JACS
JOURNAL OF THE AMERICAN CHEMICAL SOCIETY

COMMUNICATION

pubs.acs.org/JACS

A Dual-Catalysis Approach to the Asymmetric Steglich Rearrangement and Catalytic Enantioselective Addition of *O*-Acylated Azlactones to Isoquinolines

Chandra Kanta De, Nisha Mittal, and Daniel Seidel*

Department of Chemistry and Chemical Biology, Rutgers, The State University of New Jersey, Piscataway, New Jersey 08854, United States

Supporting Information

ABSTRACT: A dual-catalysis approach, namely the combination of an achiral nucleophilic catalyst and a chiral anion-binding catalyst, was applied to the Steglich rearrangement to provide α,α-disubstituted amino acid derivatives in a highly enantioselective fashion. Replacement of the nucleophilic co-catalyst for isoquinoline resulted in a divergent reaction pathway and an unprecedented transformation of *O*-acylated azlactones. This strategy provided highly substituted α,β-diamino acid derivatives with excellent levels of stereocontrol.

The rearrangement of *O*-acylated azlactones to the corresponding *C*-acylated products (**1** → **2**, Figure 1), also known as the Steglich reaction,[1,2] represents a valuable strategy for the synthesis of α,α-disubstituted amino acid derivatives.[3] Ever since the seminal work by Ruble and Fu, who described the first catalytic enantioselective version of this transformation,[4] this reaction has become and continues to be a fertile testing ground for the evaluation of new chiral nucleophilic catalysts. The latter currently include chiral variants of 4-(dimethylamino)pyridine (DMAP), phosphines, isothioureas, imidazoles, carbenes, and betaines.[5−7] These reactions typically proceed through chiral ion pairs related to **3**, with the betaine catalyst developed by Ooi et al. being a notable exception.[5i] Here we report a conceptually new strategy for the catalytic enantioselective Steglich reaction that takes advantage of a dual-catalysis approach. In addition, we describe the unprecedented reaction between *O*-acylated azlactones and isoquinolines, a transformation that is likely outside the realm of traditional nucleophilic catalysis.

We recently developed a new concept for asymmetric nucleophilic catalysis in which a simple nucleophilic catalyst such as DMAP is used in combination with a chiral hydrogen-bonding (HB) catalyst.[8,9] Anion binding[10−12] is thought to be a vital component of this strategy, which was successfully applied to a number of asymmetric acyl-transfer reactions.[13] These include the kinetic resolution of benzylic,[8a] propargylic,[8b] and allylic amines[8c] as well as the desymmetrization of *meso*-1,2-diamines.[8d] Very recently, the Jacobsen group, who pioneered much of the early work on chiral anion binding catalysis, reported a highly enantioselective acylation of silyl ketene acetals with acyl fluorides via a closely related dual-catalysis approach.[11q]

In an effort to extend our dual-catalysis strategy to other acyl-transfer reactions, we decided to apply it to the Steglich

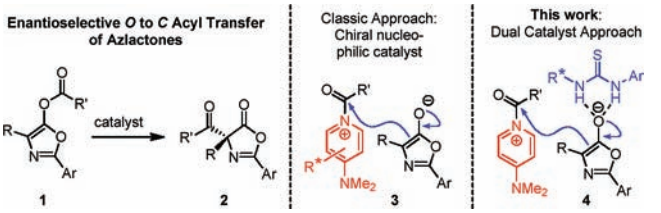


Figure 1. New concept for the azlactone rearrangement.

rearrangement. Specifically, we envisioned that intermediates such as **4** (Figure 1), featuring an achiral nucleophilic catalyst and a chiral anion receptor, should enable the efficient enantioselective conversion of **1** into **2**.

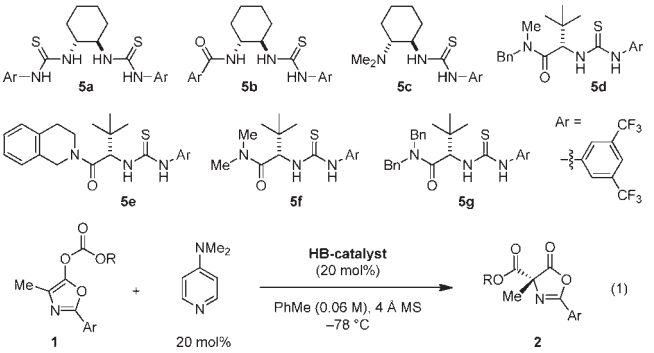
We initiated our studies by exposing *O*-acylated azlactone **1** (Ar = 4-MeO-C_6H_4) to a combination of DMAP (20 mol %) and various HB catalysts (20 mol %) at −78 °C in toluene (Table 1). Relatively fast consumption of starting material was observed in all cases. Catalysts **5a** and **5b**, compounds that were previously used successfully in the kinetic resolution and desymmetrization of amines, gave rise to poor selectivities. Promising results were obtained with the Takemoto catalyst[14] (**5c**, entry 3), while the highest level of selectivity was observed with catalyst **5d** (79% ee, entry 4), previously developed by the Jacobsen group.[11c] A brief survey of the aryl group in **1** revealed the superiority of 3,5-di-MeO-C_6H_3 over 4-MeO-C_6H_4, allowing for the recovery of product **2** in 89% ee (entry 10). Interestingly, this change also significantly decreased the reaction time from 4 h to 1 h, likely the result of an increase in nucleophilicity of the anionic intermediate. Notably, azlactone rearrangements are typically conducted at higher temperatures and to our knowledge have never been reported to proceed at temperatures as low as −78 °C. Importantly, the use of DMAP as the only catalyst under otherwise identical conditions led to very sluggish reactions. These combined observations nicely illustrate the unique reactivity profile of the dual-catalyst system.

The scope of the azlactone rearrangement was explored under the optimized conditions (Chart 1). A number of substrates were tested, and all reactions went to full conversion within short reaction times. The rearranged products **2** were recovered with high levels of enantioselectivity.[15]

Received: August 29, 2011
Published: September 29, 2011

ACS Publications © 2011 American Chemical Society

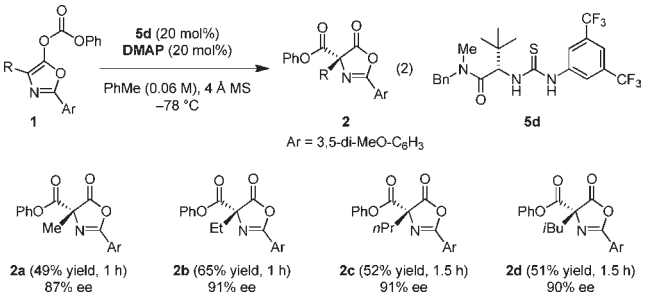
Table 1. Evaluation of Reaction Parameters for the Azlactone Rearrangement[a]



entry	R	Ar	cat	time (h)	yield (%)	ee (%)
1	Ph	4-MeO-C_6H_4	**5a**	4	57	12
2	Ph	4-MeO-C_6H_4	**5b**	4	54	10
3	Ph	4-MeO-C_6H_4	**5c**	4	44	−74
4	Ph	4-MeO-C_6H_4	**5d**	4	72	79
5	Ph	4-MeO-C_6H_4	**5e**	4	77	71
6	Ph	4-MeO-C_6H_4	**5f**	4	52	55
7	Ph	4-MeO-C_6H_4	**5g**	4	58	47
8[b]	Bn	4-MeO-C_6H_4	**5d**	8	52	60
9	Ph	1-naphthyl	**5d**	5	53	85
10	Ph	3,5-di-MeO-C_6H_3	**5d**	1	70	89

[a] Reactions were performed on a 0.1 mmol scale. The ee's were determined by HPLC analysis; see the Supporting Information for details. [b] Reaction was performed at −60 °C.

Chart 1. Scope of the Azlactone Rearrangement



In considering alternate reaction pathways, we reasoned that replacement of the nucleophilic co-catalyst DMAP for a different nucleophilic species might result in the incorporation of the latter into the final product. Specifically, we envisioned the reaction of an *O*-acylated azlactone with isoquinoline in the presence of a HB catalyst to give intermediates such as **6** (Figure 2). Ion pair **6** could rearrange in the usual manner, with isoquinoline acting as a nucleophilic promoter to give rearranged product **2** (pathway a). Alternatively, the acylisoquinolinium ion could be attacked by the enolate at the 1-position of the isoquinoline ring to give rise to the highly functionalized α,β-diamino acid derivative **7** (pathway b). While catalytic enantioselective additions to isoquinolines have been limited to relatively few examples,[16−18] significant efforts have focused on the catalytic enantioselective preparation of α,β-diamino acid derivatives.[19−21]

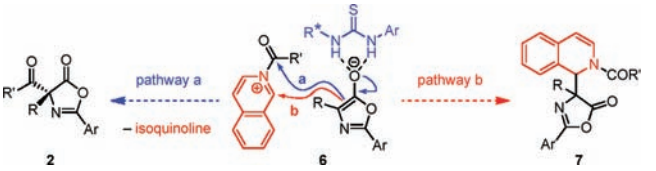
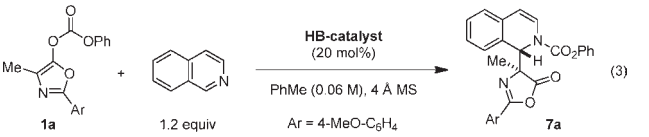


Figure 2. Potential reaction pathways for isoquinoline-derived ion pairs.

Table 2. Evaluation of Reaction Parameters for the Azlactone Addition[a]



entry	cat.	temp (°C)	solvent	time (h)	yield (%)	dr	ee (%)
1	**5a**	−10	PhMe	2	90	70:30	−10
2	**5b**	−10	PhMe	2	91	69:31	0
3	**5d**	−10	PhMe	2.5	85	86:14	64
4	**5e**	−10	PhMe	3	91	83:17	50
5	**5f**	−10	PhMe	3	91	82:18	52
6	**5g**	−10	PhMe	3	92	77:23	35
7[b]	**5d**	−10	PhMe	2.5	85	69:31	13
8	**5d**	−10	TBME	4	86	84:16	69
9	**5d**	−10	mesitylene	3	88	88:12	73
10	**5d**	−20	mesitylene	10	88	92:08	77
11[c]	**5d**	−20	pentane	24	65	92:08	82
12	**5d**	−25	mes/pent (2:1)	14	91	95:05	88
13	**5d**	−25	mes/pent (1:1)	17	90	96:04	91
14	**5d**	−25	mes/pent (1:2)	22	92	96:04	93
15	**5d**	−25	mes/hex (1:2)	20	91	91:09	84
16	**5d**[d]	−25	mes/pent (1:2)	27	92	96:04	93
17[c]	**5d**[d]	−25	mes/pent (1:3)	24	61	96:04	93
18[c]	**5d**[d]	−25	mes/pent (1:4)	24	52	95:05	93

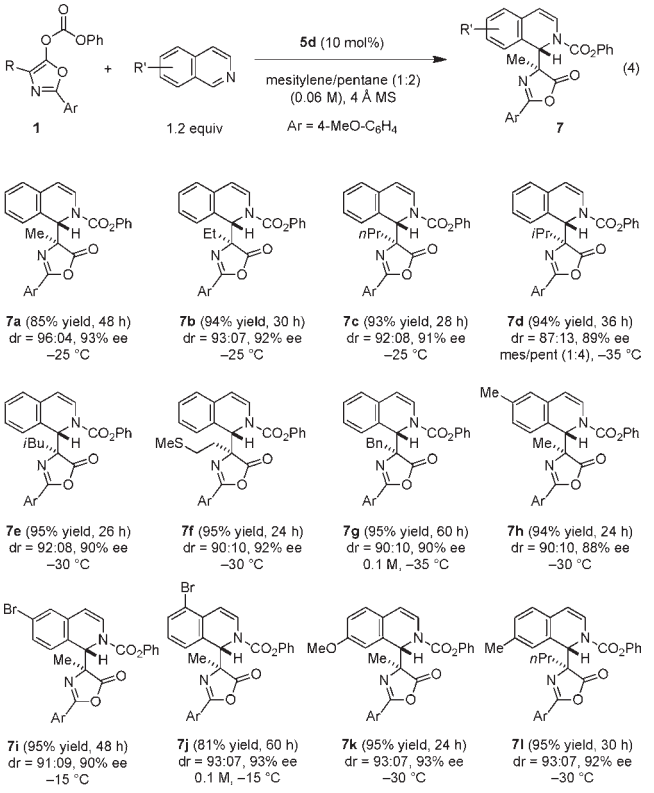
[a] Reactions were performed on a 0.1 mmol scale. The dr's and ee's were determined by HPLC analysis; see the Supporting Information for details. [b] Starting material with Ar = 3,5-di-MeO-C_6H_3 was used. [c] Reaction was incomplete. [d] 10 mol % of catalyst was used.

In order to explore this proposed transformation, we exposed **1a** to 1.2 equiv of isoquinoline in the presence of various HB catalysts (Table 2). Isoquinoline possesses a significantly lower nucleophilicity than DMAP, and consequently, the reactions were conducted at elevated temperatures. Gratifyingly, the reaction proceeded as anticipated to provide product **7a** in typically excellent yield and with promising levels of enantioselectivity. Under the initial screening conditions (toluene, −10 °C), catalyst **5d** again gave rise to the best results, enabling the isolation of **7a** in 85% yield with dr = 86:14 and 64% ee in a reaction that was completed within 2.5 h (entry 3).

The stereoselectivity could be improved to 73% ee (dr = 88:12, 3 h reaction time) upon exchange of toluene for mesitylene (entry 9). Interestingly, under the same conditions but in the absence of the HB catalyst, the reaction went to completion within 11.5 h, and **7a** was formed in 95% yield (dr = 64:36), indicating a substantial background rate. Lowering the reaction temperature to −20 °C increased the enantioselectivity to 77%

dx.doi.org/10.1021/ja208156z |*J. Am. Chem. Soc.* 2011, 133, 16802–16805

Chart 2. Scope of the Azlactone Addition to Isoquinolines



ee (entry 10). A significantly improved selectivity of 82% ee was obtained at this temperature when pentane was used as the solvent (entry 11). However, in this case, the reaction did not go to completion within a 24 h period. Ultimately, mixtures of mesitylene and pentane were evaluated at −25 °C. The best result was obtained with a 1:2 mixture of mesitylene and pentane. In this instance, **7a** was isolated in 92% yield with dr = 96:04 and 93% ee (entry 14). The catalyst loading could be reduced to 10 mol % without adverse effects on the reaction outcome (entry 16).

Under the optimized conditions, the reaction displayed a certain level of heterogeneity that appeared to be beneficial to the reaction outcome, possibly due to product precipitation driving the reaction forward.[22] However, there is a limit as to how much improvement can be achieved by a further increase in heterogeneity (see entries 17 and 18) . In these cases, the observation of retarded reaction rates is likely a consequence of the poorer solubility of the starting materials.

The scope of the reaction was explored under the optimized conditions (Chart 2). *O*-Acylated azlactones derived from different amino acids readily engaged in reactions with isoquinoline to provide products **7** in generally excellent yields and high levels of enantio- and diastereoselectivity. A number of quinolines with electronically diverse substituents at various ring positions also underwent reactions with *O*-acylated azlactones, typically with excellent results.

In summary, we have shown that *O*-acylated azlactones can be efficiently rearranged to the corresponding *C*-acylated products by using a dual-catalysis approach, further establishing the power and utility of combining a chiral HB catalyst with a simple achiral nucleophilic catalyst. We also demonstrated that replacement of the nucleophilic catalyst for a stoichiometric amount of isoquinoline enabled an unprecedented reaction of *O*-acylated azlactones, a process that provides rapid access to densely functionalized α,β-diamino acid derivatives.

■ ASSOCIATED CONTENT

Supporting Information. Experimental procedures and characterization data, including X-ray crystallographic data in CIF format for **7a** and **7j**. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author
seidel@rutchem.rutgers.edu

■ ACKNOWLEDGMENT

Financial support received from the Charles and Johanna Busch Memorial Fund at Rutgers, The State University of New Jersey, is gratefully acknowledged. We thank Dr. Tom Emge for crystallographic analysis. D.S. is a fellow of the Alfred P. Sloan Foundation and the recipient of an Amgen Young Investigator Award.

■ REFERENCES

(1) (a) Steglich, W.; Hoefle, G. *Tetrahedron Lett.* **1970**, 4727. For an early review, see:(b) Hoefle, G.; Steglich, W.; Vorbrueggen, H. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 569.

(2) For reviews on azlactone rearrangements and related reactions, see: (a) Fisk, J. S.; Mosey, R. A.; Tepe, J. J. *Chem. Soc. Rev.* **2007**, *36*, 1432. (b) Nasveschuk, C. G.; Rovis, T. *Org. Biomol. Chem.* **2008**, *6*, 240. (c) Mosey, R. A.; Fisk, J. S.; Tepe, J. J. *Tetrahedron: Asymmetry* **2008**, *19*, 2755. (d) Moyano, A.; El-Hamdouni, N.; Atlamsani, A. *Chem.—Eur. J.* **2010**, *16*, 5260. (e) Alba, A. N. R.; Rios, R. *Chem.—Asian J.* **2011**, *6*, 720.

(3) For reviews on the synthesis and importance of tetrasubstituted centers bearing nitrogen, see: (a) Vogt, H.; Braese, S. *Org. Biomol. Chem.* **2007**, *5*, 406. (b) Cativiela, C.; Diaz-De-Villegas, M. D. *Tetrahedron: Asymmetry* **2007**, *18*, 569. (c) Clayden, J.; Donnard, M.; Lefranc, J.; Tetlow, D. J. *Chem. Commun.* **2011**, *47*, 4624.

(4) Ruble, J. C.; Fu, G. C. *J. Am. Chem. Soc.* **1998**, *120*, 11532.

(5) (a) Shaw, S. A.; Aleman, P.; Vedejs, E. *J. Am. Chem. Soc.* **2003**, *125*, 13368. (b) Seitzberg, J. G.; Dissing, C.; Sotofte, I.; Norrby, P. O.; Johannsen, M. *J. Org. Chem.* **2005**, *70*, 8332. (c) Shaw, S. A.; Aleman, P.; Christy, J.; Kampf, J. W.; Va, P.; Vedejs, E. *J. Am. Chem. Soc.* **2006**, *128*, 925. (d) Nguyen, H. V.; Butler, D. C. D.; Richards, C. J. *Org. Lett.* **2006**, *8*, 769. (e) Busto, E.; Gotor-Fernandez, V.; Gotor, V. *Adv. Synth. Catal.* **2006**, *348*, 2626. (f) Dietz, F. R.; Groeger, H. *Synlett* **2008**, 663. (g) Joannesse, C.; Johnston, C. P.; Concellon, C.; Simal, C.; Philp, D.; Smith, A. D. *Angew. Chem., Int. Ed.* **2009**, *48*, 8914. (h) Dietz, F. R.; Groeger, H. *Synthesis* **2009**, 4208. (i) Uraguchi, D.; Koshimoto, K.; Miyake, S.; Ooi, T. *Angew. Chem., Int. Ed.* **2010**, *49*, 5567. (j) Zhang, Z. F.; Xie, F.; Jia, J.; Zhang, W. B. *J. Am. Chem. Soc.* **2010**, *132*, 15939. (k) Campbell, C. D.; Concellon, C.; Smith, A. D. *Tetrahedron: Asymmetry* **2011**, *22*, 797.

(6) For selected examples of related rearrangements, see: (a) Mermerian, A. H.; Fu, G. C. *J. Am. Chem. Soc.* **2003**, *125*, 4050. (b) Hills, I. D.; Fu, G. C. *Angew. Chem., Int. Ed.* **2003**, *42*, 3921. (c) Duffey, T. A.; Shaw, S. A.; Vedejs, E. *J. Am. Chem. Soc.* **2009**, *131*, 14. (d) Ismail, M.; Nguyen, H. V.; Ilyashenko, G.; Motevalli, M.; Richards, C. J. *Tetrahedron Lett.* **2009**, *50*, 6332. (e) Joannesse, C.; Morrill, L. C.; Campbell, C. D.; Slawin, A. M. Z.; Smith, A. D. *Synthesis* **2011**, 1865.

(7) For selected reviews on nucleophilic and Lewis base catalysis, see: (a) Fu, G. C. *Acc. Chem. Res.* **2000**, *33*, 412. (b) France, S.; Guerin, D. J.; Miller, S. J.; Lectka, T. *Chem. Rev.* **2003**, *103*, 2985. (c) Fu, G. C. *Acc. Chem. Res.* **2004**, *37*, 542. (d) Miller, S. J. *Acc. Chem. Res.* **2004**, *37*, 601. (e) Spivey, A. C.; Arseniyadis, S. *Angew. Chem., Int. Ed.* **2004**, *43*, 5436. (f) Vedejs, E.; Jure, M. *Angew. Chem., Int. Ed.* **2005**, *44*, 3974. (g) Wurz, R. P. *Chem. Rev.* **2007**, *107*, 5570. (h) Denmark, S. E.; Beutner, G. L. *Angew. Chem., Int. Ed.* **2008**, *47*, 1560. (i) Spivey, A. C.; Arseniyadis, S. *Top. Curr. Chem.* **2010**, *291*, 233.

(8) (a) De, C. K.; Klauber, E. G.; Seidel, D. *J. Am. Chem. Soc.* **2009**, *131*, 17060. (b) Klauber, E. G.; De, C. K.; Shah, T. K.; Seidel, D. *J. Am. Chem. Soc.* **2010**, *132*, 13624. (c) Klauber, E. G.; Mittal, N.; Shah, T. K.; Seidel, D. *Org. Lett.* **2011**, *13*, 2464. (d) De, C. K.; Seidel, D *J. Am. Chem. Soc.* **2011**, *133*, 14538.

(9) For selected reviews on HB catalysis, see: (a) Schreiner, P. R. *Chem. Soc. Rev.* **2003**, *32*, 289. (b) Takemoto, Y. *Org. Biomol. Chem.* **2005**, *3*, 4299. (c) Taylor, M. S.; Jacobsen, E. N. *Angew. Chem., Int. Ed.* **2006**, *45*, 1520. (d) Marcelli, T.; van Maarseveen, J. H.; Hiemstra, H. *Angew. Chem., Int. Ed.* **2006**, *45*, 7496. (e) Doyle, A. G.; Jacobsen, E. N. *Chem. Rev.* **2007**, *107*, 5713. (f) Yu, X.; Wang, W. *Chem.—Asian J.* **2008**, *3*, 516.

(10) For an excellent review on anion binding in the context of catalysis, see: Zhang, Z.; Schreiner, P. R. *Chem. Soc. Rev.* **2009**, *38*, 1187.

(11) For examples of anion-binding approaches to catalysis, see: (a) Kotke, M.; Schreiner, P. R. *Tetrahedron* **2006**, *62*, 434. (b) Kotke, M.; Schreiner, P. R. *Synthesis* **2007**, 779. (c) Raheem, I. T.; Thiara, P. S.; Peterson, E. A.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2007**, *129*, 13404. (d) Reisman, S. E.; Doyle, A. G.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2008**, *130*, 7198. (e) Klausen, R. S.; Jacobsen, E. N. *Org. Lett.* **2009**, *11*, 887. (f) Zuend, S. J.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2009**, *131*, 15358. (g) Zuend, S. J.; Coughlin, M. P.; Lalonde, M. P.; Jacobsen, E. N. *Nature* **2009**, *461*, 968. (h) Xu, H.; Zuend, S. J.; Woll, M. G.; Tao, Y.; Jacobsen, E. N. *Science* **2010**, *327*, 986. (i) Schreiner, P. R. *Science* **2010**, *327*, 965. (j) Knowles, R. R.; Lin, S.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2010**, *132*, 5030. (k) Brown, A. R.; Kuo, W.-H.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2010**, *132*, 9286. (l) Singh, R. P.; Foxman, B. M.; Deng, L. *J. Am. Chem. Soc.* **2010**, *132*, 9558. (m) Veitch, G. E.; Jacobsen, E. N. *Angew. Chem., Int. Ed.* **2010**, *49*, 7332. (n) Knowles, R. R.; Jacobsen, E. N. *Proc. Natl. Acad. Sci. U.S.A.* **2010**, *107*, 20678. (o) Kim, H. Y.; Oh, K. *Org. Lett.* **2011**, *13*, 1306. (p) Opalka, S. M.; Steinbacher, J. L.; Lambiris, B. A.; McQuade, D. T. *J. Org. Chem.* **2011**, *76*, 6503. (q) Birrell, J. A.; Desrosiers, J.-N.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2011**, *133*, 13872.

(12) For selected reviews on enantioselective catalysis with chiral anionic intermediates, see: (a) Lacour, J.; Hebbe-Viton, V. *Chem. Soc. Rev.* **2003**, *32*, 373. (b) Akiyama, T. *Chem. Rev.* **2007**, *107*, 5744. (c) Lacour, J.; Moraleda, D. *Chem. Commun.* **2009**, 7073. (d) Rueping, M.; Koenigs, R. M.; Atodiresei, I. *Chem.—Eur. J.* **2010**, *16*, 9350.

(13) For an excellent review on catalytic enantioselective acyl-transfer reactions, see: Mueller, C. E.; Schreiner, P. R. *Angew. Chem., Int. Ed.* **2011**, *50*, 6012.

(14) Okino, T.; Hoashi, Y.; Takemoto, Y. *J. Am. Chem. Soc.* **2003**, *125*, 12672.

(15) The moderate yields reflect the sensitivity of the products toward silica gel chromatography (hydrolytic ring opening). Other authors have previously noted the need for rapid chromatographic purification. See, for instance, refs 4 and 5a.

(16) For examples, see: (a) Takamura, M.; Funabashi, K.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2000**, *122*, 6327. (b) Takamura, M.; Funabashi, K.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2001**, *123*, 6801. (c) Alexakis, A.; Amiot, F. *Tetrahedron: Asymmetry* **2002**, *13*, 2117. (d) Taylor, M. S.; Tokunaga, N.; Jacobsen, E. N. *Angew. Chem., Int. Ed.* **2005**, *44*, 6700. (e) Yamaoka, Y.; Miyabe, H.; Takemoto, Y. *J. Am. Chem. Soc.* **2007**, *129*, 6686. (f) Black, D. A.; Beveridge, R. E.; Arndtsen, B. A. *J. Org. Chem.* **2008**, *73*, 1906.

(17) For a review on catalytic enantioselective additions to aromatic heterocycles, see: Ahamed, M.; Todd, M. H. *Eur. J. Org. Chem.* **2010**, 5935.

(18) For selected reviews on catalytic enantioselective Mannich reactions, see: (a) Friestad, G. K.; Mathies, A. K. *Tetrahedron* **2007**, *63*, 2541. (b) Ting, A.; Schaus, S. E. *Eur. J. Org. Chem.* **2007**, 5797. (c) Verkade, J. M. M.; van Hemert, L. J. C.; Quaedflieg, P.; Rutjes, F. *Chem. Soc. Rev.* **2008**, *37*, 29. (d) Kobayashi, S.; Matsubara, R. *Chem.—Eur. J.* **2009**, *15*, 10694. (e) Marques-Lopez, E.; Merino, P.; Tejero, T.; Herrera, R. P. *Eur. J. Org. Chem.* **2009**, 2401.

(19) For selected reviews on the synthesis and biological significance of α,β-diamino acids, see: (a) Viso, A.; Fernandez de la Pradilla, R.; Garcia, A.; Flores, A. *Chem. Rev.* **2005**, *105*, 3167. (b) Arrayas, R. G.; Carretero, J. C. *Chem. Soc. Rev.* **2009**, *38*, 1940. (c) Weiner, B.; Szymanski, W.; Janssen, D. B.; Minnaard, A. J.; Feringa, B. L. *Chem. Soc. Rev.* **2010**, *39*, 1656. (d) Wang, J.; Zhang, L.; Jiang, H. L.; Liu, H. *Curr. Pharm. Design* **2010**, *16*, 1252.

(20) See also: Li, L.; Ganesh, M.; Seidel, D. *J. Am. Chem. Soc.* **2009**, *131*, 11648 and references cited therein.

(21) For selected examples of azlactones in catalytic enantioselective reactions, see: (a) Daffe, V.; Fastrez, J. *J. Am. Chem. Soc.* **1980**, *102*, 3601. (b) Belokon, Y. N.; Bachurina, I. B.; Tararov, V. I.; Saporovskaya, M. B. *Bull. Acad. Sci. USSR, Div. Chem. Sci.* **1992**, *41*, 422. (c) Trost, B. M.; Ariza, X. *Angew. Chem., Int. Ed.* **1997**, *36*, 2635. (d) Liang, J.; Ruble, J. C.; Fu, G. C. *J. Org. Chem.* **1998**, *63*, 3154. (e) Trost, B. M.; Dogra, K.; Franzini, M. *J. Am. Chem. Soc.* **2004**, *126*, 1944. (f) Berkessel, A.; Cleemann, F.; Mukherjee, S.; Muller, T. N.; Lex, J. *Angew. Chem., Int. Ed.* **2005**, *44*, 807. (g) Tokunaga, M.; Kiyosu, J.; Obora, Y.; Tsuji, Y. *J. Am. Chem. Soc.* **2006**, *128*, 4481. (h) Cabrera, S.; Reyes, E.; Aleman, J.; Milelli, A.; Kobbelgaard, S.; Jorgensen, K. A. *J. Am. Chem. Soc.* **2008**, *130*, 12031. (i) Peschiulli, A.; Quigley, C.; Tallon, S.; Gun'ko, Y. K.; Connon, S. J. *J. Org. Chem.* **2008**, *73*, 6409. (j) Mosey, R. A.; Fisk, J. S.; Friebe, T. L.; Tepe, J. J. *Org. Lett.* **2008**, *10*, 825. (k) Terada, M.; Tanaka, H.; Sorimachi, K. *J. Am. Chem. Soc.* **2009**, *131*, 3430. (l) Uraguchi, D.; Ueki, Y.; Ooi, T. *Science* **2009**, *326*, 120. (m) Alba, A. N. R.; Companyo, X.; Valero, G.; Moyano, A.; Rios, R. *Chem.—Eur. J.* **2010**, *16*, 5354. (n) Dong, S. X.; Liu, X. H.; Chen, X. H.; Mei, F.; Zhang, Y. L.; Gao, B.; Lin, L. L.; Feng, X. M. *J. Am. Chem. Soc.* **2010**, *132*, 10650. (o) Misaki, T.; Takimoto, G.; Sugimura, T. *J. Am. Chem. Soc.* **2010**, *132*, 6286. (p) Weber, M.; Jautze, S.; Frey, W.; Peters, R. *J. Am. Chem. Soc.* **2010**, *132*, 12222. (q) Yang, X.; Lu, G. J.; Birman, V. B. *Org. Lett.* **2010**, *12*, 892. (r) Melhado, A. D.; Amarante, G. W.; Wang, Z. J.; Luparia, M.; Toste, F. D. *J. Am. Chem. Soc.* **2011**, *133*, 3517. See also ref 2e.

(22) See also: (a) Li, L.; Klauber, E. G.; Seidel, D. *J. Am. Chem. Soc.* **2008**, *130*, 12248. (b) Vecchione, M. K.; Li, L.; Seidel, D. *Chem. Commun.* **2010**, *46*, 4604.

(23) It is interesting to note that the facial selectivity for the azlactone addition to acylisoquinolines is opposite to that of the azlactone rearrangement. This finding suggests significant differences in the structures of the corresponding intermediate ion pairs. The origins of facial selectivity in these and related reactions are the subject of ongoing investigations.