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N-Heterocyclic Carbene-Catalyzed Cyclization of Unsaturated Acyl Chlorides and Ketones

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Abstract: A straightforward synthesis of optically active trifluoromethyl dihydropyranones and spirocyclic oxindole-dihydropyranones has been realized by the chiral N-heterocyclic carbenes-catalyzed cyclization of α,β-unsaturated β-methylacyl chlorides with activated trifluoromethyl ketones or isatin derivatives.

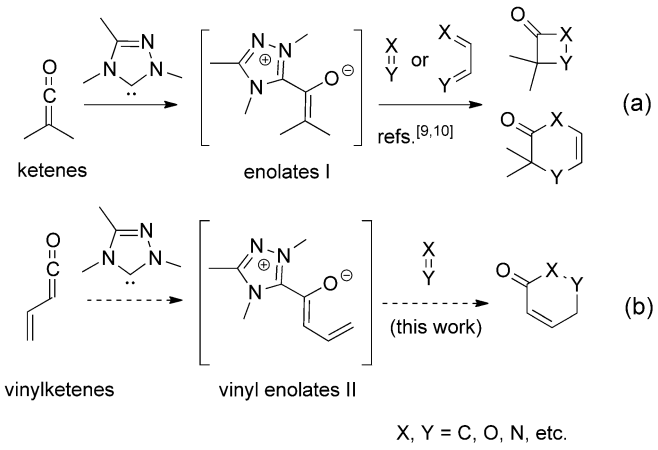
Keywords: asymmetric catalysis; cyclization; dihydropyranones; N-heterocyclic carbenes; organocatalysis; vinylketenes

Since Staudinger's discovery of ketenes and the cycloaddition of ketene with imines to form β-lactams in early 1900s,[1] the cycloaddition reactions of ketene have become one of the powerful methodologies for construction of cyclic compounds.[2] In last decades, the catalytic enantioselective [2+2] or [2+4] cycloaddition of ketenes with aldehydes,[3] imines,[4] azo compounds,[5] nitro compounds,[6] oxadienes,[7] and azadienes[8] had been well established.

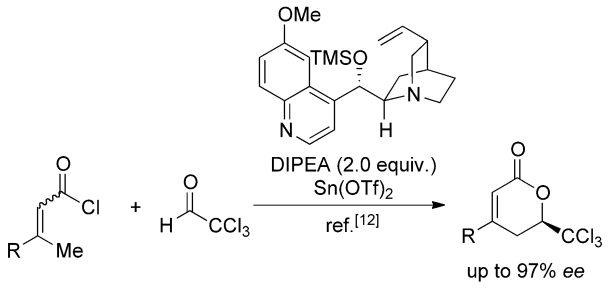
In 2008 and later, we,[9] independently with Smith et al.,[10] have demonstrated that N-heterocyclic carbenes (NHCs)[11] were efficient catalysts for the formal cycloaddition reactions of ketenes. The enolates I generated by the addition of NHC to ketenes are considered as the key intermediate for these reaction [Scheme 1, reaction (a)]. We conjecture that vinyl enolates II will be generated if vinylketenes are employed instead of ketenes, thus opening a new possibility of NHC-catalyzed reaction of vinylketenes [Scheme 1, reaction (b)].

A literature survey revealed that Peters et al. reported a pioneering asymmetric *Cinchona* alkaloids-catalyzed cyclization of unsaturated acyl halides with aldehydes (Scheme 2).[12] In this paper, we wish to report an N-heterocyclic carbene-catalyzed cyclization of unsaturated acyl chlorides with activated ketones, which did not work when *Cinchona* alkaloids were used as the catalysts.[13]

5,6-Dihydropyran-2-ones (α,β-unsaturated δ-lactones) are widely present in a number of natural and unnatural compounds which possess potent biological



Scheme 1. NHC-catalyzed cycloadditions of ketenes and vinylketenes.



Scheme 2. *Cinchona* alkaloids-catalyzed annulation of unsaturated acyl chlorides by Peters et al.

activities.[14] Consequently, many approaches have been developed for their construction.[15] However, the enantioselective synthesis of optically active 5,6-dihydropyran-2-ones is still limited.[16]

In view of the wide application of fluorinated compounds in pharmaceuticals, agrochemistry, and materials,[17] trifluoromethyl ketones[18,19] were firstly explored as the substrates for the synthesis of 6-trifluoromethyl-5,6-dihydropyran-2-ones. We are happy to find that NHC **4a′**,[20] generated *in situ* from its precursor **4a** in the presence of Cs_2CO_3, could catalyze the reaction of acyl chloride **1a** and trifluoromethyl ketone **2a** in the presence of 5 equivalents of Et_3N to give the corresponding dihydropyranone **3aa** in 50% yield with 43% *ee* (Table 1, entry 1). However, only a trace of dihydropyranone **3aa** was observed for the reaction catalyzed by the tertiary amines derived from *Cinchona* alkaloids.[12,21]

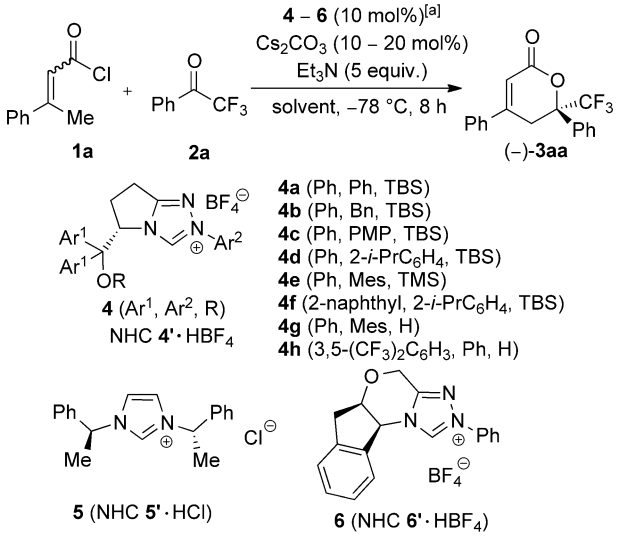
Solvent screening revealed that THF was the best choice, in which the reaction outcome was improved to 68% yield and 79% *ee* (entries 1–5). Interestingly, further improvement of the yield was realized when more Cs_2CO_3 (20 mol% *vs.* 10 mol%) was employed, which may be due to the facilitation of the formation of free NHCs (entry 6 *vs.* 5).

A series of NHCs derived from L-pyroglutamic acid was then screened for the reaction. NHCs **4b′**, **4c′**, and **4d′** (Ar^2 = Bn, PMP or 2-*i*-PrC_6H_4) gave comparable good results (entries 6–9). NHC **4e′**, with a very bulky *N*-mesityl group, gave a dramatically decreased yield and enantioselectivity (entry 10). NHC **4f′**, with a bulky diarylmethyl ether group (Ar^1 = 2-naphthyl), afforded a good yield but low enantioselectivity (entry 11). NHCs **4g** and **4h′** with a free hydroxy group led to the reaction without or with reversed but very low enantioselectivity (entries 12 and 13).[9d]

The monocyclic imidazolium NHC **5′**[22] also worked for the cyclization reaction to give the desired product in moderate yield but without enantioselectivity (entry 14). The reaction catalyzed by tetracyclic triazolium NHC **6′**[23] afforded dihydropyranone **3aa** in good yield with promising enantioselectivity (entry 15).

With the optimized reaction conditions in hand, the scope of the NHC-catalyzed reaction was investigated (Table 2). The acyl chlorides **1b** and **1c** with 4-chlorophenyl and 4-bromophenyl groups afforded the corresponding cycloadducts in high yield with high enantioselectivity (entries 2 and 3), while acyl chloride **1d** with a 4-nitrophenyl group resulted in a decreased yield (50%). The acyl chlorides **1e** and **1f** with an electron-donating group (4-MeC_6H_4, 4-MeOC_6H_4) gave the cycloadducts in good yields but with decreased enantioselectitvities (67% *ee*, 72% *ee*, respectively). The higher the steric demands of the β-aryl group (4-Cl, 3-Cl, 2-ClC_6H_4), the lower were the yield and enantioselectivity observed (entries 2, 7 and 8).

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

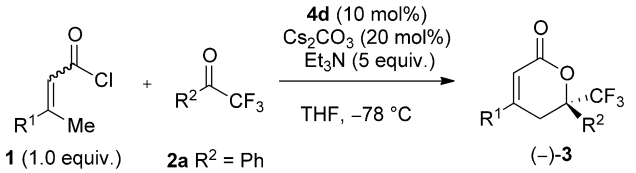


Entry	4–6	Cs_2CO_3 (X mol%)	Solvent	Yield [%][b]	*ee* [%][c]
1	**4a**	10	toluene	50	43
2	**4a**	10	benzene	35	32
3	**4a**	10	DCM	23	45
4	**4a**	10	ether	50	75
5	**4a**	10	THF	68	79
6	**4a**	20	THF	85	80
7	**4b**	20	THF	91	74
8	**4c**	20	THF	80	75
9	**4d**	20	THF	90	81
10	**4e**	20	THF	39	46
11	**4f**	20	THF	82	55
12	**4g**	20	THF	75	−13[d]
13	**4h**	20	THF	80	0
14	**5**	20	THF	43	0
15	**6**	20	THF	75	−50[d]
16	**4d**[e]	10	THF	78	68

[a] NHC **4′–6′** were generated from their precursors **4–6** (10 mol%) in the presence Cs_2CO_3 (10–20 mol%) in the stated solvent at room temperature for 30 min.
[b] Isolated yield.
[c] Determined by HPLC.
[d] The minus *ee* value indicate that (+)-**3aa** was isolated as the major isomer.
[e] 5 mol% of NHC precursor **4d** was used.

The acyl chlorides with heteroaryl groups (Ar = 2-furyl, 2-thienyl) also worked well (entries 9 and 10). It is worthwhile to note that the reaction of acyl chloride **1k** (R^1 = *i*-Pr), which may generate two regioisomers of vinylketenes, gave only one cycloadduct in high yield with moderate enantioselectivity (entry 11). However, the reaction of acyl chloride **1l** (R^1 = Me) and **1m** (R^1 = Et) gave complex mixtures with only trace or around 10% yield, respectively, of

Table 2. Enantioselective synthesis of 6-trifluoromethyl-5,6-dihydropyran-2-ones.



Entry	**1** R^1	**2**	(−)-**3**	Yield [%][a]	*ee* [%][b]
1	**1a** Ph	**2a**	**3aa**	90	81
2	**1b** 4-ClC_6H_4	**2a**	**3ba**	90	89
3	**1c** 4-BrC_6H_4	**2a**	**3ca**	90	93
4	**1d** 4-$NO_2C_6H_4$	**2a**	**3da**	50	79
5	**1e** 4-MeC_6H_4	**2a**	**3ea**	81	67
6	**1f** 4-$MeOC_6H_4$	**2a**	**3fa**	76	72
7	**1g** 3-ClC_6H_4	**2a**	**3ga**	86	86
8	**1h** 2-ClC_6H_4	**2a**	**3ha**	79	65
9	**1i** 2-furyl	**2a**	**3ia**	83	86
10	**1j** 2-thienyl	**2a**	**3ja**	83	82
11	**1k** *i*-Pr	**2a**	**3ka**	80	57
12	**1a** Ph	**2b**	**3ab**	91	75
13	**1b** 4-ClC_6H_4	**2b**	**3bb**	90	75
14	**1c** 4-BrC_6H_4	**2b**	**3cb**	92	84
15	**1e** 4-MeC_6H_4	**2b**	**3eb**	84	67
16	**1g** 3-ClC_6H_4	**2b**	**3gb**	82	71
17	**1h** 2-ClC_6H_4	**2b**	**3hb**	80	55
18	**1i** 2-furyl	**2b**	**3ib**	89	83
19	**1k** *i*-Pr	**2b**	**3kb**	82	57
20	**1c** 4-BrC_6H_4	**2c**	**3cc**	81	91
21	**1c** 4-BrC_6H_4	**2d**	**3cd**	78	84
22	**1c** 4-BrC_6H_4	**2e**	**3ce**	94	85

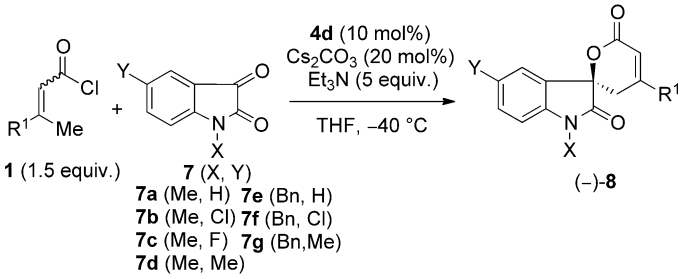
[a] Isolated yield.
[b] Determined by HPLC.

the desired cycloadduct under the current reaction conditions.[24]

When other trifluoromethyl ketones **2b–e** (R^2 = 4-ClC_6H_4, 4-MeC_6H_4, 3-MeC_6H_4, 2-thienyl) were employed, most of the investigated acyl chlorides with different β-substituents, from a phenyl, 4- or 3-substituted phenyl to a 2-furyl group, worked well to give the cycloadducts in good yields with good enantioselectivities (entries 12–22), except that the acyl chlorides **1h** (R^1 = 2-chlorophenyl) and **1k** (R^1 = *i*-propyl) afforded products in decreased enantioselectivities (entries 17 and 19).

After establishing the NHC-catalyzed reaction of acyl chlorides with trifluoromethyl ketones, we were interested to expand the reaction to the activated ketones of isatin, which will lead to the corresponding spirocyclic oxindole-dihydropyranone **8** (Table 3).[25] Indoles are regarded as one of the privileged skeletons in bioactive compounds, thus the combination of

Table 3. Enantioselective synthesis of spirocyclic oxindole-5,6-dihydropyran-2-ones.

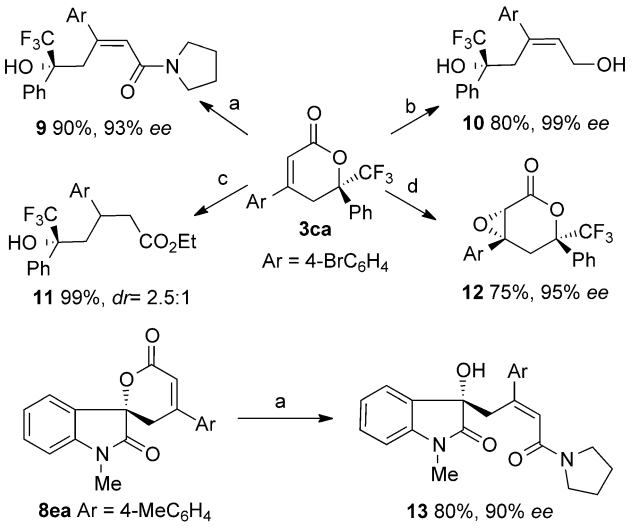


Entry	**1** R^1	**7**	**8**	Yield [%]	*ee* [%]
1	**1a** Ph	**7a**	**8aa**	55	81
2	**1c** 4-BrC_6H_4	**7a**	**8ca**	78	77
3	**1e** 4-MeC_6H_4	**7a**	**8ea**	75	89
4	**1f** 4-$MeOC_6H_4$	**7a**	**8fa**	84	87
5	**1g** 3-ClC_6H_4	**7a**	**8ga**	82	85
6	**1j** 2-thienyl	**7a**	**8ja**	80	91
7	**1f** 4-$MeOC_6H_4$	**7b**	**8fb**	78	81
8	**1c** 4-BrC_6H_4	**7c**	**8cc**	80	93
9	**1f** 4-$MeOC_6H_4$	**7c**	**8fc**	80	91
10[a]	**1c** 4-BrC_6H_4	**7d**	**8cd**	80	91
11[a]	**1f** 4-$MeOC_6H_4$	**7d**	**8fd**	71	71
12	**1c** 4-BrC_6H_4	**7e**	**8ce**	79	95
13	**1d** 4-$NO_2C_6H_4$	**7e**	**8de**	78	nd[b]
14	**1f** 4-$MeOC_6H_4$	**7e**	**8fe**	76	83
15	**1c** 4-BrC_6H_4	**7f**	**8cf**	82	77
16	**1f** 4-$MeOC_6H_4$	**7f**	**8ff**	75	93
17	**1c** 4-BrC_6H_4	**7g**	**8cg**	83	91

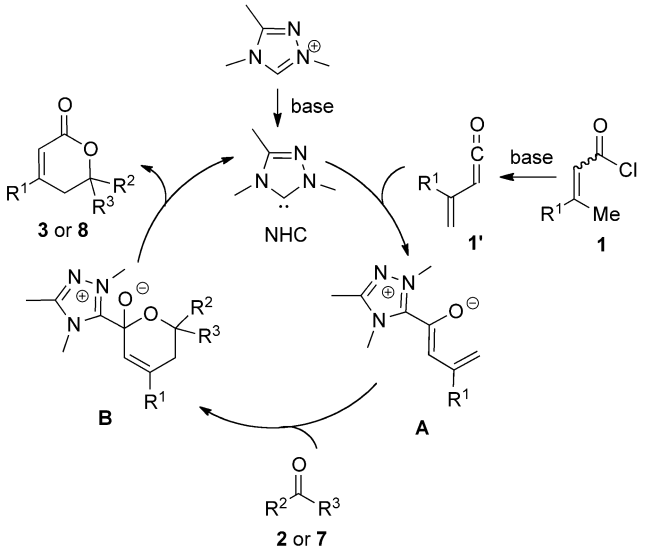
[a] The reaction was carried out at −20 °C.
[b] Not determined.

an indole and a dihydropyranone motif in one molecule will be interesting not only to synthetic but also to medicinal chemists.[26]

It was found that the reaction conditions of trifluoromethyl ketones were also good for isatins, except that 1.5 equivalents of acyl chloride were required for full consumption of isatins **7**, and a reaction temperature of −40 °C instead of −78 °C was applied to make the reaction go smoothly in most cases. The reaction of isatin **7a** reacted well with acyl chlorides **1a**, **1c**, **1e**, **1f**, **1g** and **1j**, with either phenyl, 4-bromophenyl, 4-methylphenyl, 4-methoxylphenyl, 3-chlorophenyl or 2-thienyl substituents, to give the spirocyclic product **8** in moderate to good yield with good to high enantioselectivity (entries 1–6). Isatins with electron-withdrawing groups (**7b** and **7c**) reacted well with acyl chlorides to give the products in good yields with high enantioselectivities (entries 7–9). Isatin **7d** with an electron-donating group recated slowly at −40 °C but well at −20 °C (entries 10 and 11). All the isatins **7e–7g** with an *N*-benzyl group reacted smoothly with acyl chlorides to afford the spirocyclic oxindole-dihydropyranones in good yields and high enantioselectivities (entries 12–17).



Scheme 3. Chemical transformations of dihydropyranones **3ca** and **8ea**.



Scheme 4. Possible catalytic cycle.

The absolute structures of trifluoromethyldihydropyranone (−)-**3ca** and spirocyclic indole-dihydropyranone (−)-**8ce** were unambiguous established by X-ray analysis of their crystals.[27]

In addition to their potential bioactivities, the highly functionalized dihydropyranones provided many opportunities for chemical transformations (Scheme 3). For example, the trifluoromethyl dihydropyranone **3ca** could be aminated to give the corresponding ring-opened amide **9**, and reduced by $LiAlH_4$ to give the corresponding allylic alcohol **10**. Interestingly, the Pd/C-catalyzed hydrogenation of **3ca** did not work at normal pressure, and hydrogenation plus alcoholysis occurred when 50 atm of hydrogen were applied, furnishing the corresponding ester **11** in quantitative yield with 2.5:1 diastereoselectivity. The C=C double bond in **3ca** could also be oxidized by hydroperoxide to give the corresponding epoxide **12** in high yield with high enantiopurity. Aminolysis of spirocyclic oxindole **8ea** with pyrrolidine also gave the 3-hydroxyoxindole **13** in high yield with high enantiopurity.

Similar to Peters' report,[12] the catalytic cycle of this NHC-catalyzed reaction is possibly initiated by the addition of the NHC to the vinyl ketene **1′**, which is generated from the acyl chloride **1** in the presence of base, to give the intermediate of diene **A** (Scheme 4). The diene **A** reacts with ketone **2** or **7** in a hetero-Diels–Alder reaction mode or a stepwise vinylogous aldol reaction followed by intramolecular cyclization to give the zwitterionic **B**. The collapse of zwitterionic **B** furnishes the dihydropyranone **3** or **8** and regenerates the NHC catalyst. Currently, we cannot rule out another possibility that the intermediate **A** is generated by reaction of NHC with the acyl chloride first, followed by deprotonation.

In summary, N-heterocyclic carbenes were found to be efficient catalysts for the cyclization reaction of α,β-unsaturated β-methylacyl chloride with activated ketones to give the corresponding 5,6-dihydropyran-2-ones (α,β-unsaturated δ-lactones) in good yield with good to high enantioselectivity. Two typical activated ketone systems, trifluoromethyl ketones and isatins have been successfully utilized, which provided a straightforward approach to the optically active and biologically interesting trifluoromethyldihydropyranones and spirocyclic oxindole-dihydropyranones.

Experimental Section

General Procedure for NHC-Catalyzed Annulation of Acyl chlorides and Ketones (Table 2 and Table 3)

An oven-dried 25-mL Schlenk tube equipped with a stir bar was charged with triazolium salt **4d** (15.3 mg, 0.025 mmol) and anhydrous Cs_2CO_3 (16.3 mg, 0.05 mmol). This tube was closed with a septum, evacuated, and back-filled with argon. To this mixture was added freshly distilled THF (1.5 mL) and the whole was stirred for 30 min at room temperature. Subsequently triethylamine (0.17 mL, 1.25 mmol) and ketone **2** or **7** (0.25 mmol) were successively added. Then the mixture was cooled down to −78 °C or the specific temperature given in Table 3, a solution of the corresponding acyl chloride **1** (0.25 mmol, or 0.375 mmol) in THF (1 mL) was added in 1 min. The reaction mixture was stirred for around 8 h (Table 2) or 20 h (Table 3) until full consumption of ketone **2** or **7**. The mixture was diluted with ethyl acetate and passed through a short pad of silica gel. The solvent was removed under reduced pressure and the residue was puri-

fied by chromatography on silica gel to give the desired annulation product **3** or **8**.

Acknowledgements

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References

[1] a) H. Staudinger, *Chem. Ber. Dtsch. Chem. Ges.* **1905**, *38*, 1735; b) H. Staudinger, *Justus Liebigs Ann. Chem.* **1907**, *356*, 51.

[2] a) T. T. Tidwell, *Ketenes*, 2nd edn., John Wiley & Sons, Hoboken, New Jersey, **2006**; b) T. T. Tidwell, *Angew. Chem.* **2005**, *117*, 6973; *Angew. Chem. Int. Ed.* **2005**, *44*, 6812; c) R. K Orr, M. A. Calter, *Tetrahedron* **2003**, *59*, 3545; d) D. H. Paull, A. Weatherwax, T. Lectka, *Tetrahedron* **2009**, *65*, 6771; e) G. C. Fu, *Acc. Chem. Res.* **2004**, *37*, 542.

[3] a) H. Wynberg, E. G. Staring, *J. Am. Chem. Soc.* **1982**, *104*, 166; b) S. G. Nelson, T. J. Peelen, Z. Wan, *J. Am. Chem. Soc.* **1999**, *121*, 9742; c) V. Gnandesikan, E. J. Corey, *Org. Lett.* **2006**, *8*, 4943; d) D. A. Evans, J. M. Janey, *Org. Lett.* **2001**, *3*, 2125; e) S. G. Nelson, C. Zhu, X. Shen, *J. Am. Chem. Soc.* **2004**, *126*, 14; f) M. A. Calter, O. A. Tretyak, C. Flashchenriem, *Org. Lett.* **2005**, *7*, 1809; g) G. S. Cortez, R. L. Tennyson, D. Romo, *J. Am. Chem. Soc.* **2001**, *123*, 7945; h) S. H. Oh, G. S. Cortez, D. Romo, *J. Org. Chem.* **2005**, *70*, 2835; i) J. E. Wilson, G. C. Fu, *Angew. Chem.* **2004**, *116*, 6518; *Angew. Chem. Int. Ed.* **2004**, *43*, 6358; j) P. V. G. Reddy, S, Tabassum, A. Blanrue, R. Wilhelm, *Chem. Commun.* **2009**, 5910; k) M. Mondal, A. A. Ibrahim, K. A. Wheeler, N. J. Kerrigan, *Org. Lett.* **2010**, *12*, 1664.

[4] a) A. E. Taggi, A. M. Hafez, H. Wack, B. Young, W. J. Drury III, T. Lectka, *J. Am. Chem. Soc.* **2000**, *122*, 7831; b) A. E. Taggi, A. M. Hafez, H. Wack, B. Young, D. F. Ferraris, T. Lectka, *J. Am. Chem. Soc.* **2002**, *124*, 6626; c) S. France, M. H. Shah, A. Weatherwax, H. Wack, J. P. Roth, T. Lectka, *J. Am. Chem. Soc.* **2005**, *127*, 1206; d) S. France, A. Weatherwax, A. E. Taggi, T. Lectka, *Acc. Chem. Res.* **2004**, *37*, 592; e) E. C. Lee, B. L. Hodous, E. Bergin, C. Shih, G. C. Fu, *J. Am. Chem. Soc.* **2005**, *127*. 11586; f) B. L. Hodous, G. C. Fu, *J. Am. Chem. Soc.* **2002**, *124*, 1578.

[5] J. M. Berlin, G. C. Fu, *Angew. Chem.* **2008**, *120*, 7156; *Angew. Chem. Int. Ed.* **2008**, *47*, 7048.

[6] 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.

[7] T. Bekele, M. H. Shah, J. Wolfer, C. J. Abraham, A. Weatherwax, T. Lectka, *J. Am. Chem. Soc.* **2006**, *128*, 1810.

[8] a) C. J. Abraham, D. H. Paull, M. T. Scerba, J. W. Grebinski, T. Lectka, *J. Am. Chem. Soc.* **2006**, *128*, 13370; b) J. Wolfer, T. Bekele, C. J. Abraham, C. Dogo-Isonagie, T. Lectka, *Angew. Chem.* **2006**, *118*, 7558; *Angew. Chem. Int. Ed.* **2006**, *45*, 7398.

[9] a) Y.-R. Zhang, L. He, X. Wu, P.-L. Shao, S. Ye, *Org. Lett.* **2008**, *10*, 277; b) L. He, H. Lv, Y.-R. Zhang, S. Ye, *J. Org. Chem.* **2008**, *73*, 8101; c) Y.-R. Zhang, H. Lv, D. Zhou, S. Ye, *Chem. Eur. J.* **2008**, *14*, 8473; d) X.-L. Huang, L. He, P.-L. Shao, S. Ye, *Angew. Chem.* **2009**, *121*, 198; *Angew. Chem. Int. Ed.* **2009**, *48*, 192; e) P.-L. Shao, X.-Y. Chen, S. Ye, *Angew. Chem.* **2010**, *122*, 8590; *Angew. Chem. Int. Ed.* **2010**, *49*, 8412.

[10] a) N. Duguet, C. D. Campbell, A. M. Z. Slawin, A. D. Smith, *Org. Biomol. Chem.* **2008**, *6*, 1108; b) C. Concellón, N. Duguet, A. D. Smith, *Adv. Synth. Catal.* **2009**, *351*, 3001.

[11] For the reviews of NHC-catalzyed reactions, see: a) D. Enders, T. Balensiefer, *Acc. Chem. Res.* **2004**, *37*, 534; b) K. Zeitler, *Angew. Chem.* **2005**, *117*, 7674; *Angew. Chem. Int. Ed.* **2005**, *44*, 7506; c) D. Enders, O. Niemeier, A. Henseler, *Chem. Rev.* **2007**, *107*, 5606; d) N. Marion, S. Díez-González, S. P. Nolan, *Angew. Chem.* **2007**, *119*, 3046; *Angew. Chem. Int. Ed.* **2007**, *46*, 2988; e) T. Rovis, *Chem. Lett.* **2008**, *37*, 2; f) A. J. Arduengo III, L. I. Iconaru, *Dalton Trans.* **2009**, 6903; g) J. L. Moore, T. Rovis, *Top. Curr. Chem.* **2010**, *291*, 77.

[12] a) P. S. Tiseni, R. Peters, *Angew. Chem.* **2007**, *119*, 5419; *Angew. Chem. Int. Ed.* **2007**, *46*, 5325; b) P. S. Tiseni, R. Peters, *Org. Lett.* **2008**, *10*, 2019; c) P. S. Tiseni, R. Peters, *Chem. Eur. J.* **2010**, *16*, 2503.

[13] Bode et al reported an NHC-catalyzed synthesis of 3,4-dihydropyran-2-one from α-chloroaldehydes, oxadienes: M. He, G. J. Uc, J. W. Bode, *J. Am. Chem. Soc.* **2006**, *128*, 15088.

[14] a) K. Yasui, Y. Tamura, T. Nakatani, K. Kawada, M. Ohtani, *J. Org. Chem.* **1995**, *60*, 7567; b) A. Endo, *J. Med. Chem.* **1985**, *28*, 401; c) E. S. Istvan, J. Deisenhofer, *Science* **2001**, *292*, 1160; d) S. J. Shaw, K. F. Sundermann, M. A. Burlingame, D. C. Myles, B. S. Freeze, M. Xian, I. Brouard, A. B. Smith III, *J. Am. Chem. Soc.* **2005**, *127*, 6532.

[15] V. Boucard, G. Broustal, J. M. Campagne, *Eur. J. Org. Chem.* **2007**, 225.

[16] a) Q. Fan, L. Lin, J. Liu, Y. Huang, X. Feng, G. Zhang *Org. Lett.* **2004**, *6*, 2185; b) X. Moreau, B. Bazá-Tejeda, J.-M. Campagne, *J. Am. Chem. Soc.* **2005**, *127*, 7288; c) J. Liu, X. Li, J. Wang, X. Feng, *Adv. Synth. Catal.* **2006**, *348*, 939; d) H. Du, D. Zhao, K. Ding, *Chem. Eur. J.* **2004**, *10*, 5964.

[17] a) P. Kirsch, *Modern Fluoroorganic Chemistry*, Wiley-VCH, Weinheim, **2004**; b) R. Filler, Y. Kobayashi, L. M. Yagupolskii, *Organofluorine Compounds in Medicinal Chemistry and Biomedical Applications*, Elsevier, Amsterdam, **1993**; c) P. V. Ramachandran, *Asymmetric Fluoroorganic Chemistry*, ACS Symposium Series, ACS, Washington, DC, **2000**.

[18] For examples of the reactions of trifloromethyl ketones, see: a) R. Fernández, E. Martín-Zamora, C. Pareja, J. Vázquez, E. Díez, A. Monge, J. M. Lassaletta, *Angew. Chem.* **1998**, *110*, 3598; *Angew. Chem. Int. Ed.* **1998**, *37*, 3428; b) R. Motoki, M. Kanai, M. Shibasaki, *Org. Lett.* **2007**, *9*, 2997; c) A. Bøgevig, K. V. Gothelf, K. A. Jørgensen, *Chem. Eur. J.* **2002**, *8*, 5652; d) M. Rueping, T.

Theissmann, A. Kuenkel, R. M. Koenigs, *Angew. Chem.* **2008**, *120*, 6903; *Angew. Chem. Int. Ed.* **2008**, *47*, 6798; e) J.-L. Zhao, L. Liu, C.-L. Gu, D. Wang, Y.-J. Chen, *Tetrahedron Lett.* **2008**, *49*, 1476; f) M Shi, . X.-G. Liu, Y.-W. Guo, W. Zhang, *Tetrahedron* **2007**, *63*, 12731; g) D. Enders, A. Grossmann, J. Fronert, G. Raabe, *Chem. Commun.* **2010**, 6282; h) K. Hirano, I. Piel, F. Glorius, *Adv. Synth. Catal.* **2008**, *350*, 984.

[19] We have reported an NHC-catalyzed [2+2] annulation of ketenes and trifluoromethyl ketones: X.-N. Wang, P.-L. Shao, H. Lv, S. Ye, *Org. Lett.* **2009**, *11*, 4029.

[20] For examples of the synthesis of triazolium NHCs, see: a) D. Enders, K. Breuer, G. Raabe, J. Runsink, J. H. Teles, J. P. Melder, K. Ebel, S. Brode, *Angew. Chem.* **1995**, *107*, 1119; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1021; b) R. L. Knight, F. J. Leeper, *Tetrahedron Lett.* **1997**, *38*, 3611; c) D. Enders, J. Han, *Tetrahedron: Asymmetry* **2008**. *19*. 1367.

[21] The corresponding reactions catalyzed by trimethylsilylquinidine with or without the additive of $Sc(OTf)_3$ in toluene at −78 °C or −15 °C gave complex mixtures with only a trace of the desired cycloadduct **3aa**.

[22] W. A. Herrmann, L. J. Gooßen, C. Köcher, G. R. J. Artus, *Angew. Chem.* **1996**, *108*, 2980; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 2805.

[23] . S. Kerr, J. R. deAlaniz, T. Rovis, *J. Org. Chem.* **2005**, *70*, 5725.

[24] The instability of these two vinylketenes may contribute to the by-products of these reactions.

[25] We have recently reported an NHC-catalyzed [2+2] annulation of ketenes and isatins: X.-N. Wang, Y.-Y. Zhang, S. Ye, *Adv. Synth. Catal.* **2010**, *352*, 1891–1894.

[26] a) W. C. Sumpter, *Chem. Rev.* **1945**, *37*, 443; b) M. Bandini, A. Eichholzer, *Angew. Chem.* **2009**, *121*, 9786; *Angew. Chem. Int. Ed.* **2009**, *48*, 9608; c) B. M. Trost, M. K. Brennan, *Synthesis* **2009**, 3003; d) F. Zhou, Y.-L. Liu, J. Zhou, *Adv. Synth. Catal.* **2010**, *352*, 1381.

[27] CCDC 785898 [(−)-**3ca**], CCDC 785897 (*rac*-**8fb**) and CCDC 808987 [(−)-**8ce**] contain the crystallographic data in 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. The absolute structures of other dihydropyranones **3** and **8** were assigned by comparison of the optical rotation and CD spectra with those of (−)-**3ca** and (−)-**8ce**.

