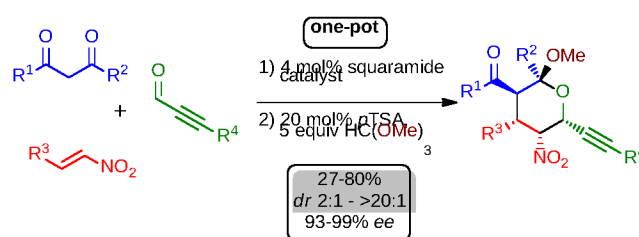


Asymmetric Synthesis of Highly Functionalized Tetrahydropyrans via a One-Pot Organocatalytic Michael/Henry/Ketalization Sequence

Robert Hahn, Gerhard Raabe and Dieter Enders*

Institute of Organic Chemistry, RWTH Aachen University, Landoltweg 1, 52074 Aachen, Germany

Supporting Information Placeholder



ABSTRACT: A diastereo- and enantioselective Michael/Henry/ketalization sequence to functionalized tetrahydropyrans is described. The multicomponent cascade reaction uses acetylacetone or β -keto esters, β -nitrostyrenes and alkynyl aldehydes as substrates affording tetrahydropyrans with five contiguous stereocenters. Employing a bifunctional quinine-based squaramide organocatalyst, the title compounds are obtained in moderate to good yields (27-80%), excellent enantiomeric excesses (93-99% *ee*) and high diastereomeric ratios (*dr* >20:1) after one crystallization.

Over the past years we have witnessed a strong increase in the number of publications on organocatalysis as the main topic.¹ Nowadays numerous groups of organocatalysts are known, with the classes of primary² and secondary amines,³ hydrogen-bonding organocatalysts,⁴ chiral phosphoric acids⁵ as well as *N*-heterocyclic carbenes⁶ being used preferentially. The catalytic asymmetric synthesis with these small organic molecules under metal-free conditions now constitutes a rapidly growing research area at the frontier of green chemistry.⁷ Hayashi and co-workers⁸ reported a cross-aldol reaction of alkynyl aldehydes **4** with other simple aliphatic aldehydes to obtain synthetically useful β -alkynyl- β -hydroxy aldehydes. Similar to the cross-aldol reactions, Henry reactions with α -acidic nitro compounds are possible as well.⁹ We wanted to combine these methods by incorporating the resulting alcohol functionality in an intramolecular fashion to generate six-membered rings. We envisaged the use of alkynyl aldehydes **4** to facilitate the 1,2-addition to be followed up by a ketalization keystone to afford 2-hydroxy tetrahydropyrans,¹⁰ which to the best of our knowledge would be the first case to generate this type of compounds via a hydrogen-bonding organocatalyst. The triple bond is a versatile structural element that can be used for several transformations, e.g. cycloadditions or selective reductions to alkenes and as a precursor of ketones. The 2-hydroxy (or rather alkoxy) tetrahydropyran unit is a characteristic structural feature of a huge number of natural products, besides carbohydrates for instance of spiroketals,¹¹ in soraphen A¹² and pederin¹³ as well as in the class of the bryostatins¹⁴.

To build up the motif of the tetrahydropyran we planned the addition of a γ -nitro carbonyl compound to an aldehyde.¹⁵ Achiral γ -nitro carbonyl compounds were extensively tested but no good asymmetric inductions could be achieved. After intensive literature research, a method provided by Rawal *et al.*¹⁶ was tested. They developed the synthesis of several Michael adducts between 1,3-diketones with β -nitrostyrenes with a novel squaramide organocatalyst based on cinchonine in excellent yields and enantiomeric excesses. Because of the pseudo-enantiomeric nature of the cinchona alkaloids, we decided to employ a quinine-based organocatalyst to prove the diversity of this method by synthesizing the corresponding enantiomer. According to the protocol of the Rawal group, acetylacetone **1a** and β -nitrostyrene **2a** reacted smoothly with catalyst **A** to the Michael adduct **3a** and in the following new step of the one-pot sequence the aldehyde **4a** was added to form the hemiketal **5a** (Scheme 1). The product was obtained in an excellent enantiomeric excess of 99%, but in a low yield of 30% after column chromatography.

Scheme 1. Initial outcome of the envisaged domino sequence

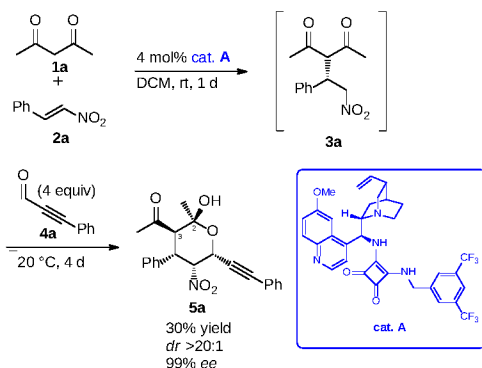
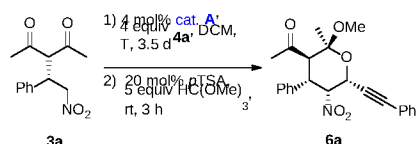


Table 1. Optimizing the reaction temperature for the Henry/ketalization sequence



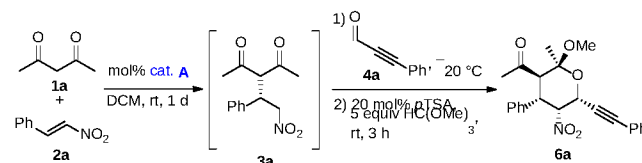
entry ^a	temp (°C)	yield (%) ^b	dr ^c
1	rt	50	3:1
2	0	61	8:1
3	-20	80	>20:1

^aThe reaction was performed on a 0.2 mmol scale. ^bCombined yield of isolated product as a mixture of diastereomers after flash chromatography. ^cDiastereomeric ratio; major vs. minor diastereomers determined by ¹H NMR.

To investigate this outcome, we stirred the intermediate Michael product **5a** over silica gel and found out that a retro-aldol reaction between C2/C3 occurred. Addition of a small amount of base during chromatography to neutralize the acidity of silica resulted in a non-characterizable product. To create a stable compound, we investigated several hydroxyl protecting groups, which all had to react under almost neutral or mild conditions. The best result was obtained with the combination of *p*TSA and HC(OMe)₃ in a quantitative yield and with no loss of enantioselectivity. With this knowledge in hand we added the protecting reagents to the reaction mixture and thus we were able to get the desired product in a good yield. Knowing how to overcome the stability problems, we screened for the best reaction conditions. A short temperature screening was conducted with Michael adduct **3a** and aldehyde **4a** (Table 1). Reducing the reaction temperature from room temperature to -20 °C (entries 1–3) was followed by an increase in yield and diastereoselectivity. Now we focused on the one-pot procedure for the synthesis of the tetrahydropyrans. Following the protocol of the Rawal group, we started with the addition of acetylacetone (**1a**) and β-nitrostyrene (**2a**) with 4 mol% of catalyst in DCM at room temperature (Table 2, entry 1). As opposed to the 2 equivalents of acetylacetone of the Rawal group, we used a 1:1 ratio, because excess acetylacetone would react with aldehyde **4a** in an aldol-condensation and thus increase the complexity of the final mixture. Reducing the amount of catalyst was not successful. Although the first step occurred quantitatively, we could obtain only 53% yield at 2 mol% catalyst loading, respectively 11% yield at 0.7 mol% (entries 2 and 3). For the next set of modifications we changed the amount of aldehyde **4a** (Table 2, entry 4–7). With 10 equivalents a lower

yield as compared to 4 or 2 equivalents was obtained indicating a concentration issue. Further reduction of the amount of the aldehyde led to a small decrease in yield (entries 6 and 7). Extending the reaction time resulted in no increase in yield (entries 8–10). The amount of solvent was reduced to a concentration of 0.5 M, which resulted in an increase of yield (Table 2, entry 11). Having the proper conditions in hand, an extension of the scope was investigated (Table 3). Several different substituents R³ on the aryl moiety of **2** (entries **b–d, f**) were introduced giving moderate to good yields of 27–65% and very good enantioselectivities (93–97% *ee*). Even a heterocyclic group, like the protected *N*-Boc-indolyl, could be used (Table 3, entry **e**).

Table 2. Screening for the optimal conditions



entry ^a	mol%	equiv of 3	time (d) ^b	yield (%) ^c	dr ^d
1	4	4	4	62	>20:1
2	2	4	5	53	>20:1
3	0.7	4	5	11	n.d. ^e
4	4	10	5	46	>20:1
5	4	2	5	61	>20:1
6	4	1.5	5	52	>20:1
7	4	1.1	5	50	>20:1
8	4	2	6	59	>20:1
9	4	2	7	57	>20:1
10	4	2	9	59	>20:1
11 ^f	4	2	5.5	79	>20:1

^aThe reaction was performed on a 0.2 mmol scale (0.2 M in DCM). ^bSum of reaction time. ^cCombined yield of isolated product as a mixture of diastereomers after flash chromatography. ^dDiastereomeric ratio; major vs. minor diastereomers determined by ¹H NMR. ^eNot determined. ^fConducted in 0.4 mL of solvent (0.5 M).

The aromatic part R⁴ of the aldehyde **4** was substituted with electron-donating and electron-withdrawing groups to yield the cascade product in modest to good yields (61–80%) and in very good enantioselectivities of 94–97% *ee* (Table 3, entries **g–i**). Switching to a cyclopentyl moiety (entry **j**) led to the same range of yield (68%) and enantioselectivity (96% *ee*). Desym-

metrization of the acetylacetone to the corresponding methyl ester gave 60% yield and 97% *ee* (Table 3, entry **k**). Increasing the bulkiness to a *tert*-butoxy group (entry **m**) resulted in a drop of obtained product (34% yield) but still impressive 98% *ee*. A further domino product was obtained in 69% yield and 96% *ee* after extending the side chain to an ethyl group (Table 3, entry **l**).

The relative configuration was determined by NOE measurements for compound **6c** (Figure 1) as well as the absolute configuration by single crystal X-ray analysis of compound **6a** (Figure 2).¹⁷

Figure 1. Determination of the relative configuration by NOE for compound **6c**.

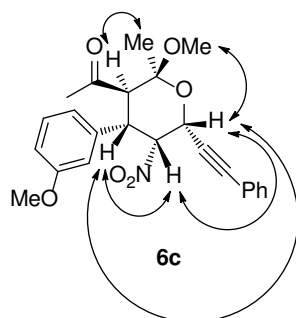
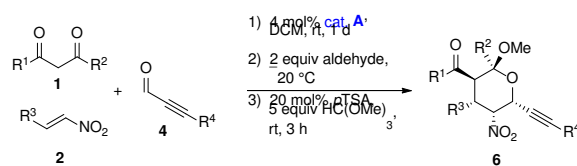


Table 3. Scope of the Michael/Henry/ketalization sequence to form tetrahydropyrans

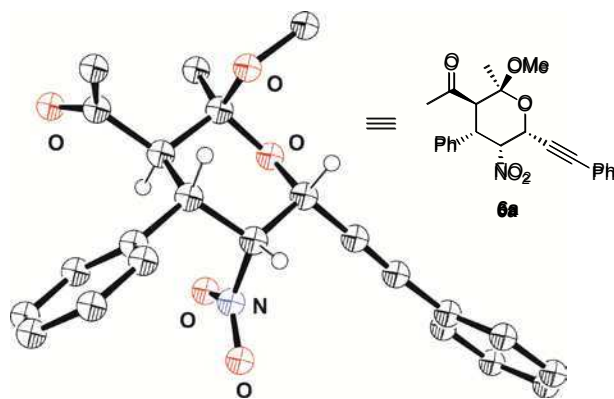


6 ^a	R ¹	R ²	R ³	R ⁴	time (d) ^b	yield (%) ^c	dr ^d	ee (%) ^e
a	Me	Me	Ph	Ph	5.5	79	>20:1	>99
b	Me	Me	2-BrC ₆ H ₄	Ph	5.5	65	13:1	93 (99)
c	Me	Me	3-MeOC ₆ H ₄	Ph	6.5	45	6:1	97 (99)
d	Me	Me	3,4-OCH ₂ OC ₆ H ₃	Ph	5	27	2:1	95 (99)
e	Me	Me	3-(<i>N</i> -Boc-indolyl)	Ph	6	38	8:1	95
f	Me	Me	4-NO ₂ C ₆ H ₄	Ph	9	46	2:1	93
g	Me	Me	Ph	3-FC ₆ H ₄	5.5	67	5:1	94 (99)
h	Me	Me	Ph	4-MeC ₆ H ₄	5.5	61	7:1	97
i	Me	Me	Ph	2-MeOC ₆ H ₄	5.5	80	3:1	95 (99)
j	Me	Me	Ph	cyclopentyl	5.5	68	4:1	96
k	OMe	Me	Ph	Ph	5.5	60	4:1	97 (99)
l	OMe	Et	Ph	Ph	5	69	3:1	96 (99)
m	O ^t Bu	Me	Ph	Ph	9	34	2:1	98

^aThe reaction was performed on a 0.4 mmol scale (0.5 M in DCM). ^bSum of reaction time. ^cCombined yield of isolated product as a mixture of diastereomers after flash chromatography. ^dDiastereomeric ratio: major vs. minor diastereomers determined by ¹H NMR; after one recrystallization *dr* >20:1. ^eDetermined by HPLC analysis on a chiral stationary phase for the major diastereomer; value in bracket after one recrystallization.

In summary, we have developed an organocatalytic Michael/Henry/ketalization cascade sequence to access highly functionalized tetrahydropyrans. A hydrogen-bonding organocatalyst on a squaramide basis was used to merge acetylacetone or different β -keto esters with nitroalkenes and ynals. In this manner tetrahydropyrans, bearing five contiguous stereocenters were obtained in moderate to good yields (27–80%), after one recrystallization in high diastereomeric ratios (*dr* >20:1) and excellent enantiomeric excesses (93–99% *ee*).

Figure 2. Determination of the absolute configuration by X-ray crystal structure analysis of compound **6a**.



ASSOCIATED CONTENT

Supporting Information

Experimental procedures and the characterization of all products are reported in the supporting information. This material is available free of charge via the Internet at <http://pubs.acs.org>.

AUTHOR INFORMATION

Corresponding Author

*E-mail: enders@rwth-aachen.de;

Fax: (+49)-241-809-2127.

Notes

The authors declare no competing financial interest.

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REFERENCES

- (1) For selected reviews, see: (a) Enders, D.; Grondal, C.; Hüttl, M. R. M. *Angew. Chem.* **2007**, *119*, 1590; *Angew. Chem. Int. Ed.* **2007**, *46*, 1570. (b) Walji, A. M.; MacMillan, D. W. C. *Synlett* **2007**, 1477. (c) Grondal, C.; Jeanty, M.; Enders, D. *Nat. Chem.* **2010**, *2*, 167. (d) Pellissier, H. *Adv. Synth. Catal.* **2012**, *354*, 237. (e) Lu, L.-Q.; Chen, J.-R.; Xiao, W.-J. *Acc. Chem. Res.* **2012**, *45*, 1278. (f) Goudedranche, S.; Raimondi, W.; Bugaut, X.; Constantieux, T.; Bonne, D.; Rodriguez, J. *Synthesis* **2013**, *45*, 1909. (g) Volla, C. M. R.; Atodiresi, I.; Rueping, M. *Chem. Rev.* **2014**, *114*, 2390.
- (2) For selected reviews and examples on cinchona alkaloid-derived primary amine catalysis, see: (a) Xu, L.-W.; Luo, J.; Lu, Y.

- Chem. Commun.* **2009**, 1807. (b) Melchiorre, P. *Angew. Chem. Int. Ed.* **2012**, *51*, 9748; *Angew. Chem.* **2012**, *51*, 9889. (c) Cassani, C.; Martín-Rapún, R.; Arceo, E.; Bravo, F.; Melchiorre, P. *Nat. Protoc.* **2013**, *8*, 325. (d) Hack, D.; Enders, D. *Synthesis* **2013**, *45*, 2904. (e) Moran, A.; Hamilton, A.; Bo, C.; Melchiorre, P. *J. Am. Chem. Soc.* **2013**, *135*, 9091. (f) Kang, Y. K.; Kim, D. Y. *Adv. Synth. Catal.* **2013**, *355*, 3131. (g) Duan, J.; Li, P. *Catal. Sci. Technol.* **2014**, *4*, 311.
- (3) For selected examples on secondary amine organocatalysts, see: (a) Rueping, M.; Kuenkel, A.; Tato, F.; Bats, J. W. *Angew. Chem. Int. Ed.* **2009**, *48*, 3699. (b) Rueping, M.; Haack, K.; Ieasuwan, W.; Sundén, H.; Blanco, M.; Schoepke, F. R. *Chem. Commun.* **2011**, *47*, 3828. (c) Enders, D.; Greb, A.; Deckers, K.; Selig, P.; Merckens, C. *Chem. Eur. J.* **2012**, *18*, 10226. (d) Enders, D.; Joie, C.; Deckers, K. *Chem. Eur. J.* **2013**, *19*, 10818. (e) Chatterjee, I.; Bastida, D.; Melchiorre, P. *Adv. Synth. Catal.* **2013**, *355*, 3124. (f) Zeng, X.; Ni, Q.; Raabe, G.; Enders, D. *Angew. Chem. Int. Ed.* **2013**, *52*, 2977. (g) Erdmann, N.; Philipps, A. R.; Atodiresei, I.; Enders, D. *Adv. Synth. Catal.* **2013**, *355*, 847. (h) Dong, L.-J.; Fan, T.-T.; Wang, C.; Sun, J. *Org. Lett.* **2013**, *15*, 204. (i) Wu, L.; Wang, Y.; Song, H.; Tang, L.; Zhou, Z.; Tang, C. *Chem. Asian J.* **2013**, *8*, 2204. (j) Alexakis, A.; Lefranc, A.; Guénée, L. *Org. Lett.* **2013**, *15*, 2172. (k) Joie, C.; Deckers, K.; Enders, D. *Synthesis* **2014**, *46*, 799.
- (4) For selected reviews and examples of hydrogenbonding catalysis, see: (a) Schreiner, P. R. *Chem. Soc. Rev.* **2003**, *32*, 289. (b) Taylor, M. S.; Jacobsen, E. N. *Angew. Chem.* **2006**, *118*, 1550; *Angew. Chem. Int. Ed.* **2006**, *45*, 1520. (c) Connon, S. J. *Chem. Eur. J.* **2006**, *12*, 5418. (d) Doyle, A. G.; Jacobsen, E. N. *Chem. Rev.* **2007**, *36*, 5713. (e) Zhang, Z.; Schreiner, P. R. *Chem. Soc. Rev.* **2009**, *38*, 1187. (f) Etzenbach-Effers, K.; Berkessel, A. *Top. Curr. Chem.* **2009**, *291*, 1. (g) Aleman, J.; Parra, A.; Jiang, H.; Jørgensen, K. A. *Chem. Eur. J.* **2011**, *17*, 6890. (h) Storer, R. I.; Aciro, C.; Jones, L. H. *Chem. Soc. Rev.* **2011**, *40*, 2330. (i) Albrecht, L.; Dickmeiss, G.; Acosta, F. C.; Rodriguez-Esrich, C.; Davis, R. L.; Jørgensen, K. A. *J. Am. Chem. Soc.* **2012**, *134*, 2543. (j) Enders, D.; Urbanietz, G.; Cassens-Sasse, E.; Kees, S.; Raabe, G. *Adv. Synth. Catal.* **2012**, *354*, 1481. (k) Loh, C. C. J.; Hack, D.; Enders, D. *Chem. Commun.* **2013**, *49*, 10230. (l) Liu, Y.; Wang, Y.; Song, H.; Zhou, Z.; Tang, C. *Adv. Synth. Catal.* **2013**, *355*, 2544. (m) Gosh, A. K.; Zhou, B. *Tetrahedron Lett.* **2013**, *54*, 3500. (n) Sun, W.; Hong, L.; Zhu, G.; Wang, Z.; Wie, X.; Ni, J.; Wang, R. *Org. Lett.* **2014**, *16*, 544. (o) Zhou, E.; Liu, B.; Dong, C. *Tetrahedron: Asymmetry* **2014**, *25*, 181. (p) Han, X.; Dong, C.; Zhou, H.-B. *Adv. Synth. Catal.* **2014**, *356*, 1275.
- (5) (a) Akiyama, T.; Itoh, J.; Yokota, K.; Fuchibe, K. *Angew. Chem.* **2004**, *116*, 1592; *Angew. Chem. Int. Ed.* **2004**, *43*, 1566. (b) Uraguchi, D.; Terada, M. *J. Am. Chem. Soc.* **2004**, *126*, 5356. (c) Rueping, M.; Azap, C. *Angew. Chem. Int. Ed.* **2006**, *45*, 7832. (d) Baudequin, C.; Zamfir, A.; Tsogoeva, S. B. *Chem. Commun.* **2008**, 4637. (e) Evans, C. G.; Gestwicki, J. E. *Org. Lett.* **2009**, *11*, 2957. (f) Terada, M. *Synthesis* **2010**, 1929. (g) Taylor, J. E.; Daniels, D. S. B.; Smith, A. D. *Org. Lett.* **2013**, *15*, 6058. (h) Courant, T.; Kumarn, S.; He, L.; Retailliau, P.; Masson, G. *Adv. Synth. Catal.* **2013**, *355*, 836. (i) Izquierdo, J.; Orue, A.; Scheidt, K. A. *J. Am. Chem. Soc.* **2013**, *135*, 10634. (j) Enders, D.; Stöckel, B. A.; Rembiak, A. *Chem. Commun.* **2014**, *50*, 4489. (k) Tian, X.; Hofmann, N.; Melchiorre, P. *Angew. Chem. Int. Ed.* **2014**, *53*, 2997. (l) Mori, K.; Wakazawa, M.; Akiyama, T. *Chem. Sci.* **2014**, *5*, 1799. (m) Zhong, S.; Nieger, M.; Bihlmeier, A.; Shi, M.; Bräse, S. *Org. Biomol. Chem.* **2014**, *12*, 3265.
- (6) For selected reviews and examples on NHC catalysis, see: (a) Heitbaum, M.; Glorius, F.; Escher, I. *Angew. Chem. Int. Ed.* **2006**, *45*, 4732. (b) Enders, D.; Niemeier, O.; Henseler, A. *Chem. Rev.* **2007**, *107*, 5606. (c) Moore, J. L.; Rovis, T. *Top. Curr. Chem.* **2010**, *291*, 118. (d) Bijou, A. K.; Kuhl, N.; Glorius, F. *Acc. Chem. Res.* **2011**, *44*, 1182. (e) Grossmann, A.; Enders, D. *Angew. Chem.* **2012**, *124*, 320; *Angew. Chem. Int. Ed.* **2012**, *51*, 314. (f) Izquierdo, J.; Hutson, G. E.; Cohen, D. T.; Scheidt, K. A. *Angew. Chem.* **2012**, *124*, 11854; *Angew. Chem. Int. Ed.* **2012**, *51*, 11686. (g) Bugaut, X.; Glorius, F. *Chem. Soc. Rev.* **2012**, *41*, 3511. (h) Ni, Q.; Zhang, H.; Grossmann, A.; Loh, C. C. J.; Merckens, C.; Enders, D. *Angew. Chem. Int. Ed.* **2013**, *52*, 13562. (i) Ryan, S. J.; Candish, L.; Lupton, D. W.; *Chem. Soc. Rev.* **2013**, *42*, 4906. (j) Song, X.; Ni, Q.; Grossmann, A.; Enders, D. *Chem. Asian J.* **2013**, *8*, 2965. (k) P. Chauhan, D. Enders, *Angew. Chem. Int. Ed.* **2014**, *53*, 1485.
- (7) (a) Wende, R. C.; Schreiner, P. R. *Green Chem.* **2012**, *14*, 1821. (b) Liu, D. D. J.; Chen, E. Y.-X. *Green Chem.* **2014**, *16*, 964.
- (8) Hayashi, Y.; Kojima, M.; Yasui, Y.; Kanda, Y.; Mukaiyama, T.; Shomura, H.; Nakamura, D.; Ritmaleni, Sato, I. *ChemCatChem* **2013**, *5*, 2887.
- (9) For recent selected examples of organocatalytic Michael–Henry domino reactions, see: (a) Xu, D.-Q.; Wang, Y.-F.; Luo, S.-P.; Zhang, S.; Zhong, A.-G.; Chen, H.; Xu, Z.-Y. *Adv. Synth. Catal.* **2008**, *350*, 2610. (b) Tan, B.; Chua, P. J.; Li, Y.; Zhong, G. *Org. Lett.* **2008**, *10*, 2437. (c) Tsakos, M.; Elsegood, M. R. J.; Kokotos, C. G. *Chem. Commun.* **2013**, *49*, 2219. (d) Qian, H.; Zhao, W.; Sung, H. H.-Y.; Williams, I. D.; Sun, J. *Chem. Commun.* **2013**, *49*, 4361. (e) Quintavalla, A.; Lombardo, M.; Sanap, S. P.; Trombini, C. *Adv. Synth. Catal.* **2013**, *355*, 938. (f) Dai, Q.; Arman, H.; Zhao, J. C.-G. *Chem. Eur. J.* **2013**, *19*, 1666. (g) Arai, T.; Yamamoto, Y. *Org. Lett.* **2014**, *16*, 1700.
- (10) For selected recent examples on tetrahydropyran syntheses, see: (a) Heumann, L. V.; Keck, G. E. *Org. Lett.* **2007**, *9*, 1951. (b) Larrosa, I.; Romea, P.; Urpi, F. *Tetrahedron* **2008**, *64*, 2683. (c) Gotoh, H.; Okamura, D.; Ishikawa, H.; Hayashi, Y. *Org. Lett.* **2009**, *11*, 4056. (d) Chandrasekhar, S.; Mallikarjun, K.; Pavankumarreddy, G.; Rao, K. V.; Jagadeesh, B. *Chem. Commun.* **2009**, *45*, 4985. (e) Olier, C.; Kaafarani, M.; Gastaldi, S.; Bertrand, M. P. *Tetrahedron* **2010**, *66*, 413. (f) Urbanietz, G.; Atodiresei, I.; Enders, D. *Synthesis* **2014**, *46*, 1261.
- (11) (a) Perron, F.; Albizzati, K. F. *Chem. Rev.* **1989**, *89*, 1617. (b) Raju, B. R.; Saikia, A. K. *Molecules* **2008**, *13*, 1942. (c) Favre, S.; Vogel, P.; Gerber-Lemaire, S. *Molecules* **2008**, *13*, 2570. (d) Sperry, J.; Liu, Y.-C.; Brimble, M. A. *Org. Biomol. Chem.* **2010**, *8*, 29.
- (12) Bedorf, N.; Schomburg, D.; Gerth, K.; Reichenbach, H.; Höfle, G. *Liebigs Ann. Chem.* **1993**, 1017.
- (13) (a) Willson, T. M.; Kocienski, P.; Jarowicki, K.; Isaac, K.; Faller, A.; Campbell, S.; Bordner, J. *Tetrahedron* **1990**, *46*, 1757. (b) Willson, T. M.; Kocienski, P.; Jarowicki, K.; Isaac, K.; Faller, A.; Campbell, S.; Bordner, J. *Tetrahedron* **1990**, *46*, 1767.
- (14) Hale, K. J.; Hummersone, M. G.; Manaviazar, S.; Frigerio, M. *Nat. Prod. Rep.* **2002**, *19*, 413.
- (15) Enders, D.; Hahn, R.; Atodiresei, I. *Adv. Synth. Catal.* **2013**, *355*, 1126.
- (16) Malerich, J. P.; Hagihara, K.; Rawal, V. H. *J. Am. Chem. Soc.* **2008**, *130*, 14416.
- (17) CCDC 999310 (**6a**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

