Organic & Biomolecular Chemistry

ROYAL SOCIETY OF CHEMISTRY

PAPER

View Article Online
View Journal

Cite this: DOI: 10.1039/d0ob00300j

Construction of 2,3-disubstituted benzo[*b*]thieno[2,3-*d*]thiophenes and benzo[4,5]selenopheno[3,2-*b*]thiophenes using the Fiesselmann thiophene synthesis†

Roman A. Irgashev, *[a,b] Nadezhda S. Demina [a,b] and Gennady L. Rusinov[a,b]

A series of 3-(hetero)aryl-substituted benzo[*b*]thieno[2,3-*d*]thiophenes, bearing various electron withdrawing groups at C-2 position of their scaffolds, were obtained using a convenient approach based on the Fiesselmann thiophene synthesis. To realize this strategy, the Friedel–Crafts acylation of (hetero)arenes with easily accessible 3-chlorobenzo[*b*]thiophene-2-carbonyl chlorides was initially performed to afford 3-chloro-2-(hetero)aroylbenzo[*b*]thiophenes. The latter ketones were treated either with methyl thioglycolate in the presence of DBU and calcium oxide powder or successively with sodium sulfide, an alkylating agent, containing methylene active component, and also DBU and calcium oxide, to form the desired benzo[*b*]thieno[2,3-*d*]thiophene derivatives. In addition, similar benzo[4,5]selenopheno[3,2-*b*]thiophene derivatives were prepared in the same manner using 3-bromobenzo[*b*]selenophen-2-yl substrates. The obtained functional derivatives of both benzo[*b*]thieno[2,3-*d*]thiophene and benzo[4,5]selenopheno[3,2-*b*]thiophene are of interest for further elaboration of organic semiconductor materials.

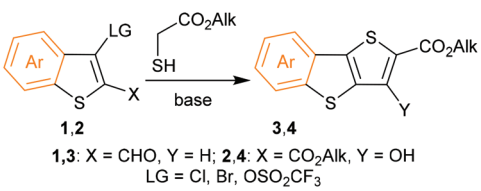
Received 10th February 2020,
Accepted 2nd April 2020

DOI: 10.1039/d0ob00300j

rsc.li/obc

Introduction

Over the past two decades, π-conjugated thiophene-based compounds with linear as well as ring-fused structures have received significant attention from researchers owing to the prospect of their application for organic electronics area.[1–5] In this context, a large number of photo- and electroactive materials based on thienothiophenes and more π-extended thieno-fused molecules have been synthesized, studied and utilized for the manufacture of various thin-film electronic and optoelectronic devices.[6–9] Among them, benzo[*b*]thieno[2,3-*d*]thiophene (BTT) framework, also named benzothieno[3,2-*b*]thiophene or thieno[3,2-*b*][1]benzothiophene, has been used in the production of dyes for dye-sensitized solar cells,[10–14] π-conjugated donor–acceptor polymers for bulk heterojunction solar cells,[15–17] p-type semiconductors for organic field-effect transistors[18–22] as well as fluorescent materials,[23] electroactive polymers,[24,25] liquid crystals[26] and photochromic materials.[27] Few protocols of preparing the simple benzo[*b*]thieno[2,3-*d*]thiophene have been reported in the literature, including reaction of 1-(3-bromobenzo[*b*]thiophen-2-yl)-2-trimethylsilylacetylene with sodium sulfide,[20] Cu- or Fe-catalyzed reaction of benzo[*b*]thieno[2,3-*d*]iodolium triflate with sulfur sources,[28,29] Pd-catalyzed C–S cyclization of 2-(2-acetylthiophenyl)thiohene[30] or 2,2′-di(thiophen-2-yl)diphenyldisulfide.[31] At the same time, BTT scaffolds can be readily formed by the Fiesselmann thiophene synthesis, which consists in reaction of thioglycolic acid derivatives or mercaptomethyl ketones with appropriate 1,3-C,C-dielectrophiles,[32] and is widely used for the construction of functional thiophenes.[33–35] With regard to BTTs synthesis, 3-unsubstituted and 3-hydroxy-substituted benzo[*b*]thieno[2,3-*d*]thiophene-2-carboxylates **3** and **4** have been prepared from benzo[*b*]thiophene substrates **1**[21,24] or **2**,[23,36,37] respectively (Scheme 1). However, the scope of the



Scheme 1 Construction of BTT compounds using the Fiesselmann reaction.

[a]*Postovsky Institute of Organic Synthesis, Ural Division, Russian Academy of Sciences, S. Kovalevskoy Str., 22, Ekaterinburg, 620990, Russia. E-mail: irgashev@ios.uran.ru; Fax: +7 343 369 30 58*

[b]*Ural Federal University named after the First President of Russia B. N. Yeltsin, Mira Str., 19, Ekaterinburg, 620002, Russia*

†Electronic supplementary information (ESI) available: Experimental procedures, copies of ^{1}H, ^{19}F and ^{13}C NMR spectra of new compounds. CCDC 1981665, 1981666 and 1981668. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/d0ob00300j

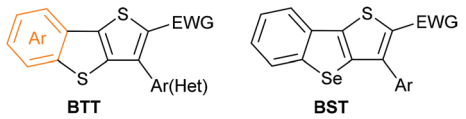


Fig. 1 Substructure of compounds, obtained in this study.

Fiesselmann reaction application for the construction of 2,3-disubstituted BTT molecules has not been fully disclosed yet.

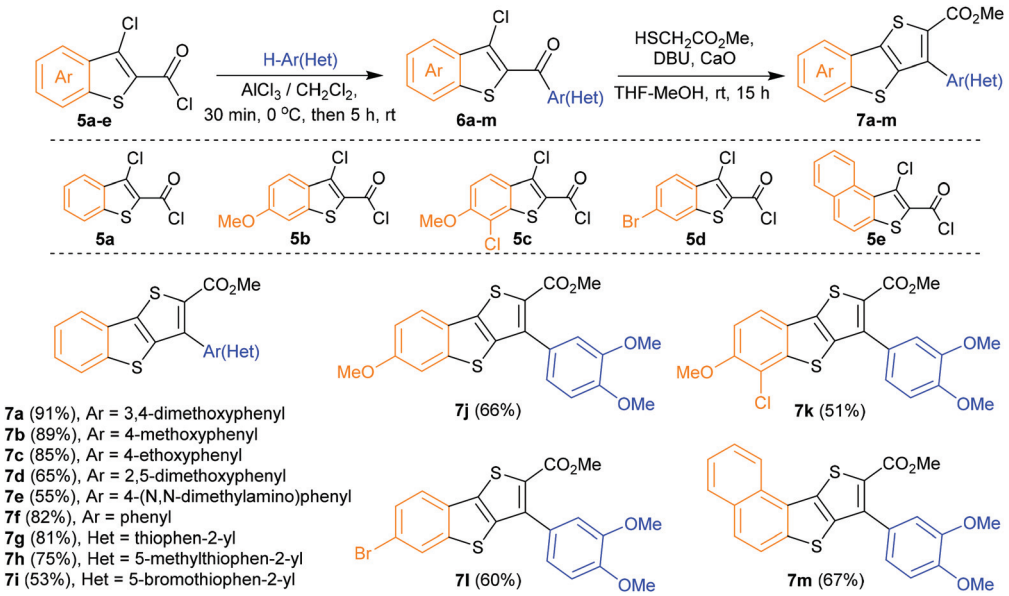
Herein, we report synthetic strategy for the preparation of 3-(hetero)aryl-substituted BTTs, bearing electron withdrawing groups (EWG), such as carbomethoxy, cyano or acyl at C-2 positions, based on the Fiesselmann reaction. In addition, we have also used this approach to obtain some similar benzo[4,5]selenopheno[3,2-*b*]thiophene (BST) derivatives (Fig. 1). Both types of these 2,3-disubstituted BTTs and BSTs have not been previously described in principle to the best of our knowledge.

Results and discussion

To perform the construction of the above mentioned BTT molecules in accordance with our synthetic strategy, we selected 2-(hetero)aroyl-substituted 3-chlorobenzo[*b*]thiophenes **6** as appropriate 1,3-C,C-dielectrophilic substrates required for the Fiesselmann reaction. Thus, ketones **6a–i** were synthesized by the Friedel–Crafts acylation of various aromatic compounds as well as thiophenes with 3-chlorobenzo[*b*]thiophene-2-carbonyl chloride **5a** in the presence of $AlCl_3$ in dry CH_2Cl_2, and ketones **6j–m** were similarly obtained by the acylation of veratrole with acyl chlorides **5b–e** (Scheme 2) in 28–87% yields. In turn, acyl chlorides **5** were readily obtained by treatment of the corresponding cinnamic acids with excess of thionyl chloride in the presence of DMF and pyridine according to previously described procedure.[38] Compounds **6a–m** were obtained in 28–87% yields, wherein moderate yields were observed for **6g** (28%) and **6h** (38%), bearing thien-2-yl and 5-methylthien-2-yl part, respectively, due to the significant degradation of thiophene and 2-methylthiophene during their reaction with acyl chloride **5a**. At the same time, our attempts to use milder Lewis acids such as $SnCl_4$ or $TiCl_4$ instead of $AlCl_3$ failed.

It should be noted, that an alternative synthesis of such type ketones, consisting in the treatment of 3-chloro-6-methoxybenzo[*b*]thiophene-2-carbonyl chloride (**5b**) or the corresponding Weinreb amide[39] with (hetero)arylmagnesium bromides in dry THF, has recently been reported.[40] This method can also be utilized for the preparation of compounds **6** in some cases.

Next, we focused on determining optimal reaction conditions for the conversion of compounds **6** to BTT derivatives using the Fiesselmann method. To this end, we studied the reaction of **6** with methyl thioglycolate. Thus, the treatment of substrate **6a** with methyl thioglycolate (1.3 equiv.) and DBU (2 equiv.) in THF–MeOH (10 : 1, v/v) under an argon atmosphere at room temperature gave a mixture of the desired ester **7a** and the corresponding carboxylic acid, which formed due to the partial saponification of **7a**. At the same time, our attempts to use NaH or NaOMe in THF or DMF solution were fruitless, since the fast degradation of raw materials occurred, complex mixture of compounds forming. To improve the result, we redid the experiment with DBU adding CaO powder (5 equiv.) to bind water released during reaction process. With this change, the desired product **7a** was obtained in 91% yield. Furthermore, since the basic nature of CaO caused the regeneration of DBU freebase from its hydrochloride, we managed to reduce the amount of DBU to 50 mol% without decrease in yield of ester **7a** (Table 1). Other BTT derivatives **7b–m** were



Scheme 2 Synthesis of BTT derivatives **7**, substrate scope and yields. $HSCH_2CO_2Me$ (1.3 equiv.), DBU (50 mol%) and CaO (5 equiv.) were used.

Table 1 Reaction conditions for the synthesis of BTT **7a**

Entry[a]	DBU (equiv.)	CaO (equiv.)	Yield of **7a** (%)
1	2.0	—	79[b]
2	2.0	5.0	91
3	0.5	5.0	91

[a] The experiments were performed with $HSCH_2CO_2Me$ (1.3 equiv.) in THF–MeOH (10 : 1, v/v) at rt for 15 h. [b] Ester **7a** was obtained in a mixture with the corresponding carboxylic acid.

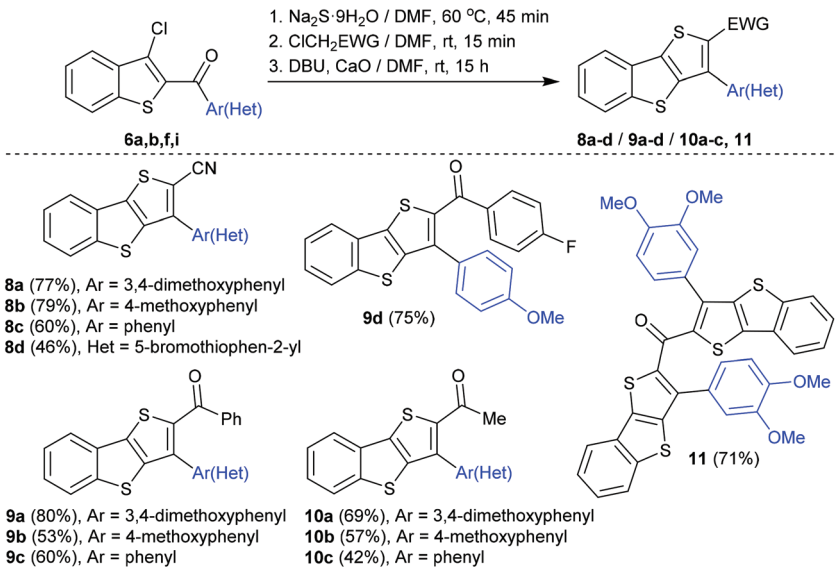
smoothly prepared in the same manner in 51–89% yields (Scheme 2).

To obtain BTT derivatives with other EWGs at C-2 position, we realized the Fiesselmann-like reaction, wherein 1,3-C,C-dielectrophilic substrate was successively treated with alkali sulfide and the alkylating agent. For instance, to substitute chlorine atom at C-3 position of compound **6a**, the latter one was involved in the reaction with sodium sulfide (1.1 equiv.) in DMF solution under an argon atmosphere at 60 °C for 45 min, thus giving thiolate anion, which was alkylated with chloroacetonitrile (1.1 equiv.) next. The formed intermediate was cyclized *in situ* under the reaction conditions similar to the derivatives **7** formation, except for a larger excess of CaO (15 equiv.), to afford product **8a** in 77% yield. Carbonitriles **8b–d** were prepared from substrates **6b,f,i** according to this one-pot procedure in 46–79% yields. In addition, 2-benzoyl- and 2-(4-fluorobenzoyl)-BTTs **9a–c** and **9d** as well as 2-acetyl-BTTs **10a–c** were obtained in the same manner using phenacyl and 4-flourophenacyl chlorides or chloroacetone as the alkylating agents, respectively (Scheme 3). Doubled BTT derivative **11** was also synthesized from substrate **6a** in 71% yield with the use of 1,3-dichloroacetone. To note, we failed to prepare 2-benzoyl and 2-acetyl BTTs from substrate **6i**, bearing 5-bromothien-2-yl unit, while carbonitrile **8d** was obtained only in moderate yield because of significant degradation of **6i** during its initial reaction with sodium sulfide in DMF solution.

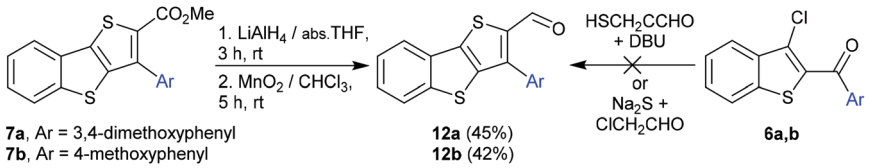
The structure of BTTs **7–11** was confirmed by the data of ^1H and ^{13}C NMR spectroscopy, and HRMS. In addition, the molecular structure of compounds **9b** and **11** was proved unequivocally by XRD analysis (see ESI† for additional information).[41]

The synthesis of 2-formyl-substituted BTT derivatives **12** was also elaborated during this study. Initially, we tried to prepare these compounds by treatment of substrates **5** with either 2,5-dihydroxy-1,4-dithiane (dimer of 2-mercaptoacetaldehyde and its synthetic equivalent) or sodium sulfide and 2-chloroacethaldehyde using the described above reaction conditions, but these attempts failed. In this respect, we performed the preparation of compounds **12** by transformation of carbomethoxy group in derivatives **7**. To this end, esters **7a,b** were reduced with $LiAlH_4$ in THF solution at room temperature, followed by mild oxidation of the obtained BTT carbinols, which were isolated by alkali workup of the reaction mixtures and used without further purification, with MnO_2 in $CHCl_3$ solution to give BTT carbaldehydes **12a,b** in 45% and 42% overall yields (Scheme 4).

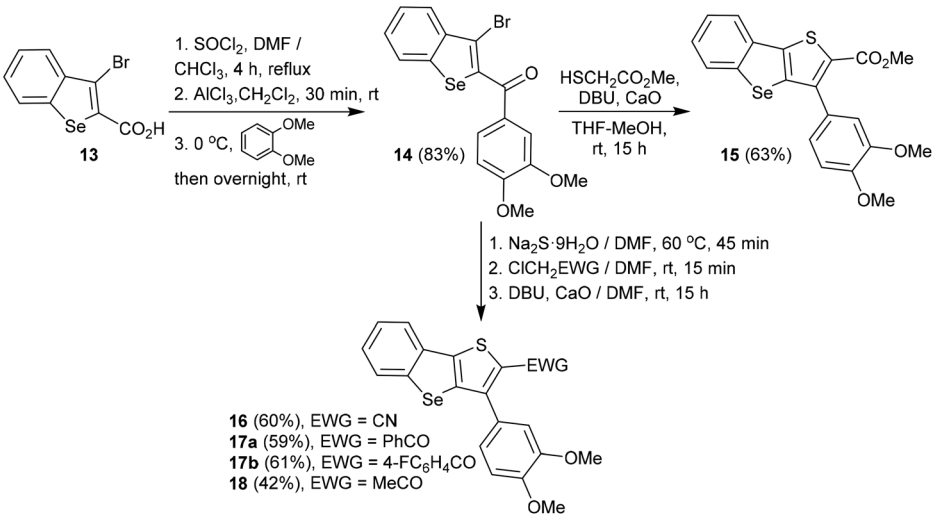
The present approach was also applied to construct 3-(3,4-dimethoxyphenyl)-substituted BST molecules. To this end, we saponified easily accessible ethyl 3-bromobenzo[*b*]selenophene-2-carboxylate[42] to obtain carboxylic acid **13**. The latter acid was treated with excess of thionyl chloride to afford the corresponding acyl chloride, which was further involved in the Friedel–Crafts reaction without any purification. Thus, ketone **14** was prepared in 83% yield by acylation of veratrole (1.2 equiv.) with this intermediate acyl chloride in the presence of $AlCl_3$ (1.3 equiv.). Then, the reaction of substrate **14** with methyl thiogly-



Scheme 3 Synthesis of BTT derivatives **8–11**, substrate scope and yields. $Na_2S·9H_2O$ (1.1 equiv.), $ClCH_2EWG$ (1.1 equiv.), DBU (50 mol%) and CaO (15 equiv.) were used.



Scheme 4 Synthesis of 2-formyl-substituted BTTs **12**.



Scheme 5 Synthesis of BST derivatives **15–18**.

colate (1.3 equiv.) in the presence of DBU (50 mol%) and CaO powder (5 equiv.) afforded ester **15** in 63% yield. In turn, 2-cyano-, 2-benzoyl-, 2-(4-fluorobenzoyl)- and 2-acetyl-substituted BSTs **16**, **17a**, **17b** and **18** were prepared by reaction of compound **14** with sodium sulfide (1.1 equiv.) to form the intermediate thiolate anion, which was successively treated with chloroacetonitrile, phenacyl or 4-fluorophenacyl chloride, or chloroacetone (1.1 equiv.), respectively, and with DBU (50 mol%) and CaO (15 equiv.) in DMF solution (Scheme 5). The molecular structure of BST derivatives **15–18** was additionally established by XRD analysis, carried out for a single crystal of compound **17a** (see ESI† for additional information).[43]

Conclusion

In summary, we have successfully applied the Fiesselmann reaction to prepare benzo[*b*]thieno[2,3-*d*]thiophene derivatives, bearing (hetero)aromatic units at C-3 position and EWGs at C-2 position, from 3-chloro-2-(hetero)aroylbenzo[*b*]thiophenes. Furthermore, the construction of the similar benzo[4,5]selenopheno[3,2-*b*]thiophene molecules in accordance with this synthetic approach has also been demonstrated. In general, being readily available and conveniently modifiable on (hetero)aromatic moieties and functional groups to get enhanced features, benzo[*b*]thieno[2,3-*d*]thiophenes and benzo[4,5]selenopheno[3,2-*b*]thiophenes described herein are of interest as building blocks for the development of π-extended BTT- and BST-based compounds for material applications.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

This study was supported by the Russian Science Foundation, Grant No. 19-13-00234.

Notes and references

1 *Handbook of Thiophene-Based Materials*, ed. I. F. Perepichka and D. F. Perepichka, John Wiley & Sons, Ltd, Chichester, UK, 2009.
2 A. Mishra, C. Q. Ma and P. Bäuerle, *Chem. Rev.*, 2009, **109**, 1141–1176.
3 G. Turkoglu, M. E. Cinar and T. Ozturk, *Top. Curr. Chem.*, 2017, 375.
4 *Organic Optoelectronic Materials*, ed. Y. Li, Springer, Cham, 2015.
5 H. Klauk, *Chem. Soc. Rev.*, 2010, **39**, 2643–2666.
6 V. P. Litvinov, *Russ. Chem. Rev.*, 2005, **74**, 217–248.

7 M. E. Cinar and T. Ozturk, *Chem. Rev.*, 2015, **115**, 3036–3140.
8 K. Strakova, L. Assies, A. Goujon, F. Piazzolla, H. V. Humeniuk and S. Matile, *Chem. Rev.*, 2019, **119**, 10977–11005.
9 J. Podlesný, O. Pytela, M. Klikar, V. Jelínková, I. V. Kityk, K. Ozga, J. Jedryka, M. Rudysh and F. Bureš, *Org. Biomol. Chem.*, 2019, **17**, 3623–3634.
10 Y. K. Eom, S. H. Kang, I. T. Choi, E. Kim, J. Kim, M. J. Ju and H. K. Kim, *RSC Adv.*, 2015, **5**, 80859–80870.
11 Y. K. Eom, I. T. Choi, S. H. Kang, J. Lee, J. Kim, M. J. Ju and H. K. Kim, *Adv. Energy Mater.*, 2015, **5**, 1500300.
12 K. Miao, M. Liang, Z. Wang, C. Zhang, Z. Sun and S. Xue, *Phys. Chem. Chem. Phys.*, 2017, **19**, 1927–1936.
13 X. Xie, Z. H. Liu, F. Q. Bai and H. X. Zhang, *Front. Chem.*, 2019, **7**, 676.
14 Y. K. Eom, S. H. Kang, I. T. Choi, Y. Yoo, J. Kim and H. K. Kim, *J. Mater. Chem. A*, 2017, **5**, 2297–2308.
15 S. Sun, P. Zhang, J. Li, Y. Li, J. Wang, S. Zhang, Y. Xia, X. Meng, D. Fan and J. Chu, *J. Mater. Chem. A*, 2014, **2**, 15316–15325.
16 W. Yue, R. S. Ashraf, C. B. Nielsen, E. Collado-Fregoso, M. R. Niazi, S. A. Yousaf, M. Kirkus, H. Y. Chen, A. Amassian, J. R. Durrant and I. McCulloch, *Adv. Mater.*, 2015, **27**, 4702–4707.
17 M. Neophytou, D. Bryant, S. Lopatin, H. Chen, R. K. Hallani, L. Cater, I. McCulloch and W. Yue, *Macromol. Rapid Commun.*, 2018, **39**, 1700820.
18 H. Chen, Q. Cui, G. Yu, Y. Guo, J. Huang, M. Zhu, X. Guo and Y. Liu, *J. Phys. Chem. C*, 2011, **115**, 23984–23991.
19 C. Mallet, G. Savitha, M. Allain, V. Kozmík, J. Svoboda, P. Frère and J. Roncali, *J. Org. Chem.*, 2012, **77**, 2041–2046.
20 P. Y. Huang, L. H. Chen, Y. Y. Chen, W. J. Chang, J. J. Wang, K. H. Lii, J. Y. Yan, J. C. Ho, C. C. Lee, C. Kim and M. C. Chen, *Chem. – Eur. J.*, 2013, **19**, 3721–3728.
21 Z. Li, J. Zhang, K. Zhang, W. Zhang, L. Guo, J. Huang, G. Yu and M. S. Wong, *J. Mater. Chem. C*, 2015, **3**, 8024–8029.
22 K. Hyodo, H. Hagiwara, R. Toyama, H. Mori, S. I. Soga and Y. Nishihara, *RSC Adv.*, 2017, **7**, 6089–6092.
23 C. Lô, J.-J. Aaron, V. Kozmík, J. Svoboda, J.-C. Brochon and L. Na, *J. Fluoresc.*, 2010, **20**, 1037–1047.
24 I. Fouad, Z. Mechbal, K. I. Chane-Ching, A. Adenier, F. Maurel, J. J. Aaron, P. Vodicka, K. Cernovska, V. Kozmik and J. Svoboda, *J. Mater. Chem.*, 2004, **14**, 1711–1721.
25 C. Lô, A. Adenier, F. Maurel, J. J. Aaron, V. Kozmik and J. Svoboda, *Synth. Met.*, 2008, **158**, 6–24.
26 K. Černovská, B. Košata, J. Svoboda, V. Novotná and M. Glogarová, *Liq. Cryst.*, 2006, **33**, 987–996.
27 S. K. Balenko, N. I. Makarova, O. G. Karamov, V. P. Rybalkin, I. V. Dorogan, L. L. Popova, E. N. Shepelenko, A. V. Metelitsa, V. V. Tkachev, S. M. Aldoshin, V. A. Bren and V. I. Minkin, *Russ. Chem. Bull.*, 2007, **56**, 2400–2406.
28 M. Shimizu, M. Ogawa, T. Tamagawa, R. Shigitani, M. Nakatani and Y. Nakano, *Eur. J. Org. Chem.*, 2016, **2016**, 2785–2788.
29 L. Liu, J. Qiang, S. Bai, Y. Li and J. Li, *Appl. Organomet. Chem.*, 2017, **31**, 2365–2371.
30 S. Chen, M. Wang and X. Jiang, *Chin. J. Chem.*, 2018, **36**, 921–924.
31 K. Nishino, Y. Ogiwara and N. Sakai, *Chem. – Eur. J.*, 2018, **24**, 10971–10974.
32 J. J. Li, in *Name Reactions*, Springer International Publishing, Cham, 2014, pp. 250–251.
33 M. Teiber and T. J. J. Müller, *Chem. Commun.*, 2012, **48**, 2080–2082.
34 A. S. Kostyuchenko, A. M. Averkov and A. S. Fisyuk, *Org. Lett.*, 2014, **16**, 1833–1835.
35 I. Karpavičienė, M. Jonušis, K. Leduskrasts, I. Misiūnaitė, E. Suna and I. Čikotienė, *Dyes Pigm.*, 2019, **170**, 107646.
36 A. F. Moretto, S. J. Kirincich, W. X. Xu, M. J. Smith, Z.-K. Wan, D. P. Wilson, B. C. Follows, E. Binnun, D. Joseph-McCarthy, K. Foreman, D. V. Erbe, Y. L. Zhang, S. K. Tam, S. Y. Tam and J. Lee, *Bioorg. Med. Chem.*, 2006, **14**, 2162–2177.
37 R. A. Irgashev, A. A. Karmatsky, G. L. Rusinov and V. N. Charushin, *Org. Lett.*, 2016, **18**, 804–807.
38 W. Ried, G. Oremek and B. Ocakcioglu, *Liebigs Ann. Chem.*, 1980, **1980**, 1424–1427.
39 S. Nahm and S. M. Weinreb, *Tetrahedron Lett.*, 1981, **22**, 3815–3818.
40 R. Xiong, J. Zhao, L. M. Gutgesell, Y. Wang, S. Lee, B. Karumudi, H. Zhao, Y. Lu, D. A. Tonetti and G. R. J. Thatcher, *J. Med. Chem.*, 2017, **60**, 1325–1342.
41 CCDC 1981665 (**9b**) and 1981668 (**11**) contain the supplementary crystallographic data for this paper.†
42 E. Paegle, S. Belyakov and P. Arsenyan, *Eur. J. Org. Chem.*, 2014, **2014**, 3831–3840.
43 CCDC 1981666 (**17a**) contains the supplementary crystallographic data for this paper.†