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N-Heterocyclic Carbene Catalyzed Dynamic Kinetic Resolution of Pyranones

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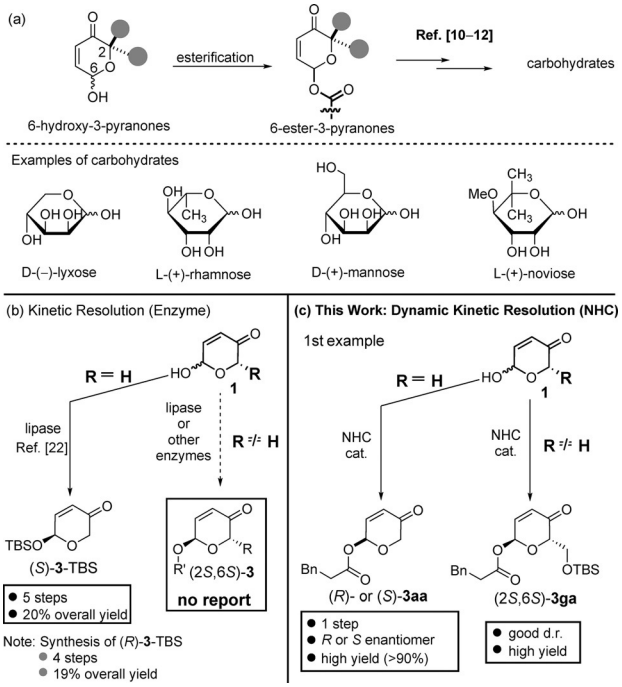
Abstract: *The dynamic kinetic resolution of 6-hydroxypyranones with enals or alkynals through an asymmetric redox esterification is catalyzed by a chiral N-heterocyclic carbene. The resulting esters are obtained in good to high yields and with high levels of enantio- and diastereocontrol. The reaction products are further derivatized to obtain functionalized sugar derivatives and natural products.*

N-Heterocyclic carbene (NHC) catalysis has emerged as a powerful method for the catalytic construction of various intermediates that can be utilized in the assembly of biologically or medicinally important chiral scaffolds.[1] Although significant progress has been made, examples of NHC-catalyzed dynamic kinetic resolution (DKR) reactions[2–5] are still rare. In 2012, Scheidt and co-workers reported the intramolecular NHC-catalyzed DKR of β-keto esters.[6] In 2014, Johnson et al. reported an NHC-catalyzed asymmetric cross-benzoin reaction of β-halo-α-keto esters and aldehydes.[7] Shortly after, NHC-catalyzed [3+2] and [4+2] annulations by DKR were independently reported by Johnson[8] and co-workers and our group.[9a] To the best of our knowledge, NHC-catalyzed DKR reactions of hemiacetals have not been reported to date. As part of our studies in this area,[9] we wish to disclose a novel NHC-catalyzed DKR of hemiacetals, which generates enantioenriched pyranone precursors for the synthesis of carbohydrates or application in glycochemistry (Scheme 1c).

Inspired by the role of 6-hydroxy-3-pyranones as key intermediates for carbohydrate synthesis,[10] O'Doherty[11] and co-workers have disclosed an elegant palladium-catalyzed stereospecific glycosidation[11–13] of 3-pyranones with an ester substituent in the 5-position (Scheme 1a) for assembling diversified libraries[14] and complex natural products.[15] Because of the significance of pyranones with a substituent (e.g., esters) in the 6-position, many efforts have been devoted to the manipulation of the hemiacetal group of pyranones, for example, by the protection or oxidation of the hemiacetal group.[16] However, most transformations involving the anomeric center have not been highly stereoselective.



Scheme 1. a) Pyranones as important building blocks in carbohydrate synthesis. b) Enzymatic kinetic resolution. c) NHC-catalyzed dynamic kinetic resolution.

In 2000, Sugawara and co-workers reported a method to generate enantiomerically pure (*R*)- or (*S*)-6-*tert*-butyldimethylsiloxy-3-pyranones ((*R*)-**3**-TBS or (*S*)-**3**-TBS) by lipase-catalyzed resolution.[17] Although the two enantiomers were obtained eventually, tedious synthetic steps were required, and only low chemical yields were achieved (Scheme 1b, R = H; (*S*)-**3**-TBS: 5 steps, 20%; (*R*)-**3**-TBS: 4 steps, 19%). Most importantly, an enzymatic resolution of the widely used racemic 2-substituted 3-pyranone synthons has not been reported to date (Scheme 1b, R ≠ H). Herein, we describe the first NHC-catalyzed dynamic kinetic resolution of 6-hydroxy-3-pyranones. A broad range of 2-substituted 6-hydroxy-3-pyranones were suitable substrates of this process and converted with good diastereoselectivity (Scheme 1c, R ≠ H).

Experimentally, we set out to achieve a DKR process with **2a** and **1a** as the model substrates. Key optimization results are summarized in Table 1. Chiral triazolium NHC catalysts with an *N*-mesityl (Mes) substituent (**A** and **B**)[18] and a backbone derived from α-amino acids were initially tested in combination with $CHCl_3$ and NaOAc as the solvent and base, respectively. The use of L-phenylalanine-derived catalyst **A** yielded the desired product **3aa** in 33% yield and

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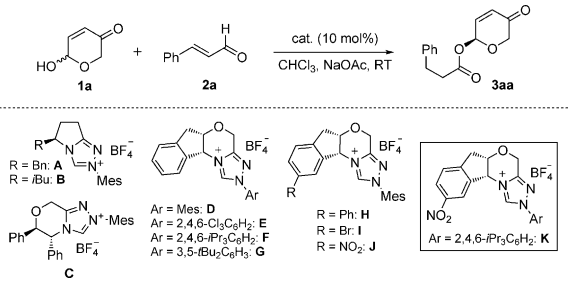
Table 1: Optimization of the reaction conditions.[a]



Entry	Catalyst	*t* [h]	Yield[b] [%]	e.r.[c]
1	**A**	36	33	−61:39
2	**B**	24	60	−70:30
3	**C**	48	85	50:50
4	**D**	48	90	82:18
5	**E**	24	90	−71:29
6	**F**	36	75	83:17
7	**G**	72	36	80:20
8	**H**	12	85	80:20
9	**I**	12	74	82:18
10	**J**	12	80	83:17
11	**K**	12	89	92:8
12[d]	**K**	3	98	91:9
13[e]	**K**	**48**	**90**	**95:5**

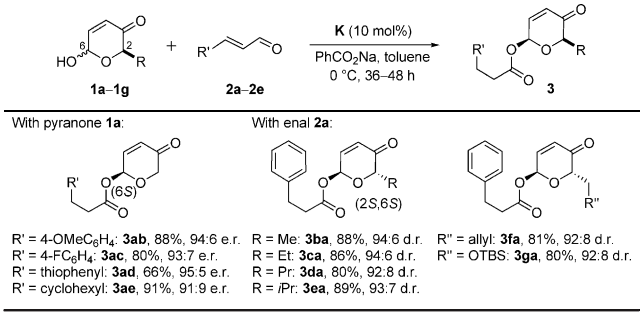
[a] Reaction conditions: A mixture of **1a** (0.20 mmol), **2a** (0.24 mmol), NaOAc (0.4 mmol), and the indicate catalyst (10 mol%) in $CHCl_3$ (2.0 mL) was stirred at room temperature. [b] Yield of isolated product. [c] Determined by HPLC analysis on a chiral stationary phase. [d] Toluene (2.0 mL), $PhCO_2Na$ (0.4 mmol). [e] Toluene (2.0 mL), $PhCO_2Na$ (0.4 mmol), 0°C.

a moderate enantiomeric ratio (entry 1, −61:39 e.r.). Use of the more bulky catalyst **B**,[19] which was prepared from L-*tert*-leucine, gave a better e.r. (entry 2, −70:30 e.r., 60% yield). Disappointingly, no enantioselectivity was observed when the morpholinone-derived triazolium catalyst **C**[20] was employed (entry 3).

Given the importance of structural diversification for the success of a given catalytic transformation, access to a wide variety of catalyst structures is crucial.[21] We herein investigated indanol-derived triazolium scaffolds.[22] A series of indanol-derived N-substituted triazolium catalysts (**D**–**G**) were synthesized and then used in the model reaction (Table 1). Pleasingly, enhanced enantioselectivity was achieved with the *N*-mesityl- or *N*-2,4,6-$iPr_3C_6H_2$-substituted triazolium catalysts **D** and **F** (entries 4 and 6). Building upon these findings, we next tested the impact of the R substituent on the triazolium scaffold (**H**–**J**). Catalyst **J**, which bears a strongly electron-withdrawing R group, not only led to good e.r. values (83:17), but also showed high catalytic activity (entry 10, 80%, 12 h). Gratifyingly, a new indanol-derived triazolium catalyst **K**, which bears a nitro group at a remote aryl position and a bulky 2,4,6-$iPr_3C_6H_2$ substituent on the nitrogen atom, performed even better (entry 11, 89%, 92:8 e.r., 12 h). Then, a variety of solvents and bases were tested, and a combination of toluene and $PhCO_2Na$ was found to be the best choice, leading to the desired product with good enantioselectivity and conversion (entry 12, 89%, 91:9 e.r., 3 h). Lowering the temperature to 0°C further improved the enantioselectivity (entry 13, 95:5 e.r.). Therefore, the reaction conditions shown in entry 13 were identified as the optimized conditions.

With the optimized reaction conditions in hand, we turned our attention to the generality of this DKR process. Both electron-donating and electron-withdrawing aryl substituents in the β-position of the enal were well tolerated (**3ab** and **3ac**; Table 2). Replacement of the β-aryl moiety with a heteroaryl

Table 2: Reaction of pyranones **1** with enals **2**.[a]



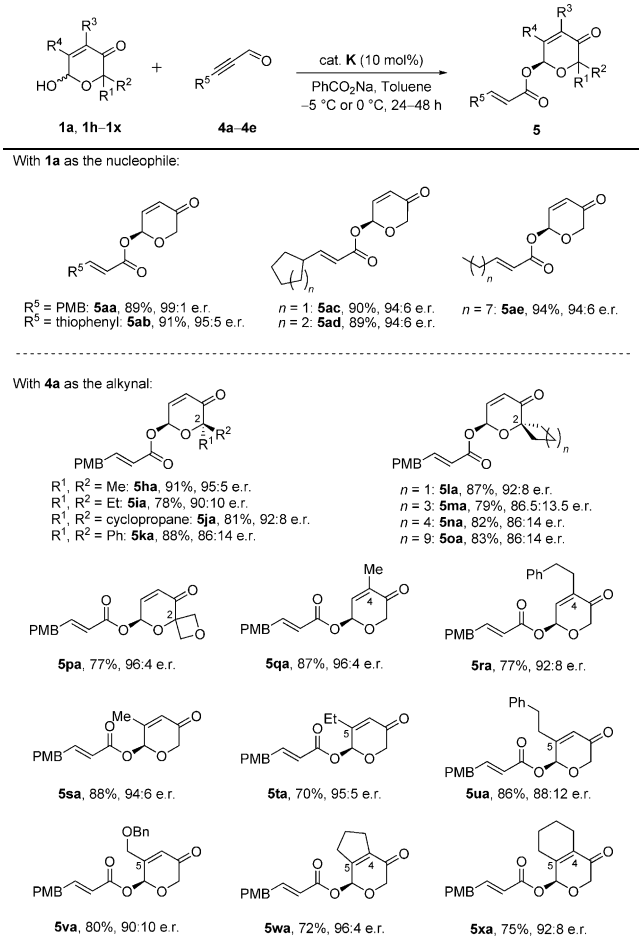
[a] Reaction conditions: **1** (0.20 mmol), **2** (0.24 mmol), $PhCO_2Na$ (0.4 mmol), **K** (10 mol%), toluene (2 mL), 0°C, 36–48 h.

(**3ad**) or alkyl (**3ae**) substituent had little effect on the outcome of the reaction. To further demonstrate the generality of this reaction, several 2-substituted 6-hydroxypyranones were examined. As shown in Table 2, pyranones with various 2-alkyl substituents gave the corresponding 2,6-disubstituted pyranones **3ba**–**3ga** in good yields and diastereoselectivities.[23]

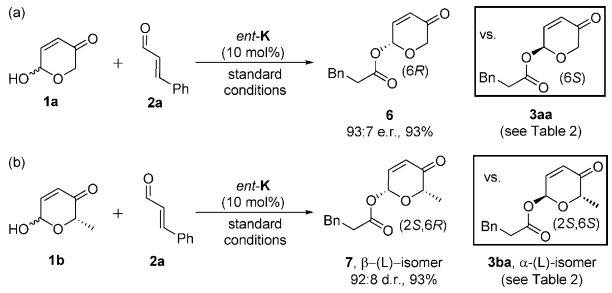
Encouraged by our success with enals, other classes of aldehydes were investigated. To our delight, the reaction was well compatible with alkynals. As shown in Table 3, alkynals with (hetero)aryl or alkyl substituents all gave the corresponding products in high yields and with good enantioselectivities (**5aa**–**5ae**). In particular, alkynal **4a**, with a *para*-methoxybenzyl (PMB) substituent, afforded the desired product **5aa** in 90% yield and with 99:1 e.r. When 2,2-disubstituted 6-hydroxy-3-pyranones were used, good enantioselectivities and excellent *E*/*Z* ratios were generally achieved (**5ha**–**5ka**). With a spirocycle attached to the C2 position, the corresponding products were still obtained in good yields and high enantioselectivities (**5la**–**5pa**). Furthermore, incorporation of substituents at the 4- and/or 5-position had little impact on the formation of the corresponding products **5qa**–**5xa**.

Access to the another enantiomer or isomer of these pyranone analogues will be essential to advance carbohydrate synthesis.[24] Enzymatic resolution and column chromatography can be used to synthesize the other enantiomer, (*R*)-**3**-TBS, but resulted in a low yield (Scheme 1b; 4 steps, 19% overall yield). Herein, we could conveniently prepare the appropriate enantiomer **6** by just utilizing the enantiomeric NHC catalyst (Scheme 2a; 1 step, 93:7 e.r., 93% yield). Moreover, β-L-isomer **7** was synthesized from **1b** and **2a** with catalyst *ent*-**K** in good diastereoselectivity and excellent yield (Scheme 2b; 92:8 d.r., 93%).

Table 3: Reaction of pyranones **1** with alkynals **4**.[a]



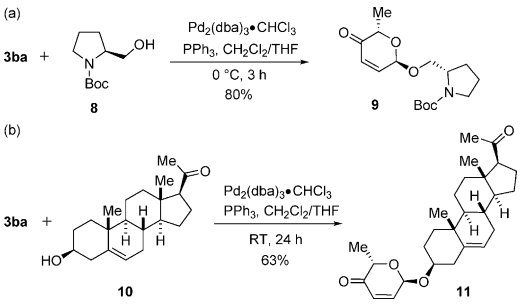
[a] Reaction conditions: **1** (0.20 mmol), **4** (0.22 mmol), $PhCO_2Na$ (0.4 mmol), **K** (10 mol%), toluene (2.0 mL), −5 °C or 0 °C, 24–48 h. The *E*/*Z* ratios were determined by ^{1}H NMR spectroscopy and were >20:1 for all products. PMB = *para*-methoxybenzyl.



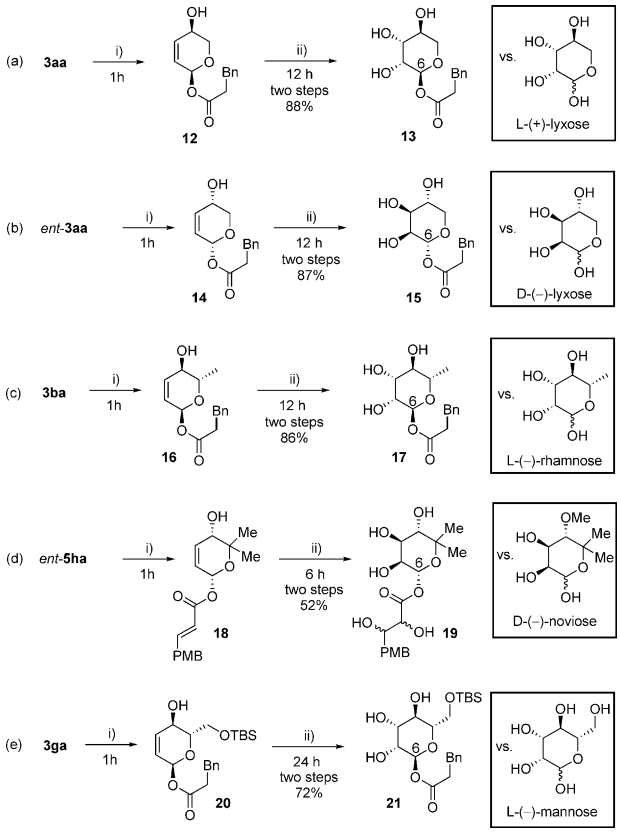
Scheme 2. Synthesis of (*R*)-**6** and **7**.

To synthesize functional sugar derivatives, we turned to glycosidation. As shown in Scheme 3, pyranone **3ba** could be reacted with chiral prolinol **8** or chiral pregnenolone **10** to generate the biologically important glycosides **9** or **11** in a straightforward palladium-catalyzed glycosylation process.[12,13]

Importantly, these enantiopure pyranones are very useful feedstocks for carbohydrates. For examples, pyranone **3aa** was converted into L-lyxose **13** in two steps through reduction



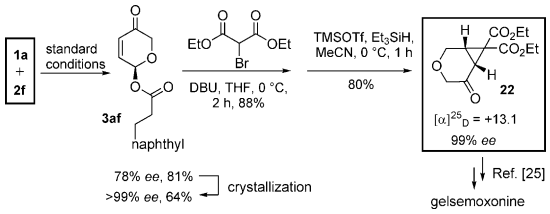
Scheme 3. Product **3ba** was converted into a) prolinol glycoside **9** and b) pregnenolone glycoside **11**. Boc = *tert*-butyloxycarbonyl, dba = dibenzylideneacetone.



Scheme 4. Synthesis of selected carbohydrates. Conditions: i) $NaBH_4$ (1.1 equiv), $CeCl_3$ (1.0 equiv), $MeOH/CH_2Cl_2$ (1:1, v/v), −78 °C; ii) *N*-methylmorpholine *N*-oxide (NMO, 1.0 mL mmol^{-1}), OsO_4 (0.05 equiv), *t*BuOH/acetone (1:1, v/v), RT.

and dihydroxylation (Scheme 4a; 88% over 2 steps). Lyxose **13** has an ester substituent at the 6-position, which could be used to assemble glycans through glycosidation. The same strategy was applied to generate D-lyxose **15** from *ent*-**3aa** (Scheme 4b; 87% over 2 steps). Pleasingly, desmethyl-D-noviose **19** could be synthesized from intermediate **18** (Scheme 4d; 52% overall yield). Furthermore, **3ba** and **3ga** were successfully converted into the sugar derivatives α-L-rhamnose **17** and α-L-mannose **21** in two steps with overall yields of 85% and 72%, respectively (Scheme 4c and e).

To further showcase the synthetic utility of this transformation, we wished to rapidly synthesize some key inter-



Scheme 5. Enantioselective synthesis of key intermediate **22**. DBU = 1,8-diazabicyclo[5.4.0]undec-7-ene, Tf = trifluoromethanesulfonyl, TMS = trimethylsilyl.

mediates of natural products. As highlighted in Scheme 5, the key intermediate **22** could be obtained in good chemical yield through a three-step sequence (for synthetic details, see the Supporting Information). On the basis of **22**, Fukuyama et al. have successfully completed the total synthesis of gelsemoxonine (Scheme 5).[25] The absolute configuration of **3af** was determined by comparing the optical rotation of **22** with values reported in the literature, and the configurations of the other products were assigned by analogy.[25,26]

In conclusion, we have developed a novel NHC-catalyzed dynamic kinetic resolution process. A variety of 6-substituted 3-pyranones were obtained in high diastereo- and enantioselectivity. The synthetic potential of this DKR process was demonstrated by concise syntheses of sugar derivatives. Further studies on complexity-generating dynamic processes are ongoing in our laboratory.

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Angew. Chem. **2016**, *128*, 1852–1856

[1] For selected reviews on NHC catalysis, see: a) K. Zeitler, *Angew. Chem. Int. Ed.* **2005**, *44*, 7506; *Angew. Chem.* **2005**, *117*, 7674; b) D. Enders, O. Niemeier, A. Henseler, *Chem. Rev.* **2007**, *107*, 5606; c) N. Marion, S. Diez-González, S. P. Nolan, *Angew. Chem. Int. Ed.* **2007**, *46*, 2988; *Angew. Chem.* **2007**, *119*, 3046; d) V. Nair, S. Vellalath, B. P. Babu, *Chem. Soc. Rev.* **2008**, *37*, 2691; e) E. M. Phillips, A. Chan, K. A. Scheidt, *Aldrichimica Acta* **2009**, *42*, 55; f) J. L. Moore, T. Rovis, *Top. Curr. Chem.* **2010**, *291*, 77; g) A. T. Biju, N. Kuhl, F. Glorius, *Acc. Chem. Res.* **2011**, *44*, 1182; h) K. Hirano, I. Piel, F. Glorius, *Chem. Lett.* **2011**, *40*, 786; i) P.-C. Chiang, J. W. Bode, *TCI MAIL* **2011**, *149*, 2; j) V. Nair, R. S. Menon, A. T. Biju, C. R. Sinu, R. R. Paul, A. Jose, V. Sreekumar, *Chem. Soc. Rev.* **2011**, *40*, 5336; k) Z. Q. Rong, W. Zhang, G. Q. Yang, S.-L. You, *Curr. Org. Chem.* **2011**, *15*, 3077; l) H. U. Vora, T. Rovis, *Aldrichimica Acta* **2011**, *44*, 3; m) D. T. Cohen, K. A. Scheidt, *Chem. Sci.* **2012**, *3*, 53; n) X. Bugaut, F. Glorius, *Chem. Soc. Rev.* **2012**, *41*, 3511; o) A. Grossmann, D. Enders, *Angew. Chem. Int. Ed.* **2012**, *51*, 314; *Angew. Chem.* **2012**, *124*, 320; p) J. Douglas, G. Churchill, A. D. Smith, *Synthesis* **2012**, 2295; q) J. Izquierdo, G. E. Hutson, D. T. Cohen, K. A. Scheidt, *Angew. Chem. Int. Ed.* **2012**, *51*, 11686; *Angew. Chem.* **2012**, *124*, 11854; r) S. J. Ryan, L. Candish, D. W. Lupton, *Chem. Soc. Rev.* **2013**, *42*, 4906; s) S. De Sarkar, A. Biswas, R. C. Samanta, A. Studer, *Chem. Eur. J.* **2013**, *19*, 4664; t) S. J. Connon, *Angew. Chem. Int. Ed.* **2014**, *53*, 1203; *Angew. Chem.* **2014**, *126*, 1225; u) J. Mahatthananchai, J. W. Bode, *Acc. Chem. Res.* **2014**, *47*, 696; v) M. N. Hopkinson, C. Richter, M. Schedler, F. Glorius, *Nature* **2014**, *510*, 485; w) M. Binanzer, S.-Y. Hsieh, J. W. Bode, *J. Am. Chem. Soc.* **2011**, *133*, 19698; x) Z. Fu, J. Xu, T. Zhu, W. Leong, Y. R. Chi, *Nat. Chem.* **2013**, *5*, 835; y) K. Namitharan, T. Zhu, J. Cheng, P. Zhang, X. Li, S. Yang, B.-A. Song, Y. R. Chi, *Nat. Commun.* **2014**, *5*, 1982; z) D. M. Flanigan, F. Romanov-Michailidis, N. A. White, T. Rovis, *Chem. Rev.* **2015**, *115*, 9307.

[2] For reviews on DKR processes, see: a) R. Noyori, M. Tokunaga, M. Kitamura, *Bull. Chem. Soc. Jpn.* **1995**, *68*, 36; b) S. Caddick, K. Jenkins, *Chem. Soc. Rev.* **1996**, *25*, 447; c) F. F. Huerta, A. B. E. Minidis, J.-E. Bäckvall, *Chem. Soc. Rev.* **2001**, *30*, 321; d) J. Steinreiber, K. Faber, H. Griengl, *Chem. Eur. J.* **2008**, *14*, 8060.

[3] For examples of metal- and/or enzyme-catalyzed dynamic kinetic resolution reactions, see: a) B. M. Trost, F. D. Toste, *J. Am. Chem. Soc.* **1999**, *121*, 3543; b) B. M. Trost, N. G. Andersen, *J. Am. Chem. Soc.* **2002**, *124*, 14320; c) B. Martín-Matute, M. Edin, K. Bogár, F. B. Kaynak, J.-E. Bäckvall, *J. Am. Chem. Soc.* **2005**, *127*, 8817; d) M. P. Rainka, J. E. Milne, S. L. Buchwald, *Angew. Chem. Int. Ed.* **2005**, *44*, 6177; *Angew. Chem.* **2005**, *117*, 6333; e) J. Paetzold, J.-E. Bäckvall, *J. Am. Chem. Soc.* **2005**, *127*, 17620.

[4] For selected organocatalytic dynamic kinetic resolution reactions, see: a) J. Liang, J. C. Ruble, G. C. Fu, *J. Org. Chem.* **1998**, *63*, 3154; b) L. Tang, L. Deng, *J. Am. Chem. Soc.* **2002**, *124*, 2870; c) M. P. Lalonde, Y. Chen, E. N. Jacobsen, *Angew. Chem. Int. Ed.* **2006**, *45*, 6366; *Angew. Chem.* **2006**, *118*, 6514; d) X. Yang, V. B. Birman, *Angew. Chem. Int. Ed.* **2011**, *50*, 5553; *Angew. Chem.* **2011**, *123*, 5667; e) S. Hoffmann, M. Nicoletti, B. List, *J. Am. Chem. Soc.* **2006**, *128*, 13074; f) J. W. Evans, M. B. Fierman, S. J. Miller, J. A. Ellman, *J. Am. Chem. Soc.* **2004**, *126*, 8134; g) J. L. Gustafson, D. Lim, S. J. Miller, *Science* **2010**, *328*, 1251.

[5] For selected organocatalytic kinetic resolution processes via chiral acyl azolium ions, see: a) T. Kano, K. Sasaki, K. Maruoka, *Org. Lett.* **2005**, *7*, 1347; b) S. Lu, S. B. Poh, W.-Y. Siau, Y. Zhao, *Angew. Chem. Int. Ed.* **2013**, *52*, 1731; *Angew. Chem.* **2013**, *125*, 1775; c) S. Lu, S. B. Poh, Y. Zhao, *Angew. Chem. Int. Ed.* **2014**, *53*, 11041; *Angew. Chem.* **2014**, *126*, 11221; d) S. E. Allen, S.-Y. Hsieh, O. Gutierrez, J. W. Bode, M. C. Kozlowski, *J. Am. Chem. Soc.* **2014**, *136*, 11783; and Ref. [1w].

[6] a) D. T. Cohen, C. C. Eichman, E. M. Phillips, E. R. Zarefsky, K. A. Scheidt, *Angew. Chem. Int. Ed.* **2012**, *51*, 7309; *Angew. Chem.* **2012**, *124*, 7421; b) R. C. Johnston, D. T. Cohen, C. C. Eichman, K. A. Scheidt, P. H.-Y. Cheong, *Chem. Sci.* **2014**, *5*, 1974.

[7] C. G. Goodman, J. S. Johnson, *J. Am. Chem. Soc.* **2014**, *136*, 14698.

[8] C. G. Goodman, M. M. Walker, J. S. Johnson, *J. Am. Chem. Soc.* **2015**, *137*, 122.

[9] a) Z. J. Wu, F. Y. Li, J. Wang, *Angew. Chem. Int. Ed.* **2015**, *54*, 1629; *Angew. Chem.* **2015**, *127*, 1649; b) F. Y. Li, Z. J. Wu, J. Wang, *Angew. Chem. Int. Ed.* **2015**, *54*, 656; *Angew. Chem.* **2015**, *127*, 666; c) Z. J. Wu, X. Wang, F. Y. Li, J.-C. Wu, J. Wang, *Org. Lett.* **2015**, *17*, 3588.

[10] For selected examples, see: a) O. Achmatowicz, Jr., P. Bukowski, *Can. J. Chem.* **1975**, *53*, 2524; b) O. Achmatowicz, B. Szechner, *Carbohydr. Res.* **1976**, *50*, 23; c) R. Bognár, P. Herczegh, *Carbohydr. Res.* **1976**, *52*, 11; d) N. L. Holder, *Chem. Rev.* **1982**,

82, 287; e) M. Takeuchi, T. Taniguchi, K. Ogasawara, *Synthesis* **1999**, 341; f) A. Ortiz, T. Benkovics, G. L. Beutner, Z. Shi, M. Bultman, J. Nye, C. Sfouggatakis, D. R. Kronenthal, *Angew. Chem. Int. Ed.* **2015**, *54*, 7185; *Angew. Chem.* **2015**, *127*, 7291; g) H.-Y. Wang, K. Yang, S. R. Bennett, S.-R. Guo, W. Tang, *Angew. Chem. Int. Ed.* **2015**, *54*, 8756; *Angew. Chem.* **2015**, *127*, 8880.

[11] a) R. S. Babu, G. A. O'Doherty, *J. Am. Chem. Soc.* **2003**, *125*, 12406; b) R. S. Babu, M. Zhou, G. A. O'Doherty, *J. Am. Chem. Soc.* **2004**, *126*, 3428; c) H. Guo, G. A. O'Doherty, *Angew. Chem. Int. Ed.* **2007**, *46*, 5206; *Angew. Chem.* **2007**, *119*, 5298; d) R. S. Babu, Q. Chen, S.-W. Kang, M. Zhou, G. A. O'Doherty, *J. Am. Chem. Soc.* **2012**, *134*, 11952; e) M. Zhou, G. A. O'Doherty, *Curr. Top. Med. Chem.* **2008**, *8*, 114.

[12] A. C. Comely, R. Eelkema, A. J. Minnaard, B. L. Feringa, *J. Am. Chem. Soc.* **2003**, *125*, 8714.

[13] X. Li, J. Zhu, *J. Carbohydr. Chem.* **2012**, *31*, 284.

[14] M. D. Burke, E. M. Berger, S. L. Schreiber, *Science* **2003**, *302*, 613.

[15] For a recent review, see: K. E. O. Ylijoki, J. M. Stryker, *Chem. Rev.* **2013**, *113*, 2244.

[16] a) J. M. Harris, G. A. O'Doherty, *Tetrahedron Lett.* **2000**, *41*, 183; b) L. Z. Zhu, A. Talukdar, G. S. Zhang, J. P. Kedenburg, P. G. Wang, *Synlett* **2005**, 1547.

[17] K. Sugawara, Y. Imanishi, T. Hashiyama, *Tetrahedron: Asymmetry* **2000**, *11*, 4529.

[18] R. L. Knight, F. J. Leeper, *Tetrahedron Lett.* **1997**, *38*, 3611.

[19] P. Chiang, M. Rommel, J. W. Bode, *J. Am. Chem. Soc.* **2009**, *131*, 8714.

[20] a) A. Chan, K. A. Scheidt, *Org. Lett.* **2005**, *7*, 905; b) A. Chan, K. A. Scheidt, *J. Am. Chem. Soc.* **2007**, *129*, 5334.

[21] a) T. Rovis, *Chem. Lett.* **2008**, *37*, 2; b) J. Mahatthananchai, J. W. Bode, *Chem. Sci.* **2012**, *3*, 192.

[22] a) M. S. Kerr, J. Read de Alaniz, T. Rovis, *J. Org. Chem.* **2005**, *70*, 5725; b) M. He, J. R. Struble, J. F. Bode, *J. Am. Chem. Soc.* **2006**, *128*, 8418; c) K. E. Ozboya, T. Rovis, *Synlett* **2014**, 2665; d) M. S. Kerr, J. Read de Alaniz, T. Rovis, *J. Am. Chem. Soc.* **2002**, *124*, 10298; e) D. A. DiRocco, K. M. Oberg, D. M. Dalton, T. Rovis, *J. Am. Chem. Soc.* **2009**, *131*, 10872.

[23] The diastereomeric ratio (d.r.) was determined by ^{1}H NMR analysis of the crude products.

[24] B. Lepenies, J. Yin, P. H. Seeberger, *Curr. Opin. Chem. Biol.* **2010**, *14*, 404.

[25] J. Shimokawa, T. Harada, S. Yoloshima, T. Fukuyama, *J. Am. Chem. Soc.* **2011**, *133*, 17634.

[26] This experiment: $[\alpha]_D^{25}$ of compound **22**: +13.1 ($c = 1.0$, $CHCl_3$); literature data: $[\alpha]_D^{22}$ of compound **22**: +11.4 ($c = 1.0$, $CHCl_3$); see Ref. [25].

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