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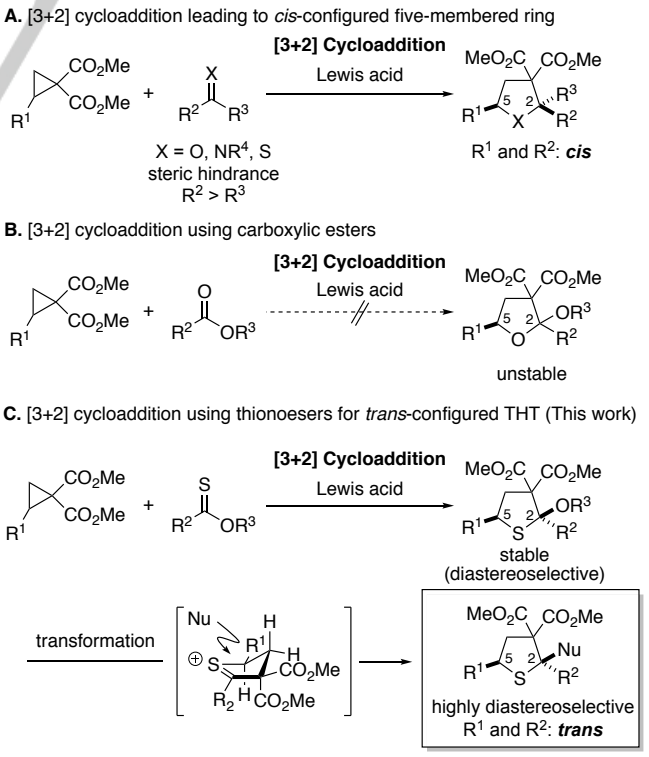
An Expeditious Route to *trans*-Configured Tetrahydrothiophenes Enabled by $Fe(OTf)_3$-Catalyzed [3+2] Cycloaddition of Donor-Acceptor Cyclopropanes with Thionoesters

Yohei Matsumoto, Daiki Nakatake, Ryo Yazaki* and Takashi Ohshima*

Abstract: A synthetic route to *trans*-configured tetrahydrothiophenes (THTs) through $Fe(OTf)_3$-promoted [3+2] cycloaddition of donor-acceptor cyclopropanes with thionoesters was developed. The cycloaddition proceeded in high yield with high diastereoselectivity, affording transient α-alkoxy THTs. Not only aromatic and aliphatic thionoesters, but also thionolactone were applicable to the present iron catalysis. Further transformation of the S,O-ketal functionality of the product was achieved in a highly *trans* diastereoselective manner. Moreover, the utility of our methodology was clearly demonstrated by the synthesis of enantioenriched *trans*-configured THTs.

Tetrahydrothiophene (THT), a heavier analog of tetrahydrofuran, is an important scaffold frequently found in biologically active natural products.[1] THT is also utilized as a ligand in synthetic chemistry to harness the preferential coordination ability to soft metals over hard metals.[2] In contrast to the methods available for the tetrahydrofuran, methods for the synthesis of THT remain to be explored, despite its importance; therefore, multistep reactions involving intramolecular cyclization are almost inevitable.[1,3,4] An intermolecular [3+2] cycloaddition reaction of donor-acceptor (D-A) cyclopropanes with heteroatom-containing dipolarophiles is one of the most powerful synthetic methods for a five-membered hetero ring system (Scheme 1A).[5] Although the chemistry of D-A cyclopropanes has considerably progressed in the last few decades, only a few examples of THT synthesis using sulfur-containing dipolarophiles are reported.[6] Furthermore, [3+2] cycloaddition of D-A cyclopropanes with hetero-dipolarophiles generally provides a 2,5-*cis*-configured five-membered ring system through a common reaction mechanism, and the synthesis of a 2,5-*trans*-configured five-membered ring system has remained a formidable task.[7] Herein, we report an expeditious synthetic route to 2,5-*trans*-configured THT derivatives through catalytic [3+2] cycloadditions of D-A cyclopropanes with thionoesters (Scheme 1C).

Thiocarbonyls are innately more reactive than the corresponding carbonyls due to the less efficient π-orbital overlap of the C-S bond.[8] For example, benzothioaldehyde is highly unstable, leading to oligomerization even at 110 K, and thioketones require thermodynamic or kinetic stabilization to be isolated.[9,10] Among thiocarbonyls, thionoesters, which can be readily synthesized from the corresponding esters by treatment with Lawesson's reagent, are relatively stable and easy to handle due to conjugative stabilization by a lone pair at oxygen.[11] The stable nature of thionoesters makes them useful for unique transformations that cannot be accessed using a common carboxylic ester.[12] Previously, Nicolaou *et al.* developed several unique transformations of thionoesters and applied them to the total synthesis of various natural products.[13] Efficient synthesis of heteroaromatic compounds from thionoesters is also well investigated.[14] Thus, we focused on the use of thionoesters for the synthesis of 2,5-*trans*-configured THT derivatives through Lewis acid-catalyzed [3+2] cycloaddition of D-A cyclopropanes. Although the use of carboxylic ester in the [3+2] cycloaddition of D-A cyclopropanes is problematic due to instability of the O,O-ketal functionality of the product (Scheme 1B), thionoesters are a good substrate due to the higher stability of the corresponding S,O-ketal functionality under Lewis or Brønsted acid-catalyzed conditions.[13] We also envisioned that further transformation of the S,O-ketal functionality through a thionium cation intermediate would deliver the 2,5-*trans*-configured THT derivatives in a highly *trans*-selective manner to avoid the steric repulsion (Scheme 1C).



Scheme 1. [3+2] Cycloaddition reactions of D-A cyclopropanes and dipolarophiles.

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ohshima@phar.kyushu-u.ac.jp

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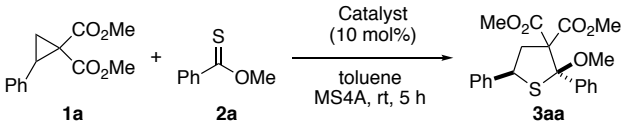


Table 1. Condition Optimization[a]

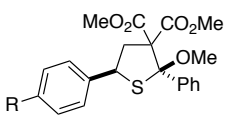
Entry	Catalyst	Yield (%)[b]	dr[b]
1	none	n.r.	n.d.
2	$Mg(OTf)_2$	n.r.	n.d.
3	$Al(OTf)_3$	n.r.	n.d.
4	$AlCl_3$	n.r.	n.d.
5	$Sc(OTf)_3$	38	7.0:1
6	$Fe(OTf)_2$	n.r.	n.d.
7	$Fe(OTf)_3$	95	10:1
8	$Cu(OTf)_2$	n.r.	n.d.
9	$Sn(OTf)_2$	5	n.d.
10	$La(OTf)_3$	n.r.	n.d.
11	$Yb(OTf)_3$	n.r.	n.d.
12[c]	$Fe(OTf)_3$	38	16:1

[a] Conditions: **1a** (0.20 mmol), **2a** (0.24 mmol), catalyst (0.020 mmol), MS4A (50 mg), toluene (1.0 ml). [b] Yield and diastereoselectivity were calculated by ^{1}H-NMR analysis using 2-methoxynaphthalene standard. n.r. = no reaction. n.d. = not determined. [c] Without MS4A.

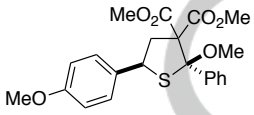
We began our investigation using cyclopropane **1a** and thionoester **2a** as model substrates, and the reactions were performed with MS4A in toluene at ambient temperature. No reaction proceeded without a catalyst (entry 1). In addition, several Lewis acid catalysts, which are commonly used in [3+2] cycloadditions of D-A cyclopropanes, exhibited no catalytic activity (entries 2–4). $Sc(OTf)_3$ provided the desired product **3aa** in moderate yield with good diastereoselectivity (entry 5). In contrast, $Fe(OTf)_3$ exhibited the highest catalytic performance and **3aa** was obtained in 95% yield with high diastereoselectivity, although $Fe(OTf)_2$ was ineffective (entries 6 and 7). Soft metal triflates, $Cu(OTf)_2$ and $Sn(OTf)_2$, were less effective, presumably due to the highly coordinative nature of soft Lewis basic thionoester **2a** (entries 8 and 9). Representative lanthanide metal catalysts $La(OTf)_3$ and $Yb(OTf)_3$ gave no desired product **3aa** (entries 10 and 11). Without MS4A, ring-opening of tetrahydrothiophene due to water contamination occurred, resulting in a low chemical yield (entry 12).[15]. TfOH, which can be generated in situ by decomposing metal triflate with water, afforded product **3aa** in very low yield, suggesting that Lewis acidic $Fe(OTf)_3$ would be an actual active species.[16]

With the optimal conditions in hand (Table 1, entry 7), we next investigated the scope with respect to D-A cyclopropanes **1** (Table 2). A range of substituents on the 2-aryl group were applicable to the present catalysis (**3ba**–**3ea**). When less reactive substrates were used, the use of CH_2Cl_2 instead of toluene as a solvent was beneficial for smooth reaction progress. An electron-rich aromatic group, 4-methoxyphenyl and 2-thienyl, afforded the products in a synthetically useful yield with high diastereoselectivity (**3fa** and **3ga**). Although alkyl-substituted

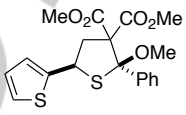
Table 2. Substrate Scope[a]



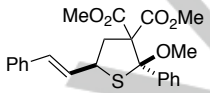
R =		
H	**3aa**	87% yield (10:1)
F	**3ba**	86% yield (9.2:1)
Cl	**3ca**	89% yield (7.1:1)
Br	**3da**	91% yield (5.2:1)
I	**3ea**	83% yield (8.9:1)



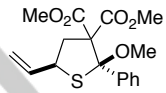
3fa
79% yield (9.3:1)[b]



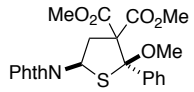
3ga
45% yield (8.5:1)[b]



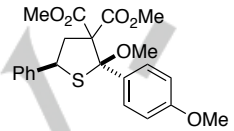
3ha
56% yield (5.8:1)[b]



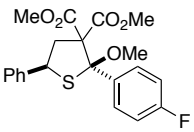
3ia
61% yield (4.5:1)[b]



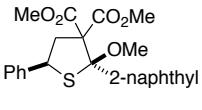
3ja
84% yield (>20:1)[b]



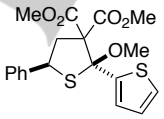
3ab
60% yield (8.9:1)



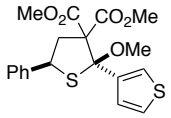
3ac
87% yield (4.0:1)[c]



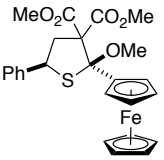
3ad
85% yield (10:1)[b]



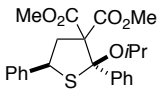
3ae
34% yield (15:1)[b,d,e]



3af
46% yield (14:1)[b,d]

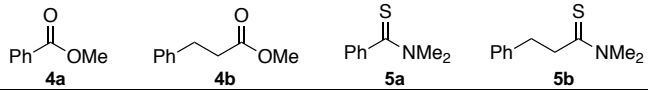


3ag
85% yield (>20:1)[b,f]



3ah
63% yield (2.5:1)[c]

No reaction (with **1a**)



[a] Reaction Conditions: **1** (0.20 mmol), **2** (0.24 mmol), $Fe(OTf)_3$ (0.020 mmol), MS4A (50 mg), toluene (1.0 ml). [b] CH_2Cl_2 was used as a solvent instead of toluene. [c] Reaction time was 12 h. [d] 30 mol% catalyst was used. [e] Reaction time was 96 h. [f] Reaction time was 24 h.

cyclopropane did not provide the product, cinnamyl and vinyl-substituted THT, which could be further transformed through a cross metathesis reaction, were obtained (**3ha** and **3ia**), confirming the synthetic utility of the present catalysis for divergent THT synthesis. Phthalimide-substituted THT **3ja** was also successfully constructed in high yield with excellent diastereoselectivity.

The scope of thionoesters **2** was also investigated with cyclopropane **1a**. Methyl 4-methoxythionobenzoate (**2b**) and 4-fluorothionobenzoate (**2c**) provided the corresponding THTs **3ab**

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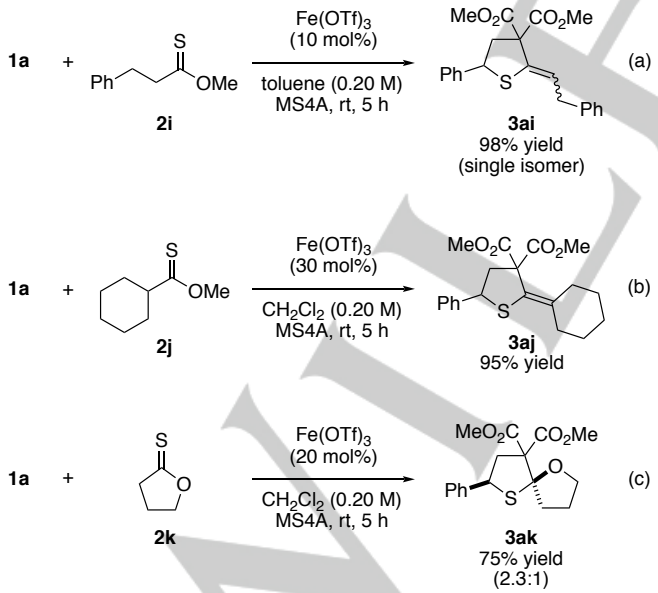
and **3ac** in good yield. The initial reaction rate decreased in the order of **2b** > **2a** > **2c**, suggesting that the reaction was initiated by nucleophilic attack of the thionoester, the same mechanism of the common D-A cyclopropane chemistry.[5,16] Time-course analysis of product **3ac** revealed low diastereoselectivity in a shorter reaction time, and as the reaction progressed, the ratio of the thermodynamically more stable isomer increased.[16]

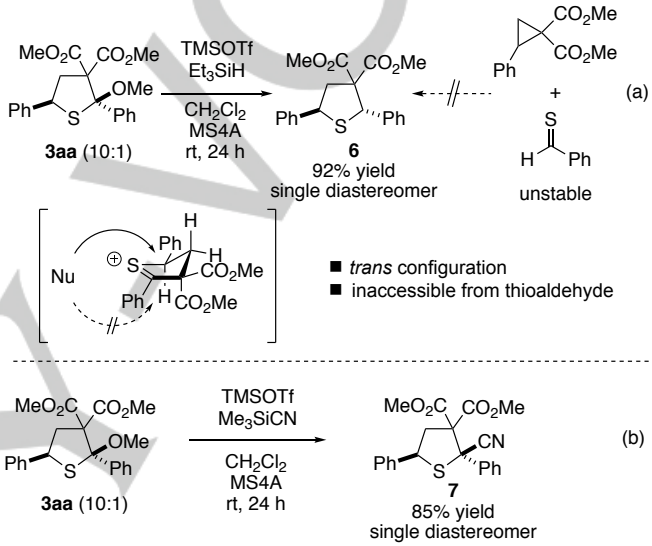
2-Naphthyl group could be used as substrate (**3ad**). Previously unexplored highly coordinative thiocarbonyls having heteroaromatic functionality could be applied and products (**3ae**, **3af**) were isolated in moderate yields with high diastereoselectivities using 30 mol% catalyst.[6d] Useful intermediate **3ag** having ferrocenyl group was obtained in high yield, verifying synthetic utility of the present catalysis.[17] Inferior reactivity and diastereoselectivity were observed when a sterically congested isopropyl thionobenzoate (**2h**) was used. No reactions were observed using aromatic/aliphatic carboxylic esters (**4a** and **4b**) or thioamides (**5a** and **5b**), highlighting the highly chemoselective nature of the present [3+2] cycloadditions.

Aliphatic thioaldehydes and thioketones are generally unstable and difficult to use in the intermolecular [3+2] cycloaddition reaction of D-A cyclopropanes.[8-10] To demonstrate further synthetic utility of the present catalysis, we next investigated the scope using aliphatic thionoesters (Scheme 2). The [3+2] cycloaddition of methyl 3-phenylthionopropionate (**2i**) and cyclopropane **1a** followed by elimination of methanol afforded olefinated product **3ai** in excellent yield (Scheme 2a). Sterically-hindered substrate **2j** was also applicable to the present catalysis using 30 mol% $Fe(OTf)_3$ (Scheme 2b). It is noteworthy that cyclic thionoester, γ-butyrothionolactone (**2k**), afforded a hitherto-inaccessible [5,5]-spiro-S,O-ketal ring system for the first time (Scheme 2c). Although the diastereoselectivity of **3ak** was moderate, those isomers could be separated by conventional column chromatography.

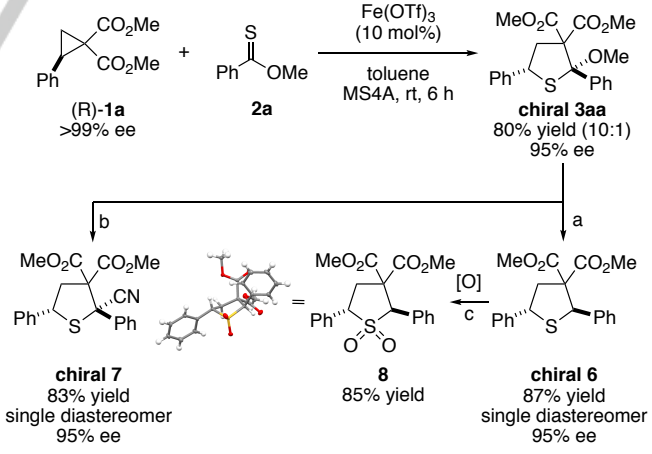


Scheme 2. [3+2] Cycloaddition reactions of cyclopropane **1a** and aliphatic thionoester **2i** and **2j** and thionolactone **2k**.

We next turned our attention to transformations of the S,O-ketal functionality (Scheme 3). A Lewis acid-mediated hydride reduction with Et_3SiH proceeded smoothly, and α-mono-substituted product **6** was obtained in 92% yield as a single diastereomer; this *trans*-product cannot be accessed from thioaldehyde due to the instability of the thioaldehyde (Scheme 3a).[9,18a] Although the previously reported [3+2] cycloaddition of D-A cyclopropanes provided *cis*-configured five-membered systems as the major isomer, this transformation proceeded in a highly *trans*-selective manner to avoid steric repulsion,[18b] demonstrating the utility of our synthetic method for *trans*-configured THT synthesis. Aside from the reduction, diastereoselective transformation of the C–O bond to the C–C bond was achieved using TMSCN, affording α-tetrasubstituted THT **7** as a single diastereomer, which cannot be synthesized by conventional S_N2 cyclization (Scheme 3b).[3]



Scheme 3. TMSOTf mediated diastereoselective transformation of **3aa**.



Scheme 4. Chiral THT synthesis using (*R*)-**1a**. Reaction conditions: a) TMSOTf (30 mol%), Et_3SiH (3.0 equiv.), MS4A, CH_2Cl_2, 0°C to RT, 24 h. b) TMSOTf (50 mol%), TMSCN (5.0 equiv.), MS4A, CH_2Cl_2, 0°C to RT, 24 h. c) *m*CPBA (2.0 equiv), CH_2Cl_2, RT, 6 h.

Finally, we applied our method to chiral THT synthesis using readily available chiral cyclopropane (*R*)-**1a** (Scheme 4). The enantioenriched THT was isolated in high yield with 95% ee. Further elaboration of the obtained chiral **3aa** provided chiral

products **6** and **7** without decreasing the enantioselectivity. Absolute stereochemistry of oxidized sulfone **8** was confirmed by X-ray crystallographic analysis, where stereochemical inversion was observed, supporting the predominance of S_N2 nucleophilic attack of the thionoester rather than the carbocation pathway.

In summary, we developed a catalytic [3+2] cycloaddition of D-A cyclopropanes with thionoesters for the synthesis of *trans*-configured THTs. Aromatic and aliphatic thionoesters were applicable to the present catalysis. Thionolactone provided the hitherto-inaccessible [5,5]-spiro-S,O-ketal ring system. Transformation mediated by TMSOTf delivered *trans*-configured THT derivatives with excellent diastereoselectivity. The present methodology was applied to an enantioenriched THT synthesis using chiral cyclopropane. Further applications of this *trans*-configured THT synthetic method to biologically active compounds are in progress.

Acknowledgements

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Keywords: cycloaddition • thionoester • iron • tetrahydrothiophene • stereoselectivity

[1] a) W. Trost, *IRCS Med. Sci.* **1986,** *14,* 905; b) P. J. De Clercq, *Chem. Rev.* **1997,** *97,* 1755; c) S.-B. Hwang, *J. Biol. Chem.* **1988,** *263,* 3225; d) M. Yoshikawa, T. Morikawa, H. Matsuda, G. Tanabe, O. Muraoka, *Bioorg. Med. Chem.* **2002,** *10,* 1547; e) P. C. B. Page, H. Vahedi, K. J. Batchelor, S. J. Hindley, M. Edgar, P. Beswick, *Synlett* **2003,** 1022; f) L. S. Jeong, D. Z. Jin, H. O. Kim, D. H. Shin, H. R. Moon, P. Gunaga, M. W. Chun, Y.-C. Kim, N. Melman, Z.-G. Gao, K. A. Jacobsen, *J. Med. Chem.* **2003,** *46,* 3775; g) D. Meng, W. Chen, W. Zhao, *J. Nat. Prod.* **2007,** *70,* 824; h) G. Tanabe, M. Sakano, T. Minematsu, H, Matsuda, M. Yoshikawa, O. Muraoka, *Tetrahedron* **2008,** *64,* 10080. i) P. Besada, M. Pérez, G. Gómez, Y. Fall, *Tetrahedron Lett.* **2009,** *50,* 6941.

[2] a) H. D. Kaesz, R. Uson, A. Laguna, M. Laguna, D. A. Briggs, H. H. Murray, J. P. Fackler Jr., *Inorganic Syntheses* **1989,** *26,* 85; b) E. Hauptman, R. Shapiro, W. Marshall, *Organometallics* **1998,** *17,* 4976.

[3] a) K. Julienne, P. Metzner, *J. Org. Chem.* **1998,** *63,* 4532; b) J. Zanardi, C. Leriverend, D. Aubert, K. Julienne, P. Metzner, *J. Org. Chem.* **2001,** *66,* 5620; c) V. K. Aggarwal, E. Alonso, G. Fang, M. Ferrara, G. Hynd, M. Porcelloni, *Angew. Chem. Int. Ed.* **2001,** *40,* 1430; *Angew. Chem.* **2001,** *113,* 1482; d) V. K. Aggarwal, I. Bae, H.-Y. Lee, J. Richardson, D. T. Williams, *Angew. Chem., Int. Ed.* **2003,** *42,* 3274; *Angew. Chem.* **2003,** *115,* 3396; e) Y. Gui, S. Shen, H.-Y. Wang, Z. Y. Li, Z.-Z. Huang, *Chem. Lett.* **2007,** *36,* 1436.

[4] a) G. Mloston, R. Huisgen, H. Huber, D. S. Stephenson, *J. Heterocyclic Chem.* **1999**, *36*, 959; b) S. Karlsson, H.-E, Hogberg, *Org. Lett.* **1999,** *1,* 1667; c) Huisgen, G. Mloston, H. Giera, E. Langhals, *Tetrahedron*, **2002**, *58*, 507; d) M. Woźnicka, M. Rutkowska, G. Mloston, A. Majchrzak, H. Heimgartner, *Polish, J. Chem.* **2006**, *80*, 1683; e) G. Luo, S. Zhang, W. Duan, W. Wang, *Tetrahedron Lett.* **2009,** *50,* 2946; f) O. Illa, M. Arshad, A. Ros, E. M. McGarrigle, V. K. Aggarwal, *J. Am. Chem. Soc.* **2010,** *132,* 1828; g) J.-B. Ling, Y, Su. H.-L. Zhu, G.-Y. Wang, P.-F. Xu, *Org. Lett.* **2012,** *14,* 1090; h) F. J. Robertson, J. Wu, *J. Am. Chem. Soc.* **2012,** *134,* 2775.

[5] For reviews on donor-acceptor cyclopropanes: a) T. F. Schneider, J. Kaschel, D. B. Werz, *Angew. Chem. Int. Ed.* **2014,** *53,* 5504; *Angew. Chem.* **2014,** *126,* 5608; b) M. A. Cavitt, L. H. Phun, S. France, *Chem. Soc. Rev*. **2014,** *43,* 804.

[6] a) A. F. G. Goldberg, N. R. O'Connor, R. A. Craig II, B. M. Stoltz, *Org. Lett.* **2012,** *14,* 5314; b) Y. X. Sun, G. S. Yang, Z. Chai, X. L. Mu, J. Chai, *Org. Biomol. Chem.* **2013,** *11,* 7859; c) S.-W. Wang, W.-S. Guo, L.-R. Wen, M. Li, *RSC Adv*. **2015,** *5,* 47418. Very recently, Werz at al reported elegant [3+2] cycloaddition of D-A cyclopropanes using relatively stable thioketones such as thiobenzophenone. When the unsymmetrical thioketones were used, 2,5-*cis*-configured THTs were obtained in moderate diastereoselectivity. See, d) A. U. Augustin, M. Busse, P. G. Jones, D. B. Werz, *Angew. Chem. Int. Ed.* **2017,** *56,* 14293; *Angew. Chem.* **2017,** *129,* 14481; e) A. U. Augustin, M. Sensse, P. G. Jones, D. B. Werz, *Org. Lett.* **2018,** *20,* 820.

[7] a) D. P. Patrick, S. J. Jeffrey, *J. Am. Chem. Soc.* **2005,** *127,* 16014; b) D. P. Patrick, D. S. Shanina, T. P. Andrew, L. Wei, S. J. Jeffrey, *J. Am. Chem. Soc.* **2008,** *130,* 8642; c) T. P. Andrew, S. J. Jeffrey, *J. Am. Chem. Soc.* **2009,** *131,* 3122; d) T. P. Andrew, G. S. Austin, J. N. Andrew, S. J. Jeffrey, *J. Am. Chem. Soc.* **2010,** *132,* 9688; e) F. de Nanteuil, E. Serrano, D. Perrotta, J. Waser, *J. Am. Chem. Soc.* **2014,** *136,* 6239.

[8] For reviews on thiocarbonyl compounds: a) P. Metzner, *Synthesis* **1992,** 1185; b) P. Metzner, *Top. Curr. Chem.* **1999,** *204,* 127.

[9] a) H. G. Giles. R. A. Marty. P. de Mayo, *Can. J. Chem.* **1976,** *54,* 537; b) E. Vedejs, J. S. Stults, R. G. Wilde, *J. Am. Chem. Soc.* **1988,** *110,* 5452; c) N. Takeda, N. Tokitoh, R. Okazaki, *Chem. Eur. J.* **1997,** *3,* 62.

[10] a) J. Kaschel, C. D. Schmidt, M. Mumby, D. Kratzert, D. Stalke, D. B. Werz, *Chem. Commun.* **2013,** *49,* 4403; b) J. Hejmanowska, M. Jasiński, G. Mlostoń, Ł. Albrecht, *Eur. J. Org. Chem.* **2017,** 950.

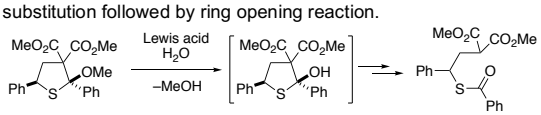
[11] a) B. A. Jones, J. S. Bradshaw, *Chem. Rev.* **1984,** *84,* 17; b) M. P. Cava, M. I. Levinson, *Tetrahedron* **1985,** *41,* 5061; c) V. S. Rajender, K. Dalip, *Org. Lett.* **1999,** *1,* 697; d) M. A. Shalaby, H. Rapoport, *J. Org. Chem.* **1999,** *64,* 1065.

[12] a) S. L. Baxter, J. S. Bradshaw, *J. Org. Chem.* **1981,** *46,* 831; b) W. H. Bunnelle, B. R. McKinnis, B. A. Narayanan, *J. Org. Chem.* **1990,** *55,* 768; c) H. K. Lee, J. Kim, C. S. Pak, *Tetrahedron Lett.* **1999,** *40,* 6267.

[13] a) K. C. Nicolaou, C.-K. Hwang, M. E. Duggan, K. Bal Reddy, B. E. Marron, D. G. McGarry, *J. Am. Chem. Soc.* **1986,** *108,* 6800; b) K. C. Nicolaou, D. G. McGarry, P. K. Sommers, *J. Am. Chem. Soc.* **1990,** *112,* 3696; c) K. C. Nicolaou, D. G. McGarry, P. K. Sommers, B. H. Kim, W.W. Ogilvie, G. Yiannikouros, C. V. C. Prasad, C. A. Veale, R. R. Hark, *J. Am. Chem. Soc.* **1990,** *112,* 6263.

[14] a) P. Reynaud, Y. E. Hamad, C. Davrinche, E. Nguyen-Tri-Xuong, G. Tran, P. Rinjard, *J. Heterocyclic Chem.* **1992,** *29,* 991; b) T. Miura, Y. Funakoshi, Y. Fujimoto, J, Nakahashi, M. Murakami, *Org. Lett.* **2015,** *17,* 2454.

[15] Without strict drying technique, by-product was observed via water substitution followed by ring opening reaction.



[16] See Supporting Information for details.

[17] G. Mloston, P. Grzelak, R. Hamera-Fałdyga, M. Jasiński, P. Pipiak, *Phosphorus Sulfur Silicon Relat. Elem.* **2017**, 192, 204.

[18] a) T. Tsunoda, M. Suzuki, R. Noyori, *Tetrahedron Lett.* **1979,** *48,* 4679; b) S. R. Shenoy, D. M. Smith, K. A. Woerpel, *J. Am. Chem. Soc.* **2006,** *128,* 8671.

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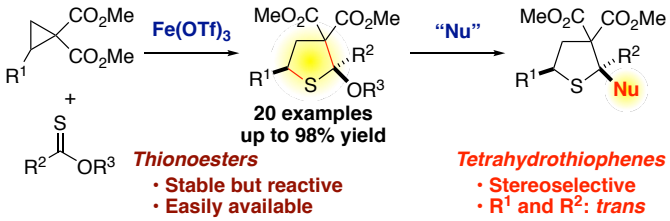

A synthetic route to *trans*-configured tetrahydrothiophenes (THTs) through $Fe(OTf)_3$-promoted [3+2] cycloaddition of donor-acceptor cyclopropanes with thionoesters was developed. The cycloaddition proceeded in high yield with high diastereoselectivity, affording transient THTs bearing S,O-ketal functionality. Further transformation of the S,O-ketal functionality was achieved in a highly *trans* diastereoselective manner.

Y. Matsumoto, D. Nakatake, R. Yazaki and T. Ohshima**

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An Expeditious Route to *trans*-Configured Tetrahydrothiophenes Enabled by $Fe(OTf)_3$-Catalyzed [3+2] Cycloaddition of Donor-Acceptor Cyclopropanes and Thionoesters