ISSN 1990-7931, Russian Journal of Physical Chemistry B, 2019, Vol. 13, No. 8, pp. 1284–1289. © Pleiades Publishing, Ltd., 2019.
Russian Text © The Author(s), 2019, published in Sverkhkriticheskie Flyuidy. Teoriya i Praktika, 2019, Vol. 14, No. 2, pp. 31–39.

Cyclization of *o*-Phenylenediamine and *o*-Substituted Anilines with Supercritical Carbon Dioxide

Yu. M. Panov[a], L. V. Erkhova[a], A. G. Balybin[a], D. P. Krut'ko[a], *, and D. A. Lemenovskii[a]

[a] *Lomonosov Moscow State University, Chemistry Department, Moscow, 119991 Russia*

**e-mail: kdp@org.chem.msu.ru*

Received January 23, 2019; revised February 7, 2019; accepted February 7, 2019

Abstract—It is demonstrated that tin(II) 2-ethylhexanoate and tin(II) oxide are effective catalysts for the reaction of cyclization of model arylamines *o*-$NH_2(C_6H_4)XH$ (X = NH, O, S, CH_2NH) in supercritical carbon dioxide with the formation of benzo-1,3-azol-2-ones and 3,4-dihydroquinazolin-2-one. Optimal conditions for these reactions are found. Possible mechanisms for these processes are proposed, depending on the catalyst used.

Keywords: supercritical carbon dioxide, cyclization, benz-1,3-azol-2-ones, tin(II) derrivatives

DOI: 10.1134/S1990793119080062

INTRODUCTION

Supercritical carbon dioxide has been attracting constant attention for several decades, not only as a convenient reaction medium but also as an environmentally friendly and safe reagent [1, 2]. The interaction of supercritical carbon dioxide with various amines is within the class of such reactions.

The reactions of aliphatic diamines with carbon dioxide, leading to cyclic or linear derivatives of urea, proceed quite easily and are well established [1–6]. By contrast, aromatic amines are dramatically less active with respect to CO_2. The comparative rates of their reactions were clearly demonstrated in [6]. At the same time, benzo-1,3-azol-2-ones, the products of the cyclization of aromatic *o*-diamines and O- and S-containing analogues with carbon dioxide, are important in practical heterocyclic compounds exhibiting a wide range of biological activity [7–10]. Known methods of their synthesis, including industrial methods, include the using phosgene [10, 11], carbon monoxide [12, 13], dimethyl carbonate [14] and urea [15, 16]. Despite the high yields of the target compounds and the short reaction time, these methods have several disadvantages: the use of toxic reagents (CO, phosgene), volatile organic solvents, and an excess of reagents and catalysts, many of which are quite expensive. On this basis, the direct cyclization of aromatic *o*-diamines and their heteroatomic analogues, with cheap and environmentally friendly CO_2, is a very attractive alternative, despite their low reactivity with carbon dioxide.

Progress in this direction has been achieved only in recent years with the use of polytungstates (cyclization of *o*-phenylenediamines) [17, 18] or ionic liquids based on a superbase (cyclization of *o*-phenylenediamines and *o*-aminothiophenol) [19] as catalysts. In both cases, to obtain high yields of the cyclic product, starting from *o*-phenylenediamines or its derivatives, stringent conditions are required (120–140°C, reaction time 24–40 h, 0.1–1 eq. catalyst). The advantage of using tungstates $(Bu_4N)_2(WO_4)$ as a catalyst is the low pressure of CO_2, but the disadvantage is the need for an expensive solvent, N-methylpyrrolidone. In the presence of an excess of triethoxysilane as a reducing agent and ionic liquids as a catalyst (1 equiv.), The derivatives of *o*-aminothiophenol cyclize with carbon dicoside (P = 5 MPa) to form benzithiazole. In this case, the reaction conditions are milder (40–60°C, and a reaction time of 24 h) [20].

In this work, we used tin compounds (II)—2-tin ethylhexanoate ($Sn(Oct)_2$) and tin oxide as catalysts for cyclization of model arylamines *o*-$NH_2(C_6H_4)XH$ (X = NH, O, S) in supercritical carbon dioxide (SC-CO_2) with the formation of benzo-1,3-azol-2-ones. Despite the more stringent conditions used (170°C for the case X = NH, S and 210°C for X = O), they have noticeable advantages over $(Bu_4N)_2(WO_4)$ or [DBUH][OAc] (where DBUH is diazabicycloundecene). With comparable activity, tin ethylhexanoate and tin oxyl are favorably low-cost, especially the first (due to its large-capacity industrial production as a catalyst for the polymerization of lactides for biodegradable packaging), and does not require a solvent. For comparison, we also carried out a cyclization reaction with a mixed diamine *o*-$NH_2(C_6H_4)CH_2NH_2$, which contains both aryl and benzyl amino groups.

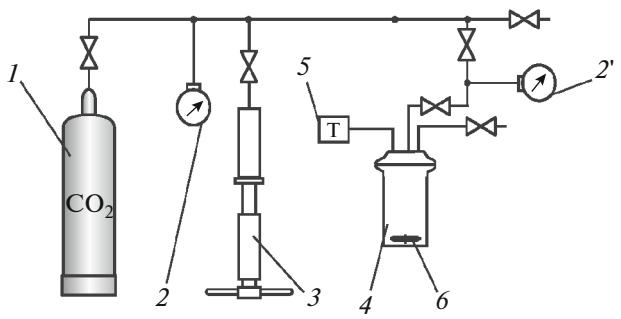


Fig. 1. Installation for high pressure: (*1*) ballon, (*2*, *2*') manometres, (*3*) hand screw press, (*4*) reactor, (*5*) thermocouple, (*6*) magnetic stir bar anchor.

EXPERIMENTAL

We used commercially available reagents from Aldrich. Spectra ^1H and ^{13}C were recorded on a Bruker Avance-400 spectrometer (at 400 and 100 MHz, respectively). The values of chemical shifts are measured relative to the signals of the deuterium solvent: 2.49 and 39.5 ppm (DMSO-d_6).

Reactions at high pressures were carried out in a diamagnetic steel reactor with an internal volume of 47 mL. A simplified view of the experimental setup is shown in Fig. 1.

Pressure monitoring in the system was carried out using internal (*2*') and external (*2*) manometers. The temperature in the reactor was maintained using a glycerin bath and controlled using a thermocouple mounted in the reactor lid and placed in the center of the reaction volume. The reaction mixture was stirred using a magnetic stirrer. To a liquid state, the gas was compressed using a hand press.

The Method of Cyclization of o-$NH_2(C_6H_4)XH$ (X = NH, O, S, CH_2NH) with CO_2 and Using $Sn(Oct)_2$ or SnO as a Catalyst

In a high-pressure reactor equipped with a magnetic stirrer, 100 mg starting compound was placed *o*-$NH_2(C_6H_4)XH$ (X = NH, O, S, CH_2NH), along with the required amount of Sn or SnO catalyst (N_{eqv}) (Table 1), then the reactor was closed and 6 MPa CO_2 was pumped. Using a hand press, the amount of liquid CO_2 in the reactor was adjusted to ~35 mL (substrate/CO_2 ratio of approximately 1/750 mol). The reaction mixture was stirred for a time *t* at the required temperature *T* (Table 1). The pressure in the reaction mixture varied from 25.1 (160°C) to 31.4 MPa (210°C). After completion of the reaction, the reactor was cooled and CO_2 was released for 30 min. Part of the reaction mixture was dissolved in DMSO-d_6 for analysis by NMR. The ratio of components in the reaction mixtures was determined by integrating the corresponding signals in the NMR ^1H spectra.

Table 1. Cyclization of compounds **1a–4a** with CO_2 using a catalyst $Sn(Oct)_2$ or SnO

Experiment, no.[1]	*t*, h	*T*, °C	Catalyst	N_{eq}	Yield[1], %
1	12	160	–	0	(**1b**) 0
2	12	160	$Sn(Oct)_2$	0.15	(**1b**) 14
3	12	170	$Sn(Oct)_2$	0.15	(**1b**) 35
4	36	170	$Sn(Oct)_2$	0.15	(**1b**) 60
5	36	170	$Sn(Oct)_2$	0.25	(**1b**) 72
6	36	170	$Sn(Oct)_2$	0.40	(**1b**) 90
7	36	170	$Sn(Oct)_2$	0.40	(**2b**) 0
8	12	170	SnO	0.40	(**1b**) 18
9	12	180	SnO	0.40	(**1b**) 18
10	36	170	SnO	0.40	(**1b**) 18
11	12	210	SnO	0.40	(**2b**) 22
12	36	210	SnO	0.40	(**2b**) 28
13	12	170	SnO	0.40	(**3b**) 50
14	12	180	SnO	0.40	(**3b**) 37
15	36	170	SnO	0.40	(**3b**) 64
16	6	170	$Sn(Oct)_2$	0.05	(**4b**) ~100

[1] The yield corresponds to the content of the cyclization product in the reaction mixture.

The Method of the Isolation of the Reaction Products 1b–4b

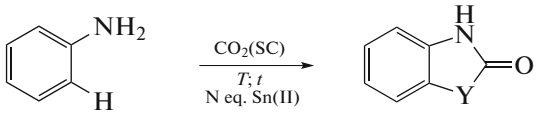
Then, 12 mL EtOH was added to the reaction mixture, and the solution was stirred for 30 min at 50°C. An insoluble residue (tin(II) ethylate or SnO) was precipitated by centrifugation, the ethanol solution was separated by decantation. After evaporation of the solvent, the mixture of the starting compound and the cyclization product was separated by column chromatography on silica gel (40/100 μm) (eluent-THF : hexane = 2 : 1) and recrystallized from EtOH. The yields of cyclization products after isolation were 80–90% (taking into account the conversion of the starting amine).

The parameters of the ^{1}H and ^{13}C NMR spectra of the obtained compounds (benzimidazol-2-one (**1b**) [18], bezoxazol-2-one (**2b**) [21], benzothiazol-2-one (**3b**) [19] and 3,4-dihydroquinazolin-2-one (**4b**) [22]) coincide with the data in the literature.

The structure of 2- (heptyl-3) -benzoxazole (5, see below) was established on the basis of ^{1}H and ^{13}C NMR spectra by analogy with related compounds [23] (reaction mixture (**2a : 5** = 0.8 : 1.0). **5** (atom numbering is shown in the diagram in the next section): NMR^1 H (DMSO-d_6): δ = 0.71; 0.75 (both t, $^3J_{HH}$ = 7.3 Hz, $CH_3^{1',7'}$); 1.05–1.75 (overlapp. m, $CH_2^{2',4'-6'}$); 2.84 (m, $H^{3'}$); 7.24 (m, $H^{5,6}$); 7.55; 7.62 (both m, $H^{4,7}$). NMR ^{13}C (DMSO-d_6): δ = 11.59 ($CH_3^{1'}$); 13.79 ($CH_3^{7'}$); 22.20 ($CH_2^{6'}$); 26.29 ($CH_2^{2'}$); 29.18 ($CH_2^{5'}$); 32.57 ($CH_2^{4'}$); 41.14 ($CH^{3'}$); 110.53 (CH^7); 119.44 (CH^4); 124.23, 124.63 ($CH^{5,6}$); 141.02 (CH^{3a}); 150.34 (C^{7a}); 169.46 (C^2).

RESULTS AND CONCLUSION

The general reaction of arylamine *o*-$NH_2(C_6H_4)XH$ cyclization has the form:

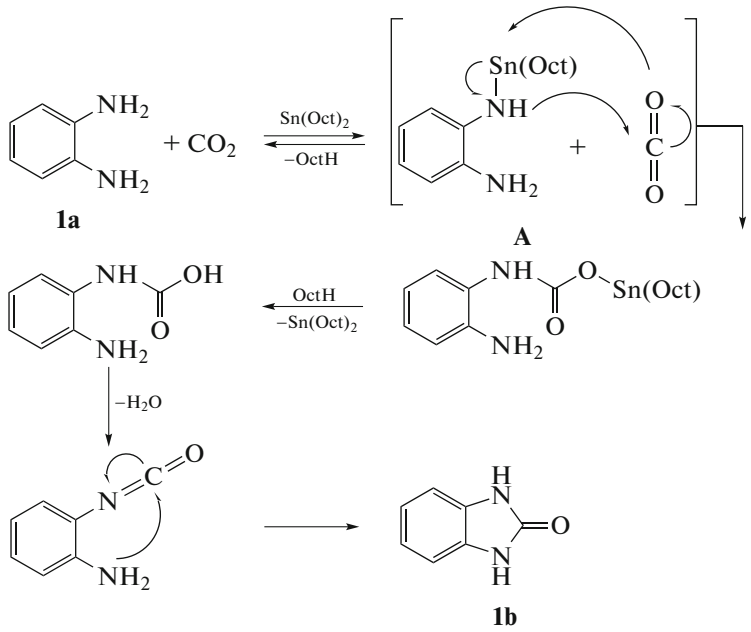


X = **1a** –NH, **2a** –O, Y = **1b** –NH, **2b** –O,
3a –S, **4a** –CH_2NH, **3b** –S, **4b** –CH_2NH.

To optimize the cyclization conditions for the model arylamines of *o*-$NH_2(C_6H_4)XH$ (X = NH, O, S, CH_2NH) with CO_2, at the first stage, we carried out a series of experiments on the cyclization of *o*-phenylenediamines (**1a**) using the $Sn(Oct)_2$ catalyst. It was found that this process proceeds with high selectivity (>95%), and the yield of benzimidazole-2-one depends on temperature, reaction time and the amount of catalyst used (Table 1). A control experiment (experiment 1) showed that in the absence of a catalyst, the reaction does not proceed.

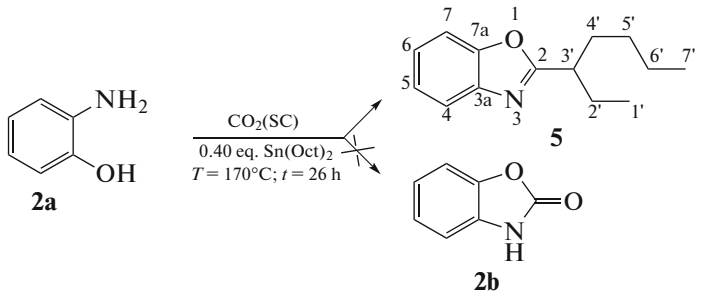
When using 0.15 equiv. ($Sn(Oct)_2$) the yield of **1b** was only 14% (experiment 2). An increase in temperature to 170°C increased the yield to 35% (experiment 3). A three-fold increase in the reaction time allowed it to be brought up to 60% (experiment 4). A sequential increase in the amount of catalyst under the same conditions (experiments 5.6) increases the yield to 90% (0.40 equiv. $Sn(Oct)_2$). Note that the only minor (<5%) by-product in this reaction is 2 (-heptyl-3)-benzimidazole, similar in structure to benzoxazole **5**.

We suggest that the cyclization of *o*-phenylenediamine with CO_2 in the presence of $Sn(Oct)_2$ proceeds according to the following mechanism:

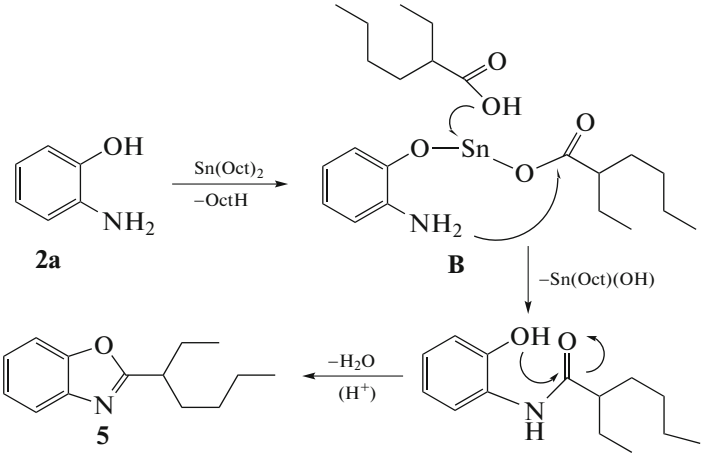


Since the Sn–N bond is rather labile [24], the first stage of the formation of adduct **A** is most likely reversible. The last two stages through the formation of an intermediate isocyanate are common [1].

Cyclization of 2-aminphenol (**2a**) under conditions optimized for **1a** showed that almost the only product in the reaction mixture was 2-(-heptyl-3)-benzoxazole (**5**), and not the expected benzoxazol-2-one (**2b**) (experiment 7)



Conversion **2a** was 56%. Apparently, this is due to the fact that the affinity of tin to oxygen is greater than to nitrogen, and the reaction proceeds in a different way. We suggest that cyclization of 2-aminophenol with CO_2 proceeds according to the following mechanism:



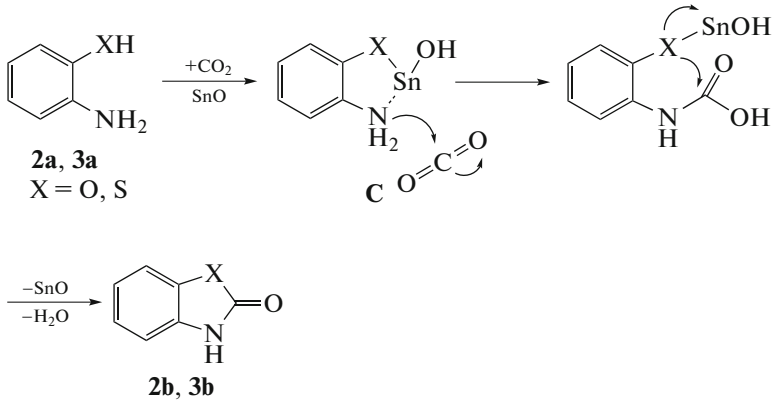
In contrast to cyclization **1a**, the first stage of cyclization **2a** is irreversible and forms (**B**), the intramolecular rearrangement of which leads to product **5**. In this case, the electrophilicity of the CO_2 molecule is too small for interaction with the weakly nucleophilic O–Aryl atom in adduct **B**, in contrast to the more nucleophilic atom NH–Aryl in adduct **A** in case of cyclization **1a** (see above).

The second catalyst we studied is tin oxide(II), a cheap and affordable reagent, which, however, unlike $Sn(Oct)_2$, soluble in SC-CO_2, is a solid substance, and reactions with its participation can proceed only heterogeneously. As initial conditions for the synthesis of compound **1b**, 0.40 equiv. SnO, time 12 h, temperature 170°C (experiment 8). The yield for **1b** was 18%. It turned out that increasing the temperature to 180°C (experiment 9) or increasing the reaction time to 36 h (experiment 10) does not increase the yield of the target product. This is probably due to a change in the reaction mechanism during the transition from $Sn(Oct)_2$ to SnO (see the discussion of the mechanism for **2a** and **3a** below). Thus, for cyclization of *o*-aryl diamides with CO_2, the use of SnO is impractical in comparison with $Sn(Oct)_2$.

Because 2-aminophenol is less reactive with respect to CO_2 than o-phenylenediamine, its cyclization in the presence of SnO was carried out at a higher temperature (210°C). The yield of **2b** was 22% in 12 h (experiment 11). An increase in the duration of the reaction to 36 h) (experiment 12) led only to a slight increase in the yield of the target product (28%). Nevertheless, despite the low yield, this reaction is the first example of direct cyclization of 2-aminophenol with CO_2.

For the synthesis of benzothiazol-2-one (**3b**), 0.40 equiv. SnO, the time was 12 h, and the temperature was 170°C (experiment 13). Yield **3b** was 50%. Moreover, an increase in temperature of only 10°C leads to a decrease in the yield of **3b** to 37% (experiment 14), and an increase in the reaction time by a factor of three increases it to 64% (experiment 15).

We assume that in the presence of a hydroxy or thio group, a stable adduct (**C**) is irreversibly formed with an amino group intramolecularly activated by the tin atom. Without such activation, the aryl amino group is not able to interact with carbon dioxide (experiment 1). Then, the resulting carbamic intermediate cyclizes:



Because the affinity of sulfur to tin is greater than that of oxygen, the activity of SnO in the reaction of CO_2 with 2-aminothiophenol is higher than with 2-aminophenol, which leads to much better yields **3b** compared to **2b** at a significantly lower reaction temperature. At the same time, due to the lability of the Sn–N bond, the formation of the type **C** intermediate adduct for *o*-phenylenediamine is apparently reversible; its concentration is insignificant, which leads to low **1b** yields upon SnO catalysis.

An analysis of the NMR ^1H and ^{13}C spectra showed that aniline is present in the reaction mixture during cyclization of **3a** as a byproduct (~25%), which is apparently formed due to desulfurization of 2-aminothiophenol with tin oxide(II) to form mixed SnOS sulfyl oxide. This explains the decrease in the yield of **3b** with an increase in the temperature of the reaction; it is obvious that in this case, the side process of desulfurization is accelerated and becomes dominant.

To evaluate the catalytic activity of $Sn(Oct)_2$ in the cyclization of diamine more reactive with respect to CO_2, we performed this reaction with *o*-aminomethylaniline (**4a**), which simultaneously contains an aryl and benzyl amino groups. With a significantly lower catalyst load (0.05 equiv.) and a shorter reaction time (6 h), the yield of the target product **4b** was practically quantitative (experiment 16). That is, the presence of an alkyl (benzyl) amino group in the starting diamine accelerates the reaction by an order of magnitude.

CONCLUSION

The results obtained show that tin compounds(II) are a good alternative to the few known catalyst for the cyclization of arylamines *o*-$NH_2(C_6H_4)XH$ (X = NH, O, S) in SC-CO_2 with the formation of benzo-1,3-azol-2-ones. Their advantage is low cost with comparable activity. Moreover, cyclization of 2-aminophenol with CO_2, catalyzed by SnO and leading to benzoxazol-2-one, was carried out by us for the first time. On the other hand, the formation of 2-(heptyl-3)-benzoxazole in the same reaction, but in the presence of $Sn(Oct)_2$, opens up the prospect of producing 2-alikl-substituted benzo-1,3-azoles by the reaction of *o*-$NH_2(C_6H_4)XH$ ariamines with carboxylic acids under the catalysis of tin oxide(II).

FUNDING

The authors are grateful to the Russian Foundation for Basic Research (project 18-29-06010) for the financial support and the LLC IPK Lik for the technical support of this work.

REFERENCES

1. *Carbon Dioxide as Chemical Feedstock,* Ed. by M. Aresta (Wiley-VCH, Weinheim, 2010).
2. *Carbon Dioxide and Organometallics,* Ed. by Xiao-Bing Lu (Springer, New York, 2016).
3. Ts. Seki and T. Ikariya, Phys. Chem. Chem. Phys. **11**, 10073 (2009).
4. Ts. Seki, Y. Kokubo, Sh. Ichikawa, T. Suzuki, Y. Kayaki, and T. Ikariya, Chem. Commun., No. 3, 349 (2009).
5. Jianpeng Shang, Shimin Liu, Xiangyuan Ma, Liujin Lu, and Youquan Deng, Green Chem. **14**, 2899 (2012).
6. Feng Shi, Youquan Deng, Tianlong SiMa, Jiajian Peng, Yanlong Gu, and Botao Qiao, Angew. Chem. Int. Ed. **42**, 3257 (2003).
7. Q. Li, T. Li, K. Woods, V-G. Gu, J. Cohen, F. Stoll, T. Galicia, Ch. Hutchins, D. Frost, S. Rosenberg, and H. Sham, Bioorg. Med. Chem. Lett. **15**, 2918 (2005).
8. E. A. Terefenko, J. Kern, A. Fensome, J. Wrobel, Y. Zhu, J. Cohen, R. Winneker, Zh. Zhang, and P. Zhang, Bioorg. Med. Chem. Lett. **15**, 3600 (2005).
9. A. Hammach, A. Barbosa, F. C. Gaenzler, T. Fadra, D. Goldberg, M-H. Hao, R. Kroe, P. Liu, K. Qian, M. Ralph, Ch. Sarko, and N. Moss, Bioorg. Med. Chem. Lett. **16**, 6316 (2006).
10. M. L. Barreca, A. Rao, L. De Luca, N. Iraci, A.-M. Monforte, G. Maga, Ch. Pannecouque, J. Balzarini, and A. Chimirri, Bioorg. Med. Chem. Lett. **17**, 1956 (2007).
11. H.-Y. Chen, M. Kulkarni, C.-H. Chen, and C.-M. Sun, Tetrahedron Lett. **64**, 6387 (2008).
12. T. Yoshida, N. Kambe, Sh. Murai, and N. Sonoda, Tetrahedron Lett. **27**, 3037 (1986).
13. L. Troisi, C. Granito, S. Perrone, and F. Rosato, Tetrahedron Lett. **52**, 4330 (2011).

14. F. Yue, B. Toshihide, and O. Yoshio, J. Catal. **197**, 91 (2001).

15. Z. Yang, J. Wang, L. Li, Ch. Ye, and H. Liu, J. Heterocycl. Chem. **46**, 788 (2009).

16. D. S. Recunge and Ch. Khatri, Tetrahedron Lett. **58**, 4304 (2017).

17. Kamata Keigo, Kimura Toshihiro, Sunaba Hanako, and Mizuno Noritaka, Catal. Today **226**, 160 (2014).

18. Kimura Toshihiro, Kamata Keigo, and Mizuno Noritaka, Angew. Chem., Int. Ed. Engl. **51**, 6700 (2012).

19. Bo Yu, Hongye Zhang, Yanfei Zhao, Sha Chen, Jilei Xu, Leiduan Hao, and Zhimin Liu, ACS Catal. **3**, 2076 (2013).

20. Gao Xiang, Yu Bo, Yang Zhenzhen, Zhao Yanfei, Zhang Hongye, Hao Leiduan, Han Buxing, and Liu Zhimin, ACS Catal. **5**, 6648 (2015).

21. P. Liu, Z. Wang, and X. Hu, Eur. J. Org. Chem., No. 10, 1994 (2012).

22. J. Paz, C. Perez-Balado, B. Iglesias, and L. Munoz, Org. Chem. **75**, 3037 (2010).

23. J. A. Seijas, M. P. Vazquez-Tato, M. R. Carballido-Reboredo, J. Crecente-Campo, and L. Romar-López, Synlett., No. 2, 313 (2007).

24. A. Kowalski, J. Libiszowski, T. Biela, M. Cypryk, A. Duda, and S. Penczek, Macromolecules **38**, 8170 (2005).

Translated by M. Aladina