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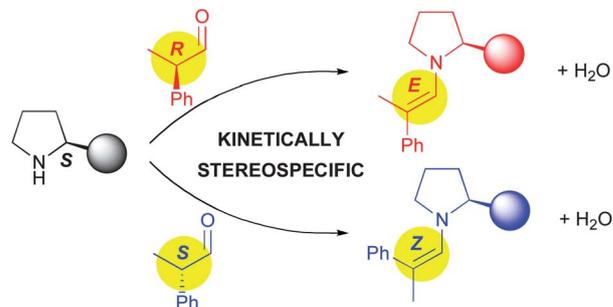
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Kinetic correlation between aldehyde/enamine stereoisomers in reactions between aldehydes with α -stereocenters and chiral pyrrolidine-based catalysts

Jordi Bures, Alan Armstrong and Donna G. Blackmond*

Reaction between aldehydes with α -stereocenters and pyrrolidine-based catalysts leads to “kinetically stereospecific” formation of *E* and *Z* enamines.



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Kinetic correlation between aldehyde/enamine stereoisomers in reactions between aldehydes with α -stereocenters and chiral pyrrolidine-based catalysts†

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The formation of enamines between aldehydes with α -stereocenters and pyrrolidine-based catalysts that lack an acidic proton is examined by kinetic and spectroscopic studies. The reaction exhibits “kinetic stereospecificity” in that each enantiomer of the aldehyde initially reacts to form a specific enamine stereoisomer, prior to thermodynamic equilibration of the *E* and *Z* enamines. For the case of proline catalysts, each of the stereoisomeric enamines is correlated with a specific stereoisomeric oxazolidinone. The reactions of *E* and *Z* enamines with electrophiles such as DEAD lead to products of opposite stereochemistry. The product enantioselectivity observed depends on the extent to which the *E* and *Z* enamines are pre-equilibrated prior to reaction with the electrophile. General implications for selectivity in organocatalytic reactions are discussed.

Introduction

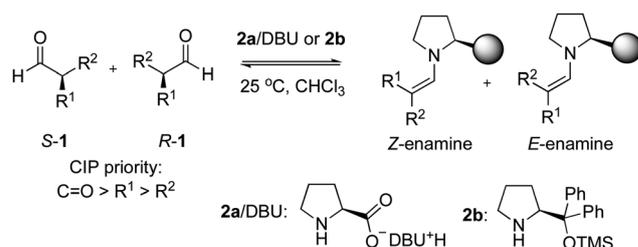
Enamine formation is a key step in a wide variety of organocatalytic reactions.¹ The experimental detection of these intermediates in pyrrolidine-based catalytic reactions remained elusive, however, until Gschwind and coworkers² demonstrated the application of NMR methodology³ allowing quantitative identification and temporal monitoring of enamines. We recently carried out kinetic, spectroscopic and computational studies of the formation of enamine carboxylates between linear aldehydes and proline catalysts either pre-formed or formed *in situ* from proline in the presence of a base.^{4,5} Because of the synthetic importance of molecules with quaternary stereocenters, we began to focus on applying these tools to probe organocatalytic intermediates formed from aldehydes with α -stereocenters.⁶ We report here several examples of unusual experimental observations in organocatalytic reactions involving enamines from α,α -disubstituted aldehydes and catalysts that lack the acidic proton of proline, demonstrating that the formation and reaction of stereoisomeric enamines is kinetically stereospecific.⁷ This concept has important general consequences in asymmetric catalytic reactions that follow an enamine pathway.

Results and discussion

We reported that the sense of the stereochemical outcome of the α -amination reaction of linear aldehydes using proline in the presence of bases such as DBU is opposite that for proline.^{4,5} The proline-catalyzed α -amination of α,α -disubstituted aldehydes such as **1a** ($R^1 = \text{Ph}$, $R^2 = \text{Me}$) has been reported by Bräse,^{6a} and we expected again to observe a reversal in enantioselectivity in this reaction using proline/DBU. Surprisingly, however, racemic product was observed in the reaction of **1a** with DEAD using **2a**/DBU. This result prompted us to examine the stereochemical outcome of trisubstituted enamine formation (Scheme 1), which has not yet received detailed attention in mechanistic organocatalysis.

NMR studies of interactions between **1a** and **2a**/DBU

When aldehyde *rac*-**1a** was allowed to equilibrate at ambient temperature with **2a**/DBU, a mixture of *ca.* 9 : 1 *E* : *Z* enamines was observed by ¹H NMR spectroscopy, as identified



Scheme 1 Enamine formation between aldehydes and pyrrolidine catalysts.

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by nOe contacts.⁹ Monitoring the process over time, however, revealed that enamine concentrations were roughly equal immediately after mixing substrate and catalyst and that equilibration required about 30 min (Fig. 1). Equilibration of the *E* : *Z* enamine mixture is accelerated in the presence of acid. NMR spectra of *rac*-**1a** and **2a**/DBU with 1 equiv CH₃COOH taken immediately after mixing reveal the system has already reached the thermodynamic ratio of enamines.

The addition of acid also promotes the formation of oxazolidinones, and we have shown previously for linear aldehydes and catalyst **2a**/DBU that the *E*-enamine first identified by Gschwind is quantitatively converted to two diastereomeric oxazolidinones in the presence of acid;^{5a} however, in the case of α,α -disubstituted aldehydes, the system equilibrates to give a mixture containing both enamines and oxazolidinones. 1D-gNOESY and 2D-ROESY NMR studies reveal that each enamine exhibits a more intense EXSY cross-peak with a particular oxazolidinone peak (Fig. 2). In order to assign the stereochemistry at the C1' center of each oxazolidinone, we studied oxazolidinone formation from *S*-**1a** and *R*-**1a** separately with *S*-**2a**, as shown in Scheme 2. Reaction of *S*-**1a** with *S*-**2a** produces the oxazolidinone diastereomer *S*-**4** with the upfield C(2) proton at 4.96 ppm, while *R*-**1a** with *S*-**2a** yields the oxazolidinone diastereomer *R*-**4** with the C(2) proton downfield at 4.99 ppm. This experiment allows us to assign the enamine – oxazolidinone relationship for *rac*-**1a** with *S*-**2a**/DBU, as shown in Scheme 2.⁸

The EXSY data in Fig. 2 reveal a stereoisomeric correlation between the enamines and oxazolidinones, with *2S,1'R,2'R*-**4** associated with the *E*-enamine and *2S,1'R,2'S*-**4** with the *Z*-enamine. One important consequence of such a relationship is that the formation of the two oxazolidinones from **2a**/DBU and *rac*-**1a** cannot proceed through a common intermediate. This supports Gschwind's studies^{2a} proposing that oxazolidinones formed from enamines of linear aldehydes do not share a common iminium ion as a precursor, in contrast to conventional descriptions of the reaction pathway.

Our results also help to settle an intriguing question raised by Seebach⁹ about two possible pathways for enamine formation from an oxazolidinone, namely bond dissociation vs. *E2*-elimination, which provide different stereochemical outcomes. Seebach suggested that deuterium labeling might be used to determine which mechanism is extant; however, as illustrated in Scheme 3, application of our EXSY results to the Seebach

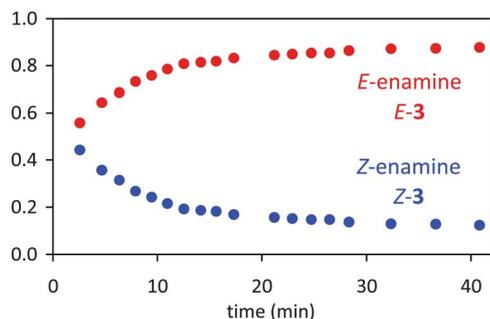


Fig. 1 Temporal profiles for enamine formation *E*-3 and *Z*-3 from **1a** (0.45 M) and *S*-**2a**/DBU (0.15 M) in CDCl₃ at 25 °C measured by NMR.⁸

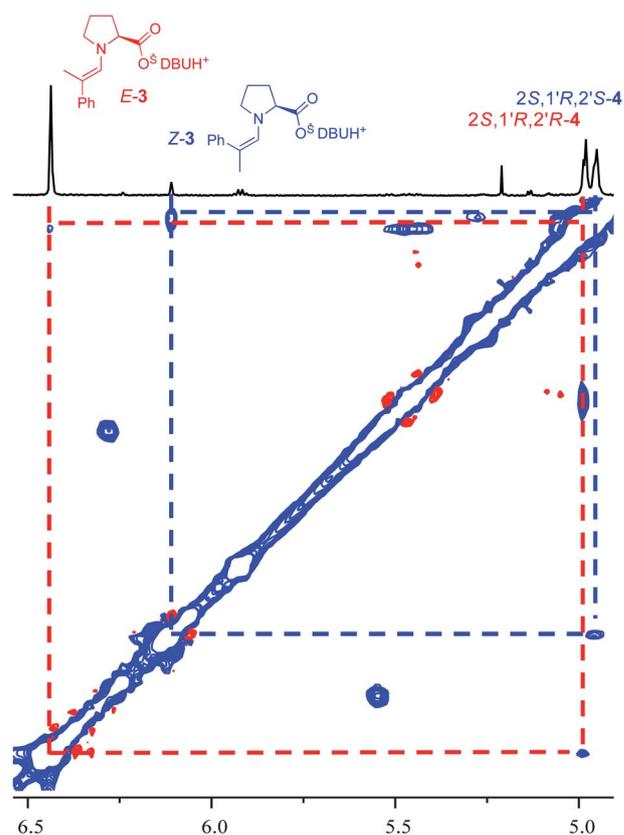
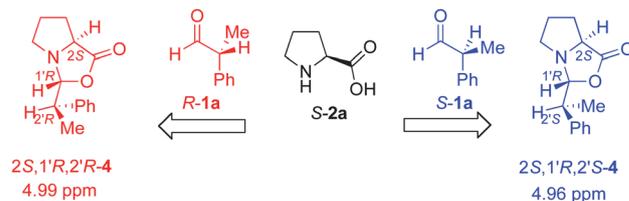


Fig. 2 2D-ROESY ¹H-NMR spectrum of an equilibrated mixture of *rac*-**1a** (0.45 M) and *S*-**2a**/DBU (0.15 M) in CDCl₃ at 25 °C in the presence of 1 equiv CH₃COOH.⁹ *E*-enamine *E*-3 (red) correlates with oxazolidinone *R*-**4** at 4.99 ppm (red); *Z*-enamine *Z*-3 (blue) correlates with oxazolidinone *S*-**4** at 4.96 ppm (blue) (see Scheme 2).⁸

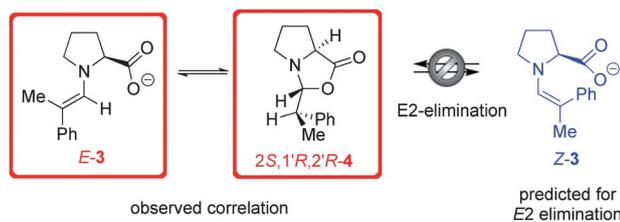
proposal reveals that the *E2*-elimination pathway predicts the wrong enamine-oxazolidinone correlation.

NMR studies of enamine formation with **1a** and **2b**

The initial kinetic formation of a *ca.* 1 : 1 mixture of enamines from racemic aldehyde **1a**, and the enamine/oxazolidinone correlation revealed in Fig. 2, raise the intriguing question of a stereoisomeric relationship between enamine configuration and that of the starting aldehyde. To probe this idea, we turned to the study of intermediates derived from catalyst **2b** and aldehyde **1a**. As with **2a**/DBU, this catalyst has been shown to give product selectivity opposite to that of proline in reactions such as the α -amination of aldehydes. From the viewpoint of NMR study, **2b**



Scheme 2 ¹H-NMR assignments of oxazolidinones formed from enantiopure *S*-**1a** and **2a**.



Scheme 3 Enamine-oxazolidinone correlation predicted for $E2$ elimination pathway compared to that experimentally observed.

has the advantage that enamine formation in the absence of acid is sufficiently slow to allow observation of the initial rates of E and Z isomer formation. As shown in Fig. 3, the initial E and Z enamine concentrations from *rac*-**1a** again differ from the equilibrium composition, which ultimately gives enamines E -**5** and Z -**5** in a thermodynamic ratio of $E : Z \approx 5 : 1$ for the equilibrated system of **S-2b** and *rac*-**1a**. The initial rate of enamine formation was also monitored for reaction of each separate enantiomer of **1a**, as shown in Fig. 4.⁸ Interestingly, the thermodynamically less stable Z -enamine forms more quickly initially for **S-1a**, while **R-1a** shows both a kinetic and thermodynamic preference for E -**5**.

The observed stereochemical relationship can be rationalized by invoking selective formation of the E iminium intermediate and removal of the proton from the α -carbon in a stereo-electronically controlled orientation parallel to the iminium π -system, with the proton placed on the sterically more accessible face opposite to the catalyst sidechain (Scheme 4). The stereochemical relationship is maintained in the reverse reaction by protonation on the less hindered face of the S -*trans*-enamine conformer. Eventual equilibration of the E and Z enamines is possible because of the accessibility of alternative (but less favored) transition states for the deprotonation of the intermediate iminium, e.g., reaction *via* the Z iminium, or in a conformation of the E iminium where the C–H bond is oriented *syn* to the sidechain. Similar arguments apply to less favored transition states for the reverse reaction.¹⁰

Rationalization of catalytic results

These studies of enamine formation may help to rationalize the results of catalytic reactions using α,α -disubstituted aldehydes and catalysts such as **2a**/DBU and **2b**, such as the α -amination (Table 1). A general network shown in Scheme 5 describes the

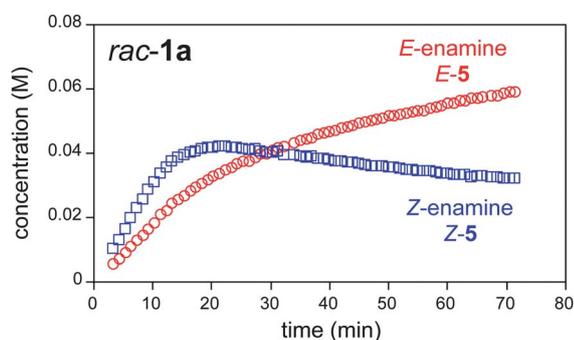


Fig. 3 Temporal profiles for enamine formation E -**5** and Z -**5** from *rac*-**1a** (0.45 M) and **S-2b** (0.15 M) in CDCl_3 at 25 °C measured by NMR.

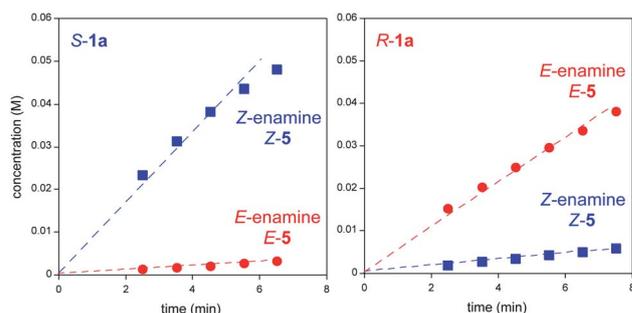
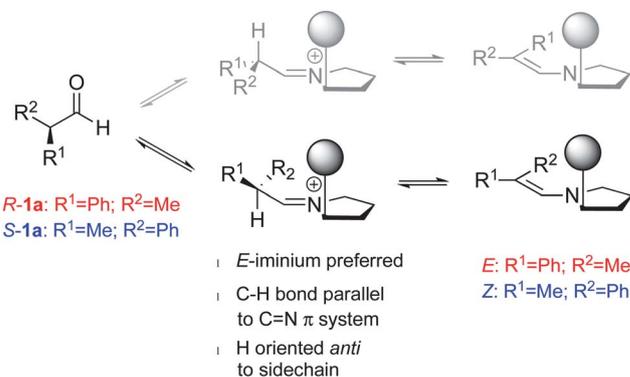


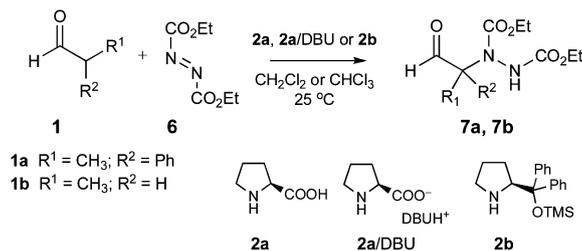
Fig. 4 Temporal profiles for enamine formation E -**5** and Z -**5** from 0.15 M **S-2b** with 0.45 M **S-1a** (left) or **R-1a** (right) in CDCl_3 at 25 °C measured by NMR.

rate of formation of the major and minor products, τ_{maj} and τ_{min} , where the concentration of the electrophile and species such as water in the hydrolysis step are equal in each pathway and are thus suppressed for simplicity. We propose (and will test) a simplifying assumption for aldehydes with R^1 and R^2 of approximate C_{nv} symmetry that the E and Z -enamines exhibit the same reactivity,¹¹ which then gives $k_{\text{maj}} = k'_{\text{maj}}$ and $k_{\text{min}} = k'_{\text{min}}$ and the expression for product enantiomeric excess as eqn (1). A selectivity factor is defined for product formation as $s = k_{\text{maj}}/k_{\text{min}}$. The selectivity factor s is equivalent to the enantiomeric ratio in the case where only one enamine forms, as for reactions of linear aldehydes such as propanal **1b**, where the E -enamine is formed essentially exclusively.^{2a} With **2a**/DBU as catalyst, the α -amination of **1b** with DEAD (52% ee, entry 3) gives $s = 3.2$, while for catalyst **2b** (79% ee, entry 10), $s = 8.5$. Interestingly these values and the experimentally determined equilibrium enamine E/Z ratios for aldehyde **1a** into eqn (1) gives predicted product ee values of 38% **S-7a** for catalyst **2a**/DBU and 55% **S-7a** for **2b**, in excellent agreement with the experimental values in Table 1 (entries 6 and 8) of 34% and 53% **S-7a** respectively. This concordance supports the validity of the simplifying assumption that the E and Z enamines react with similar facial selectivities. It also suggests that in the case of both catalysts **2a**/DBU and **2b**, the disubstituted enamine derived from **1b** reacts with facial selectivity similar to that of its trisubstituted counterpart derived from **1a**, thus providing what might be considered an intrinsic selectivity for reaction of enamines formed from each catalyst.



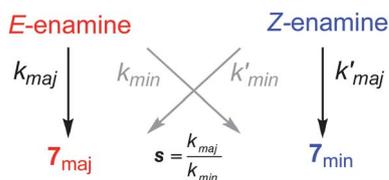
Scheme 4 Rationale for kinetic stereospecificity in enamine formation.

Table 1 α -Amination of linear and branched aldehydes^a



Entry	Catalyst	Aldehyde R ¹ , R ²	Additive	Product ee ^d (%)
1 ^b	2a	1b CH ₃ , H	none	85 (<i>R</i>)
2 ^b	2a/DBU	1b CH ₃ , H	none	48 (<i>S</i>)
3 ^b	2a/DBU	1b CH ₃ , H	CH ₃ COOH (1 eq)	52 (<i>S</i>)
4 ^c	2a/DBU	1a CH ₃ , Ph	none	racemic
5 ^c	2a/DBU	1a CH ₃ , Ph	none	21 (<i>S</i>) ^d
6 ^c	2a/DBU	1a CH ₃ , Ph	CH ₃ COOH (1 eq)	34 (<i>S</i>)
7 ^c	2b	1a CH ₃ , Ph	none	38 (<i>S</i>) - eqn (1) ^e
8 ^c	2b	1a CH ₃ , Ph	CH ₃ COOH (1 eq)	53 (<i>S</i>)
9 ^c	2b	1b CH ₃ , H	none	55 (<i>S</i>) - eqn (1) ^e
10 ^c	2b	1b CH ₃ , H	CH ₃ COOH (1 eq)	79 (<i>S</i>)

^a Enantiomeric excess of the oxazolidinone derivative of product **7a** or **7b** measured by chiral GC. ^b See ref. 4. ^c Reaction conditions: 0.3 M **2**; 0.32 M **1a** or **1b**; 0.11 M **2a/DBU** or **2b**; CHCl₃ at 5 °C. ^d Reaction carried out by adding **6** to a pre-equilibrated mixture of *rac*-**1a** and **2a/DBU**. ^e Predicted ee from eqn (1). ^f Irreversible reaction between **6** and catalyst **2b** suppresses the reaction in the absence of added acid; see ref. 5b.



Scheme 5 General network for reaction of stereoisomeric enamines.

$$\%ee = 100 \cdot \frac{(k_{maj} - k_{min})([E] - [Z])}{(k_{maj} + k_{min})([E] + [Z])} = 100 \cdot \frac{(s - 1) \left(1 - \frac{[Z]}{[E]}\right)}{(s + 1) \left(1 + \frac{[Z]}{[E]}\right)} \quad (1)$$

Eqn (1) also rationalizes the racemic product observed for **1a** with catalyst **2a/DBU** (Table 1, entry 4) for reaction occurring prior to equilibration, when $[E] \approx [Z]$ initially as shown in Fig. 1. Thus this unexpected result of 0% ee may be attributed to the interception of the kinetic mixture of enamines by the electrophile prior to equilibration (*i.e.*, *ca.* 1 : 1 *E* : *Z*, Fig. 1). This is in agreement with our previous results for linear aldehydes showing that enamine formation is rate-determining. Supporting this conclusion is the outcome of reactions carried out when *rac*-**1a** is allowed to pre-equilibrate with **2a/DBU** prior to reaction,¹² and that for reactions carried out with addition of acid, which gave product enantioselectivities 21% and 34% ee *S*-**7a** (Table 1, entries 5 and 6), respectively.

Finally, an important general consequence for any α,α -disubstituted aldehyde/catalyst system comes from consideration of eqn (1) together with the experimental *E/Z* value. This

provides an estimate of the maximum product enantioselectivity achievable for an electrophile with perfect selectivity: for example, in the case of **1a** with **2b**, eqn (1) predicts $ee_{\max} = ca.$ 68%, while for **1a** with **2a/DBU**, $ee_{\max} = ca.$ 80%. Reaction optimization efforts should take into account both the kinetic and thermodynamic *E/Z* values as well as the relative rates of enamine formation and enamine reaction. Catalyst design that provides a higher equilibrium enamine *E/Z* ratio together with reaction conditions that allow pre-equilibration of the enamines will allow for high enantioselectivity; alternatively, catalyst design focused on establishing a strong kinetic preference for one enamine, coupled with conditions that allow rapid attack on the electrophile, provides another approach that may afford high enantioselectivity. In either case the stereochemical outcome is determined by the facial preference for attack of the enamine — at its prevailing concentration ratio at the instant of attack — on the electrophile.

Conclusions

The development of asymmetric reactions to form quaternary stereogenic centers is an important research goal, and the use of aldehydes with α -stereocenters as substrates in organocatalytic transformations *via* enamine catalysis is a promising approach. Our work reveals that both the kinetics and thermodynamics of reversible enamine reactions must be considered in the design of selective catalytic solutions to this challenge. Our work shows for the first time that reversible enamine formation between asymmetric catalysts and aldehydes with α -stereocenters is kinetically stereospecific, with a distinct correlation between one enantiomer of the aldehyde and one stereoisomeric enamine. The reactions of

1 these enamines with electrophiles also proceed with high selectivity, with each enamine correlating directly with one stereoisomeric reaction product. A theoretical analysis allows a general model to be advanced that predicts the enantiomeric excess of the product in reactions of enamines with electrophiles. Establishment of a stereogenic center from enamine intermediates, and preservation of the stereogenic integrity of reaction products that may themselves form enamines, particularly for cascade reaction networks, are critical processes that may be influenced by the thermodynamic vs. kinetic selectivity of enamine formation and reaction. We demonstrate that kinetic stereospecificity in ultimately reversible enamine reactions may contribute to the efficacy of enamine-based catalysis in complex reaction networks.

15 Acknowledgements

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Notes and references

- 1 (a) S. Mukherjee, J. W. Yang, S. Hoffmann and B. List, *Chem. Rev.*, 2007, **107**, 5471–5569; (b) P. Melchiorre, M. Marigo, A. Carlone and G. Bartoli, *Angew. Chem., Int. Ed.*, 2008, **47**, 6138–6171; (c) S. Bertelsen and K. A. Jorgensen, *Chem. Soc. Rev.*, 2009, **38**, 2178–2189; (d) C. Palomo and A. Mielgo, *Angew. Chem., Int. Ed.*, 2006, **45**, 7876–7880; (e) S. Sulzer-Mosse and A. Alexakis, *Chem. Commun.*, 2007, 3123–3135.
- 2 (a) M. B. Schmid, K. Zeitler and R. M. Gschwind, *Angew. Chem., Int. Ed.*, 2010, **49**, 4997–5003; (b) M. B. Schmid, K. Zeitler and R. M. Gschwind, *J. Am. Chem. Soc.*, 2011, **133**, 7065–7074; (c) M. B. Schmid, K. Zeitler and R. M. Gschwind, *Chem. Sci.*, 2011, **2**, 1793–1803.
- 3 J. Schleucher, B. Schworer, R. K. Thauer and C. Griesinger, *J. Am. Chem. Soc.*, 1995, **117**, 2941–2942.

- 4 D. G. Blackmond, A. Moran, M. Hughes and A. Armstrong, *J. Am. Chem. Soc.*, 2010, **132**, 7598–7599.
- 5 (a) J. E. Hein, J. Bures, Y. H. Lam, M. Hughes, K. N. Houk, A. Armstrong and D. G. Blackmond, *Org. Lett.*, 2011, **13**, 5644–5647; (b) J. E. Hein, A. Armstrong and D. G. Blackmond, *Org. Lett.*, 2011, **13**, 4300–4303.
- 6 (a) H. Vogt, S. Vanderheiden and S. Brase, *Chem. Commun.*, 2003, 2448–2449; (b) S. Sulzer-Mosse, A. Alexakis, J. Mareda, G. Bollot, G. Bernardinelli and Y. Filinchuk, *Chem.–Eur. J.*, 2009, **15**, 3204–3220; (c) D. D. Steiner, N. Mase and C. F. Barbas 3rd, *Angew. Chem., Int. Ed.*, 2005, **44**, 3706–3710.
- 7 The IUPAC definition of stereospecificity states: “A reaction is termed stereospecific if starting materials differing only in their configuration are converted into stereoisomeric products. According to this definition, a stereospecific process is necessarily stereoselective but not all stereoselective processes are stereospecific. Stereospecificity may be total (100%) or partial.” Since the formation and reaction of enamines are reversible processes that equilibrate to a thermodynamic selectivity outcome, we introduce the term “kinetic stereospecificity” to highlight the initial preference for one stereoisomer to form one enamine, prior to equilibration. We use this term to indicate the connection between aldehyde configuration and configuration of the initially formed enamine (a) A. D. McNaught in *IUPAC Compendium of Chemical Terminology*, 2nd ed. V. Gold, K. L. Loening, P. Shemi, Blackwell Science, Oxford, 1996, p 2193; (b) A. D. McNaught in *IUPAC Compendium of Chemical Terminology*, 2nd ed. V. Gold, K. L. Loening, P. Shemi, Blackwell Science, Oxford, 1994, p 1077.
- 8 See Supporting Information†.
- 9 D. Seebach, A. K. Beck, D. M. Badine, M. Limbach, A. Eschenmoser, A. M. Treasurywala, R. Hobi, W. Prikoszovich and B. Linder, *Helv. Chim. Acta*, 2007, **90**, 425.
- 10 The accessibility of less favored transition states for the protonation of the enamine from the less hindered face of the *S-cis*-enamine or the more hindered face of the *S-trans*-enamine may also be considered.
- 11 This simplification may break down for aldehydes where the conformational preferences of the R¹ and R² substituents result in different facial selectivities for the *E*- and *Z*-enamines; see ref. 5b.
- 12 **1a** was mixed with 33 mol% catalyst **2a**/DBU for 30 min prior to three consecutive additions of 33 mol% **6**, for a total of three catalytic turnovers. See Supporting Information†.

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