Construction of Heteroacenes with Fused Thiophene and Pyrrole Rings via the Fischer Indolization Reaction
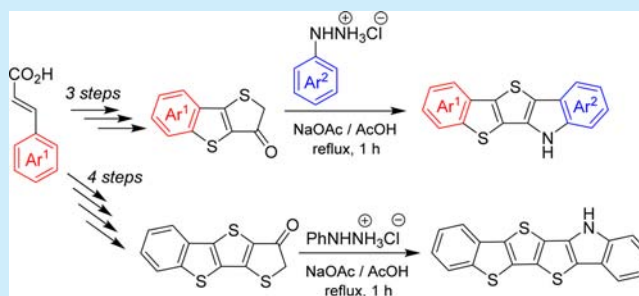
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S *Supporting Information*

ABSTRACT: A convenient approach to ladder-type 6*H*-benzo[4′,5′]thieno[2′,3′:4,5]thieno[3,2-*b*]indoles bearing various substituents in both terminal benzene rings has been developed. The protocol suggested for preparing these *N,S*-heteroacenes is based on using easily available reagents, such as cinnamic acids and arylhydrazines, which can be involved in the Fischer indole synthesis, as the key step. A similar condensed system of 12*H*-benzo[4″,5″]thieno[2″,3″:4′,5′]-thieno[2′,3′:4,5]thieno[3,2-*b*]indole, bearing six rings, has also been obtained.

A significant and growing number of publications dealing with various classes of π-conjugated polycyclic molecules, including acenes and their heteroanalogues (heteroacenes), have emerged during the past decade. Successful applications of these compounds have been presented, specifically as active materials for high-performance organic electronic devices, such as organic field-effect transistors (OFETs),[1] organic light-emitting diodes (OLEDs),[2] and different kinds of organic photovoltaics (OPVs).[3] Pentacene and some higher acenes, such as hexa- or heptacenes, are excellent organic semiconductors, showing outstanding characteristics of charge carrier mobility.[4] However, these compounds possess low stability under ambient conditions due to high-lying HOMO energy levels, which strongly restrict their practical applications.[5] Compared with acenes, electron-rich heteroacenes, bearing fused thiophene and/or pyrrole rings, instead of the benzene units in the parent aromatic hydrocarbons, not only exhibit better electronic characteristics but are also more resistant to degradation. Generally, heteroacenes have a higher structural versatility because of a variety of combinations of aromatic and heteroaromatic units that provide desired tuning for target structures. Many heteroacene derivatives based on thiophene and/or pyrrole units have recently been suggested as promising materials for electronic and optoelectronic devices.[6] In this context, there is a strong demand for new heteroacenes; therefore, the development of convenient synthetic approaches to their frameworks is an important topic for both organic chemistry and material science. From an organic synthesis point of view, a good strategy should provide easy access to a diversity of heteroacene derivatives for further design of more complicated molecules to develop materials with improved properties.

In this paper, we report a robust and convenient way for the synthesis of new asymmetric *N,S*-heteroacenes, having a ladder-

type structure, namely 6*H*-benzo[4′,5′]thieno[2′,3′:4,5]thieno-[3,2-*b*]indoles (BTTIs). Moreover, the suggested approach enables one to vary substituents in both terminal benzene rings of the BTTI scaffold. It is noteworthy that three isomeric heteroacenes **1−3** with different dispositions of two thiophene and one pyrrole rings, located between two terminal benzene fragments, have been described previously in the literature (Figure 1).[7]
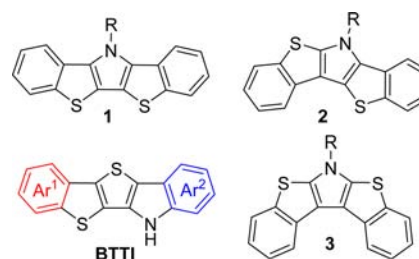

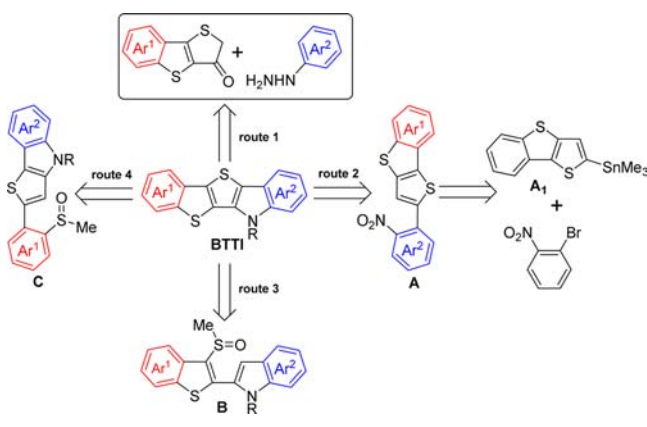**Figure 1.** Structures of BTTI and the known isomers.

The key step in the synthesis of heteroacenes **1−3** is the formation of central pyrrole ring using the Cadogan reductive cyclization[7a] or the Buchwald−Hartwig amination,[7b] although variation of substituents merely at the nitrogen atom in these heterocycles has also been demonstrated.

Several ring-closure reactions appear suitable for construction of the BTTI core, and they should be discussed in order to select the most acceptable route. In fact, the BTTI structure can be formed using the Cadogan cyclization[8a] of 2-nitrophenyl, containing benzo[*b*]thieno[2,3-*d*]thiophenes **A** (route 2, Scheme 1), triflic acid catalyzed cyclization[8b] of 2-methyl-

Scheme 1. Synthetic Routes to the Formation of BTTI Scaffold

Scheme 2. Synthesis and Structures of Benzo[*b*]thieno[2,3-*d*]thiophenes Derivatives 5 and 6

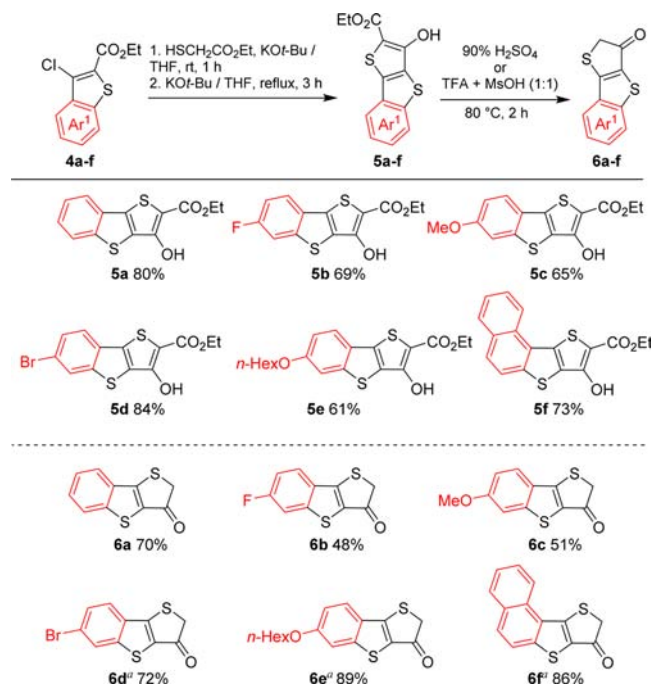[a]TFA/MsOH (v/v, 1:1) was used instead of sulfuric acid.

sulfinylphenyl-containing indoles **B** (route 3, Scheme 1), or related cyclization of thieno[3,2-*b*]indoles **C** (route 4, Scheme 1). A reasonable approach to precursors **A**−**C** is provided by the Suzuki−Miyaura or the Stille cross-coupling reactions between properly selected (hetero)aryl halides and organoboron or organotin (hetero)arenes, respectively (for instance, the formation of precursor **A** using the Stille cross-coupling of stannane **A₁**[8c] with 1-bromo-2-nitrobenzene, Scheme 1).

However, synthetic routes to the BTTI scaffold discussed above have some disadvantages; namely, they require expensive and nonenvironmentally friendly transition metals, highly toxic phosphine ligands and organotin compounds (for the Stille reaction), as well as some pyrophoric reagents (e.g., *n*-BuLi) for prefunctionalization of (het)aromatic fragments. All these features eventually lead to a low availability of the target compounds. The synthesis of BTTI structure can also be realized via the Fischer reaction,[9] which avoids the mentioned above difficulties, and thereby the Fischer indolization process has been selected as the key step for the synthesis of the BTTI core (route 1, Scheme 1). It should be mentioned that, for instance, the double-Fischer cyclization of bis-arylhydrazones of cyclohexa-1,4-dione provides an easy access to 5,11-dihydroindolo[3,2-*b*]carbazoles, which constitute an important class of *N*-heteroacenes with a wide range of applications in organic electronic devices.[10]

According to the selected synthetic procedure, benzo[*b*]-thieno[2,3-*d*]thiophen-3(2*H*)-ones proved to be major precursors of BTTI compounds, and their preparation became the starting point for its implementation. The closest analogues of these tricyclic ketones, such as thieno[3,2-*b*]thiophen-3(2*H*)-ones, have been synthesized previously by cyclization of 2-(thien-3-ylthio)acetic acids in polyphosphoric acid in low yields.[11] At the same time, compounds with the thiophen-3(2*H*)-one moiety were synthesized in good yields by facile decarboxylation of the corresponding 3-hydroxythiophene-2-carboxylic acids.[12] In this connection, tricyclic 3-hydroxyesters **5a**−**f** were prepared by the Fiesselmann-like reaction[13] from ethyl 3-chlorobenzo[*b*]thiophene-2-carboxylates **4a**−**f** and ethyl mercaptoacetate in the presence of an excess of potassium *tert*-butoxide (Scheme 2). The starting materials **4a**−**f** bearing the benzo[*b*]thiophene scaffold have been obtained by treatment of the corresponding cinnamic acids with thionyl chloride, according to the reported procedure.[14]

All attempts to cause saponification of ester **5a** in a refluxing solution of potassium hydroxide in ethanol for 12 h, as well as

to realize its hydrolysis with a mixture of concentrated hydrochloric and glacial acetic acids (v/v, 1:1) under similar conditions, have failed, and the starting material **5a** was recovered in both cases. Successful hydrolysis of the ester **5a** followed by decarboxylation of the formed acid has been performed in a solution of 90% sulfuric acid on mild heating of the reaction mixture up to 80 °C, thus affording tricyclic ketone **6a** in 75% yield. It is especially important to maintain the temperature of the current process below 80 °C because the yield of the product **6a** becomes lower in the case of even a short-term overheating of the reaction mixture. Other ketones **6b**−**f** have been synthesized from the corresponding esters **5b**−**f** in the same manner.
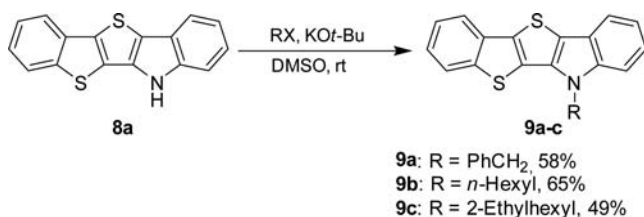
However, conversion of raw materials **5d**−**f** in sulfuric acid was very slow, and it caused significant degradation of the reaction products **6d**−**f** due to a prolonged contact with a strong acid under heating. This problem was solved using a mixture of trifluoroacetic (TFA) and methanesulfonic (MsOH) acids (v/v, 1:1), instead of sulfuric acid, for hydrolysis of esters **5d**−**f** resulting in ketones **6d**−**f** in good yields (Scheme 2).

It has been found that ketones **6a**−**f** react with phenylhydrazine hydrochloride **7a** (1.2 equiv) in the presence of anhydrous sodium acetate (2 equiv) in a glacial acetic acid when heated under reflux for 1 h, and the initially formed hydrazones of **6** are easily indolized into BTTIs **8a**−**f** under these conditions without isolation of intermediates (field A, Scheme 3). The synthesis of compounds **8g**−**k** with substituents in the fused benzene ring of the indole part of the molecules has been performed easily by treatment of ketone **6a** with hydrochloric salts of the corresponding arylhydrazines **7b**−**f** under the same reaction conditions (field B, Scheme 3). Therefore, two sets of the target BTTI heteroacenes **8** containing various substituents in both benzene rings have been prepared successfully using the Fischer reaction as the key step of these transformations.

Scheme 3. Synthesis and Structures of BTTI Derivatives 8 Prepared by the Fischer Indolization Reaction

N-Substituted derivatives **9a−c** were prepared by alkylation of the starting compound **8a** as an example of modification of the BTTI core. This synthesis was carried out in DMSO solution at room temperature in the presence of potassium *tert*-butoxide as a base (Scheme 4). Evidence for the structure of

Scheme 4. Synthesis of N-Substituted BTTIs 9a−c

9a: R = PhCH$_2$, 58%
9b: R = *n*-Hexyl, 65%
9c: R = 2-Ethylhexyl, 49%

BTTI compounds **8** has been obtained unequivocally by X-ray crystallography analysis performed for the single-crystal sample of 6-benzyl-substituted derivative **9a** (Figure 2; see also the SI), thus supporting the ^{1}H and ^{13}C NMR spectroscopic data.

The suggested approach to the formation of BTTI molecules has also been applied successfully for the synthesis of heteroacenes bearing six rings with one extra thiophene block in its ladder-type BTTI framework. Thus, treatment of 3-hydroxyester **5a** with triflic anhydride (Tf$_2$O) in the presence of triethylamine and 4-(dimethylamino)pyridine (DMAP) has

afforded the corresponding triflate **10** in a quantitative yield. The latter readily reacts with ethyl mercaptoacetate under conditions similar to those used for preparation of compound **5a** to obtain tetracyclic 3-hydroxyester **11**. Hydrolysis of the ester **11**, followed by decarboxylation in a mixture of trifluoroacetic (TFA) and methanesulfonic (MsOH) acids, has produced the key precursor **12**, which has been transformed consequently into the target six-ring heterocyclic system **13** (BTTTI) according to the Fischer reaction (Scheme 5).
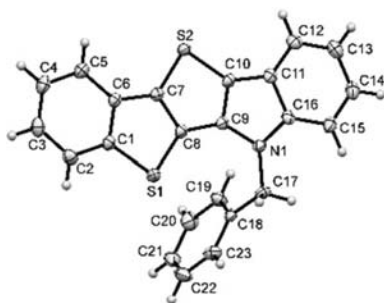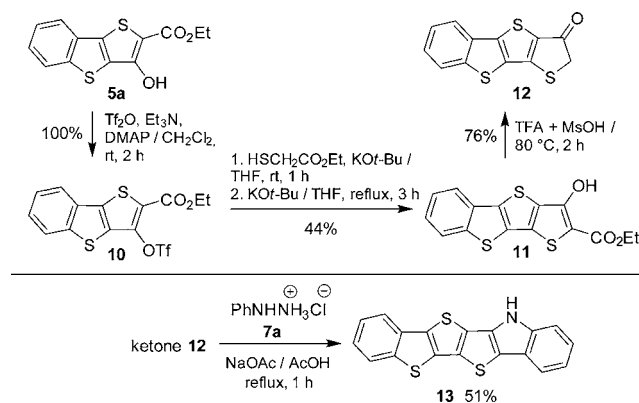
Scheme 5. Synthesis of Six-Ring Heteroacene 13

In summary, we have described a convenient approach to construct derivatives of an unknown heterocyclic system, namely 6H-benzo[4′,5′]thieno[2′,3′:4,5]thieno[3,2-b]indoles, bearing substituents in both terminal benzene rings, on the basis of the Fischer indole synthesis, as the key step. The three-step synthesis of these N,S-heteroacenes has been realized, starting from ethyl 3-chlorobenzo[b]thiophene-2-carboxylates, which have been prepared from easily accessible cinnamic acids. In addition, the synthesis of a six-ring heterocyclic system of 12H-benzo[4″,5″]thieno[2″,3″:4′,5′]thieno[2′,3′:4,5]thieno-[3,2-b]indole has been performed using this strategy. The further design and synthesis of new heteroacene structures using this reaction sequence, as well as the elucidation of optic

Figure 2. X-ray single crystal structure of derivative **9a**. Thermal ellipsoids of 50% probability are presented.

and electronic properties of BTTI and BTTTI compounds, are currently in progress.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.6b00081.

> Experimental procedures, UV−vis absorption spectra of compounds **8a−c,f,h,i,k** and **13**, characterization data for all new compounds, and ^{1}H, ^{13}C, and ^{19}F NMR spectra (PDF)
> Crystallographic data for **9a** (CIF)

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Notes

The authors declare no competing financial interest.

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REFERENCES

(1) (a) Wu, W.; Liu, Y.; Zhu, D. *Chem. Soc. Rev.* **2010**, *39*, 1489−1502. (b) Zschieschang, U.; Ante, F.; Kälblein, D.; Yamamoto, T.; Takimiya, K.; Kuwabara, H.; Ikeda, M.; Sekitani, T.; Someya, T.; Nimoth, J. B.; Klauk, H. *Org. Electron.* **2011**, *12*, 1370−1375. (c) Watanabe, M.; Chen, K. Y.; Chang, Y. J.; Chow, T. J. *Acc. Chem. Res.* **2013**, *46*, 1606−1615. (d) Wang, M.; Li, J.; Zhao, G. Y.; Wu, Q. H.; Huang, Y. G.; Hu, W. P.; Gao, X.; Li, H.; Zhu, D. *Adv. Mater.* **2013**, *25*, 2229−2233. (e) Takimiya, K.; Osaka, I.; Nakano, M. *Chem. Mater.* **2014**, *26*, 587−593.

(2) (a) *Organic Light Emitting Devices: Synthesis, Properties and Applications*; Müllen, K., Scherf, U., Eds.; Wiley-VCH: Weinheim, 2006. (b) Lo, S.-C.; Burn, P. L. *Chem. Rev.* **2007**, *107*, 1097−1116. (c) Zhu, M.; Yang, C. *Chem. Soc. Rev.* **2013**, *42*, 4963−4976. (d) Liu, Z. Y.; Xiao, J. C.; Fu, Q.; Feng, H. R.; Zhang, X. M.; Ren, T. J.; Wang, S.; Ma, D.; Wang, X.; Chen, H. *ACS Appl. Mater. Interfaces* **2013**, *5*, 11136−11141.

(3) (a) Lin, Y. Z.; Li, Y. F.; Zhan, X. W. *Chem. Soc. Rev.* **2012**, *41*, 4245−4272. (b) *Organic Photovoltaics: Materials, Device Physics, and Manufacturing Technologies*, 2nd ed.; Brabec, C., Scherf, U., Dyakonov, V., Eds.; Wiley-VCH: Mannheim, 2014. (c) Im, J.-H.; Jang, I.-H.; Pellet, N.; Grätzel, M.; Park, N.-G. *Nat. Nanotechnol.* **2014**, *9*, 927−932. (d) Kazim, S.; Nazeeruddin, M. K.; Grätzel, M.; Ahmad, S. *Angew. Chem., Int. Ed.* **2014**, *53*, 2812−2824. (e) Mazzio, K. A.; Luscombe, C. K. *Chem. Soc. Rev.* **2015**, *44*, 78−90. (f) Steck, C.; Franckevičius, M.; Zakeeruddin, S. M.; Mishra, A.; Bäuerle, P.; Grätzel, M. *J. Mater. Chem. A* **2015**, *3*, 17738−17746.

(4) (a) Kelley, T. W.; Boardman, L. D.; Dunbar, T. D.; Muyres, D. V.; Pellerite, M. J.; Smith, T. P. *J. Phys. Chem. B* **2003**, *107*, 5877−5881. (b) Payne, M. M.; Parkin, S. R.; Anthony, J. E. *J. Am. Chem. Soc.* **2005**, *127*, 8028−8029. (c) Mondal, R.; Adhikari, R. M.; Shah, B. K.; Neckers, D. C. *Org. Lett.* **2007**, *9*, 2505−2508. (d) Purushothaman, B.; Parkin, S. R.; Anthony, J. E. *Org. Lett.* **2010**, *12*, 2060−2063. (e) Watanabe, M.; Chang, Y. J.; Liu, S.-W.; Chao, T.-H.; Goto, K.; Islam, M. M.; Yuan, C.-H.; Tao, Y.-T.; Shinmyozu, T.; Chow, T. J. *Nat. Chem.* **2012**, *4*, 574−578.

(5) (a) Maliakal, A.; Raghavachari, K.; Katz, H.; Chandross, E.; Siegrist, T. *Chem. Mater.* **2004**, *16*, 4980−4986. (b) Einholz, R.;

Bettinger, H. F. *Angew. Chem., Int. Ed.* **2013**, *52*, 9818−9820. (c) Zade, S. S.; Bendikov, M. *J. Phys. Org. Chem.* **2012**, *25*, 452−461. (d) Zade, S. S.; Bendikov, M. *Angew. Chem., Int. Ed.* **2010**, *49*, 4012−4015.

(6) (a) Anthony, J. E. *Chem. Rev.* **2006**, *106*, 5028−5048. (b) Izawa, T.; Takimiya, K. *J. Am. Chem. Soc.* **2007**, *129*, 2224−2225. (c) Miyazaki, E.; Takimiya, K. *Chem. Mater.* **2009**, *21*, 903−912. (d) Gao, P.; Cho, D.; Yang, X. Y.; Enkelmann, V.; Baumgarten, M.; Müllen, K. *Chem. - Eur. J.* **2010**, *16*, 5119−5128. (e) Simokaitiene, J.; Stanislovaityte, E.; Grazulevicius, J. V.; Jankauskas, V.; Gu, R.; Dehaen, W.; Hung, Y. C.; Hsu, C. P. *J. Org. Chem.* **2012**, *77*, 4924−4931. (f) Mori, T.; Nishimura, T.; Yamamoto, T.; Doi, I.; Miyazaki, E.; Osaka, I.; Takimiya, K. *J. Am. Chem. Soc.* **2013**, *135*, 13900−13913. (g) Park, J.-I.; Chung, J. W.; Kim, J.-Y.; Lee, J.; Jung, J. Y.; Koo, B.; Lee, B.-L.; Lee, S. W.; Jin, Y. W.; Lee, S. Y. *J. Am. Chem. Soc.* **2015**, *137*, 12175−12178. (h) Niebel, C.; Kim, Y.; Ruzié, C.; Karpinska, J.; Chattopadhyay, B.; Schweicher, G.; Richard, A.; Lemaur, V.; Olivier, Y.; Cornil, J.; Kennedy, A. R.; Diao, Y.; Lee, W. Y.; Mannsfeld, S.; Bao, Z.; Geerts, Y. H. *J. Mater. Chem. C* **2015**, *3*, 674−685. (i) Jung, I. H.; Kim, J.-H.; Nam, S. Y.; Lee, C.; Hwang, D.-H.; Yoon, S. C. *Macromolecules* **2015**, *48*, 5213−5221.

(7) (a) Qi, T.; Guo, Y.; Liu, Y.; Xi, H.; Zhang, H.; Gao, X.; Liu, Y.; Lu, K.; Du, C.; Yu, G.; Zhu, D. *Chem. Commun.* **2008**, 6227−6229. (b) Balaji, G.; Valiyaveettil, S. *Org. Lett.* **2009**, *11*, 3358−3361.

(8) (a) Cadogan, J. I. G.; Mackie, R. K. *Chem. Soc. Rev.* **1974**, *3*, 87−137. (b) Huang, J.; Luo, H.; Wang, L.; Guo, Y.; Zhang, W.; Chen, H.; Zhu, M.; Liu, Y.; Yu, G. *Org. Lett.* **2012**, *14*, 3300−3303. (c) Mallet, C.; Savitha, G.; Allain, M.; Kozmik, V.; Svoboda, J.; Frere, P.; Roncali, J. *J. Org. Chem.* **2012**, *77*, 2041−2046.

(9) Robinson, B. *Chem. Rev.* **1963**, *63*, 373−401.

(10) (a) Tholander, J.; Bergman, J. *Tetrahedron* **1999**, *55*, 12577−12594. (b) Yudina, L. N.; Bergman, J. *Tetrahedron* **2003**, *59*, 1265−1275.

(11) Archer, W. J.; Taylor, R. *J. Chem. Soc., Perkin Trans. 2* **1982**, 295−299.

(12) (a) Carpenter, W.; Snyder, H. R. *J. Am. Chem. Soc.* **1960**, *82*, 2592−2597. (b) Dinescu, L.; Maly, K. E.; Lemieux, R. P. *J. Mater. Chem.* **1999**, *9*, 1679−1686.

(13) (a) Fiesselmann, H.; Schipprak, P. *Chem. Ber.* **1954**, *87*, 835−841. (b) Fiesselmann, H.; Schipprak, P.; Zeitler, L. *Chem. Ber.* **1954**, *87*, 841−848. (c) Fiesselmann, H.; Pfeiffer, G. *Chem. Ber.* **1954**, *87*, 848−856. (d) Fiesselmann, H.; Thoma, F. *Chem. Ber.* **1956**, *89*, 1907−1912. (e) Fiesselmann, H.; Schipprak, P. *Chem. Ber.* **1956**, *89*, 1897−1902.

(14) (a) Higa, T.; Krubsack, A. J. *J. Org. Chem.* **1975**, *40*, 3037−3045. (b) Ried, W.; Oremek, G.; Ocakcioglu, B. *Liebigs Ann. Chem.* **1980**, *1980*, 1424−1427.