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Site-Selective and Enantioselective α,β,γ-Functionalization of 5-Alkylidenefuran-2(5*H*)-ones: A Route to Polycyclic γ-Lactones

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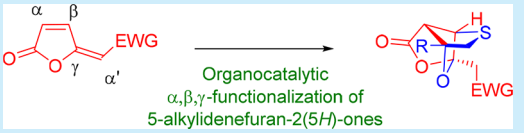
Supporting Information

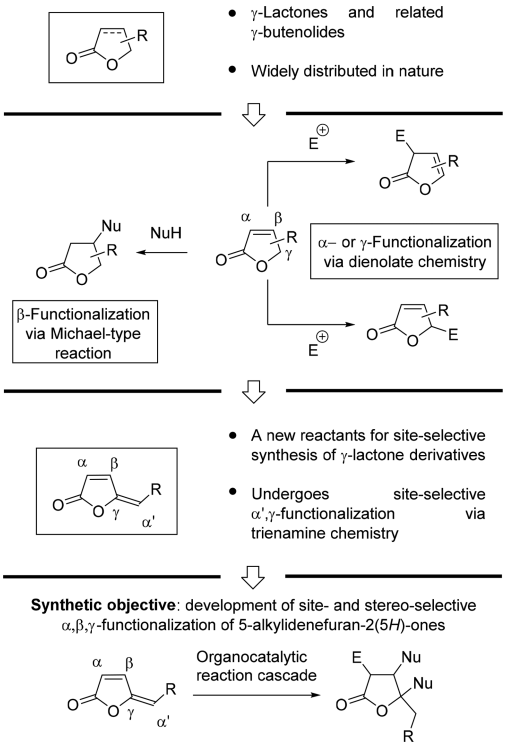
ABSTRACT: A new strategy for a direct α,β,γ-functionalization of the γ-lactone framework in the corresponding 5-alkylidenefuran-2(5*H*)-ones is reported. The developed approach is based on a stereocontrolled cascade reaction with 2-mercaptocarbonyl compounds proceeding in a sequence of thia-Michael/aldol/oxa-Michael reactions. Such a synthetic strategy allows for a construction of a unique polycyclic architecture containing γ-lactone, tetrahydrofuran, and tetrahydrothiophene ring systems. Excellent enantioselectivities and diastereoselectivities have been obtained in the presence of bifunctional catalyst derived from cinchona alkaloids.



The design of new functionalization strategies constitutes one of the most important goals in the modern organic synthesis, thereby providing access to novel reaction profiles and new types of products. The realization of this task has recently been dominated by the asymmetric catalysis.[1] In such a setup, the chiral catalyst employed serves a dual purpose. First, it activates the substrate, making the devised strategy feasible. Second, it provides a well-defined chiral environment, making it possible for the transformation to proceed in an enantioselective fashion. Among various asymmetric catalytic strategies for the stereoselective functionalization of organic molecules, in the past 20 years, organocatalysis has emerged as a method of choice.[2,3] Notably, organocatalytic reactions can be realized according to various activation strategies, with bifunctional catalysis being a highly relevant approach.[3]

γ-Lactones and related γ-butenolides constitute privileged structural motifs widely distributed in nature and exhibiting a wide range of biological activities (Scheme 1, top).[4] They are also employed as key synthetic intermediates in natural product synthesis. As a consequence, much effort has been devoted toward the development of methods for their preparation, in particular in a stereoselective fashion (Scheme 1).[5−8] One strategy involves the use of furan-2(5*H*)-ones as a template for further structural modifications. These highly useful building blocks undergo Michael-type addition with selected nucleophiles, thus introducing new substituents in the β-position.[6] In contrast, site-selective α- or γ-functionalization of the γ-butenolide architecture is possible via the corresponding dienolate formation or related systems.[7] Recently, we have developed an alternative approach for the synthesis of γ,γ-disubstituted-γ-butenolides.[8] It involves the usage of 5-alkylidenefuran-2(5*H*)-ones as a new type of building block. We have demonstrated that their site-selective α′,γ-functionalization can be realized under trienamine activation conditions, providing an excellent route to spirocyclic derivatives. Interestingly, a literature survey revealed that a strategy allowing for the direct introduction of substituents at the α-, β-, and γ-positions of the γ-lactone moiety is missing.

Scheme 1. Strategies for the Site-Selective Functionalization of γ-Lactone Framework



Therefore, we became interested in the development of organocatalytic strategy for α,β,γ-functionalization of 5-alkylidenefuran-2(5*H*)-ones (Scheme 1, bottom).

Organocatalytic cascade reactions where more than one chemical bond is formed in a single manual operation

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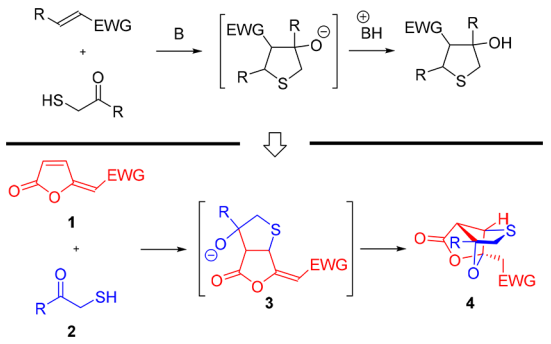
constitute a powerful strategy in modern asymmetric synthesis.[9] Enantioselective synthesis of tetrahydrothiophenes is an interesting example of such an approach to organic synthesis (Scheme 2, top).[10] In such a cascade, 2-

Scheme 2. Cascade Synthesis of Tetrahydrothiopenes

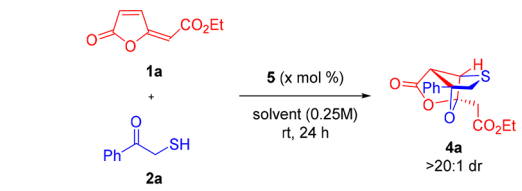


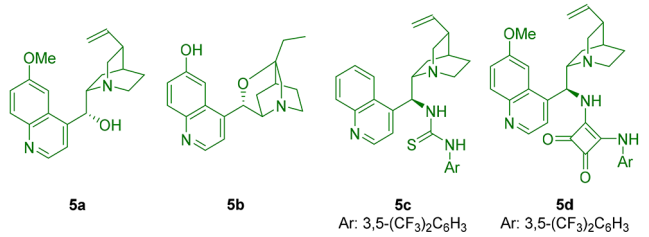
mercaptocarbonyl compounds are reacted with electron-deficient double bonds. The reaction is initiated by the thia-Michael addition, followed by the intramolecular aldol reaction. Protonation of the originally formed alkoxide results in the formation of tetrahydrothiophene bearing a hydroxyl group in the 3-position.

Taking advantage of the formation of the nucleophilic alkoxide in such a cascade, we decided to use it as a template for the α,β,γ-functionalization of 5-alkylidenefuran-2(5*H*)-ones (Scheme 2, bottom). It was anticipated that the initial thia-Michael addition should occur at the least sterically demanding endocyclic double bond in **1**. Subsequent intramolecular aldol reaction introduces oxygen-centered nucleophile into the molecule capable of undergoing intramolecular oxa-Michael reaction, thus accomplishing the devised α,β,γ-functionalization of 5-alkylidenefuran-2(5*H*)-ones. Herein, we report our studies on the development of organocatalytic synthesis of polycyclic γ-lactones bearing a tetrahydrothiophene and tetrahydrofuran moieties via stereocontrolled thia-Michael/aldol/oxa-Michael reaction cascade.

Optimization studies were performed using (*E*)-ethyl 2-(5-oxofuran-2(5*H*)-ylidene)acetate **1a** and 2-mercaptoacetophenone **2a** as model reactants (Table 1). Initially catalyst screening was performed (Table 1, entries 1−4). To our delight, it was found that the devised cascade consisting of thia-Michael/aldol/oxa-Michael reactions proved possible to realize employing bifunctional organocatalysts **5a**−**5d** derived from cinchona alkaloids. Notably, the diastereoselectivity of the transformation was excellent, because γ-lactone **4a** was obtained as a single diastereoisomer in all of the cases, despite the presence of four stereogenic centers. Interestingly, already simple quinine **5a** promoted the reaction, affording **4a** in unsatisfactory yield and enantioselectivity (Table 1, entry 1). The use of β-isocupreidine **5b** did not enhance the result (Table 1, entry 2). However, the introduction of a stronger hydrogen-bonding unit into the structure of the catalyst (Table 1, entries 3 and 4) allowed for significant improvement of the results with catalyst **5d** bearing a squaramide moiety being the best (Table 1, entry 4). Subsequently, the solvent screening was initiated (Table 1, entries 4−9) leading to the identification of chloroform (Table 1, entry 4) as the best-suited solvent, in terms of enantioselectivity for the developed α,β,γ-functionalization of furan-2(5*H*)-one **1a**. Further optimization studies were focused on the evaluation of

Table 1. Organocatalytic, Stereocontrolled α,β,γ-Functionalization of 5-Alkylidenefuran-2(5*H*)-ones 1: Optimization Studies[a]





	solvent	cat. (mol %)	NMR yield[b] [%]	enantiomeric ratio, er[c]
1	$CHCl_3$	**5a** (20)	31	56:44
2	$CHCl_3$	**5b** (20)	36	54:46
3	$CHCl_3$	**5c** (20)	63	90:10
4	$CHCl_3$	**5d** (20)	75 (74)	97.5:2.5
5	CH_2Cl_2	**5d** (20)	83 (75)	95:5
6	CCl_4	**5d** (20)	61	96:4
7	toluene	**5d** (20)	63	95:5
8	CH_3CN	**5d** (20)	47	93:7
9	THF	**5d** (20)	54	94:6
10[d]	$CHCl_3$	**5d** (20)	73 (69)	97:3
11[e]	$CHCl_3$	**5d** (20)	73 (71)	99:1
12[f]	$CHCl_3$	**5d** (20)	48	99:1
13	$CHCl_3$	**5d** (5)	83 (78)	>99:1

[a]All reactions were performed in a 0.1 mmol scale using **1a** (1.0 equiv) and **2a** (1.3 equiv) in 0.4 mL of the corresponding solvent (for details, see the Supporting Information). [b]As determined by ^{1}H NMR of a crude reaction mixture, with respect to the signal of 1,3,5-tris(trifluoromethyl)benzene as internal standard. Isolated yield is given in parentheses. [c]As determined by the chiral stationary phase UPC^2. [d]Reaction performed in 0.2 mL of the solvent. [e]Reaction performed in 0.8 mL of the solvent. [f]Reaction performed using **1a** (1.3 equiv) and **2a** (1.0 equiv).

concentration effect (Table 1, entries 10 and 11) and relative ratio of reactants (Table 1, entry 12). Neither of these changes led to improvement of the results. Finally, the attempt to reduce the catalyst loading to 5 mol % was made (Table 1, entry 13). Delightfully, the transformation proceeded with high chemical and stereochemical efficiency, thus identifying the final reaction parameters.

With the optimization studies accomplished, studies on the scope of the methodology were initiated (Table 2). Initially, various 2-mercaptocarbonyl compounds **2** were employed in the reaction (Table 2, entries 1−11). To our delight, the developed, organocatalytic α,β,γ-functionalization of 5-alkylidenefuran-2(5*H*)-ones **1** proved unbiased toward the electronic character of substituents on the aromatic ring in **2** (compare entries 2, 3, and 4−7 in Table 2). Furthermore, the position of the substituents on the aromatic ring in **2** had no significant influence on either the yield of the cascade or its diastereoselectivity (compare entries 2, 3, and 5−7 in Table 2) with very good results obtained for *ortho*-substituted derivatives (Table 2, entries 3 and 7) being particularly

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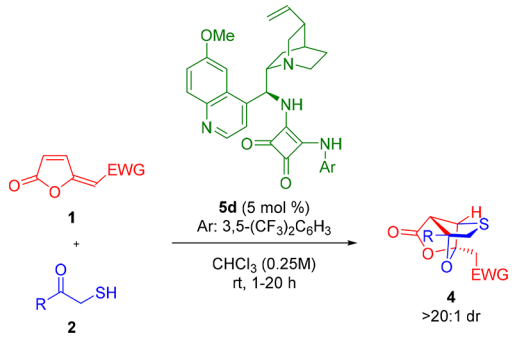
Table 2. Organocatalytic, Stereocontrolled α,β,γ-Functionalization of 5-Alkylidenefuran-2(5*H*)-ones 1: Scope Studies[a]



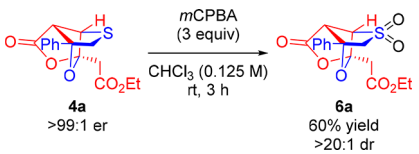
entry	R	electron-withdrawing group, EWG	yield[b] [%]	enantiomeric ratio, er[c]
1	Ph	CO_2Et	**4a**: 78	>99:1
2	4-FC_6H_4	CO_2Et	**4b**: 69	98:2
3	2-FC_6H_4	CO_2Et	**4c**: 70	98:2
4	4-$CH_3C_6H_4$	CO_2Et	**4d**: 70	98.5:1.5
5	4-$CH_3OC_6H_4$	CO_2Et	**4e**: 76	99:1
6	3-$CH_3OC_6H_4$	CO_2Et	**4f**: 76	99:1
7	2-$CH_3OC_6H_4$	CO_2Et	**4g**: 73	98.5:1.5
8	benzofuran-2-yl	CO_2Et	**4h**: 45	99:1
9	thiophen-3-yl	CO_2Et	**4i**: 68	98:2
10	2-naphthyl	CO_2Et	**4j**: 75	99:1
11	3,4-$Cl_2C_6H_3$	CO_2Et	**4k**: 75	97.5:2.5
12	Ph	CO_2Me	**4l**: 70	98:2
13	Ph	CN	**4m**: 63	89:11
14[d]	Ph	CO_2Et	**4a**: 70	>99:1

[a]All reactions were performed in a 0.1 mmol scale using **1a** (1.0 equiv) and **2a** (1.3 equiv) in 0.4 mL of the corresponding solvent (for details, see the Supporting Information). [b]Isolated yields are given. [c]As determined by the chiral stationary phase UPC². [d]Reaction performed in a gram scale.

noticeable. Interestingly, heteroaromatic substituents were also well-tolerated with products **4h** and **4i** efficiently synthesized. Moreover, disubstituted aromatic rings could also be present in the structure of **2**, as demonstrated in the synthesis of **4j** and **4k** (Table 2, entries 10 and 11). In the course of further scope studies, the possibility to modify the structure of olefinic counterpart was attempted. Delightfully, selected electron-withdrawing groups proved possible to be present at the exocyclic double bond in **1** with good results being observed (Table 2, entries 12 and 13). Finally, a 1-g scale experiment was performed, leading to the formation of **4a** with comparable results (Table 2, entry 14).

The cascade product **1a** has been subjected to oxidation of the sulfide moiety into the sulfone **6a** (Scheme 3). The reaction has been efficiently realized using *m*-chloroperbenzoic acid (*m*CPBA) as the oxidant in chloroform at room

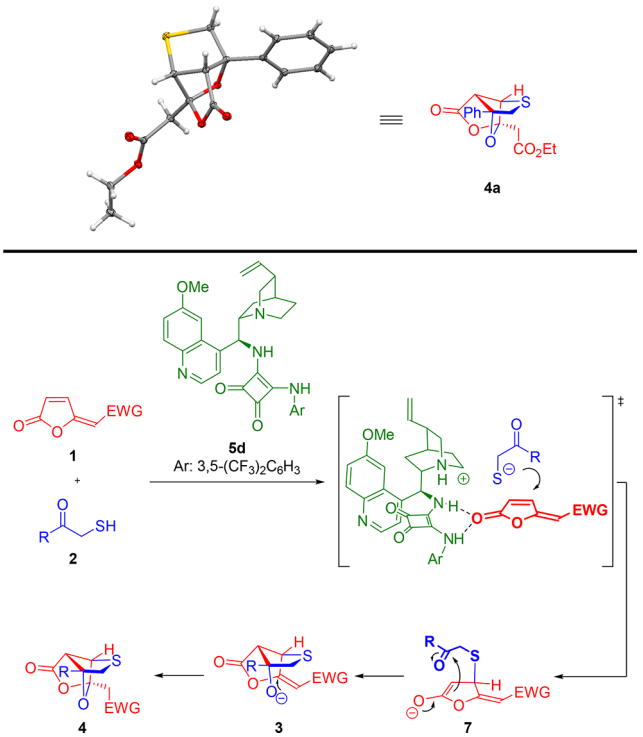
Scheme 3. Oxidation of Sulfide Moiety in 4a to the Corresponding Sulfone 6a



temperature. It was terminated within 3 h providing **6a** in 60% yield. To our delight, the transformation proceeded with preservation of stereochemical information introduced at the organocatalytic cascade as **6a** was obtained as a single stereoisomer.

In order to assign the absolute configuration of the polycyclic products obtained, the single-crystal X-ray analysis was performed. To our delight, **4a** provided crystals suitable for such an analysis (Scheme 4, top). Given the result

Scheme 4. Organocatalytic, Stereocontrolled α,β,γ-Functionalization of 5-Alkylidenefuran-2(5*H*)-ones 1: Mechanistic Considerations



obtained, it was established as 3*S*,3a*R*,6*S*,6a*R* with the absolute configuration of remaining products being assigned by analogy. Based on the stereochemical reaction outcome, a plausible mechanism of a cascade was proposed (Scheme 4, bottom). The developed transformation is initiated by the sulfa-Michael addition of 2-mercaptocarbonyl compound **2** to the endocyclic double bond of the corresponding 5-alkylidenefuran-2(5*H*)-one **1**. The reaction is promoted by the bifunctional catalyst **5d** that is responsible for the activation of electrophile **1** through the hydrogen-bonding interactions. At the same time, **2** is activated by deprotonation. Such a recognition profile determines both site selectivity and enantioselectivity of the cascade. The fact that the Michael reaction occurs at the less-hindered electrophilic position of the molecule is also of importance with the observed site selectivity being in contrast to our previous results concerning the reactivity of **1**, where the nucleophilic attack that occurs at the exocyclic double bond has been preferred.[8] Intramolecular aldol reaction takes place in the second stage of a cascade, leading to the introduction of the oxygen-centered nucleophile into the molecule. Notably, when it is positioned in the pseudoaxial position, it is in the spatial proximity of the electron-deficient double bond present in the molecule and the oxa-Michael addition occurs, thus

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terminating the cascade. It is postulated that the excellent diastereoselectivity of the transformation is a consequence of reversibility of the aldol reaction. The diasteroisomeric aldol product with pseudoequatorial alignment of the alkoxide anion cannot participate in the subsequent oxa-Michael addition and undergoes a retro-aldol reaction. This is in accordance with the fact that only the thia-Michael adduct (protonated intermediate **7**) was possible to be experimentally observed in the ^{1}H NMR spectrum of the crude reaction mixture.

In summary, we have developed the first strategy for a direct α,β,γ-functionalization of the γ-lactone framework. It was found that when the reaction between 5-alkylidenefuran-2(5*H*)-ones **1** and 2-mercaptocarbonyl compounds **2** is performed, polycyclic γ-lactone derivatives **4** bearing tetrahydrofuran and tetrahydrothiophene ring systems have been efficiently obtained. Good to high yields and excellent stereocontrol has been achieved when a quinine-derived bifunctional catalyst **5d** bearing a squaramide moiety has been employed.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.8b03796.

Experimental procedures, characterization of the products, NMR data, and UPC^2 traces (PDF)

Accession Codes

CCDC 1879289 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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All authors have given approval to the final version of the manuscript.

Author Contributions

†These authors contributed equally.

Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) Jacobsen, E. N.; Pfaltz, A.; Yamamoto, H. *Comprehensive Asymmetric Catalysis*; Springer: Berlin, 1999. (b) Mikami, K.; Lautens, M. *New Frontiers in Asymmetric Catalysis*; Wiley−Interscience: Hoboken, NJ, 2007.

(2) For selected reviews on organocatalysis, see: (a) Gaunt, M. J.; Johansson, C. C. C.; McNally, A.; Vo, N. C. *Drug Discovery Today* **2007**, *12*, 8. (b) Bella, M.; Gasperi, T. *Synthesis* **2009**, *2009*, 1583. (c) Palomo, C.; Oiarbide, M.; López, R. *Chem. Soc. Rev.* **2009**, *38*, 632. (d) Melchiorre, P. *Angew. Chem., Int. Ed.* **2012**, *51*, 9748. (e) Goudedranche, S.; Raimondi, W.; Bugaut, X.; Constantieux, T.; Bonne, D.; Rodriguez, J. *Synthesis* **2013**, *45*, 1909. (f) Krawczyk, H.; Dzięgielewski, M.; Deredas, D.; Albrecht, A.; Albrecht, Ł. *Chem. - Eur. J.* **2015**, *21*, 10268.

(3) For selected reviews on the enantioselective bifunctional catalysis, see: (a) Marcelli, T.; van Maarseveen, J. H.; Hiemstra, H. *Angew. Chem., Int. Ed.* **2006**, *45*, 7496. (b) Jew, S.-S.; Park, H.-G. *Chem. Commun.* **2009**, 7090. (c) Alemán, J.; Parra, A.; Jiang, H.; Jørgensen, K. A. *Chem. - Eur. J.* **2011**, *17*, 6890. (d) Quigley, C.; Rodríguez-Docampo, Z.; Connon, S. J. *Chem. Commun.* **2012**, *48*, 1443. (e) Albrecht, Ł.; Jiang, H.; Jørgensen, K. A. *Chem. - Eur. J.* **2014**, *20*, 358.

(4) (a) Rao, Y. S. *Chem. Rev.* **1964**, *64*, 353. (b) Hoffmann, H. M. R.; Rabe, J. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 94. (c) Negishi, E.; Kotora, M. *Tetrahedron* **1997**, *53*, 6707. (d) Alali, F. Q.; Liu, X.-X.; McLaughlin, J. L. *J. Nat. Prod.* **1999**, *62*, 504. (e) Bandichhor, R.; Nosse, B.; Reiser, O. *Top. Curr. Chem.* **2005**, *243*, 43. (f) Quintavalla, A. *Curr. Med. Chem.* **2018**, *25*, 917.

(5) For selected reviews, see: (a) Mao, B.; Fañanás-Mastral, M.; Feringa, B. L. *Chem. Rev.* **2017**, *117*, 10502. (b) Yanai, H. In *Green and Catalytic Methods for γ-Lactone Synthesis. Green Synthetic Approaches for Biologically Relevant Heterocycles*; Brahmachari, G., Ed.; Elsevier: Boston, 2015; pp 257−289. (c) Albrecht, A.; Albrecht, Ł.; Janecki, T. *Eur. J. Org. Chem.* **2011**, *2011*, 2747. (d) Kitson, R. R. A.; Millemaggi, A.; Taylor, R. J. K. *Angew. Chem., Int. Ed.* **2009**, *48*, 9426. (e) Gil, S.; Parra, M.; Rodriguez, P.; Segura, J. *Mini-Rev. Org. Chem.* **2009**, *6*, 345. (f) Seitz, M.; Reiser, O. *Curr. Opin. Chem. Biol.* **2005**, *9*, 285. (g) Carter, N. B.; Nadany, A. E.; Sweeney, J. B. *J. Chem. Soc., Perkin Trans.* **2002**, *1*, 2324.

(6) For selected examples, see: (a) De Lange, B.; van Bolhuis, F.; Feringa, B. L. *Tetrahedron* **1989**, *45*, 6799. (b) Trost, B. M.; Aponick, A. *J. Am. Chem. Soc.* **2006**, *128*, 3931. (c) Busqué, F.; de March, P.; Figueredo, M.; Font, J.; González, L. *Eur. J. Org. Chem.* **2004**, *2004*, 1492. (d) Fukata, Y.; Okamura, T.; Asano, K.; Matsubara, S. *Org. Lett.* **2014**, *16*, 2184. (e) Brito, G. A.; Sarotti, A. M.; Wipf, P.; Pilli, R. A. *Tetrahedron Lett.* **2015**, *56*, 6664.

(7) For selected reviews, see: (a) Schneider, C.; Abels, F. *Org. Biomol. Chem.* **2014**, *12*, 3531. (b) Jusseau, X.; Chabaud, L.; Guillou, C. *Tetrahedron* **2014**, *70*, 2595. (c) Zhang, Q.; Liu, X.; Feng, X. *Curr. Org. Synth.* **2013**, *10*, 764. (d) Frías, M.; Cieślik, W.; Fraile, A.; Rosado-Abón, A.; Garrido-Castro, A. F.; Yuste, F.; Alemán, J. *Chem. - Eur. J.* **2018**, *24*, 10906. For selected examples, see: (e) Brown, S. P.; Goodwin, N. C.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2003**, *125*, 1192. (f) Huang, Y.; Walji, A. M.; Larsen, C. H.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2005**, *127*, 15051. (g) Singh, R. P.; Foxman, B. M.; Deng, L. *J. Am. Chem. Soc.* **2010**, *132*, 9558. (h) Quintard, A.; Lefranc, A.; Alexakis, A. *Org. Lett.* **2011**, *13*, 1540. (i) Manna, M. S.; Kumar, V.; Mukherjee, S. *Chem. Commun.* **2012**, *48*, 5193. (j) Joannesse, C.; Morrill, L.; Campbell, C.; Slawin, A.; Smith, A. *Synthesis* **2011**, *2011*, 1865. (k) Kemppainen, E. K.; Sahoo, G.; Valkonen, A.; Pihko, P. M. *Org. Lett.* **2012**, *14*, 1086. (l) Chen, J.; Ni, S.; Ma, S. *Adv. Synth. Catal.* **2012**, *354*, 1114. (m) Fournier, J.; Lozano, O.; Menozzi, C.; Arseniyadis, S.; Cossy, J. *Angew. Chem., Int. Ed.* **2013**, *52*, 1257. (n) Li, X.; Lu, M.; Dong, Y.; Wu, W.; Qian, Q.; Ye, J.; Dixon, D. J. *Nat. Commun.* **2014**, *5*, 4479. (o) Manna, M. S.; Mukherjee, S. *Chem. Sci.* **2014**, *5*, 1627. (p) Kemppainen, E. K.; Sahoo, G.; Piisola, A.; Hamza, A.; Kótai, B.; Pápai, I.; Pihko, P. M. *Chem. - Eur. J.* **2014**, *20*, 5983. (q) Sekikawa, T.; Kitaguchi, T.; Kitaura, H.; Minami, T.; Hatanaka, Y. *Org. Lett.* **2015**, *17*, 3026. (r) Wang, Y.; Li, Z.; Lv, L.; Xie, Z. *Org. Lett.* **2016**, *18*, 792. (s) Lagoutte, R.; Besnard, C.; Alexakis, A. *Eur. J. Org. Chem.* **2016**, *2016*, 4372. (t) Rout, S.; Joshi, H.; Singh, V. K. *Org. Lett.* **2018**, *20*, 2199.

DOI: 10.1021/acs.orglett.8b03796
Org. Lett. XXXX, XXX, XXX−XXX

(8) Skrzyńska, A.; Drelich, P.; Frankowski, S.; Albrecht, Ł. *Chem. - Eur. J.* **2018**, *24*, 16543.
(9) For selected reviews on organocatalytic cascade reactivities, see: (a) Enders, D.; Grondal, C.; Hüttl, M. R. M. *Angew. Chem., Int. Ed.* **2007**, *46*, 1570. (b) Yu, X.; Wang, W. *Org. Biomol. Chem.* **2008**, *6*, 2037. (c) Alba, A.-N.; Companyo, X.; Viciano, M.; Rios, R. *Curr. Org. Chem.* **2009**, *13*, 1432. (d) Grondal, C.; Jeanty, M.; Enders, D. *Nat. Chem.* **2010**, *2*, 167. (e) Ramachary, D. B.; Jain, S. *Org. Biomol. Chem.* **2011**, *9*, 1277. (f) Wende, R. C.; Schreiner, P. R. *Green Chem.* **2012**, *14*, 1821. (g) Wende, R. C.; Schreiner, P. R. *Green Chem.* **2012**, *14*, 1821.
(10) For reviews, see: (a) Benetti, S.; De Risi, C.; Pollini, G. P.; Zanirato, V. *Chem. Rev.* **2012**, *112*, 2129. (b) Chauhan, P.; Mahajan, S.; Enders, D. *Chem. Rev.* **2014**, *114*, 8807. For selected examples of thia-Michael/aldol reaction sequences realized under organocatalytic conditions, see: (c) Brandau, S.; Maerten, E.; Jørgensen, K. A. *J. Am. Chem. Soc.* **2006**, *128*, 14986. (d) Ling, J.-B.; Su, Y.; Zhu, H.-L.; Wang, G.-Y.; Xu, P.-F. *Org. Lett.* **2012**, *14*, 1090. (e) Su, Y.; Ling, J.-B.; Zhang, S.; Xu, P.-F. *J. Org. Chem.* **2013**, *78*, 11053. (f) Zhao, B.; Liu, L.; Du, D. *Eur. J. Org. Chem.* **2014**, *2014*, 7850. (g) Liang, J.-J.; Pan, J.-Y.; Xu, D.-C.; Xie, J.-W. *Tetrahedron Lett.* **2014**, *55*, 6335. (h) Kowalczyk, D.; Wojciechowski, J.; Albrecht, Ł. *Tetrahedron Lett.* **2016**, *57*, 2533. (i) Przydacz, A.; Kowalczyk, R.; Albrecht, Ł. *Org. Biomol. Chem.* **2017**, *15*, 9566.

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