ACS Catalysis

Letter

Cite This: ACS Catal. 2019, 9, 11614−11618

pubs.acs.org/acscatalysis

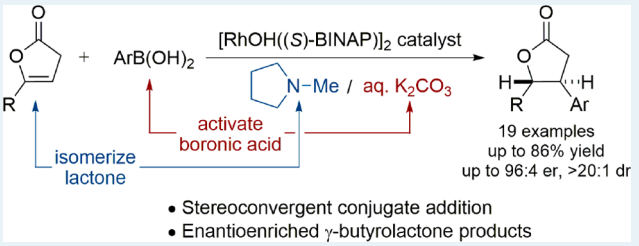
Stereoconvergent Conjugate Addition of Arylboronic Acids to α-Angelica Lactone Derivatives: Synthesis of Stereochemically Complex γ-Butyrolactones

Jessica A. Griswold and Jeffrey S. Johnson*

Department of Chemistry, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina 27599-3290, United States

Supporting Information

ABSTRACT: Catalyzed stereoconvergent 1,4-additions to unsaturated carbonyls are rare but of high potential value. This letter details the development of enantioselective arylation reactions of boronic acids and β,γ-butenolides. These reactions are catalyzed by commercially available hydroxy[(*S*)-BINAP]-rhodium(I) dimer to afford stereochemically complex γ-butyrolactone derivatives. The reaction products provide functionality amenable to further manipulation and can lead to products with up to three contiguous stereocenters. The reaction proceeds under a dynamic kinetic resolution manifold by isomerizing the achiral starting material into an interconverting mixture of enantiomeric conjugate acceptors, followed by catalyst-controlled, enantiomer-selective 1,4-addition. Base-promoted racemization of the intermediate α,β-butenolide is possible due to the high kinetic and thermodynamic acidity of the γ-proton.

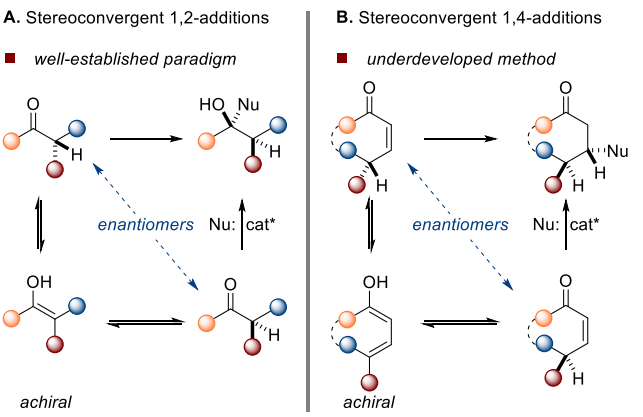


KEYWORDS: *asymmetric catalysis, conjugate addition, lactones, rhodium, dynamic kinetic resolution*

The need for enantioenriched drug molecules has provided a significant impetus for breakthroughs in the field of dynamic kinetic resolution (DKR). DKR has proven to be a powerful tool for the synthesis of enantiomerically pure products from racemic starting materials.[1] DKR reactions commonly take advantage of a stereogenic center adjacent to an activating group to promote racemization. For example, DKR transformations of β-keto esters and α-keto esters have been widely explored, as these types of substrates can be easily racemized via the achiral enol or enolate, followed by catalyst-controlled enantio- and diastereoselective 1,2-addition (Scheme 1A).[2,3] One could imagine a complementary scenario, in which an α,β-unsaturated substrate containing a stereocenter at the γ-position could be racemized via the dienol or dienolate (Scheme 1B). One enantiomer of the starting material could then be trapped via an asymmetric 1,4-addition, to afford useful products with vicinal stereocenters at the β- and γ-positions. This reaction manifold remains unknown to the best of our knowledge, despite its direct analogy to the vast body of enantioconvergent 1,2-additions.[4]

It may be worth considering possible reasons for this gulf, especially in the context of attempting to identify an electrophile that could potentially be appropriate for such a transformation. Successful DKR reactions of this type would require the γ-proton of the substrate to be of sufficient kinetic acidity to racemize at a rate faster than the irreversible π-bond addition. We were interested in testing the notion that α-angelica lactone (**A**) and related structures might serve as useful proelectrophiles for the transformation outlined in Scheme 1B. Enantioconvergent conjugate additions to α-angelica lactone are especially enticing because of that reagent's lignocellulosic origin[5] and the prevalence of the core scaffold in bioactive structures: nearly 10% of all natural products contain a γ-butyrolactone.[6]

Scheme 1. Enantioconvergent Additions of π-Functional Groups

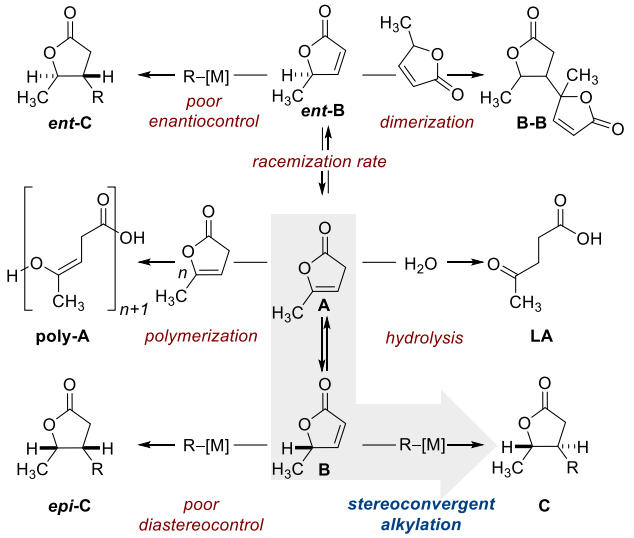


Catalyzed enantioconvergent reactions are complex because of the need to engineer both a competent racemization pathway and an enantiomer-selective addition to a prochiral functional group. Scheme 2 illustrates the higher level of

Received: October 14, 2019
Revised: November 12, 2019

DOI: 10.1021/acscatal.9b04405
ACS Catal. 2019, 9, 11614−11618

Scheme 2. Kinetic Issues Involved in the Stereoconvergent Alkylation of α-Angelica Lactone (Gray Arrow)

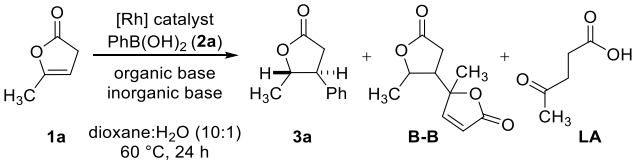


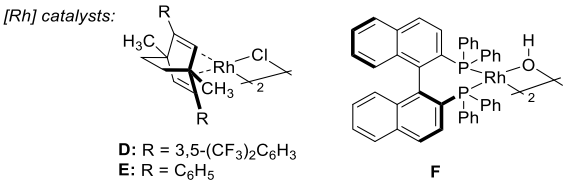
potential complication associated with the projected application. The desired path is **A** → **C** traced by the background gray arrow, while other mechanistically validated paths radiate from the center. The substrate **A** is a proelectrophile: the olefin must migrate into conjugation for it to be armed in its active form as a conjugate acceptor (**A** ⇆ **B** (≡ β-angelica lactone)). Prior reports indicate γ-substituted α,β-unsaturated butenolides racemize (**B** ⇆ *ent*-**B**) at reaction rates and under conditions that vary widely.[7] Enantioenriched β,γ-substituted γ-butyrolactones are commonly accessed via diastereoselective 1,4-additions to enantioenriched γ-substituted α,β-unsaturated butenolide, allaying some concern about diastereocontrol (*epi*-**C**); however, there are no reports of accessing enantioenriched products from racemic starting materials.[6a,7d,e,8] In its "unarmed" form, α-angelica lactone is known to hydrolyze to levulinic acid (**A** → **LA**)[9] and polymerize (*n***A** → **poly(A)**),[10] while the conjugated isomer **B** dimerizes (2 **B** → **B-B**).[11] Critically, identification of an appropriate catalyst that can differentiate between the two enantiomers of starting material is an inherent challenge of any stereoconvergent transformation (**A** → **C** vs **A** → *ent*-**C**).

Because the asymmetric rhodium-catalyzed 1,4-addition of arylboronic acids to butenolide substrates is well-precedented,[6a] and requires conditions known to be tolerant of amine bases,[3b] we believed this system would be appropriate for an enantioconvergent conjugate addition to α-angelica lactone. Herein, we report the stereoconvergent arylation of γ-substituted α,β-unsaturated butenolides via isomerization of α-angelica lactone derivatives and concomitant rhodium-catalyzed 1,4-addition of arylboronic acids.

We began our studies with reaction of lactone **1a**, phenylboronic acid, and a bicyclo[2.2.2]octadiene rhodium dimer **D**.[12] While the reaction proceeded with high conversion and diastereoselectivity to the desired product **3a**, the reaction displayed only modest enantioselectivity and was accompanied by an appreciable amount of the undesired dimer **B-B** (Table 1, entry 1). By switching the aryl group on the complex **E**, dimerization could be greatly suppressed; however, both diastereoselectivity and enantioselectivity of the transformation were compromised (Table 1, entry 2). Employing the commercially available (*S*)-BINAP hydroxy-rhodium dimer

Table 1. Reaction Optimization





entry[a]	catal. (mol %)	org. base (equiv)	inorg. base (equiv)	conversion, % (**3a**/**B-B**/**LA**)	er[b]
1[c,d]	**D** (2.5)	Et_3N (6)	CsF (6)	100 (1.7:1:0)	24:76
2[c,d]	**E** (2.5)	Et_3N (6)	CsF (6)	100 (11:1:0)	44:56
3[e]	**F** (2.0)	Et_3N (1)	CsF (2)	15 (1.5:1:0)	92:8
4	**F** (2.0)	Et_3N (1)	none	7 (1:0:0)	97:3
5	**F** (2.0)	Et_3N (1)	K_2CO_3 (1)	100 (2.5:0:1)	85:15
6[f]	**F** (2.0)	Et_3N (1)	K_2CO_3 (1)	20 (1:0:0)	*i*
7	**F** (2.0)	NMP[g] (1)	K_2CO_3 (1)	100 (6.7:0:1)	96:4
8[e]	**F** (2.0)	NMP[g] (1)	K_2CO_3 (1)	56 (3:1:0)	97:3
9	**F** (2.0)	NMP[g] (6)	K_2CO_3 (1)	80 (5.0:0:1)	96:4
10	**F** (2.0)	NMP[g] (10)	K_2CO_3 (1)	100 (10:0:1)	95:5
11[h]	**F** (2.0)	NMP[g] (10)	K_2CO_3 (1)	90 (1:0:0)	95:5

[a]All reactions were run on a 0.20 mmol scale. [b]Determined by HPLC using a chiral stationary phase. [c]Reaction solvent CH_2Cl_2. [d]Reaction run at room temperature. [e]Reaction T = 40 °C. [f]Reaction solvent 1,4-dioxane. [g]NMP = *N*-methylpyrrolidine. [h]Reaction time = 1 h. [i]Not determined.

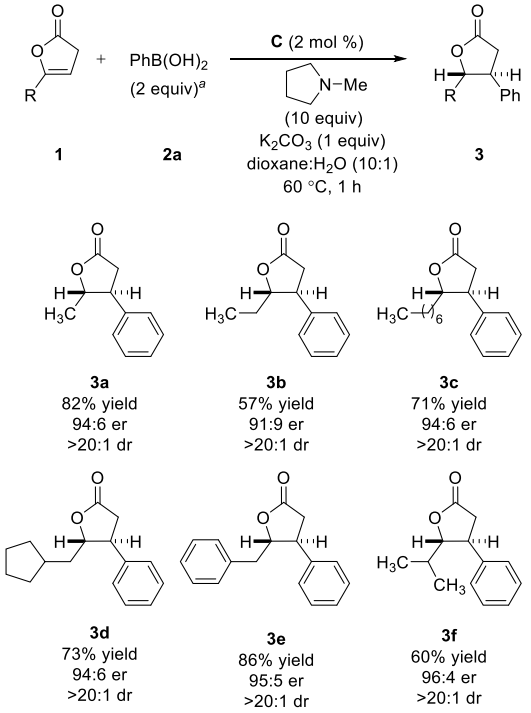
catalyst **F**,[13] we obtained poor conversion to the desired product **3a** but observed excellent enantio- and diastereoselectivity (Table 1, entry 3). Further investigation revealed that CsF rapidly induces dimerization of the α-angelica lactone, and when it was omitted, dimerization did not occur (Table 1, entry 4). Given the inorganic base's role in facilitating transmetalation, we considered alternative additives in order to increase conversion.[14] The addition of K_2CO_3 successfully improved conversion, but also accelerated the undesired hydrolysis of α-angelica lactone to levulinic acid, **LA** (Table 1, entry 5). Water is necessary to achieve high conversion to the desired product (Table 1, entry 6). Additionally K_2CO_3 decreases the enantioselectivity of the reaction, a fact that we attribute to a relatively fast rate of arylation relative to the rate of racemization of the substrate. Our group previously reported that the rate of racemization of configurationally labile substrates in the context of DKR reactions can be accelerated by smaller organic bases.[3b] Accordingly, use of *N*-methylpyrrolidine (NMP), a less sterically encumbered organic base, restored excellent levels of enantioselectivity (Table 1, entry 7). Although hydrolysis is suppressed at lower temperatures, arylation is slowed significantly, leading to increased dimerization (Table 1, entry 8). Increasing the amount of organic base had a dual effect of accelerating isomerization to the requisite butenolide isomer, effectively inhibiting hydrolysis, and promoting faster racemization relative to the arylation to afford the desired product in good enantioselectivity (Table 1, entry 9). By use of 10 equiv of *N*-methylpyrrolidine, the

DOI: 10.1021/acscatal.9b04405
ACS Catal. 2019, 9, 11614−11618

desired product was prepared in excellent conversion, diastereo- and enantioselectivity in 1 h (Table 1, entry 11). Additional studies confirmed that dioxane, K_2CO_3, and arylboronic acid are the best solvent, inorganic base, and organoboron source, respectively (see Supporting Information).

With optimized conditions in hand, we sought to explore their applicability to other reaction partners, beginning with unsaturated lactones bearing other substituents at the γ-position (Table 2). Substrates containing both short and long

Table 2. Scope of γ-Substituted β,γ-Unsaturated Butenolides

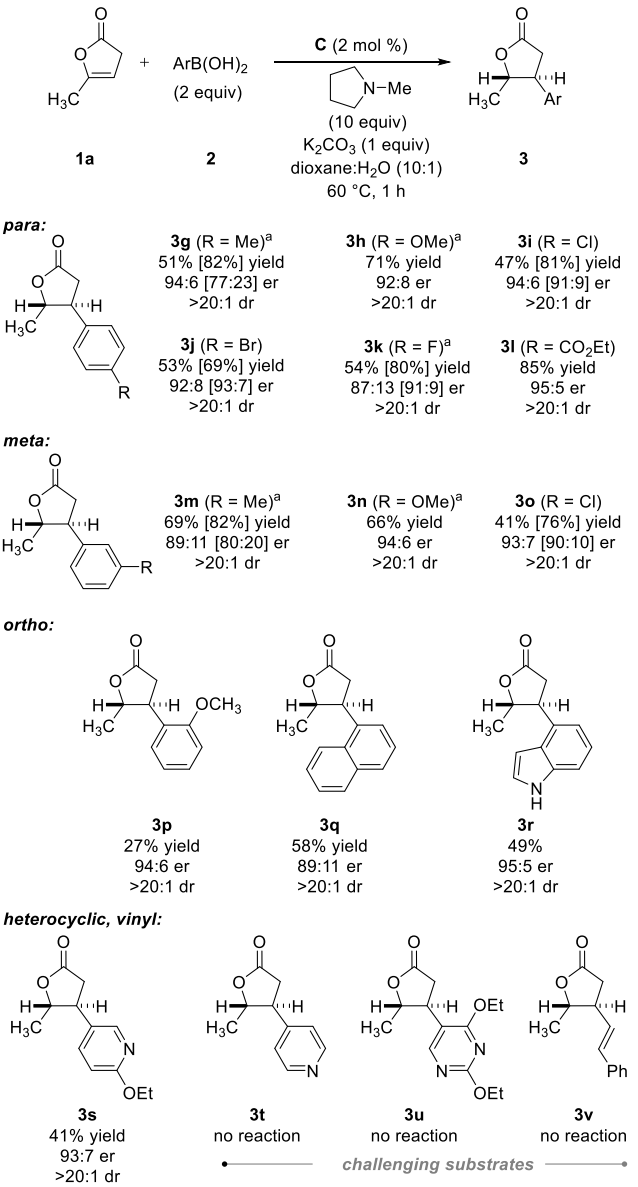


[a]Excess boronic acid is needed because of background hydrolysis (to benzene, see ref 16) and competitive angelica lactone dimerization.

alkyl chains afforded the desired products, **3a**, **3b**, and **3c**, in good yields and excellent stereoselectivities. Homologated carbocycles at the γ-position gave desired product **3d** in good yield and enantioselectivity. The benzyl group is also tolerated at the γ-position and gives lactone **3e** in excellent yield and stereoselectivity. A branched alkyl group worked well in the transformation to afford **3f**, albeit in slightly diminished yield, presumably due to the steric bulk at the γ-position. All products were obtained as a single diastereomer.

The scope of boronic acids tolerated in this reaction was then explored (Table 3). We found a wide variety of *para*-substituted arylboronic acids could be employed to generate products containing electron-donating groups, such as *p*-tolyl **3g** and *p*-anisyl **3h**. We could also obtain products containing *para*-substituted halogens, **3i–k**, and electron-withdrawing *para*-ester **3l** in modest to good yields and good enantioselectivities. Electron-rich arylboronic acids highlight the delicate balance between the rates of arylation and racemization. Reactions employing electron-rich arylboronic acids require catalytic quantities of K_2CO_3 to achieve desirable levels of enantioselectivity; a full equivalent of inorganic base results in loss of enantioselectivity. We hypothesize that the erosion is due to the accelerated arylation relative to

Table 3. Scope of Arylboronic Acid[b]



[a]Reaction run with 5 mol % K_2CO_3. [b]Results in brackets are for reactions run with 4.0 equiv of $ArB(OH)_2$.

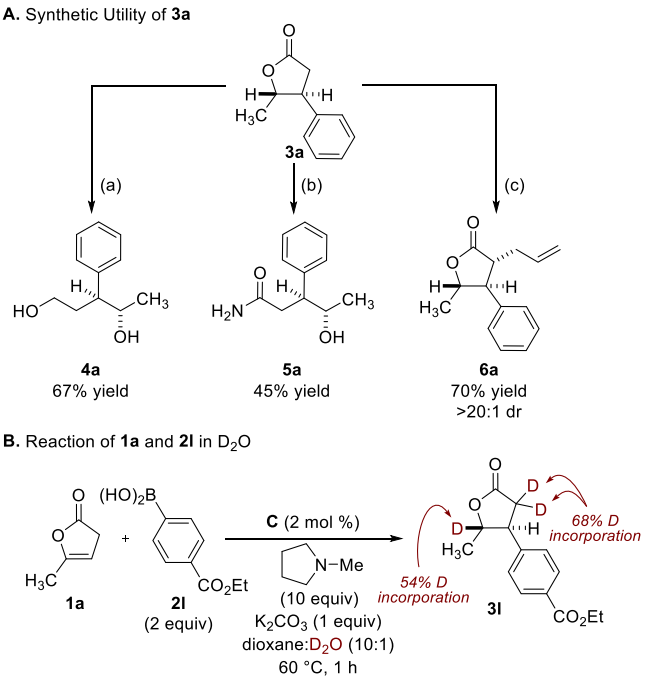
racemization. This trend continues for *meta*-substituted arylboronic acids. Products with electron-releasing substituents at the *meta*-position, **3m** and **3n**, can be obtained in good yields and enantioselectivities when substoichiometric K_2CO_3 is used. Halogen substitution at the *meta*-position (**3o**) is tolerated as well. Pleasingly, a sterically bulky *ortho*-substituted arylboronic acid provided product **3p** with excellent enantioselectivity, though greatly decreased yield. Naphthylboronic acid coupled product **3q** can be attained. Electron-rich heteroaromatic boronic acids work to afford heteroaromatic-containing lactones **3r** and **3s**. X-ray diffraction studies revealed the stereochemistry of **3g**, **3j**, and **3q** to be (4*S*,5*S*) (See Supporting Information).[15] The absolute stereochemistry agrees with the results of Hayashi and co-workers.[13,14,16,17] On a 1 mmol scale using 1 mol % catalyst **C**, α-angelica lactone and phenylboronic acid reacted to provide the derived lactone **3a** in 89% yield, >20:1 diastereoselection, and 93:7 er.

DOI: 10.1021/acscatal.9b04405
ACS Catal. 2019, 9, 11614–11618

Current limitations of the substrate scope include electron-poor heteroaromatic and styrenyl boronic acids.[3b] Higher yields can generally be achieved by employing more arylboronic acid, but in cases of electron-rich arylboronic acids, enantioselectivity typically suffers, presumably due to the rate of arylation relative to the rate of racemization. We hypothesize that under the optimized conditions, protodeborylation of the arylboronic acids occurs rapidly, accounting for moderate yields with some boronic acids. In most cases, longer reaction times do not improve yields.[14]

Further chemical transformations of the enantioenriched β,γ-substituted γ-butyrolactones were performed in order to access synthetically useful organic intermediates (Scheme 3).

Scheme 3. Synthetic Utility of Lactone Products[a]



[a]Reagents and conditions: (a) $LiAlH_4$, THF, 23 °C, 2 h; (b) aq. NH_4OH, 23 °C, 5 h; (c) LDA, allyl iodide, THF, −78 to 0 °C, 3 h.

The disubstituted lactone **3a** can be reduced to 1,4-diol **4a** with a primary and secondary alcohol. Lactone amidolysis of **3a** with ammonium hydroxide afforded enantioenriched amide **5a**, which can be further reduced to afford its derived 1,4-amino alcohol (see the Supporting Information). Finally, the β,γ-substituted γ-butyrolactone **3a** can be alkylated at the α-position in excellent diastereoselectivity to afford γ-butyrolactone **6a** with three contiguous stereocenters. The relative stereochemistry of this transformation was confirmed by a 1D NOE NMR study (see the Supporting Information).[18]

When the catalyzed addition of **2l** to **1a** was carried out in dioxane/D_2O (10:1), partial deuterium incorporation was observed at both the α- and γ-positions of **3l** (Scheme 3B). The fact that the product is obtained with less than 100% of $^1H/^2H$ exchange carries ramifications for the mechanism of the obligatory 1,3-prototropy. The results in part implicate $[R_3N–H]^+$, rather than D_2O, as the partner that reacts with the dienolate[7b] and concurrently confirm the importance of the organic base in the process.

In summary, we have developed an enantioconvergent 1,4-arylation of γ-substituted α,β-unsaturated butenolides. This reaction is one of the first dynamic kinetic resolutions that takes advantage of racemization of a γ-stereocenter through formation of a dienolate. A wide range of β-aryl, γ-substituted γ-butyrolactones can be accessed in good yields, excellent enantioselectivities, and as a single diastereomer. These lactones can be further manipulated to generate useful organic building blocks, including 1,4-diols and 1,4-amino alcohols. Additionally, the products can be diastereoselectively alkylated to afford stereochemically complex trisubstituted lactones. Extension of this work to other classes of nucleophiles, as well as application of the DKR conjugate addition manifold to additional substrates is currently underway in our laboratory.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acscatal.9b04405.

Experimental procedures and spectral and analytical data (PDF)

Crystallographic data for **3j** (CIF)

Crystallographic data for **3g** (CIF)

Crystallographic data for **3q** (CIF)

■ AUTHOR INFORMATION

Corresponding Author

*Email: jsj@unc.edu.

ORCID

Jeffrey S. Johnson: 0000-0001-8882-9881

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

The project described was supported by Award R35 GM118055 from the National Institute of General Medical Sciences. X-ray crystallography was performed by Dr. Josh Chen (UNC Chemistry X-ray Core Laboratory). We thank Dr. Brandie Ehrmann and Diane Weatherspoon (UNC Chemistry Mass Spectrometry Core Laboratory) for their assistance with mass spectrometry analysis using instrumentation acquired under National Science Foundation Grant CHE-1726291.

■ REFERENCES

(1) Reviews on dynamic kinetic resolution: (a) Huerta, F. F.; Minidis, A. B. E.; Bäckvall, J.-E. Racemisation in Asymmetric Synthesis. Dynamic Kinetic Resolution and Related Processes in Enzyme and Metal Catalysis. *Chem. Soc. Rev.* **2001**, *30*, 321−331. (b) Pellissier, H. Recent Developments in Dynamic Kinetic Resolution. *Tetrahedron* **2011**, *67*, 3769−3802. (c) Bhat, V.; Welin, E. R.; Guo, X.; Stoltz, B. M. Advances in Stereoconvergent Catalysis from 2005 to 2015: Transition-Metal-Mediated Stereoablative Reactions, Dynamic Kinetic Resolutions, and Dynamic Kinetic Asymmetric Transformations. *Chem. Rev.* **2017**, *117*, 4528−4561. (d) Bartlett, S. L.; Johnson, J. S. Synthesis of Complex Glycolates by Enantioconvergent Addition Reactions. *Acc. Chem. Res.* **2017**, *50*, 2284−2296. (e) Pellissier, H. Dynamic Kinetic Resolution. *Tetrahedron* **2003**, *59*, 8291−8327. (f) Caddick, S.; Jenkins, K. Dynamic Resolutions in Asymmetric Synthesis. *Chem. Soc. Rev.* **1996**, *25*, 447−456.

(2) Select examples of DKR of β-ketoesters: (a) Noyori, R.; Ikeda, T.; Ohkuma, T.; Widhalm, M.; Kitamura, M.; Takaya, H.; Akutagawa, S.; Sayo, N.; Saito, T.; Taketomi, T.; Kumobayashi, H. Stereoselective Hydrogenation via Dynamic Kinetic Resolution. *J. Am. Chem. Soc.* **1989**, *111*, 9134−9135. (b) Genêt, J.; Pfister, X.; Ratovelomanana-

DOI: 10.1021/acscatal.9b04405
ACS Catal. 2019, 9, 11614−11618

Vidal, V.; Pinel, C.; Laffitte, J. Dynamic Kinetic Resolution of Cyclic β-Ketoesters with Preformed or Prepared in Situ Chiral Diphosphine-Ruthenium (II) Catalysts. *Tetrahedron Lett.* **1994**, *35*, 4559−4562. (c) Yang, J.; Wang, T.; Ding, Z.; Shen, Z.; Zhang, Y. Highly Diastereo- and Enantioselective Organocatalytic Addition of Acetone to β-Substituted α-Ketoesters via Dynamic Kinetic Resolution. *Org. Biomol. Chem.* **2009**, *7*, 2208−2213. (d) Cohen, D. T.; Eichman, C. C.; Phillips, E. M.; Zarefsky, E. R.; Scheidt, K. A. Catalytic Dynamic Kinetic Resolutions with N-Heterocyclic Carbenes: Asymmetric Synthesis of Highly Substituted β-Lactones. *Angew. Chem., Int. Ed.* **2012**, *51*, 7309−7313. (e) Zhang, G.; Yang, S.; Zhang, X.; Lin, Q.; Das, D. K.; Liu, J.; Fang, X. Dynamic Kinetic Resolution Enabled by Intramolecular Benzoin Reaction: Synthetic Applications and Mechanistic Insights. *J. Am. Chem. Soc.* **2016**, *138*, 7932−7938.

(3) Select examples of DKR of α-keto esters: (a) Steward, K. M.; Gentry, E. C.; Johnson, J. S. Dynamic Kinetic Resolution of α-Keto Esters via Asymmetric Transfer Hydrogenation. *J. Am. Chem. Soc.* **2012**, *134*, 7329−7332. (b) Bartlett, S. L.; Keiter, K. M.; Johnson, J. S. Synthesis of Complex Tertiary Glycolates by Enantioconvergent Arylation of Stereochemically Labile α-Keto Esters. *J. Am. Chem. Soc.* **2017**, *139*, 3911−3916.

(4) Additions to α,β-enones with thermodynamic or kinetic stereoconvergence at the α′-position: (a) Pandey, G.; Adate, P. A.; Puranik, V. G. Organocatalytic Dynamic Kinetic Resolution via Conjugate Addition: Synthesis of Chiral Trans-2,5-Dialkylcyclohexanones. *Org. Biomol. Chem.* **2012**, *10*, 8260−8267. Stereoconvergence by alkene (*E*)/(*Z*)-isomerization: (b) Misaki, T.; Tatsumi, T.; Okamoto, T.; Hayashi, Y.; Jin, N.; Sugimura, T. Stereoconvergent 1,4-Addition Reaction of 5 *H* -Oxazol-4-Ones with *E, Z* Isomeric Mixture of Alkylidene β-Ketoesters Catalyzed by Chiral Guanidines. *Chem. - Eur. J.* **2018**, *24*, 9778−9782. Stereoconvergent additions to α,β-enones by reversible ring opening: (c) Orue, A.; Uria, U.; Roca-López, D.; Delso, I.; Reyes, E.; Carrillo, L.; Merino, P.; Vicario, J. L. Racemic Hemiacetals as Oxygen-Centered Pronucleophiles Triggering Cascade 1,4-Addition/Michael Reaction through Dynamic Kinetic Resolution under Iminium Catalysis. Development and Mechanistic Insights. *Chem. Sci.* **2017**, *8*, 2904−2913.

(5) Lima, C. G. S.; Monteiro, J. L.; de Melo Lima, T.; Weber Paixão, M.; Corrêa, A. G. Angelica Lactones: From Biomass-Derived Platform Chemicals to Value-Added Products. *ChemSusChem* **2018**, *11*, 25−47.

(6) (a) Mao, B.; Fañanás-Mastral, M.; Feringa, B. L. Catalytic Asymmetric Synthesis of Butenolides and Butyrolactones. *Chem. Rev.* **2017**, *117*, 10502−10566. (b) Seitz, M.; Reiser, O. Synthetic Approaches towards Structurally Diverse γ-Butyrolactone Natural-Product-like Compounds. *Curr. Opin. Chem. Biol.* **2005**, *9*, 285−292.

(7) (a) Panfil, I.; Abramski, W.; Chmielewski, M. Conjugate Addition of Hydroxylamines to 4-Subtituted Butenolides. *J. Carbohydr. Chem.* **1998**, *17*, 1395−1403. See also: (b) Wu, Y.; Singh, R. P.; Deng, L. Asymmetric Olefin Isomerization of Butenolides via Proton Transfer Catalysis by an Organic Molecule. *J. Am. Chem. Soc.* **2011**, *133*, 12458−12461. (c) Sorg, A.; Blank, F.; Brückner, R. Stepwise Cross-Couplings of a Dibromo-γ-Methylenebutenolide as an Access to *Z* -Configured α-Alkenyl-γ-Alkylidenebutenolides. Straightforward Synthesis of the Antibiotic Lissoclinolide. *Synlett* **2005**, *2005*, 1286−1290. (d) Jones, C. R.; Greenhalgh, M. D.; Bame, J. R.; Simpson, T. J.; Cox, R. J.; Marshall, J. W.; Butts, C. P. Subtle Temperature-Induced Changes in Small Molecule Conformer Dynamics − Observed and Quantified by NOE Spectroscopy. *Chem. Commun.* **2016**, *52*, 2920−2923. (e) Lindström, M.; Hedenström, E.; Bouilly, S.; Velonia, K.; Smonou, I. Synthesis of Diastereo- and Enantiomerically Pure Anti-3-Methyl-1,4-Pentanediol via Lipase Catalysed Acylation. *Tetrahedron: Asymmetry* **2005**, *16*, 1355−1360. (f) Zhou, L.; Lin, L.; Ji, J.; Xie, M.; Liu, X.; Feng, X. Catalytic Asymmetric Vinylogous Mannich-Type (AVM) Reaction of Non-activated α-Angelica Lactone. *Org. Lett.* **2011**, *13*, 3056−3059. (g) Newland, M. J.; Rea, G. J.; Thüner, L. P.; Henderson, A. P.; Golding, B. T.; Rickard, A. R.; Barnes, I.; Wenger, J. Photochemistry of 2-Butenedial and 4-Oxo-2-Pentenal under Atmospheric Boundary Layer Conditions. *Phys. Chem. Chem. Phys.* **2019**, *21*, 1160−1171. (h) Mathews, C. J.; Taylor, J.; Tyte, M. J.; Worthington, P. A. Microwave Assisted Suzuki Reactions for the Preparation of the Antifungal 3-Aryl-5-Methyl-2,5-Dihydrofuran-2-ones. *Synlett* **2005**, *2005*, 538−540.

(8) Select examples of diastereoselective conjugate addition to γ-substituted α,β-unsaturated butenolides: (a) Harcken, C.; Brückner, R. Synthesis of Optically Active Butenolides and γ-Lactones by the Sharpless Asymmetric Dihydroxylation Of β,γ-Unsaturated Carboxylic Esters. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2750−2752. (b) Navarro, C.; Moreno, A.; Csákÿ, A. G. Stereoselective Rhodium-Catalyzed Conjugate Addition of Boronic Acids to Unprotected δ-Hydroxy-γ-butenolides. Synthesis of (−)-7-Oxamuricatacin and β-Substituted Derivatives. *J. Org. Chem.* **2009**, *74*, 466−469. (c) Mao, B.; Geurts, K.; Fañanás-Mastral, M.; van Zijl, A. W.; Fletcher, S. P.; Minnaard, A. J.; Feringa, B. L. Catalytic Enantioselective Synthesis of Naturally Occurring Butenolides via Hetero-Allylic Alkylation and Ring Closing Metathesis. *Org. Lett.* **2011**, *13*, 948−951. (d) Koschker, P.; Kähny, M.; Breit, B. Enantioselective Redox-Neutral Rh-Catalyzed Coupling of Terminal Alkynes with Carboxylic Acids toward Branched Allylic Esters. *J. Am. Chem. Soc.* **2015**, *137*, 3131−3137.

(9) Al-Shaal, M. G.; Ciptonugroho, W.; Holzhäuser, F. J.; Mensah, J. B.; Hausoul, P. J. C.; Palkovits, R. Catalytic Upgrading of α-Angelica Lactone to Levulinic Acid Esters under Mild Conditions over Heterogeneous Catalysts. *Catal. Sci. Technol.* **2015**, *5*, 5168−5173.

(10) Chen, T.; Qin, Z.; Qi, Y.; Deng, T.; Ge, X.; Wang, J.; Hou, X. Degradable Polymers from Ring-Opening Polymerization of α-Angelica Lactone, a Five-Membered Unsaturated Lactone. *Polym. Chem.* **2011**, *2*, 1190−1194.

(11) Mascal, M.; Dutta, S.; Gandarias, I. Hydrodeoxygenation of the Angelica Lactone Dimer, a Cellulose-Based Feedstock: Simple, High-Yield Synthesis of Branched C_7 -C_{10} Gasoline-like Hydrocarbons. *Angew. Chem., Int. Ed.* **2014**, *53*, 1854−1857.

(12) Luo, Y.; Carnell, A. J. Chemoenzymatic Synthesis and Application of Bicyclo[2.2.2]Octadiene Ligands: Increased Efficiency in Rhodium-Catalyzed Asymmetric Conjugate Additions by Electronic Tuning. *Angew. Chem., Int. Ed.* **2010**, *49*, 2750−2754.

(13) Hayashi, T.; Takahashi, M.; Takaya, Y.; Ogasawara, M. Catalytic Cycle of Rhodium-Catalyzed Asymmetric 1,4-Addition of Organoboronic Acids. Arylrhodium, Oxa-π-Allylrhodium, and Hydroxorhodium Intermediates. *J. Am. Chem. Soc.* **2002**, *124*, 5052−5058.

(14) Itooka, R.; Iguchi, Y.; Miyaura, N. Rhodium-Catalyzed 1,4-Addition of Arylboronic Acids to α,β-Unsaturated Carbonyl Compounds: Large Accelerating Effects of Bases and Ligands. *J. Org. Chem.* **2003**, *68*, 6000−6004.

(15) CCDC 1918980 (**3j**), CCDC 1919324 (**3g**), and CCDC 1920098 (**3q**) contain the supplementary crystallographic data for this paper. This data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

(16) Takaya, Y.; Ogasawara, M.; Hayashi, T.; Sakai, M.; Miyaura, N. Rhodium-Catalyzed Asymmetric 1,4-Addition of Aryl- and Alkenylboronic Acids to Enones. *J. Am. Chem. Soc.* **1998**, *120*, 5579−5580.

(17) Takaya, Y.; Senda, T.; Kurushima, H.; Ogasawara, M.; Hayashi, T. Rhodium-Catalyzed Asymmetric 1,4-Addition of Arylboron Reagents to α,β-Unsaturated Esters. *Tetrahedron: Asymmetry* **1999**, *10*, 4047−4056.

(18) Gross, A.; Borcherding, D. R.; Friedrich, D.; Sabol, J. S. A Stereocontrolled Approach to Substituted Piperidones and Piperidines: Flavopiridol D-Ring Analogs. *Tetrahedron Lett.* **2001**, *42*, 1631−1633.

DOI: 10.1021/acscatal.9b04405
ACS Catal. 2019, 9, 11614−11618