Asymmetric Catalysis

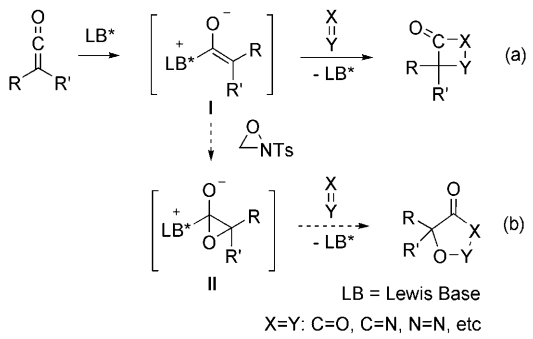
DOI: 10.1002/anie.201003532

Formal [3+2] Cycloaddition of Ketenes and Oxaziridines Catalyzed by Chiral Lewis Bases: Enantioselective Synthesis of Oxazolin-4-ones**

*Pan-Lin Shao, Xiang-Yu Chen, and Song Ye**

The oxidation of enolates with oxaziridine derivatives has been widely utilized for the synthesis of α-hydroxy carbonyl compounds since Davis et al. reported their pioneering work in 1980s.[1,2] Asymmetric Davis' oxaziridine oxidation reactions generally require a stoichiometric amount of chiral oxaziridine or auxiliary. It is therefore highly desirable to develop a catalytic, enantioselective version of Davis' oxidation and related reactions.[3]

During the past decades, great success has been achieved through enantioselective [2+2] and [4+2] cycloaddition reactions of ketenes[4] catalyzed by chiral Lewis bases such as cinchona alkaloids,[5] planar-chiral DMAP derivatives,[6] and N-heterocyclic carbenes (NHCs)[7,8] (Scheme 1a; DMAP = 4-dimethylaminopyridine).[9] The key intermediate

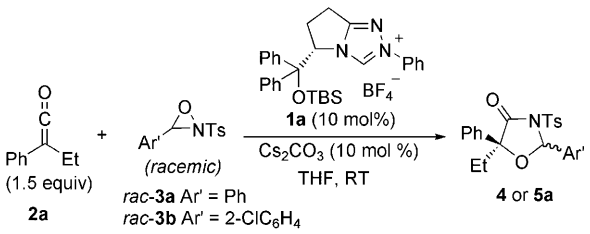


Scheme 1. a) LB-catalyzed cycloaddition reactions of ketene derivatives; b) Possible oxidation of generated zwitterionic enolate **II** with oxaziridine compounds. Ts = 4-toluenesulfonyl.

of these catalytic reactions involves the zwitterionic enolate intermediate **I** generated by the addition of a Lewis base to ketene compounds. We envision that this zwitterionic enolate **I** could be subject to oxidation with oxaziridine derivatives to produce a new intermediate **II**, and thus open new possibilities for catalytic ketene reactions (Scheme 1b).

Based on the above analysis, herein we report a novel enantioselective formal [3+2] cycloaddition of ketenes and oxaziridines for the synthesis of oxazolin-4-ones,[10] which are not only biologically interesting intermediates[11] but are also masked α-hydroxy carbonyl compounds.[12]

Initially, we observed that the NHC **1a′**, which was generated in situ from the triazolium salt **1a** in the presence of Cs_2CO_3, catalyzed the cycloaddition reaction of ketene **2a** and racemic oxaziridine **3a** and furnished the desired oxazolin-4-one **4** in 47% yield with 1:1 diastereoselectivity and promising enantioselectivity (Scheme 2). When oxaziridine *rac*-**3b** bearing a 2-chlorophenyl group was used, the corresponding cycloadduct **5a** was obtained in better yield with 3:1 diastereoselectivity and decreasing enantioselectivity.



4 (Ar' = Ph), 47%, *cis*/*trans* = 1:1, 73% *ee* (*cis*), 60% *ee* (*trans*)
5a (Ar' = 2-ClC$_6$H$_4$), 80%, *cis*/*trans* = 3:1, 56% *ee* (*cis*), 30% *ee* (*trans*)

Scheme 2. Cycloaddition reaction of ketene **2a** and racemic oxaziridines **3a** and **3b** catalyzed by NHC **1a′**. TBS = *tert*-butyldimethylsilyl, THF = tetrahydrofuran.

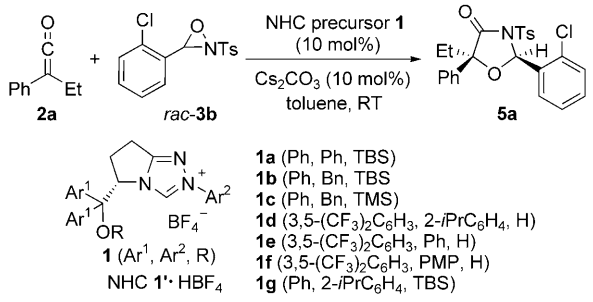
A series of NHCs,[7a,13] derived from L-pyroglutamic acid, were then screened for the model reaction of phenyl(ethyl)ketene **2a** and racemic oxaziridine **3b** (Table 1). It was found that both NHC **1c′** and **1d′** could afford the desired cycloadduct **5a** in good yield with high diastereoselectivities and enantioselectivities (Table 1, entries 3 and 4). More interestingly, we noticed that the opposite enantioselectivity could be induced by appropriate NHC catalysts, although they all bear the same chiral center (Table 1, entries 1–3 vs. entries 4–7). Not only NHCs **1e′**,**f′** bearing a proximal free hydroxy group (Table 1, entries 5 and 6), but also NHC **1g′** bearing a bulky *N*-aryl group (Table 1, entry 7) showed some sort of reversed enantioselectivity. N-heterocyclic carbene **1d′**, which has both of the above features, afforded the best result (Table 1, entry 4). In other words, both the free hydroxy group and the bulky N-substituent are believed to contribute to the reverse of enantioselectivity.[14]

[*] P.-L. Shao, X.-Y. Chen, Prof. Dr. S. Ye
Beijing National Laboratory for Molecular Sciences
CAS Key Laboratory of Molecular Recognition and Function
Institute of Chemistry, Chinese Academy of Sciences
Beijing 100190 (China)
Fax: (+86) 10-6255-4449
E-mail: songye@iccas.ac.cn

[**] Financial support from the National Natural Science Foundation of China (nos. 20872143, 20932008), the Ministry of Science and Technology of China (no. 2009ZX-5909501-018), and the Chinese Academy of Sciences is gratefully acknowledged.

Supporting information (including experimental procedures, characterization data, and NMR spectra) for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201003532.

Table 1: Screening of NHC catalysts and optimization of reaction conditions.



Entry	1	2a/3b	5a	Yield [%][a]	*cis*/*trans*[b]	*ee* [%][c]
1	**1a**	1:1.2	(−)-**5a**	64	3:1	52
2	**1b**	1:1.2	(−)-**5a**	50	7:1	74
3	**1c**	1:1.2[d]	(−)-**5a**	65	9:1	90
4	**1d**	1:1.2[e]	(+)-**5a**	71	14:1	91
5	**1e**	1:1.2	(+)-**5a**	62	8:1	32
6	**1f**	1:1.2	(+)-**5a**	42	7:1	10
7	**1g**	1:1.2	(+)-**5a**	38	5:1	55
8	**1d**	1:2	(+)-**5a**	68	14:1	92
9	**1d**	2:1	(+)-**5a**	80	10:1	82
10	**1d**	1:1.2[f]	(+)-**5a**	91	15:1	95
11	**1d**	1:1.2[g]	(+)-**5a**	24	4:1	12

[a] Yield of isolated product. [b] Determined by ^{1}H NMR spectroscopy (300 MHz) of the reaction mixture. [c] Determined by HPLC on a chiral stationary phase. [d] (+)-**3b** was recovered in 28% yield with 67% *ee*. [e] (−)-**3b** was recovered in 21% yield with 98% *ee*. [f] (+)-**3b** (with 55% *ee*) was used instead of *rac*-**3b**. [g] (−)-**3b** (with 88% *ee*) was used instead of *rac*-**3b**. Bn = benzyl, PMP = *para*-methoxyphenyl, TMS = trimethylsilyl.

Increasing the loading of the oxaziridine benefited the enantioselectivity, while the reaction with excess ketene provided the cycloadduct in better yield but with compromised enantioselectivity (Table 1, entries 8 and 9).

Notably, when 1.2 equivalents of racemic oxaziridine *rac*-**3b** was used, the optically active oxaziridine (−)- or (+)-**3b** could be recovered in reasonable yield with good enantiopurity (67% *ee* or 98% *ee*) for the reactions catalyzed by NHC **1c′** or **1d′**, respectively (Table 1, entries 3 and 4). On the other hand, employing optically active oxaziridines as the reagents had a great effect on the yield and enantioselectivity of the cycloaddition reaction. For example, better yield (91% vs. 71%) and enantioselectivity (95% *ee* vs. 91% *ee*) were observed when (+)-**3b** (with 55% *ee*) was used instead of *rac*-**3b** for the reaction catalyzed by **1d′** (Table 1, entry 10 vs. 4). On the contrary, utilizing (−)-**3b** (with 88% *ee*) dramatically diminished the yield and enantioselectivity (Table 1, entry 11 vs. 4). Notably, both reactions, no matter which oxaziridine (+)-**3b** or (−)-**3b** was used,[15] afforded (+)-**5a** as the major enantiomer when NHC **1d′** was chosen as the catalyst (Table 1, entries 10 and 11).

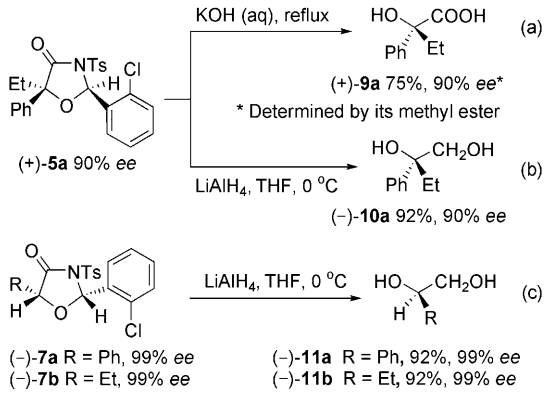
A number of aryl(alkyl)ketenes were then examined for the cycloaddition catalyzed by NHC **1c′** or **1d′** (Table 2). Ketenes with a *para*-substituted aryl group (with both electron-withdrawing 4-Cl and 4-Br, and electron-donating 4-Me) and a *meta*-substituted aryl group (3-Cl), provided the corresponding oxazolin-4-ones **5** in good yields with high diastereo- and enantioselectivities (Table 2, entries 1–5). However, only a trace amount of cycloadduct was observed for the reaction of 2-chlorophenyl(ethyl)ketene (**2f**; Table 2, entry 6). Moreover, 2-naphthyl(ethyl)ketene (**2g**) worked well, while 1-naphthyl(ethyl)ketene (**2h**) did not (Table 2, entries 7 and 8). In addition, when aryl(alkyl)ketene with a methyl, *n*Pr, or *n*Bu group was employed, good yield, high diastereo-, and enantioselectivities were observed (Table 2, entries 9–12).

Consistent with the model reaction in Table 1, cycloaddition reactions catalyzed by NHC **1c′** furnished the desired products with opposite enantioselectivities but in somewhat lower yields compared with those catalyzed by NHC **1d′** (Table 2, entries 1′, 2′, and 9′–12′).

The kinetic resolution of racemic oxaziridine **3b** was also observed for the NHC-catalyzed reaction. Optically active (−)-**3b** was recovered in 15–26% yield with 76–99% *ee* for the reactions catalyzed by NHC **1d′** (Table 2, entries 1–12). Meanwhile, (+)-**3b** was recovered in 28–36% yield with 10–67% *ee* for the reactions catalyzed by NHC **1c′** (Table 2, entries 1′, 2′, and 9′–12′).

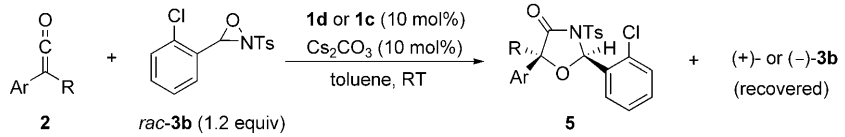
In contrast to stable disubstituted ketenes, unstable monosubstituted ketenes, which were generated in situ from the acyl chlorides, did not react with oxaziridine **3b** in the presence of NHCs. However, cinchona alkaloids **8a** and **8b** were found to be suitable catalysts for the reaction of monosubstituted ketenes and the oxaziridine **3b** (Table 3). Both phenylketene and ethylketene worked well and gave the cycloadducts in moderate to good yields with high enantioselectivities (Table 3, entries 1 and 3). The pseudoenantiomers, TMS-quinidine (**8a**) and TMS-quinine (**8b**), led to the cycloadducts in high but opposite enantioselectivities (Table 3, entries 2 and 4). It should be noted that while cinchona alkaloids **8a**,**b** worked well as the catalysts for the reaction of monosubstituted ketenes, they did not work for the reaction of disubstituted ketenes **2**.[16]

The resulting oxazolin-4-one products present opportunities for further chemical transformations. For example, the α-hydroxy acid **9a** and the 1, 2-diols **10a**, **11a** and **11b** could be readily synthesized by saponification and reduction of the corresponding cycloadducts, respectively, without erosion of enantiopurity (Scheme 3).

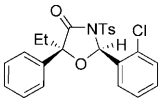
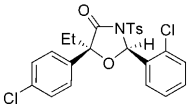
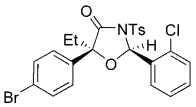
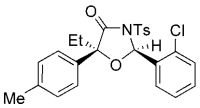
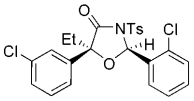
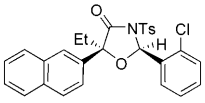
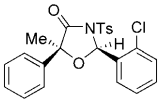
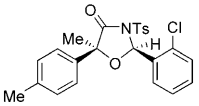
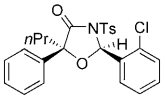
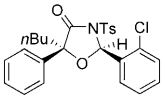


Scheme 3. Synthesis of optically active hydroxy acid and diols derived from oxazolin-4-one derivatives.

Table 2: Formal [3+2] cycloaddition reaction of disubstituted ketenes and oxaziridine **3b** catalyzed by NHC **1d′** or **1c′**.



2 *rac*-**3b** (1.2 equiv) **5**

Entry	2	Ar, R	Cat.	5		Yield [%][a]	*cis/trans*[b]	*ee* [%][c]	3b	Yield [%][a]	*ee* [%][c]
1	**2a**	Ph, Et	**1d**	(+)-**5a**		71	14:1	91	(−)-**3b**	21	98
1′	**2a**		**1c**	(−)-**5a**		65	9:1	90	(+)-**3b**	28	67
2	**2b**	4-ClC_6H_4, Et	**1d**	(+)-**5b**		71	8:1	89	(−)-**3b**	19	98
2′	**2b**		**1c**	(−)-**5b**		38	8:1	87	(+)-**3b**	36	27
3	**2c**	4-BrC_6H_4, Et	**1d**	(+)-**5c**		78	14:1	91	(−)-**3b**	15	99
4	**2d**	4-MeC_6H_4, Et	**1d**	(+)-**5d**		57	16:1	92	(−)-**3b**	26	76
5	**2e**	3-ClC_6H_4, Et	**1d**	(+)-**5e**		68	10:1	91	(−)-**3b**	25	87
6	**2f**	2-ClC_6H_4, Et	**1d**	**5f**	–	trace	–	–	–	–	–
7	**2g**	2-naphthyl, Et	**1d**	(−)-**5g**		61	10:1	94	(−)-**3b**	21	77
8	**2h**	1-naphthyl, Et	**1d**	**5h**	–	trace	–	–	–	–	–
9	**2i**	Ph, Me	**1d**	(+)-**5i**		52	15:1	85	(−)-**3b**	25	92
9′	**2i**		**1c**	(−)-**5i**		42	6:1	86	(+)-**3b**	35	36
10	**2j**	4-ClC_6H_4, Me	**1d**	(+)-**5j**		72	10:1	91	(−)-**3b**	17	92
10′	**2j**		**1c**	(−)-**5j**		37	8:1	79	(+)-**3b**	36	42
11	**2k**	Ph, *n*Pr	**1d**	(+)-**5k**		60	14:1	92	(−)-**3b**	21	76
11′	**2k**		**1c**	(−)-**5k**		43	10:1	90	(+)-**3b**	32	21
12	**2l**	Ph, *n*Bu	**1d**	(+)-**5l**		61	14:1	95	(−)-**3b**	18	94
12′	**2l**		**1c**	(−)-**5l**		41	14:1	91	(+)-**3b**	36	10

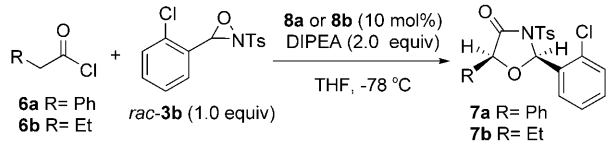
[a] Yield of isolated product. [b] Determined by ^{1}H NMR spectroscopy (300 MHz) of the reaction mixture. [c] Determined by HPLC on a chiral stationary phase.

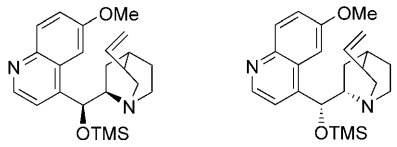
The structure of oxazolinone *cis*-**4** (see Scheme 2) was established by X-ray crystal structure analysis.[17] The absolute configuration of oxazolin-4-one **5a** and **7a**,**b** were assigned after their chemical transformations into hydroxy acid and/or diols.[18] The *cis*/*trans* isomers of oxazolin-4-one **7** was assigned by the NOE interactions of the two isomers.[19]

The formal cycloaddition reaction described here is believed to be initialized by the addition of a Lewis base to a ketene substrate, which results in the formation of a zwitterionic enolate intermediate **I**. The subsequent oxidation of enolate **I** with an oxaziridine compound affords the intermediate **II** as well as the imine **III**. Further addition of the intermediate **II** with the imine **III** gives a zwitterionic complex **IV**, which collapses to furnish the final cycloadduct and regenerate the Lewis base catalyst (Scheme 4).

In summary, an unprecedented catalytic formal [3+2] cycloaddition of ketenes and oxaziridines was reported. N-heterocyclic carbenes and cinchona alkaloids were found to be the catalysts of choice for the reaction of disubstituted and monosubstituted ketenes, respectively. Both enantiomers of oxazolin-4-one derivatives were obtained in moderate to good yields with good diastereo- and enantioselectivities by

Table 3: Formal [3+2] cycloaddition of monosubstituted ketenes and oxaziridine **3b** catalyzed by cinchona alkaloids.

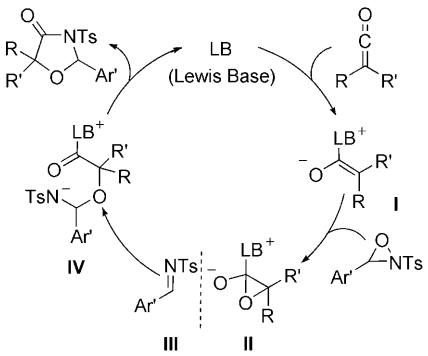




8a TMS-quinidine **8b** TMS-quinine

Entry	6	Cat.	7	Yield [%][a]	*cis*/*trans*[b]	*ee* [%][c]
1	**6a**	**8a**	(−)-**7a**	62	5:1	99, 99
2	**6a**	**8b**	(+)-**7a**	44	8:1	99, 20
3	**6b**	**8a**	(−)-**7b**	47	6:1	99, 99
4	**6b**	**8b**	(+)-**7b**	42	5:1	99, 70

[a] Yield of isolated product. [b] Determined by ^{1}H NMR spectroscopy (300 MHz) of the reaction mixture. [c] Determined by HPLC on a chiral stationary phase; *ee* value of the *cis* isomer, *ee* value of the *trans* isomer. DIPEA = *N*,*N*-diisopropylethylamine.



Scheme 4. Possible catalytic cycle.

choosing the appropriate NHCs with suitable substituents or the appropriate pseudoenantiomers of the cinchona alkaloids. The resulting oxazolin-4-one derivatives are successfully converted into the corresponding α-hydroxy acids or 1,2-diols in one step. In addition, the kinetic resolution of racemic oxaziridine compounds was also observed in some cases. Further studies of this intriguing kinetic resolution are underway.

Received: June 10, 2010
Revised: August 3, 2010
Published online: September 28, 2010

Keywords: asymmetric catalysis · cycloaddition · ketenes · oxaziridines · oxazolidin-4-ones

[1] For the synthesis and application of α-hydroxy acids, see: a) G. M. Coppola, H. F. Schuster, *α-Hydroxy Acids in Enantioselective Synthesis*, VCH, Weinheim, Germany, **1997**; b) J. M. Janey, *Angew. Chem.* **2005**, *117*, 4364; *Angew. Chem. Int. Ed.* **2005**, *44*, 4292; c) N. Momiyama, H. Yamamoto, *J. Am. Chem. Soc.* **2003**, *125*, 6038.

[2] a) F. A. Davis, N. F. Abdul-Malik, S. B. Awad, M. E. Harakal, *Tetrahedron Lett.* **1981**, *22*, 917; b) F. A. Davis, M. E. Harakal, S. B. Awad, *J. Am. Chem. Soc.* **1983**, *105*, 3123; c) F. A. Davis, L. C. Vishwakarma, J. M. Billmers, J. Finn, *J. Org. Chem.* **1984**, *49*, 3241.

[3] a) F. A. Davis, B. C. Chen, *Chem. Rev.* **1992**, *92*, 919; b) F. A. Davis, A. C. Sheppard, B. C. Chen, M. S. Haque, *J. Am. Chem. Soc.* **1990**, *112*, 6679; c) F. A. Davis, R. E. Reddy, P. V. N. Kasu, *J. Org. Chem.* **1997**, *62*, 3625; d) T. Ishimaru, N. Shibata, J. Nagai, S. Nakamura, T. Toru, S. Kanemasa, *J. Am. Chem. Soc.* **2006**, *128*, 16488; e) D. S. Reddy, N. Shibata, J. Nagai, S. Nakamura, T. Toru, *Angew. Chem.* **2009**, *121*, 817; *Angew. Chem. Int. Ed.* **2009**, *48*, 803.

[4] For reviews on the reaction of ketenes, see: a) T. T. Tidwell, *Angew. Chem.* **2005**, *117*, 5926; *Angew. Chem. Int. Ed.* **2005**, *44*, 5778; b) T. T. Tidwell, *Eur. J. Org. Chem.* **2006**, 563; c) R. K. Orr, M. A. Calter, *Tetrahedron* **2003**, *59*, 3545; d) D. H. Paull, A. Weatherwax, T. Lectka, *Tetrahedron* **2009**, *65*, 6771.

[5] a) H. Wynberg, E. G. J. Staring, *J. Am. Chem. Soc.* **1982**, *104*, 166; b) M. A. Calter, *J. Org. Chem.* **1996**, *61*, 8006; c) M. A. Calter, W. Liao, *J. Am. Chem. Soc.* **2002**, *124*, 13127; d) M. A. Calter, O. A. Tretyak, C. Flaschenriem, *Org. Lett.* **2005**, *7*, 1809; e) R. Tennyson, D. Romo, *J. Org. Chem.* **2000**, *65*, 7248; f) R. J. Duffy, K. A. Morris, D. Romo, *J. Am. Chem. Soc.* **2005**, *127*, 16754; g) A. E. Taggi, A. M. Hafez, H. Wack, B. Young, W. J. Drury III, T. Lectka, *J. Am. Chem. Soc.* **2000**, *122*, 7831; h) S. France, A. Weatherwax, A. E. Taggi, T. Lectka, *Acc. Chem. Res.* **2004**, *37*, 592; i) T. Bekele, M. H. Shah, J. Wolfer, C. J. Abraham, A. Weatherwax, T. Lectka, *J. Am. Chem. Soc.* **2006**, *128*, 1810; j) C. J. Abraham, D. H. Paull, M. T. Scerba, J. W. Grebinski, T. Lectka, *J. Am. Chem. Soc.* **2006**, *128*, 13370; k) J. Wolfer, T. Bekele, C. J. Abraham, C. Dogo-Isonagie, T. Lectka, *Angew. Chem.* **2006**, *118*, 7558; *Angew. Chem. Int. Ed.* **2006**, *45*, 7398; l) E. Alden-Danforth, M. T. Scerba, T. Lectka, *Org. Lett.* **2008**, *10*, 4951; m) X. Xu, K. Wang, S. G. Nelson, *J. Am. Chem. Soc.* **2007**, *129*, 11690; n) C. Zhu, X. Shen, S. G. Nelson, *J. Am. Chem. Soc.* **2004**, *126*, 5352.

[6] a) G. C. Fu, *Acc. Chem. Res.* **2004**, *37*, 542; b) B. L. Hodous, J. C. Ruble, G. C. Fu, *J. Am. Chem. Soc.* **1999**, *121*, 2637; c) J. E. Wilson, G. C. Fu, *Angew. Chem.* **2004**, *116*, 6518; *Angew. Chem. Int. Ed.* **2004**, *43*, 6358; d) C. Schaefer, G. C. Fu, *Angew. Chem.* **2005**, *117*, 4682; *Angew. Chem. Int. Ed.* **2005**, *44*, 4606; e) X. Dai, T. Nakai, J. A. C. Romero, G. C. Fu, *Angew. Chem.* **2007**, *119*, 4445; *Angew. Chem. Int. Ed.* **2007**, *46*, 4367; f) J. M. Berlin, G. C. Fu, *Angew. Chem.* **2008**, *120*, 7156; *Angew. Chem. Int. Ed.* **2008**, *47*, 7048.

[7] a) Y.-R. Zhang, L. He, X. Wu, P.-L. Shao, S. Ye, *Org. Lett.* **2008**, *10*, 277; b) N. Duguet, C. D. Campbell, A. M. Z. Slawin, A. D. Smith, *Org. Biomol. Chem.* **2008**, *6*, 1108.

[8] For reviews on NHC-catalzyed reactions, see: a) D. Enders, O. Niemeier, A. Henseler, *Chem. Rev.* **2007**, *107*, 5606; b) N. Marion, S. Díez-González, S. P. Nolan, *Angew. Chem.* **2007**, *119*, 3046; *Angew. Chem. Int. Ed.* **2007**, *46*, 2988; c) K. Zeitler, *Angew. Chem.* **2005**, *117*, 7674; *Angew. Chem. Int. Ed.* **2005**, *44*, 7506; d) D. Enders, T. Balensiefer, *Acc. Chem. Res.* **2004**, *37*, 534.

[9] For the asymmetric reactions of ketenes catalyzed by Lewis acids or bifunctional catalysts, see: a) Y. Tamai, H. Yoshiwara, M. Someya, J. Fukumoto, S. Miyano, *J. Chem. Soc. Chem. Commun.* **1994**, 2281; b) H. W. Yang, D. Romo, *Tetrahedron Lett.* **1998**, *39*, 2877; c) S. G. Nelson, T. J. Peelen, Z. Wan, *J. Am. Chem. Soc.* **1999**, *121*, 9742; d) D. A. Evans, J. M. Janey, *Org. Lett.* **2001**, *3*, 2125; e) V. Gnanadesikan, E. J. Corey, *Org. Lett.* **2006**, *8*, 4943; f) Y. M. Lin, J. Boucau, Z. Li, V. Casarotto, J. Lin, A. N. Nguyen, J. Ehrmantraut, *Org. Lett.* **2007**, *9*, 567; g) P. S. Tiseni, R. Peters,

Angew. Chem. **2007**, *119*, 5419; *Angew. Chem. Int. Ed.* **2007**, *46*, 5325.

[10] The synthesis of oxazolin-4-ones from ketenes and sulfilimines: a) D. M. Ketcha, M. Abou-Gharbia, F. X. Smith, D. Swern, *Tetrahedron Lett.* **1983**, *24*, 2811; b) M. Abou-Gharbia, D. M. Ketcha, D. E. Zacharias, D. Swern, *J. Org. Chem.* **1985**, *50*, 2224.

[11] For bioactive oxazolin-4-ones, see: V. R. Macherla, J. Liu, M. Sunga, D. J. White, J. Grodberg, S. Teisan, K. S. Lam, B. C. M. Potts, *J. Nat. Prod.* **2007**, *70*, 1454.

[12] The asymmetric synthesis of α-hydroxy acids through the [2+2] cycloaddition of ketenes and nitroso compounds: a) M. Dochnahl, G. C. Fu, *Angew. Chem.* **2009**, *121*, 2427; *Angew. Chem. Int. Ed.* **2009**, *48*, 2391; b) I. Chatterjee, C. K. Jana, M. Steinmetz, S. Grimme, A. Studer, *Adv. Synth. Catal.* **2010**, *352*, 945.

[13] a) D. Enders, J. Han, *Tetrahedron Lett.* **2008**, *49*, 1367; b) D. Enders, J. Han, A. Henseler, *Chem. Commun.* **2008**, 3989; c) D. Enders, J. Han, *Synthesis* **2008**, 3864.

[14] The switch of enantioselectivity was previously observed by our research group: X.-L. Huang, L. He, P.-L. Shao, S. Ye, *Angew. Chem.* **2009**, *121*, 198; *Angew. Chem. Int. Ed.* **2009**, *48*, 192.

[15] (+)-**3b** and (−)-**3b** were prepared from the resolution of *rac*-**3b** by the cycloaddition reaction of ketenes catalyzed by NHC **1c′** and **1d′**, respectively.

[16] As reported (Refs. [4–7]), NHCs are efficient catalysts for reactions of disubstituted ketenes but not for monosubstituted ones, while cinchona alkaloids are good for monosubstituted ketenes but not for disubstituted ones.

[17] CCDC 787203 (*cis*-**4**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[18] The absolute configuration of other oxazolinone derivatives **5b–l** was assigned by the comparison of their optical rotation and/or CD spectra with compound **5a**.

[19] See the Supporting Information for details.

