgI-nanoparticles as the mediator in water-methanol media. The products were obtained in excellent yields and the reaction times were significantly reduced in comparison to using bulk silver iodide. The diastereoselectivity of reactions did not change using nanoparticles. The present protocol represents a simple and remarkable method for C-N bond formation in order to prepare some amino ester derivatives in the presence of novel nano-scale materials.

AKNOWLEDGMENTS

The authors are grateful to the University of Kashan for supporting this work by Grant No: 159196/III.

Received 22 March 2012
Accepted 30 April 2012

References

1. J. Samec, S. M. Mony, L. Backvall, *Can. J. Chem*., **83**, 909 (2005).
2. X. Liu, S. Zhu, S. Wang, *Synthesis*, **5**, 683 (2004).
3. A. Toti, P. Frediani, A. Salvani, C. Giannelli, C. C. R. Giolli, *Chimia*, **7**, 769 (2004).
4. C. Baar, M. C. Jennings, J. J. Vittal, R. Puddephatt, *Organometallics*, **19**, 4150 (2004).
5. D. Dallinger, C. O. Kappe, *Chem. Rev.*, 107, 2563 (2007).
6. C. J. Li, *Chem. Rev.*, **105**, 3095 (2005).
7. Y.-S. Yang, Z.-L. Shen, T.-P. Loh, *Org. Lett*., **11**, 1209 (2009).
8. Y. Hayashi, W. Tsuboi, I. Ashimine, T. Urushima, M. Shoji, K. Sakai, *Angew. Chem. Int. Ed.*, **42**, 3677 (2003).
9. S.-G. Lee, J. K. Lee, C. E. Song, D.-C. Kim, *Bull. Korean Chem. Soc.*, **23**, 667 (2002).
10. N. Gommermann, C. Koradin, K. Polborn, P. Knochel, *Angew. Chem. Int. Ed*, **115**, 5941 (2003).
11. J.-Y. Zhou, Y. Jia, G.-F. Sun, S.-H. Wu, *Synth. Commun*., **27**, 1899 (1997).
12. L. A. T. Cleghorn, I. R. Cooper, R. Grigg, W. S. MacLachlan, V. Sridharan, *Tetrahedron Lett*., **44**, 7969 (2003).
13. J. Auge, N. Lubin-Germain, A. Thiaw-Woaye, *Tetrahedron Lett*., **40**, 9245 (1999).
14. A. S.-Y. Lee, L.-S. Lin, *Tetrahedron Lett*., **41**, 8803 (2000).
15. Z.-L. Shen, H.-L. Cheong, T.-P. Loh, *Chem. Eur. J.*, **14**, 1875 (2008).
16. U. Heiz, U. Landman, *Nanocatalysis,* Springer, Berlin, Heidelberg, New York (2006).
17. Y. Kim, J. Park, M.-Joo. Kim, *Tetrahedron Lett*., **51**, 5581 (2010).
18. A. Jagminas, *Chemija*, **14**, 151 (2003).
19. L. T. Tamasiunaite, R. Tarozaite, A. Vaskelis, *Chemija*, **17**, 13 (2006).
20. M. Kidwai, V. Bansal, A. Kumarb, S. Mozumdar, *Green Chem*., **9**, 742 (2007).
21. M. L. Kantam, S. Laha, J. Yadav, S. Bhargava, *Tetrahedron Lett.*, **49**, 3083 (2008).
22. H. Sharghi, R. Khalifeh, M. M. Doroodmand, *Adv. Synth. Catal.*, **351**, 207 (2009).
23. L. Hong-Yan, A. S. Yang, A. J. Deng, Z. H. Zhang, *Aust. J. Chem.*, **63**, 1290 (2010).
24. L. Rout, S. Jammi, T. Punniyamurthy, *Org. Lett*., **9**, 3397 (2007).
25. S. Uk Son, H. Young Jang, *Bull. Korean Chem. Soc.*, **29**, 1561 (2008).
26. Z. Mirjafary, H. Saeidian, A. Sadeghi, F. M. Moghaddam, *Catal. Commun.*, **9**, 299 (2008).
27. K. H. Vardhan Reddy, V. Prakash Reddy, A. Ashwan Kumar, G. Kranthi, Y. V. D. Nageswar, *Beilstein J. Org. Chem*., **7**, 886 (2011).

Javad Safaei-Ghomi, Abdolrazzagh Gaderi-Zefre, Mohammad Ali Ghasemzadeh, Ahmad Kakavand-Ghalenoei, Masoud Salavati-Niasari

AGI NANODALELĖS KAIP HETEROGENINIS KATALIZATORIUS VIENOS STADIJOS CHIRALINIŲ AMINŲ (L-VALINO METILO ESTERIO) ALKILINIMO REAKCIJOJE, VANDENS-ALKOHOLIO TERPĖJE

S a n t r a u k a

Aprašytas efektyvus ekologiškas chiralinių aminų alkilinimo metodas. Metodo esmę sudaro vienos stadijos aldehidų, aminų ir alkiljodidų reakcija vandens-alkoholio terpėje naudojant AgI nanodaleles kaip katalizatorių.