A Journal of the Gesellschaft Deutscher Chemiker

Angewandte International Edition GDCh Chemie

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Accepted Article

Title: Facile Stereoselective Approach to Diverse Spiroheterocyclic Tetrahydropyrans: Concise Synthesis of (+)-Broussonetine G and H

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To be cited as: *Angew. Chem. Int. Ed.* 10.1002/anie.201907353
Angew. Chem. 10.1002/ange.201907353

Link to VoR: http://dx.doi.org/10.1002/anie.201907353
http://dx.doi.org/10.1002/ange.201907353

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Facile Stereoselective Approach to Diverse Spiroheterocyclic Tetrahydropyrans: Concise Synthesis of (+)-Broussonetine G and H

Li Zhou, Shu-Yang Yu, Yong Tang and Lijia Wang*

Abstract: A highly diastereoselective copper catalyzed multi-components tandem cyclization of exocyclic enol ethers/enamines with methylene malonate and aldehydes has been developed to furnish the spiroheterocyclic tetrahydropyrans in high yields with >95/5 dr. This method is very practical that 36 examples reacted smoothly over a very broad range of aldehydes and many different exo-vinyl heterocycles. By applying the newly developed method, the total synthesis of (+)-broussonetine G and formal synthesis of (+)-broussonetine H were achieved in a concise way.

Spiroheterocyclic tetrahydropyran motifs widely exist in natural products.[1-2] These compounds with diverse structures are endowed with various biological activities.[3] For example, (+)-broussonetine G and H, which containing [6,5]- and [6,6]-spiroketal fragments, were potent glycosidase inhibitors;[3a] virgatolide C with a [6,6]-spiroketal core showed cytotoxicity against HeLa cells;[3b] penicitrinine A bearing N,O-spiroketal structure was found anti-proliferative activity on multiple tumor types.[3c] For a long time, the synthesis of such compounds has been mainly focused on the intramolecular cyclization strategy,[4-5] which depends on designing elaborate substrates that usually require long linear routes to prepare. Thus, developing general methods for the rapid construction of these motifs from simple starting materials are highly in demand.

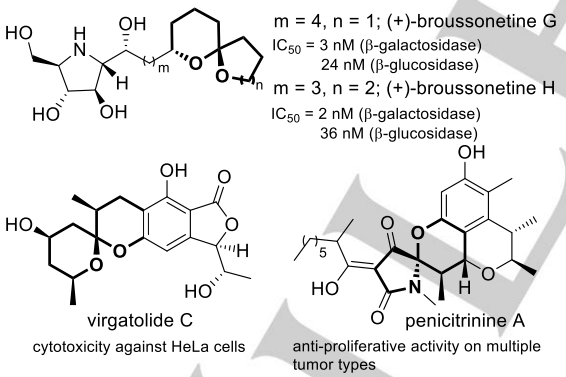

Figure 1. Bioactive Molecules with Spiroheterocyclic Tetrahydropyran Motifs.

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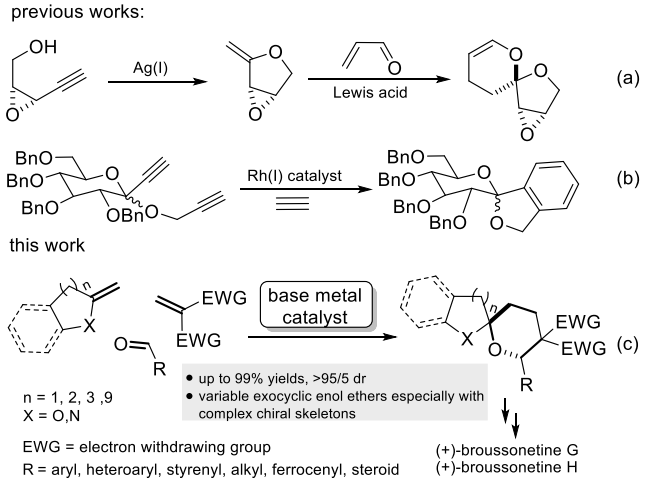
Intermolecular reactions are vested in more facility in the construction of diverse spiroketals from simple starting materials in views of step economy. In fact, as early as 1988, Pale and coworkers pioneered a two-step synthesis strategy involving a silver ion catalyzed intramolecular cyclization of ω-acetylenic alcohols followed by a Lewis acid catalyzed hetero-Diels-Alder (HDA) reaction for the build of unsaturated spiroketals (Scheme 1a).[6-7] Recent years, with similar strategy,[8-9] remarkable progress has been made by Barluenga[8a] and Xu[8b] respectively, in terms of employing noble metals, such as Pd and Au, cooperated with different Lewis acids as catalysts to achieve [6,5]-spiroketalizations between alkynols and salicylaldehyde derivatives or oxa-dienophiles. McDonald and co-workers developed a rhodium-catalyzed alkyne cyclotrimerization strategy to synthesize the spiroglycoside from bisalkynylcarbohydrate derivatives (Scheme 1b)[10]. These above-mentioned methods provide effective protocols for the construction of [6,5]-spiroketals.[11] In contrast, for [6,6]-spiroketals, which are also core structures of a series of biologically active natural products, the reported intermolecular examples are still challenging. For example, Feng and co-workers developed an elegant gold(I)/nickel(II) relay catalysis on the synthesis of spiroketals with alkynyl alcohols and keto esters.[9b] They found that by employing hex-5-yn-1-ol instead of pent-4-yn-1-ol, the yield of the corresponding [6,6]-spiroketal was dramatically decreased from 94% to 50% compared with the [6,5]-spiroketal product, probably due to the fact that the intramolecular alkynols cyclization step is gradually more difficult with the longer carbon chain. Thus, facile approaches to variable spiroheterocyclic tetrahydropyran, especially containing larger rings or complicated structures, are still very limited. In this study, we conceived a new tandem cyclization protocol for a base metal catalyzed stereoselective spiroketalization (Scheme 1c).



Scheme 1. Intermolecular Approaches to Build Spiroheterocyclic Tetrahydropyrans.

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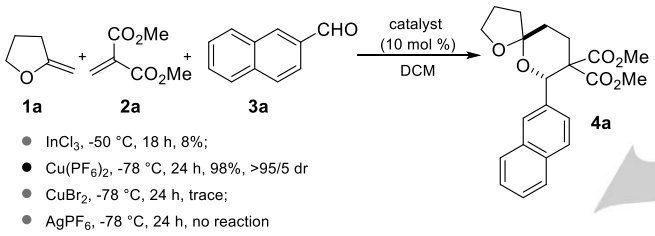
A diverse range of spiroheterocyclic tetrahydropyranes can be constructed with high efficiency and diastereoselectivity from various exocyclic enol ethers/enamines, methylene malonate and a very wide scope of aldehydes. Applying this method, the total synthesis of (+)-broussonetine G, the formal synthesis of (+)-broussonetine H, as well as the core structure framing of natural product cycloethaliacumarin[12] were completed in a concise way. Herein, we report the preliminary results.

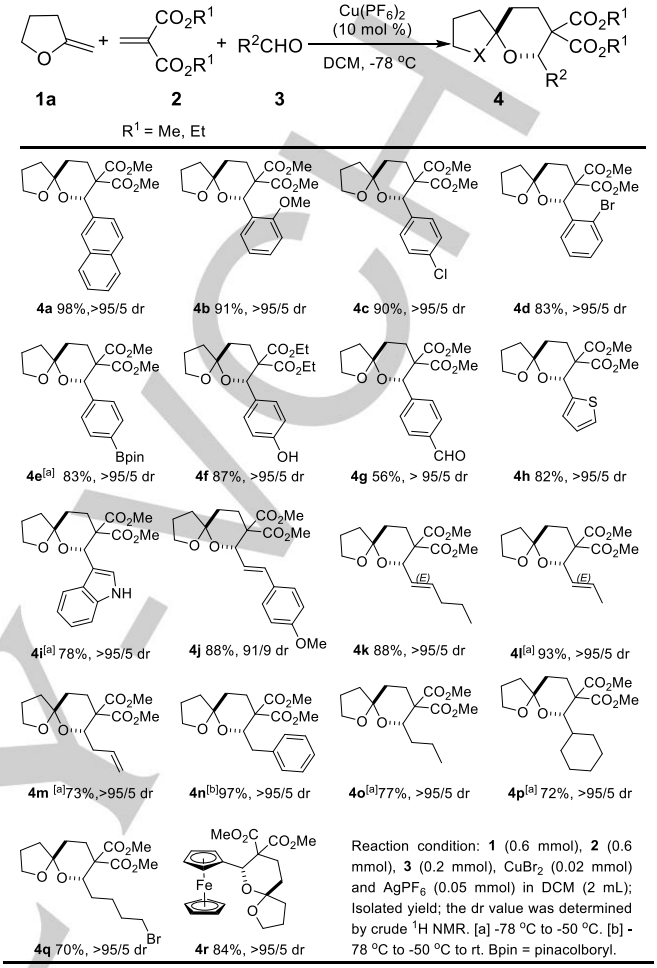
Recent years, we have developed a series of cyclization reactions by employing methylene malonate (**2a**) as synthetic building block.[13] In this study, exocyclic enol ether (**1a**), methylene malonate (**2a**) and 2-naphthaldehyde (**3a**) were initially reacted with 10 mol % of $InCl_3$ as catalyst in dichloromethane (DCM) at -50 °C, leading to the desired spiroketal (**4a**) in only 8% yield (Scheme 2). Further screening on the reaction conditions was carried out [14] and the *in situ* generated $Cu(PF_6)_2$ from $CuBr_2$ and $AgPF_6$ was found to be the best catalyst, giving **4a** in 98% yield with >95/5 dr at -78 °C after 24 h. It was worth to mention that both $CuBr_2$ and $AgPF_6$ could not promote the current reaction at -78 °C. The relative configuration of **4a** was confirmed by X-ray crystallography.[15]



Scheme 2. Tandem reaction of exocyclic enol ether (**1a**), methylene malonate (**2a**) and 2-naphthaldehyde (**3a**) with different Lewis acids.

Under the optimized reaction conditions, the substrate scope of the reaction was investigated as summarized in Table 1. A very wide range of aldehydes were found as suitable substrates, even those with sensitive functional groups. Aromatic aldehydes bearing substituents at different positions of the phenyl groups, such as 2-MeO, 4-Cl and 2-Br groups, led to spiroketals **4b-4d** in 83-91% yields with >95/5 dr. Aromatic aldehydes containing easily transformed functional groups, such as 4-bpin, 4-hydoxy and formyl groups, were tolerated, providing **4e-4g** in up to 87% yield with >95/5 dr. In addition, 2-formylthiophene and 3-formylindole were also suitable reaction candidates, giving the **4h** and **4k** in high yields with >95/5 dr, respectively. This method could also deliver spiroketals with olefin moiety. For examples, when 4-methoxycinnamaldehyd, 2-hexenal and crotonaldehyde were employed as substrates, **4j-4l** were obtained in 88-93% yields with excellent diastereoselectivities. With 3-butenal as substrate, **4m** was afforded in 73% yield with >95/5 dr. Remarkably, aliphatic aldehydes were totally compatible with the current reaction system. Various aliphatic aldehydes, including 2-phenylacetaldehyde, butyraldehyde, cyclohexanaldehyde and 5-bromopentanal were employed, and high yields with >95/5 dr were achieved to give **4n-4q**. Furthermore, spiroketal **4r** bearing a ferrocene moiety could also be prepared by using this method in 84% yield with >95/5 dr.

Table 1. Substrate Scope of Aldehydes



Further study shown that this method was compatible with various exocyclic enol ethers. As shown in Table 2, the enol ethers, bearing two phenyl groups at the five-membered ring, could give **4s** and **4t** in 88-91% yields with >95/5 dr. Compared with those previously reported strategies that involving noble metal catalysed intramolecular cyclization of alkynols, the current method broke the limitation of the five-membered ring enol ether substrates. Six-membered exocyclic enol ethers were very good substrates, which could react with a broad range of aldehydes smoothly including both aromatic and aliphatic aldehydes (**4u-4z**, 80-99% yields, >95/5 dr). It was found that the excellent diastereoselectivity was controlled by a thermodynamic process.[14] Seven-membered exocyclic enol ethers, and even 13-membered enol ethers, were also suitable substrates, leading to the **4aa** and **4bb** in 92% and 58% yields with excellent diastereoselectivities, respectively. Furthermore, these good performances were observed not only for enol ethers, but also for exocyclic enamines, and the corresponding products **4cc-4ee** were obtained in good to high yields with excellent dr values for both aromatic and aliphatic aldehydes. Remarkably, in order to test the practicability of this reaction on transforming complex molecules at late stage in organic synthesis, asymmetric reactions on modifying the (*R*)-(+)-sclareolide were carried out. With 2-naphthaldehyde, the resulting optically active product (+)-

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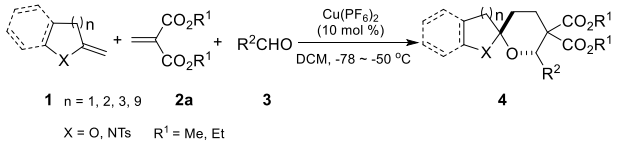
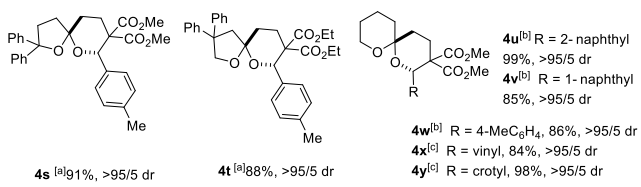
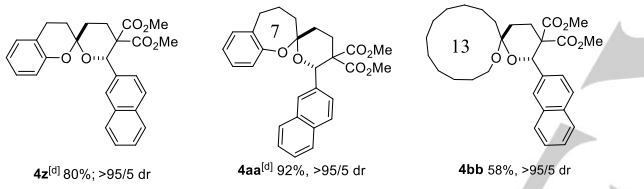
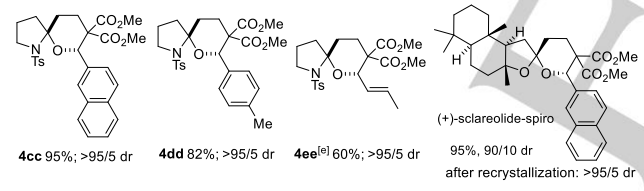
sclareolide-spiro was obtained in 95% yield with 90/10 dr (>95/5 dr, after recrystallization). This reaction could even serve as a flexible toolbox that could easily joint two complex moieties by one tetrahydropyranic cycle. With a lithocholic acid derived aldehyde, the (*R*)-(+)-sclareolide was connected with a steroid moiety to give the corresponding optically active product (+)-sclareolide-spiro-(+)-steroid in 73% yield with 88/12 dr. The relative configurations of **4u** and (+)-sclareolide-spiro were confirmed by X-ray crystallography.[15] These examples shown a high degree of remote stereocontrol in a thermodynamic process.

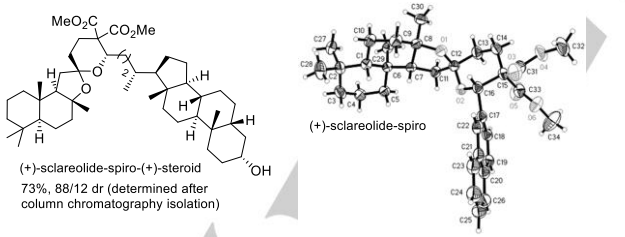
Table 2. Substrate Scope of **1**.







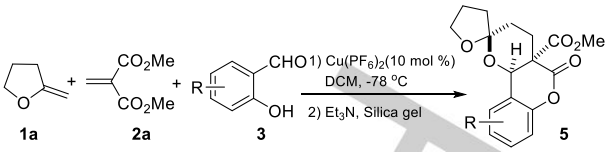


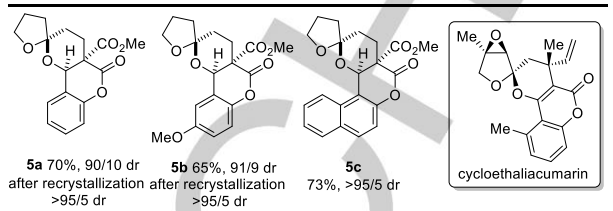


Reaction condition: **1** (0.6 mmol), **2** (0.6 mmol), **3** (0.2 mmol), $CuBr_2$ (0.02 mmol) and $AgPF_6$ (0.05 mmol) in DCM (2 mL); Isolated yield; the dr value was determined by crude ^1H NMR. [a] -78 °C; [b] -78 °C to rt; [c] -78 °C to -50 °C to rt.; [d] Purified by recrystallization; [e] $Cu(OTf)_2$ was used as catalyst. Ts = tosyl; Tf = trifluoromethanesulfonyl.

Moreover, when salicylaldehydes were employed as substrates, the spiroketalization followed by an intramolecular transesterification occurred to give the corresponding tetracyclic spiroketals **5a-5c** in 65-73% yields with excellent dr value. It is worth to mention that those tetracyclic spiroketals are core structure of natural product cycloethaliacumarin.[12] The relative configuration of **5c** was confirmed by X-ray crystallography.[15]

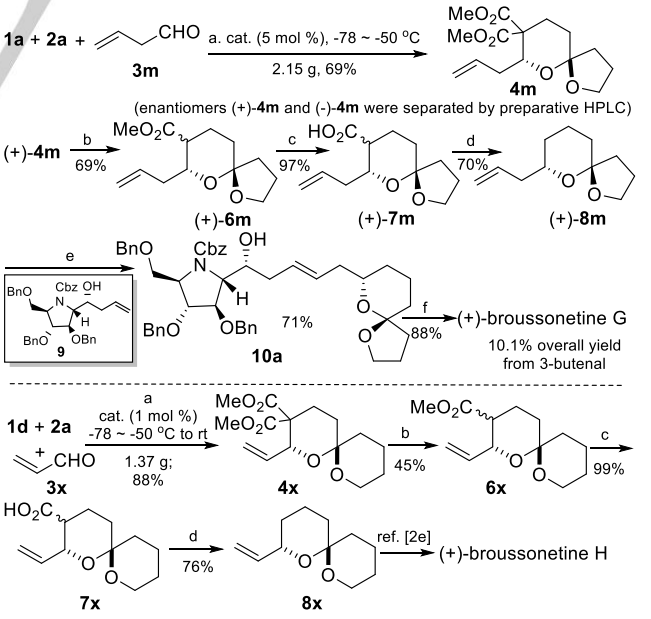
Table 3. Construction of Tetracyclic Spiroketals with Salicylaldehydes.





Reaction condition: **1** (0.6 mmol), **2** (0.6 mmol), **3** (0.2 mmol), $CuBr_2$ (0.02 mmol) and $AgPF_6$ (0.05 mmol) in DCM (2 mL) at -78 °C, then Et_3N (0.5 mL) and silica gel was added at -78 °C until **3** disappeared; Isolated yield; the dr value was determined by ^1H NMR.

Inspired by the synthetic efficiency to form spiroketals of the current method, we tried to apply it to construct the basic skeletons of biologically active natural products (+)-broussonetine G and H.[3a] In Scheme 3, the catalyst loading could be decreased to 1 mol %, and the scale-up tandem cyclization reactions with both five- and six- membered ring enol ethers were applied as the key step to build the **4m** and **4x** with excellent diastereoselectivity. The two enantiomers (+)-**4m** and (-)-**4m** could be easily separated by preparative high-performance liquid chromatography (HPLC).[14] (+)-**4m** was then treated with LiCl to give mono-decarboxylated products (+)-**6m**, followed by a hydrolysis reaction, affording (+)-**7m** in 97% yield. The carboxyl group was removed through a Barton ester free-radical reaction, and the resulting (+)-**8m** was then connected with an arabinofuranose derived synthetic intermediate **9**[16] by employing Hoveyda-Grubbs(II) catalyst to



Scheme 3. Gram-scale synthesis, total synthesis of (+)-broussonetine G and formal synthesis of (+)-broussonetine H. Reagents and conditions: a. $Cu(PF_6)_2$, DCM; b. LiCl, H_2O, dimethyl sulfoxide (DMSO), 130 °C; c. $LiOH{\cdot}H_2O$, $MeOH/H_2O$, 50 °C; d. dipyrithione, *n*-Bu_3P, *n*-Bu_3SnH, dark, benzene at rt for 3 h, then azodiisobutyronitrile (AIBN) at 80 °C; e. Hoveyda-Grubbs(II), DCM, 55 °C; f. Pd/C, H_2, MeOH, HCl (aq), rt.

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give **10a**. The total synthesis of (+)-broussonetine G was completed by the final hydrogenation of **10a** in a linear sequence of 6 steps from 3-butenal with 10.1% overall yield. Meanwhile, with (-)-**4m,** the diastereomer of (+)-broussonetine G was also prepared in the same way, [14] which provided a useful method in view of the demanding of structural diversity for the study of structure-activity relationship (SAR). Similarly, **4x** was converted into **8x,** which could be transformed to (+)-broussonetine H in two steps by a known procedure. [2e]

In summary, the first stereoselective multi-components tandem cyclizations of exocyclic enol ethers/enamines, methylene malonate and aldehydes were developed catalyzed by a copper (II) catalyst to furnish the spiroheterocyclic tetrahydropyrans in up to 99% yields with >95/5 dr. The reaction has a broad substrate scope that includes 36 examples. A very wide range of aldehydes, as well as different exo-vinyl heterocycles can all work well. This newly developed method was competent in modifying complex molecules at late stage, and was applied to the total synthesis of (+)-broussonetine G and formal synthesis of (+)-broussonetine H. The spiroketal was transformed to (+)-broussonetine G in a linear sequence of 6 steps from 3-butenal with 10.1% overall yield. Further application of this reaction is still underway in our laboratory.

Acknowledgements

We thank the NSFC (Nos. 21432011, 21772224), the CAS (Nos. QYZDY-SSW-SLH016, XDB20000000, 2017301), and the STCSM (Nos. 17JC1401200, 17ZR1436900) for the financial.

Keywords: spiroketal • diastereoselectivity • copper catalyst • tandem cyclization • (+)-broussonetine G

[1] a) F. Perron, K. F. Albizati, *Chem. Rev.* **1989**, *89*, 1617-1661; b) J. A. Beavo, L. L. Brunton, *Nat. Rev. Mol. Cell Biol.* **2002**, *3*, 710; c) J. E. Aho, P. M. Pihko, T. K. Rissa, *Chem. Rev.* **2005**, *105*, 4406-4440; d) J. A. Palmes, A. Aponick, *Synthesis* **2012**, *44*, 3699-3721; e) M. Wilsdorf, H.-U. Reissig, *Angew. Chem.* **2012**, *124*, 9624-9626; *Angew. Chem. Int. Ed.* **2012**, *51*, 9486-9488; f) F. M. Zhang, S. Y. Zhang, Y. Q. Tu, *Nat. Prod. Rep.* **2018**, *35*, 75-104.

[2] a) B. M. Trost, D. B. Horne, M. J. Woltering, *Angew. Chem.* **2003**, *115*, 6169-6172; *Angew. Chem. Int. Ed.* **2003**, *42*, 5987-5990; b) B. M. Trost, D. B. Horne, M. J. Woltering, *Chem. Eur. J.* **2006**, *12*, 6607-6620; c) M. Wilsdorf, H.-U. Reissig, *Angew. Chem.* **2012**, *126*, 4420-4424; *Angew. Chem. Int. Ed.* **2014**, *53*, 4332-4336; d) H. Cheng, Z. Zhang, H. Yao, W. Zhang, J. Yu, R. Tong, *Angew. Chem.* **2017**, *129*, 9224-9228; *Angew. Chem. Int. Ed.* **2017**, *56*, 9096-9100; e) S. L. Rössler, B. S. Schreib, M. Ginterseder, J. Y. Hamilton, E. M. Carreira, *Org. Lett.* **2017**, *19*, 5533-5536.

[3] a) M. Shibano, S. Nakamura, N. Akazawa, G. Kusano, *Chem. Pharm. Bull.* **1998**, *46*, 1048-1050; b) J. Li, L. Li, Y. Si, X. Jiang, L. Guo, Y. Che, *Org. Lett.* **2011**, *13*, 2670-2673; c) Q.-Y. Liu, T. Zhou, Y.-Y. Zhao, L. Chen, M.-W. Gong, Q.-W. Xia, M.-G. Ying, Q.-H. Zheng, Q.-Q. Zhang, *Marine Drugs* **2015**, *13*, 4733-4753.

[4] For selected examples on intramolecular spiroketalizations, see: a) B. M. Trost, E. D. Edstrom, *Angew. Chem.* **1990**, *102*, 102, 541 - 542; *Angew. Chem. Int. Ed.* **1990**, *29*, 520-522; b) S. K. Ghosh, R. P. Hsung, J. Liu, *J. Am. Chem. Soc.* **2005**, *127*, 8260-8261; c) B. D. Sherry, L. Maus, B. N. Laforteza, F. D. Toste, *J. Am. Chem. Soc.* **2006**, *128*, 8132-8133; d) L.-Z. Dai, M.-J. Qi, Y.-L. Shi, X.-G. Liu, M. Shi, *Org. Lett.* **2007**, *9*, 3191-3194; e) H. H. Jung, J. R. Seiders, 2nd, P. E. Floreancig, *Angew. Chem.* **2007**, *119*, 8616-8619; *Angew. Chem. Int. Ed.* **2007**, *46*, 8464-8467; f) J. M. Wurst, G. Liu, D. S. Tan, *J. Am. Chem. Soc.* **2011**, *133*, 7916-7925. g) A. N. Butkevich, A. Corbu, L. Meerpoel, I. Stansfield, P. Angibaud, P. Bonnet, J. Cossy, *Org. Lett.* **2012**, *14*, 4998-5001.

[5] For selected examples on enantioselective intramolecular spiroketalizations, see: a) I. Coric, B. List, *Nature* **2012**, *483*, 315-319; b) Z. Sun, G. A. Winschel, A. Borovika, P. Nagorny, *J. Am. Chem. Soc.* **2012**, *134*, 8074-8077; c) X. Wang, Z. Han, Z. Wang, K. Ding, *Angew. Chem.* **2012**, *124*, 960-964; *Angew. Chem. Int. Ed.* **2012**, *51*, 936-940; d) N. Yoneda, Y. Fukata, K. Asano, S. Matsubara, *Angew. Chem.* **2015**, *127*, 15717-15720; *Angew. Chem. Int. Ed.* **2015**, *54*, 15497-15500; e) J. Y. Hamilton, S. L. Rossler, E. M. Carreira, *J. Am. Chem. Soc.* **2017**, *139*, 8082-8085.

[6] a) P. Pale, J. Chuche, *Tetrahedron Lett.* **1988**, *29*, 2947-2950; b) G. Zhou, J. Zhu, Z. Xie, Y. Li, *Org. Lett.* **2008**, *10*, 721-724; c) M. A. Marsini, Y. Huang, C. C. Lindsey, K.-L. Wu, T. R. R. Pettus, *Org. Lett.* **2008**, *10*, 1477-1480.

[7] M. A. Rizzacasa, A. Pollex, *Org. Biomol. Chem.* **2009**, *7*, 1053-1059.

[8] a) J. Barluenga, A. Mendoza, F. Rodriguez, F. J. Fananas, *Angew. Chem.* **2009**, *121*, 1672-1675; *Angew. Chem. Int. Ed.* **2009**, *48*, 1644-1647; b) X. Wang, S. Dong, Z. Yao, L. Feng, P. Daka, H. Wang, Z. Xu, *Org. Lett.* **2014**, *16*, 22-25; c) M. Liang, S. Zhang, J. Jia, C.-H. Tung, J. Wang, Z. Xu, *Org. Lett.* **2017**, *19*, 2526-2529.

[9] For asymmetric version of intermolecular spiroketalizations, see: a) H. Wu, Y.-P. He, L.-Z. Gong, *Org. Lett.* **2013**, *15*, 460-463; b) J. Li, L. Lin, B. Hu, X. Lian, G. Wang, X. Liu, X. Feng, *Angew. Chem.* **2016**, *128*, 6179-6182; *Angew. Chem. Int. Ed.* **2016**, *55*, 6075-6078; c) J. Gong, Q. Wan, Q. Kang, *Adv. Syn. Catal.* **2018**, *360*, 4031-4036; d) S. Ge, W. Cao, T. Kang, B. Hu, H. Zhang, Z. Su, X. Liu, X. Feng, *Angew. Chem.* **2019**, *131*, 4057-4061; *Angew. Chem. Int. Ed.* **2019**, *58*, 4017-4021.

[10] F. E. McDonald, H. Y. H. Zhu, C. R. Holmquist, *J. Am. Chem. Soc.* **1995**, *117*, 6605-6606.

[11] a) C. C. Lindsey, K. L. Wu, T. R. R. Pettus, *Org. Lett.* **2006**, *8*, 2365-2367; b) K.-L. Wu, S. Wilkinson, N. O. Reich, T. R. R. Pettus, *Org. Lett.* **2007**, *9*, 5537-5540; c) K.-L. Wu, E. V. Mercado, T. R. R. Pettus, *J. Am. Chem. Soc.* **2011**, *133*, 6114-6117.

[12] a) F. Bohlmann, C. Zdero, *Phytochemistry* **1977**, *16*, 1092-1095; b) A. A. Mahmoud, A. A. Ahmed, M. Iinuma, T. Tanaka, *Phytochemistry* **1998**, *48*, 543-546.

[13] a) J. L. Hu, L. W. Feng, L. Wang, Z. Xie, Y. Tang, X. Li, *J. Am. Chem. Soc.* **2016**, *138*, 13151-13154; b) J. Zhu, Y. J. Cheng, X. K. Kuang, L. Wang, Z. B. Zheng, Y. Tang, *Angew. Chem.* **2016**, *128,* 9370-9374; *Angew. Chem. Int. Ed.* ***2016****, 55*, 9224-9228; c) H. Chen, L. Wang, F. Wang, L. P. Zhao, P. Wang, Y. Tang, *Angew. Chem.* **2017***, 129,* 7046-7049; *Angew. Chem. Int. Ed.* **2017**, *56*, 6942-6945; d) X.-K. Kuang, J. Zhu, L. Zhou, L. Wang, S. R. Wang, Y. Tang, *ACS Catal.* **2018**, *8*, 4991-4995.

[14] For details, see supporting information.

[15] CCDC 1921542 (**4a**), 1921543 (**4u**), 1921546 (**5c**) and 1921531 ((+)-sclareolide-spiro) contain the supplementary crystallographic data, which can be obtained free of charge from The Cambridge Crystallographic Data Centre.

[16] a) N. Hama, T. Aoki, S. Miwa, M. Yamazaki, T. Sato, N. Chida, *Org. Lett.* **2011**, *13*, 616-619; b) Y.-X. Li, Y. Shimada, K. Sato, A. Kato, W. Zhang, Y.-M. Jia, G. W. J. Fleet, M. Xiao, C.-Y. Yu, *Org. Lett.* **2015**, *17*, 716-719.

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10.1002/anie.201907353

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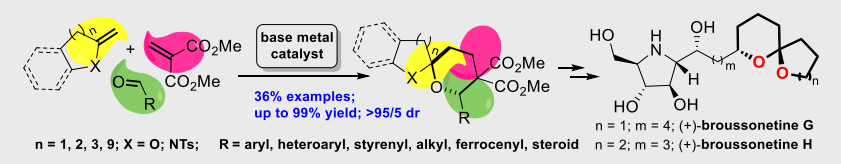

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Facile Stereoselective Approach to Diverse Spiroheterocyclic Tetrahydropyrans: Concise Synthesis of (+)-Broussonetine G and H

General method! An effective diastereoselective spiroketalization has been realized over a broad range of aldehydes in up to 99% yield with >95/5 dr. This method was applied to the total synthesis of (+)-broussonetine G and formal synthesis of (+)-broussonetine H.

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