Taylor & Francis
Taylor & Francis Group

Synthetic Communications

An International Journal for Rapid Communication of Synthetic Organic Chemistry

ISSN: 0039-7911 (Print) 1532-2432 (Online) Journal homepage: https://www.tandfonline.com/loi/lsyc20

Iodine mediated synthesis of diaryl diselenides using SeO_2 as a selenium source

Dileep Kommula, Qing Li, Siyang Ning, Wujun Liu, Qian Wang & Zongbao K. Zhao

To cite this article: Dileep Kommula, Qing Li, Siyang Ning, Wujun Liu, Qian Wang & Zongbao K. Zhao (2020): Iodine mediated synthesis of diaryl diselenides using SeO_2 as a selenium source, Synthetic Communications, DOI: 10.1080/00397911.2020.1728775

To link to this article: https://doi.org/10.1080/00397911.2020.1728775

SYNTHETIC COMMUNICATIONS®
https://doi.org/10.1080/00397911.2020.1728775

Taylor & Francis
Taylor & Francis Group

Iodine mediated synthesis of diaryl diselenides using SeO_2 as a selenium source

Dileep Kommula[a], Qing Li[a], Siyang Ning[a], Wujun Liu[b], Qian Wang[a], and Zongbao K. Zhao[a]

[a]Dalian Institute of Chemical Physics, Chinese Academy of Sciences, Dalian, China; [b]Institute of Cancer Stem Cell, Dalian Medical University, Dalian, China

ABSTRACT

A simple, eco-friendly and convenient procedure has been developed for the synthesis of diphenyl diselinides from readily available aryl boronic acids by reaction with SeO_2 in the presence of iodine under simple conditions. The methodology is reported about 19 examples and applicable to a broad scope of aryl boronic acids containing electron-rich and electron-poor substituents. Apart from being milder and environmentally benign conditions, this synthetic protocol comprises a novel, reliable methodology to give good to high yields of the desired diaryl diselenides.

GRAPHICAL ABSTRACT

ARTICLE HISTORY
Received 13 December 2019

KEYWORDS
Aryl boronic acids; selenium dioxide; iodine; diaryl diselenides. 2-Me-THF

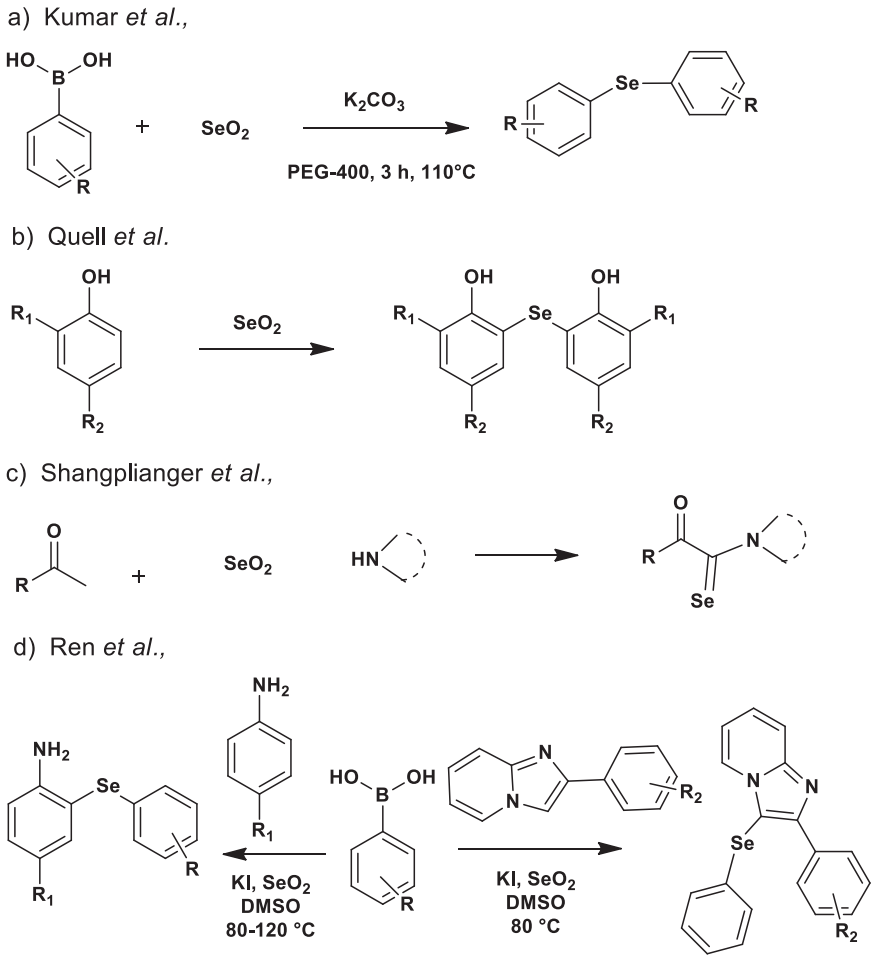
Introduction

Organoselenium compoounds, those containing selenium is considered an important class of chemical entity, and their chemistry, toxicology, and pharmacology are well documented in numerous reports.[1,2] The main chemistry of symmetric and unsymmetric organoselenium compounds is a field of great interest owing to their special structural motifs and unique reactivity.[3] For instance, organoselenium compounds of diselenides are important synthetic intermediates[1] and have been reported as essential moieties of pharmaceutically and biologically active compounds such as antioxidant,[4] anti-ulcer[5] and anti-infammatory agents.[6]

Generally, the preparation of organoselenium (to construct C-Se bond) compounds involves traditional methods such as cross coupling of aryl halides with selenium metal employing metal salts[7], oxidation of selenoles,[8] reaction of alkali metal diselenides

CONTACT Kommula Dileep dilip.kommula@gmail.com, dileepkommula@dicp.ac.cn Dalian Institute of Chemical Physics, Chinese Academy of Sciences, Dalian, China.

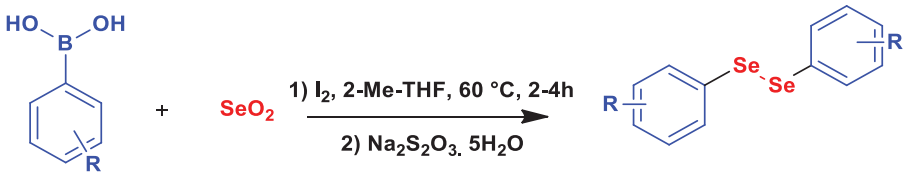
Supplemental data for this article can be accessed on the publisher's website.



Scheme 1. Some of the methods for organoselenium synthesis using SeO_2 as the selenium source.

with different electrophiles[9] and reduction of selenocyanates.[10] Since numerous methods have been reported for synthesize organoseleniums, there is still much scope and research gap in exploring new C–Se construction methods due to the most of the approaches reported so far using harsh reaction conditions such as the use of polar and toxic solvents, some reactions must be performed at relatively high temperatures, and longer reaction times, which mostly result in lower yields. Usually, synthetic chemists are commonly focused on using RSeSeR, Se or KSeCN as a selenium sources for synthesis of organoselenium compounds.[11] Recently, Leng et al.[11e] reported the synthesis of diaryl diselenides by taking aryl boronic acids and Se metal in the presence of silver nitrate catalyst. Later, Zhu et al.[12] described Nickel-catalyzed synthesis of diaryl diselenides using aryl boronic acids and Se metal as a selenium source.

In recent years, utilization of SeO_2 as a selenium source has been gaining a remarkable approach for the synthesis of organoselenium compounds. For instance, Kumar et al.[13a] reported using SeO_2 and phenylboronic acid to make diarylselenides (Scheme 1(a)). Quell et al.[13b] described the synthesis of diarylselenides and biphenols by using SeO_2 and phenols (Scheme 1(b)). Later, Shangplianger et al.[13c] reported to



Scheme 2. Synthesis of diaryl diselenides from aryl boronic acids.

construct C=Se double bonds without any catalyst using SeO_2 as a selenium source (Scheme 1(c)). Recently, Ren et al.[13d] described the synthesis of R-Se Substituted Aniline and Imidazo[1,2-a]pyridine derivatives using SeO_2 as a selenium source (Scheme 1(d)).

On the other hand, researchers are focusing on replacement of volatile organic compounds (VOCs) by biomass derived solvents. Biomass derived solvents are a type of green solvent that have attracted intensive investigations due to their advantages over conventional VOCs, such as low toxicity, biodegradability and renewability.[14] Among the biomass derived solvents, 2-methyl-tetrahydrofuran (2-Me-THF) has gained attention as a promising alternative solvent in the search for environmentally benign synthesis strategies because of its physical and chemical properties, such as its low miscibility with water, boiling point, remarkable stability compared to other cyclic-based solvents such as THF.[15] Hence, 2-Me-THF have been extensively used for applications in syntheses involving organometallics, organocatalysis, and biotransformations or for processing lignocellulosic materials.[14–16]

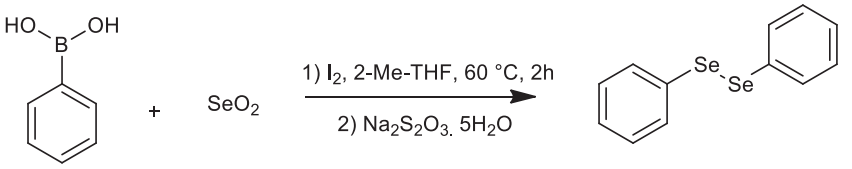
In our continued search for the development of novel green novel protocols,[17] here in, we report a novel method for the synthesis of diayrl diselenides from arylboronic acids and SeO_2 using 2-Me-THF solvent in the presence of molecular Iodine at 60°C for 2–4 h (Scheme 2).

Result and discussion

We began our study by optimizing the reaction conditions for the synthesis of diphenyl diselenide **2a** as a model reaction (Table 1). Initially, the reaction of phenyl boronic acid **1a** (1.0 mmol), SeO_2 (1.0 mmol), molecular Iodine (1.0 mmol) was carried out in DMSO as a solvent (1 mL) at room temperature gave the corresponding compound **2a** in yield 69% (Table 1, entry 2). While checking the reaction parameters, it was observed that reaction did not proceeded without presence of iodine after prolonged reaction time 24 h, (Table 1, entry 1). Later, the temperature effect on reaction conditions was carried out, and it was observed that the increase in reaction temperature from rt to 40 °C, resulted in improved the yield from 69% to 82% (Table 1, entry 6). When increases the temp from 40 °C to 60 °C, resulted in enhanced to 90% yield (Table 1, entry 4). Further, increasing the temperature to 80 °C observed that there was no obvious improvement of product **2a** yield (Table 1, entry 8).

In order to optimize the protocol, the impact of the loading molecular Iodine on the reaction efficiency was investigated. We found that increasing I_2 from 1.0 to 1.2, 1.5 and 2.0 equiv. there was no substantial improvement of yield (Table 1, entry 4, 5, 6). Finally, the effect of solvents was studied and it was observed that the reaction was also

Table 1. Optimization table for the synthesis of diphenyl diselenide[a].



1a **2a**

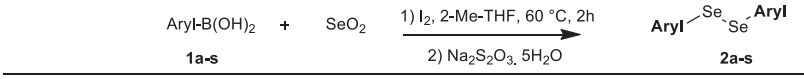
Entry	Catalyst	Catalyst (m.mol)	Solvent	Temperature (°C)	Yield[b] (%)
1	–	–	DMSO	rt	0
2	I_2	1.0	DMSO	rt	69
3	I_2	1.0	DMSO	60	90
4	I_2	1.2	DMSO	60	90
5	I_2	1.5	DMSO	60	91
6	I_2	2.0	DMSO	60	92
7	I_2	1.0	DMSO	40	82
8	I_2	1.0	DMSO	60	90
9	I_2	1.0	DMSO	80	91
10	I_2	1.0	2-Me-THF	60	89
11	I_2	1.0	THF	60	84
12	I_2	1.0	1,4-Dioxane	60	85
13	I_2	1.0	DMF	60	66
14	I_2	1.0	C_2H_3CN	60	60
15	I_2	1.0	C_2H_5OH	60	55
16	I_2	1.0	Toulene	60	40
17	I_2	1.0	H_2O	60	0

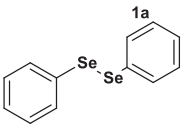
[a]The reactions were carried out as follows: Phenyl boronic acid (1.0 equiv.), I_2 (1.0 equiv.), SeO_2 (1.0 equiv.), 2-Me-THF (1 mL), at 60 °C, 2 h.
[b]Isolated yields are based on reactant.

effective in 2-Me-THF, 1,4-Dioxane, THF, DMF, CH_3CN, CH_3OH, EtOH and Toluene, obtained the product **2a** in 89%, 85%, 84%, 69%, 60%, 55% and 40% yield (Table 1, entry 10–17), respectively. It's noteworthy to mention that the desired product **2a** formation was not observed in aqueous medium (entry 18). However, the reaction was highly effective with polar aprotic solvents (entries 10–15). Among the different solvents examined, 2-Me-THF (Table 1, entry 10) was provided the highest product **2a** in 89% yield after the DMSO solvent which was afforded product **2a** in 90% yield (Table 1, entry 8). Therefore, 2-Me-THF was chosen as a preferred solvent over DMSO, because of its economical and greenery properties (derived from biomass). From exhaustive study, the optimized reaction conditions were chosen as phenyl boronic acid (1.0 equiv), SeO_2 (1.0 equiv), Iodine (1.0 equiv) was carried out in 2-Me-THF as a solvent (2 mL) at 60 °C for the preparation of diaryl diselenide compounds. Under the selected optimum reaction condition, different electron-withdrawing and electron-donating groups on the aryl boronic acids were selected and reacted with SeO_2 in the presence of Iodine gave the corresponding diaryl diselenides in good to excellent yields were presented in Table 2.

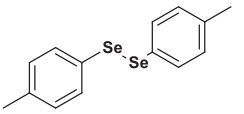
From the Table 2 it was indicated that present method was effective in the case of all aromatic boronic acid substrates bearing either electron-withdrawing or electron-donating groups provided good yields. Aryl boronic aicds bearing EDGs on the benzene ring showed higher reactivity's and afforded a little bit higher yields than

Table 2. Synthesis of various substituted diaryl diselenides[a].

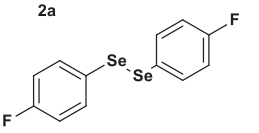




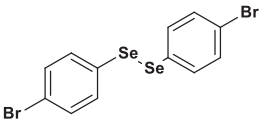
2a (90%)



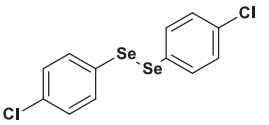
2b (89%)



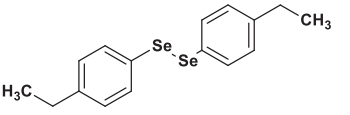
2c (85%)



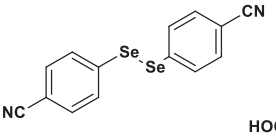
2d (82%)



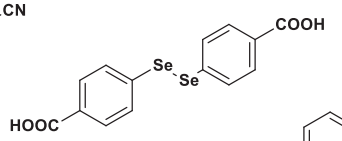
2e (80%)



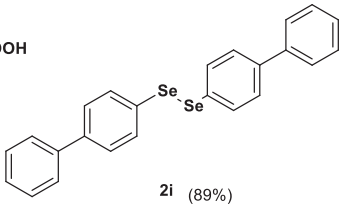
2f (89%)



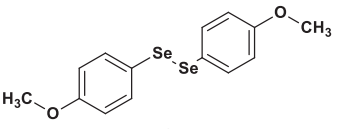
2g (73%)



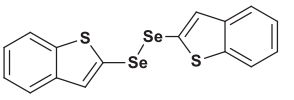
2h (60%)



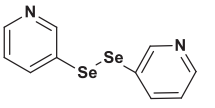
2i (89%)



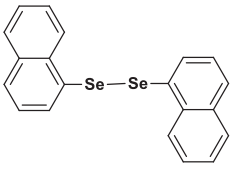
2j (79%)



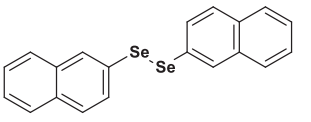
2k (65%)



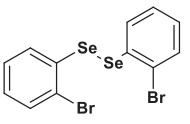
2l (68%)



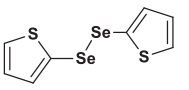
2m (70%)



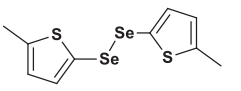
2n (88%)



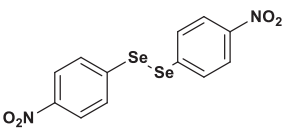
2o (70%)



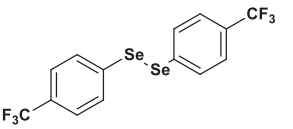
2p (75%)



2q (75%)

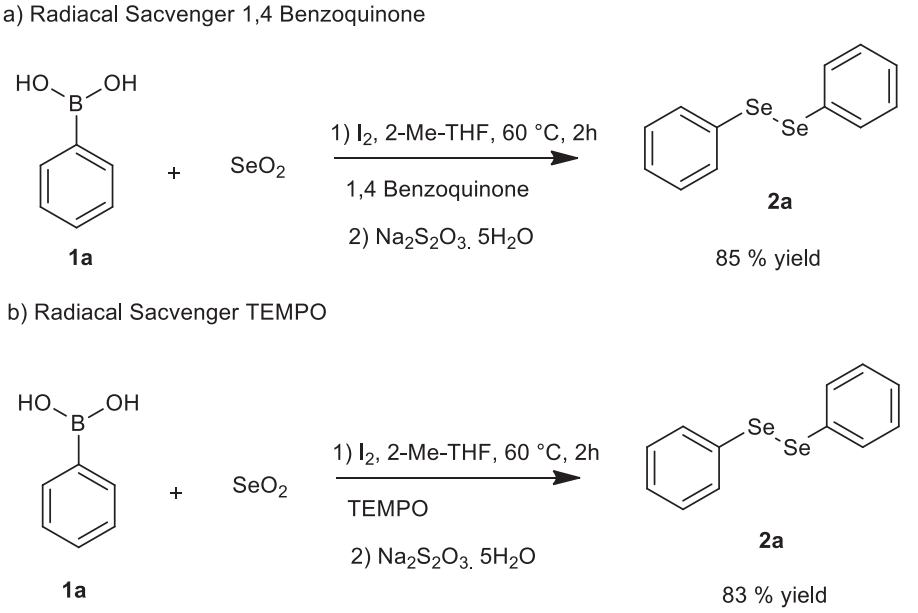


2r (75%)

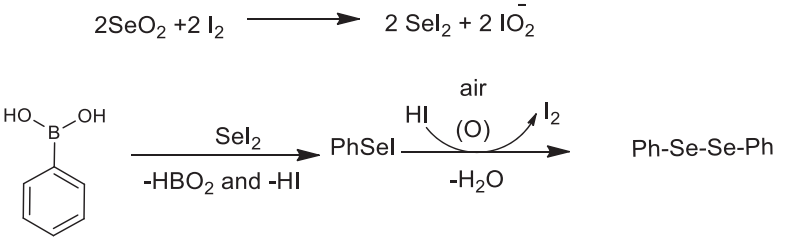


2s (69%)

[a]The reactions were carried out as follows: Phenyl boronic acid (1.0 equiv.), I_2 (1.2 equiv.), SeO_2 (1.0 equiv.), 2-Me-THF (1 mL), at 60 °C, 2 h.
[b]Isolated yields are based on reactant.



Scheme 3. Radical scavenger experiments of iodine mediated synthesis of diphenyl diselenides.



Scheme 4. Proposed plausible mechanism for the synthesis of diaryl diselenides.

those bearing EWG. Later, we checked this protocol on some alkylboronic acids; unfortunately, this protocol was not successful for converting to corresponding alkyl diselenides.

To gain insight into the mechanism of this reaction, free radical trapping experiments were conducted (Scheme 3). It was found that compound **2a** could be isolated in 85% and 83% yields in the presence of 1,4 Benzoquinone (1.0 equiv.) and 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO, 1.0 equiv.), respectively, under the optimized conditions, indicating a non-radical process involved in these transformations.

In Scheme 4, a plausible mechanism for iodine mediated facile synthesis of aryl diphenyl diselenides is outlined. Initially, the molecular iodine and selenium dioxide interact to form selenium iodide and iodide, then, nucleophilic aryl group from the phenylboronic acid reacts with selenium iodide to give phenylselenium iodide, which was detected by GC mass (obtained at *m/z* 281) and ^{77}Se NMR data[18] (peak appeared at $\delta = 507$ ppm (See the supporting information). Later, it was reduced by HI to give the product diphenyl diselenide.

Experimental

General experimental procedure for the synthesis of diaryl diselenides

The reaction was carried out in a 25 mL round bottom flask equipped with magnetic stirbar charged with aryl boronic acid (1.0 equiv), selenium dioxide (1.0 equiv), I_2 (1.0 equiv), and 2-Me-THF (2 mL). The resulting reaction mixture was stirred at 60 °C temperature for 2–4 h. The reaction progress was monitored by TLC. After completion of the reaction, iodine quenched with hypo solution and it was worked up with ethyl acetate (3 × 10 mL) and saturated brine solution. Crude product was purified by column chromatography (petroleum ether/ethyl acetate, 100:0–95:5). The identity and purity of the product was confirmed by ^{1}H NMR, 13C NMR, and EI-MS.

Data of representative example: **Diphenyl Diselenide (2a)**[19]: Orange solid; mp 57–59 °C.; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (dd, $J = 8.0$, 1.4 Hz, 4 H), 7.55 − 7.49 (m, 2 H), 7.48 − 7.41 (m, 4 H).; 13C NMR (101 MHz, $CDCl_3$) δ 134.7, 131.0, 128.9, 127.9.; MS (EI, *m/z*): 312 [M+].

Conclusion

In summary, we developed metal free, base free procedure, highly efficient and can proceed under mild and environmentally friendly conditions for the synthesis of diaryl diselenides. The transformation feature is use of SeO_2 as a selenium source, is operational simple with high functional group compatibility, high yields, base free, avoiding harmful organic solvents, and toxic catalysts. We hope that this novel method may be useful for basic as well as industrial research.

Full experimental details, spectral data of the products, and ^{1}H NMR, ^{13}C NMR and HRMS spectra of all the new compounds can be found via the Supplementary content section of this article's Web page.

Funding

We thank DICP for providing Analytical instruments data, this study was funded by the National Natural Science Foundation of China [Nos. 21721004].

ORCID

Dileep Kommula http://orcid.org/0000-0003-1195-665X

References

[1] (a) Perin, G.; Alves, D.; Jacob, R. G.; Barcellos, A. M.; Soares, L. K.; Lenardão, E. *J. Chem. Select* **2016**, *1*, 205. DOI: 10.1002/slct.201500031.(b) Perin, G.; Lenardão, E. J.; Jacob, R. G. ; Panatieri, R. B. *Chem. Rev.* **2009**, *109*, 1277–1301. DOI: 10.1021/cr8004394.(c) Zeni, G.; Ludtke, D. S.; Panatieri, R. B.; Braga, A. L. *Chem. Rev.* **2006**, *106*, 1032–1076. DOI: 10.1021/cr0505730.(d) Zeni, G.; Braga, A. L.; Stefani, H. A. *Acc. Chem. Res.* **2003**, *36*, 731–738. DOI: 10.1021/ar0202621.(e) Nogueira, C. W.; Zeni, G.; Rocha, J. B. T. *Chem. Rev.* **2004**, *104*, 6255–6286. DOI: 10.1021/cr0406559.

[2] Santi, C. *Organoselenium Chemistry Between Synthesis and Biochemistry*; Sharjah, U.A.E: Bentham Books, 2014. DOI: 10.2174/9781608058389114010 1.
[3] Singh, F. V.; Thomas, W. *Catal. Sci. Technol.* **2019**, *9*, 1073–1091. DOI: 10.1039/C8CY02274G.
[4] Ibrahim, M.; Hassan, W.; Meinerz, D. F.; Santos, M.; Klimaczewski, C.; Deobald, A.; Costa, M. S.; Nogueira, C. W.; Barbosa, N. B. V.; Rocha, J. B. T. *Mol. Cell. Biochem.* **2012**, *371*, 97–104. DOI: 10.1007/s11010-012-1426-4.
[5] Savegnago, L.; Trevisan, M.; Alves, D.; Rocha, J. B. T.; Nogueira, C. W.; Zen, G. *Environ. Toxicol. Pharmacol.* **2006**, *21*, 86–92. DOI: 10.1016/j.etap.2005.07.017.
[6] Savegnago, L.; Pinto, L. G.; Jesse, C. R.; Alves, D.; Rocha, J. B.; Nogueira, C. W.; Zeni, G. *Eur. J. Pharmacol.* **2007**, *555*, 129–138. DOI: 10.1016/j.ejphar.2006.10.003.
[7] Zhengkai, L.; Fang, K.; Hang, D.; Hualong, X.; Haifeng, X.; Xiangge, Z. *Org. Biomol. Chem.* **2013**, *11*, 2943. DOI: 10.1039/c3ob40464a.
[8] Prabhu, K.; Chandrasekaran, S. *Chem. Commun.* **1997**, 983–1072. DOI: 10.1039/a701512g.
[9] (a) Syper, L.; Mlochowski, J. *Tetrahedron* **1988**, *44*, 6119–6130. DOI: 10.1016/S0040-4020(01)89801-X.(b) Krief, A.; Delmotte, C.; Colaux-Castillo, C. *Pure Appl. Chem.* **2000**, *72*, 1709–1713. DOI: 10.1351/pac200072091709.(c) Krief, A.; Dumont, W.; Delmotte, C. *Angew. Chem. Int. Ed.* **2000**, *39*, 1669–1672. DOI: 10.1002/(sici)1521-3773(20000502)39:9<1669::aid-anie1669>3.0.co;2-6.
[10] Salama, P.; Bernard, C. *Tetrahedron Lett.* **1995**, *36*, 5711–5714. DOI: 10.1016/0040-4039(95)01112-U.
[11] (a) Wang, M.; Fan, Q. L.; Jiang, X. F. *Org. Lett.* **2016**, *18*, 5756–5759. DOI: 10.1021/acs.orglett.6b03078.(b) Maity, P.; Kundu, D.; Roy, R.; Ranu, B. C. *Org. Lett.* **2014**, *16*, 4122–4125. DOI: 10.1021/ol501820e. (c) Guan, Y.; Townsend, S. D. *Org. Lett.* **2017**, *19*, 5252–5255. DOI: 10.1021/acs.orglett.7b02526.(d) Guo, T.; Wei, X. N.; Wang, H. Y.; Zhu, Y. L.; Zhao, Y. H.; Ma, Y. C. *Org. Biomol. Chem.* **2017**, *15*, 9455–9464. DOI: 10.1039/C7OB02278F.(e) Leng, T.; Wu, G.; Zhou, Y. B.; Gao, W. X.; Ding, J. H.; Huang, X. B.; Liu, M. C.; Wu, H. Y. *Adv. Synth. Catal.* **2018**, *360*, 4336–4340. DOI: 10.1002/adsc.201800896.(f) Heredia, A. A.; Penenory, A. B. *RSC Adv.* **2015**, *5*, 105699–105706. DOI: 10.1039/C5RA20883A.(g) Liu, Y. H.; Ling, H.; Chen, C.; Xu, Q.; Yu, L.; Jiang, X. F. *Synlett.* **2019**, *30*, 207–212. DOI: 10.1055/s-0037-1612083.
[12] Zhu, J.; Zhu, W.; Xie, P.; Pittman, C. U.; Zhou, A. *Tetrahedron* **2018**, *74*, 6569–6576. DOI: 10.1016/j.tet.2018.09.037.
[13] (a) Kumar, R. U.; Reddy, K. H. V.; Satish, G.; Swapna, K.; Nageswar, Y. V. D. *Tetrahedron Lett.* **2016**, *57*, 4138–4141. DOI: 10.1016/j.tetlet.2016.07.075.(b) Quell, T.; Mirion, M.; Schollmeyer, D.; Dyballa, K. M.; Franke, R.; Waldvogel, S. R. *ChemistryOpen* **2016**, *5*, 115–119. DOI: 10.1002/open.201500206.(c) Shangpliang, O. R.; Kshiar, B.; Wanniang, K.; Marpna, I. D.; Lipon, T. M.; Laloo, B. M.; Myrboh, B. *J. Org. Chem.* **2018**, *83*, 5829–5835. DOI: 10.1021/acs.joc.8b00558.(d) Ren, Y. K.; Xu, B. J.; Zhong, Z. J.; Pittman, C. U.; Zhou, A. H. *Org. Chem. Front* **2019**, *6*, 2023–2027. DOI: 10.1039/C9QO00299E.
[14] Monticelli, S.; Castoldi, L.; Murgia, I.; Senatore, R.; Mazzeo, E.; Wackerlig, J.; Urban, E.; Langer, T.; Pace, V. *Monatsh. Chem.* **2017**, *148*, 37–48. DOI: 10.1007/s00706-016-1879-3.
[15] Pace, V.; Hoyos, P.; Castoldi, L.; Domínguez de María, P.; Alcántara, A. R. *Chem. Sus. Chem* **2012**, *5*, 1369–1379. DOI: 10.1002/cssc.201100780.
[16] David, F. A. *Org. Process Res. Dev.* **2007**, *11*, 156. DOI: 10.1021/op060155c.
[17] (a) Dileep, K.; Murty, M. S. R. *J. Iran. Chem. Soc.* **2017**, *14*, 1665. DOI: 10.1007/s13738-017-1107-z.(b) Dileep, K.; Murty, M. S. R. *Synlett.* **2017**, *28*, 2295–2298. DOI: 10.1055/s-0036-1590972.(c) Uday Kumar, R.; Dileep, K.; Harshavardhan, R. K.; Nageswar, Y. V. D. *CMIC.* **2018**, *5*, 62–72. DOI: 10.2174/2213335605666180227154226.(d) Kumar, R. U.; Dileep, K.; Reddy, K. H. V.; Nageswar, Y. V. D. *LOC.* **2019**, *16*, 110–116. DOI: 10.2174/1570178615666180627111437.(e) Li, C. Z.; Zhang, Z. H.; Zhao, Z. K. *Tetrahedron Lett.* **2009**, *50*, 5403–5405. DOI: 10.1016/j.tetlet.2009.07.053.(f) Zhang, Z. H.; Zhao, Z. K. *Bioresour. Technol.* **2010**, *101*, 1111–1114. DOI: 10.1016/j.biortech.2009.09.010.(g) Zhang,

Z. H.; Wang, Q.; Xie, H. B.; Liu, W. J.; Zhao, Z. K. *ChemSusChem*. **2011**, *4*, 131–138. DOI: 10.1002/cssc.201000279.

[18] (a) Salzen, A. M-V.; Meyer, H.-U.; Du Mont, W.-W. *Phosphorus Sulfur Silicon Relat. Elem.* **1992**, *67*, 67–71. DOI: 10.1080/10426509208045820.(b) Du Mont, W.-W.; Martens, A.; Pohl, S.; Saak, W. *Inorg. Chem.* **1990**, *29*, 4847–4848. DOI: 10.1021/ic00349a003.

[19] Singh, D.; Deobald, A. M.; Camargo, L. R. S.; Tabarelli, G.; Rodrigues, O. E. D.; Braga, A. L. *Org. Lett.* **2010**, *12*, 3288–3291. DOI: 10.1021/ol100558b.