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α′-Hydroxyenones as Mechanistic Probes and Scope-Expanding Surrogates for *α,β*-Unsaturated Aldehydes in NHC-Catalyzed Reactions

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Abstract

N-heterocyclic carbene catalyzed reactions of *α,β*-unsaturated aldehydes and a variety of electrophiles allow the facile preparation of a diverse array of annulation products including tri-substituted cyclopentenes, *γ*-lactams, and bicyclic *β*-lactams. The substrate scope of these reactions, however, is limited by the difficulties of preparing the starting*α,β*-unsaturated aldehydes. We now report that *α′*-hydroxyenones, which can be prepared in a single convenient step from aromatic and heteroaromatic aldehydes, can serve as efficient surrogates for enals in the annulation reactions. This protocol allows the facile preparation and use of substrates bearing nitrogen heterocycles. These reagents have also allowed us to demonstrate that, in contrast to other classes of aldehydes, the formation of the Breslow intermediate from enals and N-heterocyclic carbenes is irreversible under the reaction conditions.

Introduction

The explosion of synthetic methods catalyzed by organic molecules has opened new pathways to the rapid construction of structurally and stereochemically complex small molecules from *α,β*-unsaturated aldehydes. These are the key starting materials in numerous emerging processes including both iminium catalysis[i] and N-heterocyclic carbene (NHC) catalyzed annulations.[ii] For example, in our own work we have employed *α,β*-unsaturated aldehydes as substrates for the synthesis of *γ*-lactones, [iii]*γ*-lactams, [iv,v] dihydropyridinones, [vi] cyclopentenes, [vii] bicyclic cyclopentanes, [viii] esters, [ix] and amides[x] all under simple, atom-economical, and mild reaction conditions (Figure 1). In complimentary efforts, other groups have also utilized the combination of *α,β*-unsaturated aldehydes and azolium precatalysts for a variety of other reactions including the formation of *γ*-lactones, [xi] cyclopentanones, [xii] pyridazinones,[xiii] and for *β*-amidations.[xiv]

Despite these exciting new reactions of *α,β*-unsaturated enals, their application to chemically diverse libraries and a full exploration of their substrate scope has been hampered by the relative paucity of *α,β*-unsaturated aldehyde starting materials. This is particularly true of the synthetically valuable cinnamaldehyde derivatives, of which only a few members are commercially available at reasonable cost. Other derivatives must be prepared by multi-step approaches or capricious and expensive cross-coupling reactions. Our own substrate syntheses have relied largely on homologation of readily available aldehydes via a Wittig or

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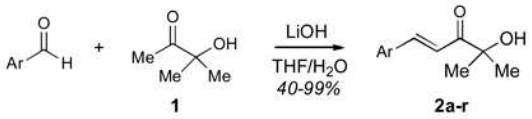
Supporting Information Available. Experimental procedures and characterization data for all compounds. This material is available free of charge via the internet at http://pubs.acs.org.

Horner-Emmons reaction followed by conversion of the resulting unsaturated amide or ester to the aldehyde, a process often requiring three steps.[xv] A direct route to cinnamaldehyde derivatives by Heck reactions with acrolein derivatives is also useful, but requires large quantities of expensive catalysts and additives and does not readily tolerate many heterocycles.[xvi] Organometallic routes such as the transformation of aldehydes to *α*,*β*-unsaturated aldehydes by additions of nucleophilic species derived from 1-alkoxyacetylene are attractive but are again constrained by high reagent costs and relatively poor functional group compatibility.[xvii,xviii] Olefin cross metathesis improves functional group tolerance, but is limited by the availability of the requisite styrenes.[xix] The most attractive route, direct condensations of acetaldehyde and an aromatic aldehyde are conceptually possible but in practice require extensive optimization and are often plagued by the formation of side products.[xx] All of these processes have played an important role in the preparation of substrates for the iminium and NHC-catalyzed reaction manifolds, but the lack of straightforward methods to access these starting materials have constrained the throughput and application of organocatalytic methodologies and discourage the use of many heteroaromatic groups.



(1)

In this article, we report a simple and broadly applicable surrogate to *α*,*β*-unsaturated aldehydes that can be easily prepared, stored, and employed directly in NHC-catalyzed annulations (Scheme 1). Our approach takes advantage of the fact that *α*′-hydroxyenones (**2**) are easily prepared by a one-step aldol condensation of aromatic aldehydes with commercially available 3-hydroxy-3-methylbutanone (eq 1). [xxi,xxii] Furthermore, they are almost always stable, crystalline solids that can be stored indefinitely without special precautions. Palomo [xxiii] and others[xxiv] have extensively utilized these substrates as electrophiles in an impressive range of organo- and metal-catalyzed reactions. We wished, instead, to use these compounds as precursors to catalytically generated homoenolates, or their formal equivalents, that could take the place of the more difficult to prepare *α*,*β*-unsaturated aldehydes in NHC-catalyzed annulation reactions. In essence, we sought to employ Palomo's hydroxyenones as protonucleophiles rather than as electrophiles.

NHC-catalyzed annulations of *α*,*β*-unsaturated aldehydes are thought to occur via the intermediacy of **V**, often referred to as the Breslow intermediate (Scheme 1). [xxv] This species arises via tautomerization of **III**, the initial adduct of an NHC and an aldehyde. We reasoned that the identical reactive intermediate could be reached by retro-benzoin reaction of the *α*′-hydroxyenones. Indeed, it has long been known that cyanide and azolium salts can generate acyl anion equivalents by retro-benzoin reactions of benzoin-dimers.[xxvi] These processes, along with the related use of *α*-ketoacids as aldehyde surrogates, have found use in azolium-catalyzed benzoin and Stetter reactions. [xxvii] Unfortunately, these strategies do not offer operational improvements to reactions of *α*,*β*-unsaturated aldehydes as they do not provide an improved synthesis of the starting materials and the dimeric products do not undergo clean retro-benzoin reactions. These limitations are also the case for acyl silanes, the preparation of which is usually more involved than the aldehydes they replace.[xxviii]

Results and Discussion

In developing the use of α′-hydroxyenones as substrates for NHC-catalyzed reactions, we selected the formation of cyclopentenes via a remarkable cascade reaction for our initial attempts. This process was originally reported by Nair using an achiral imidazolium catalyst,[xxix] and we have reported a highly enantioselective variant using electron-deficient enones and chiral triazolium salts.[vii] We were pleased to observe product formation under conditions originally optimized for α,β-unsaturated aldehydes (Table 1, entry 1). Reaction optimization identified slightly elevated reaction temperatures (40 °C), increased DBU (50 mol %), and a slight excess of the α′-hydroxyenone as ideal (entries 2–9). Shorter reaction times and higher dilution (0.05 M) were preferred due to slow decomposition of **4a** during the reaction, accounting for the mass balance (entry 10). Notably, the acetone byproduct does not appear to significantly affect the reactions and similar results were observed when acetone was added to the annulations.

We found these optimized conditions to be applicable for the vast majority of substrates tested in the cyclopentene-forming annulation reaction. In cases where we had previously prepared the identical products from the corresponding enals, the yields and diastereoselectivities were comparable or slightly superior when the α′-hydroxyenones were employed. Most importantly, the facile access to the startingα′-hydroxyenones made possible a dramatic expansion of the substrate scope (Table 2). Unlike the corresponding enals, the α′-hydroxyenone starting materials could be prepared from a wide range of aromatic and heteroaromatic aldehydes in a single step. The cyclopentene-forming annulations readily tolerated all of these diverse substituent groups, affording the cyclized products in good yields. We were particular pleased to find that the reaction was ideally suited for substrates containing an array of nitrogen heterocycles, attesting to the synthetic utility and tolerance of the NHC-catalyzed reactions. In most cases, pure *cis*-cyclopentene products could be obtained by a single crystallization. Unfortunately, the *trans*-isomers often could not be separated from residual *cis*-product except by preparative HPLC. The reported yields of cyclopentene formation are for a single set of reaction conditions; further substrate dependent optimization is possible. The use of degassed solvent did not significantly improve the reaction yields.[xxx]

We have also found the α′-hydroxyenones to be excellent surrogates for enals in other NHC-catalyzed processes. We have recently reported an efficient annulation of enals and saccharin-derived ketimines to afford highly substituted γ-lactams.[v] These annulation products, along with the cyclopentenes, are excellent starting materials for lead discovery and development in a medicinal chemistry setting. In extending the use of the α′-hydroxyenones to this lactam-forming annulation, we found that we could lower the catalyst and base loadings and perform the reactions at room temperature. These conditions gave good yields and diastereoselectivities for the formation of diverse γ-lactam products bearing aromatic, aliphatic, and heteroaromatic substituents (Table 3). The yields and diastereoselectivities of lactams prepared via this method were in general identical or slightly superior to reactions performed using α,β-unsaturated aldehydes. The higher reactivity of the saccharins stem from their increased electrophilicity. Due to this property, they react rapidly, but reversibly, with the nucleophilic triazolium-derived catalyst. With more electron deficient saccharin-derived substrates, for example **8j** and **8k**, this catalyst inhibition pathway led to poor results when the α′-hydroxyenones were employed, reflecting the lower reactivity (vide supra) of these protonucleophiles.

In preliminary efforts, we have also explored the utility of these substrates for other annulation reactions promoted by azolium precatalysts. We were pleased to find that the conditions identified for cyclopentene formation were directly applicable to the formation of

bicyclo-cyclopentyl-β-lactams (Scheme 2). Likewise, it can also be applied to the synthesis of γ-lactones, albeit in somewhat diminished yields as compared to prior reports using α,β-unsaturated aldehydes.[iii] The lower conversion, however, may reflect the fact that triazolium-derived catalysts are usually inferior to imidazolium-derived catalysts for this particular annulation.[xxxi]

Annulations employing α'-hydroxyenones **2** were generally cleaner than those starting from the corresponding aldehyde; however, these surrogates proved to be somewhat different than α,β unsaturated aldehydes in their reactivity with the catalysts. Direct comparisons of **2** to the enals revealed that the enals were about four times more reactive than the α'-hydroxyenones under identical conditions (Scheme 3). These reactions also suggest that the difference between the two starting materials is in the rate of the formation of the nucleophilic intermediate; once the Breslow intermediate is formed the reactions follow an identical pathway. We attribute the difference in rate to the increased steric demands and decreased electrophilicity of the α'-hydroxyenones, rather than a slow retro-benzoin reaction.

This observation is further supported by the extreme sensitivity of these processes to the size of the NHC-catalyst. Chiral triazolium precatalyst **15**, which is highly effective in numerous enantioselective NHC-catalyzed reactions, proved unproductive even under forcing conditions. We confirmed that the lack of reactivity with precatalyst **15** is due to steric, rather than electronic effects, by preparing and testing the achiral morpholinone-derived triazolium salt **19**, which did promote the retro-benzoin and annulation reaction. This subtle steric effect was further probed by preparing achiral triazolium precatalysts **20** and **21**,[xxxii] whose reactivity diminished as a function of size. As with other triazolium-catalyzed annulations, the presence of an *N*-mesityl substituent proved essential for the success of the reaction; 4-methoxyphenyl or pentafluorophenyl substituted precatalysts **22** and **23** failed to give the desired product. These results suggested that *N*-mesityl substituted pyrrolidine-derived chiral triazolium salts might promote the reaction. Indeed, smaller, chiral NHC-catalysts[xxxiii] such as **17**, do provide the desired products with good enantioselectivity, but at severely diminished levels of conversion. For this reason, the use of α'-hydroxyenones is currently limited to the preparation of racemic annulation products with achiral catalyst **5**.

This finding allowed us to demonstrate that aldehydes are not formed during the reaction or involved in the mechanism. The combination of achiral catalyst **5**, which executes the retro-benzoin, and chiral precatalyst **15** provided only racemic annulations products in good yield. Achiral thiazolium precatalysts are known to promote aldehyde-ketone retro-benzoin reactions but not the annulation.[xxxiv] The combination of an achiral thiazolium **24** and chiral triazolium **15**, however, does not afford the annulation product. These studies establish that, under these conditions, the Breslow intermediate, once formed, does not revert to the aldehyde and the NHC-catalyst (Scheme 4). This contrasts to studies involving aldehydes other than enals, as these undergo reversible formation of the Breslow intermediate [xxxv] and attest to the unique reactivity and properties of extended Breslow-type intermediate **I**. These results also suggest that, at least under these conditions, this process will not be useful for the in situ generation of α,β-unsaturated aldehydes for use in other types of catalytic reactions.

We hasten to emphasize that we do not view the failure of chiral triazolium precatalyst **15** in these processes as a severe limitation. For many purposes, the preparation of racemic annulation products is sufficient or even desirable. In the event that homochiral cyclopentenes are needed for further studies, they can be prepared from the corresponding α,β-unsaturated aldehydes and commercially available chiral triazolium **15**. Other than the fact that the unsaturated aldehyde may be more difficult to access, we do not anticipate

annulation reactions that work with the α'-hydroxyenone and achiral triazolium **5** failing when α,β-unsaturated aldehydes are employed.

Conclusions

In conclusion, we have demonstrated that α'-hydroxyenones of the type popularized by Palomo are outstanding protonucleophiles in azolium catalyzed annulation reactions. The main advantage lies in their facile preparation and handling, making possible the synthesis of diverse cinnamaldehyde surrogates in a single step from commercial materials. These studies extend the scope of azolium catalyzed annulation reactions to include an assortment of heterocyclic substituents. Other advantages include cleaner reactions by avoiding or diminishing side reactions such as decomposition or dimerization of the α,β-unsaturated aldehydes. The one disadvantage of the use of α'-hydroxyenones as substrates for catalytic annulation reactions is that they are not presently compatible with chiral triazolium **15** and are limited to the preparation of racemic products. We believe that the present method is therefore best suited to the rapid synthesis of annulation products for screening or derivatization. Should the enantiopure products be needed they may be prepared from the corresponding, but less conveniently accessed, α,β-unsaturated aldehyde.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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References

i. Erkkilä A, Majander I, Pihko PM. Chem Rev 2007;107:5416–5470. [PubMed: 18072802]

ii. For selected reviews, see: (a) Enders D, Niemeier O, Henseler A. Chem Rev 2007;107:5606–5655. [PubMed: 17956132] (b) Zeitler K. Angew Chem Int Ed 2005;44:7506–7510. (c) Johnson JS. Angew Chem Int Ed 2004;43:1326–1328. (d) Nair V, Vellalath S, Babu BP. Chem Soc Rev 2008;37:2691–2698. [PubMed: 19020682]

iii. (a) Sohn SS, Rosen EL, Bode JW. J Am Chem Soc 2004;126:14370–14371. [PubMed: 15521753] (b) Burstein C, Glorius F. Angew Chem Int Ed 2004;43:6205–6208. (b) Burstein C, Tschan S, Xie X, Glorius F. Synthesis 2006:2418–2439.

iv. He M, Bode JW. Org Lett 2005;7:3131–3134. [PubMed: 15987223]

v. Rommel M, Fukuzumi T, Bode JW. J Am Chem Soc 2008;130:17266–17267. [PubMed: 19053399]

vi. He M, Struble JR, Bode JW. J Am Chem Soc 2006;128:8418–8420. [PubMed: 16802805]

vii. Chiang PC, Kaeobamrung J, Bode JW. J Am Chem Soc 2007;129:3520–3521. [PubMed: 17335218] (b) For the first report of a reaction of this type, see reference [xxix].

viii. (a) He M, Bode JW. J Am Chem Soc 2008;130:418–419. [PubMed: 18092785] (b) Kaeobamrung J, Bode JW. Org Lett 2009;11:677–680. [PubMed: 19175349]

ix . (a) Sohn SS, Bode JW. Org Lett 2005;7:3873–3876. [PubMed: 16119920] (b) Chan A, Scheidt KA. Org Lett 2005;7:905–908. [PubMed: 15727471]

x . (a) Bode JW, Sohn SS. J Am Chem Soc 2007;129:13798–13799. [PubMed: 17956104] (b) Vora HU, Rovis T. J Am Chem Soc 2007;129:13796–13797. [PubMed: 17929821]

xi . (a) Li Y, Zhao ZA, He H, You SL. Adv Synth Catal 2008;350:1885–1890. (b) Nair V, Vellalath S, Poonoth M, Suresh E, Viji S. Synthesis 2007:3195–3200. (c) Nair V, Vellalath S, Poonoth M, Mohan R, Suresh E. Org Lett 2006;8:507–509. [PubMed: 16435871]

xii . Nair V, Babu BP, Vellalath S, Suresh E. Chem Commun 2008:747–749.

xiii . Chan A, Scheidt KA. J Am Chem Soc 2007;129:5334–5335. [PubMed: 17407298]

xiv . (a) Seayad J, Patra PK, Zhang Y, Ying JY. Org Lett 2008;10:953–956. [PubMed: 18247633] (b) Chan A, Scheidt KA. J Am Chem Soc 2008;130:2740–2741. [PubMed: 18260665]

xv . Chuzel O, Piva O. Synth Commun 2003;33:393–402.

xvi . Battistuzzi G, Cacchi S, Fabrizi G. Org Lett 2003;5:777–780. [PubMed: 12605513]

xvii. Wollenberg RH, Albizati KF, Peries R. J Am Chem Soc 1977;99:7365–7367.

xviii . (a) Maeta H, Hashimoto T, Hasegawa T, Suzuki K. Tetrahedron Lett 1992;33:5965–5968. (b) Maeta H, Suzuki K. Tetrahedron Lett 1993;34:341–344.

xix . (a) Paul T, Sirasani G, Andrade RB. Tetrahedron Lett 2008;49:3363–3367. (b) Lee BT, Schrader TO, Martín-Matute B, Kauffman CR, Zhang P, Snapper ML. Tetrahedron 2004;60:7391–7396.

xx . (a) Keinan E, Peretz M. J Org Chem 1983;48:5302–5309. (b) Waley SG. J Chem Soc 1948:2008–2011. (c) Lu X, Li Z, Gao F. Ind Eng Chem Res 2006;45:4145–4149.

xxi . As suggested by a referee, we refer to the α,β-unsaturated, α',α'-dimethyl-α'-hydroxyketones as α'-hydroxyenones.

xxii. (a) Palomo C, Oiarbide M, García JM, González A, Arceo E. J Am Chem Soc 2003;125:13942–13943. [PubMed: 14611214] (b) Reiter M, Turner H, Mills-Webb R, Gouverneur V. J Org Chem 2005;70:8478–8485. [PubMed: 16209595] (c) King GG, Karabinos JV. J Chem Eng Data 1968;13:565–566.

xxiii . (a) Palomo C, Oiarbide M, Halder R, Kelso M, Gómez-Bengoa E, García JM. J Am Chem Soc 2004;126:9188–9189. [PubMed: 15281801] (b) Palomo C, Pazos R, Oiarbide M, García JM. Adv Synth Catal 2006;348:1161–1164. (c) Palomo C, Oiarbide M, Arceo E, García JM, López R, González A, Linden A. Angew Chem Int Ed 2005;44:6187–6190. (d) Palomo C, Oiarbide M, Kardak BG, García JM, Linden A. J Am Chem Soc 2005;127:4154–4155. [PubMed: 15783181]

xxiv . (a) Monge D, Martín-Zamora E, Vázquez J, Alcarazo M, Álvarez E, Fernández R, Lassaletta JM. Org Lett 2007;9:2867–2870. [PubMed: 17580886] (b) Lee S, Lim CJ, Kim S, Subramaniam R, Zimmerman J, Sibi MP. Org Lett 2006;8:4311–4313. [PubMed: 16956214] (c) Sakai T, Yamawaki A, Ito H, Utaka M, Takeda A. J Heterocycl Chem 1986;23:1199–1201.

xxv . Breslow R. J Am Chem Soc 1958;80:3719–3726.

xxvi. For recent examples of highly reversible formation of the Breslow intermediate in NHC-catalyzed reactions, see: (a) Read de Alaniz J, Rovis T. J Am Chem Soc 2005;127:6284–6289. [PubMed: 15853335] (b) Enders D, Han J, Henseler A. Chem Commun 2008:3989–3991.

xxvii . (a) Myers MC, Bharadwaj AR, Milgram BC, Scheidt KA. J Am Chem Soc 2005;127:14675–14680. [PubMed: 16231921] (b) Stetter H, Lorenz G. Chem Ber 1985;118:1115–1125.

xxviii. (a) Mattson AE, Bharadwaj AR, Zuhl AM, Scheidt KA. J Org Chem 2006;71:5715–5724. [PubMed: 16839153] (b) Mattson AE, Bharadwaj AR, Scheidt KA. J Am Chem Soc 2004;126:2314–2315. [PubMed: 14982429]

xxix . Nair V, Vellalath S, Poonoth M, Suresh E. J Am Chem Soc 2006;128:8736–8737. [PubMed: 16819860]

xxx. The use of degassed solvents in azolium catalyzed reactions is sometimes advantageous. For examples, see: (a) Supporting Information of reference [ixa]. Phillips EM, Wadamoto M, Scheidt KA. Synthesis 2009:687–690.

xxxi . Struble JR, Kaeobamrung J, Bode JW. Org Lett 2008;10:957–960. [PubMed: 18266380]

xxxii. An N-phenyl substituted triazolium similar to precatalyst 21 has been reported: Chen D-D, Hou X-L, Dai L-X. J Org Chem 2008;73:5578–5581. [PubMed: 18557643]

xxxiii. (a) Kerr MS, Read de Alaniz J, Rovis T. J Am Chem Soc 2002;124:10298–10299. [PubMed: 12197730] (b) Kerr MS, Read de Alaniz J, Rovis T. J Org Chem 2005;70:5725–5728. [PubMed: 15989360]

xxxiv. Takikawa H, Hachisu Y, Bode JW, Suzuki K. Angew Chem Int Ed 2006;45:3492–3494.

xxxv. For selected examples, see: (a) Enders D, Han J, Henserler A. Chem Commun 2008:3989–3991. (b) Li GQ, Dai LX, You SL. Chem Commun 2007:852–854. (c) Li GQ, Li Y, Dai LX, You SL. Org Lett 2007;9:3519–3521. [PubMed: 17685621]

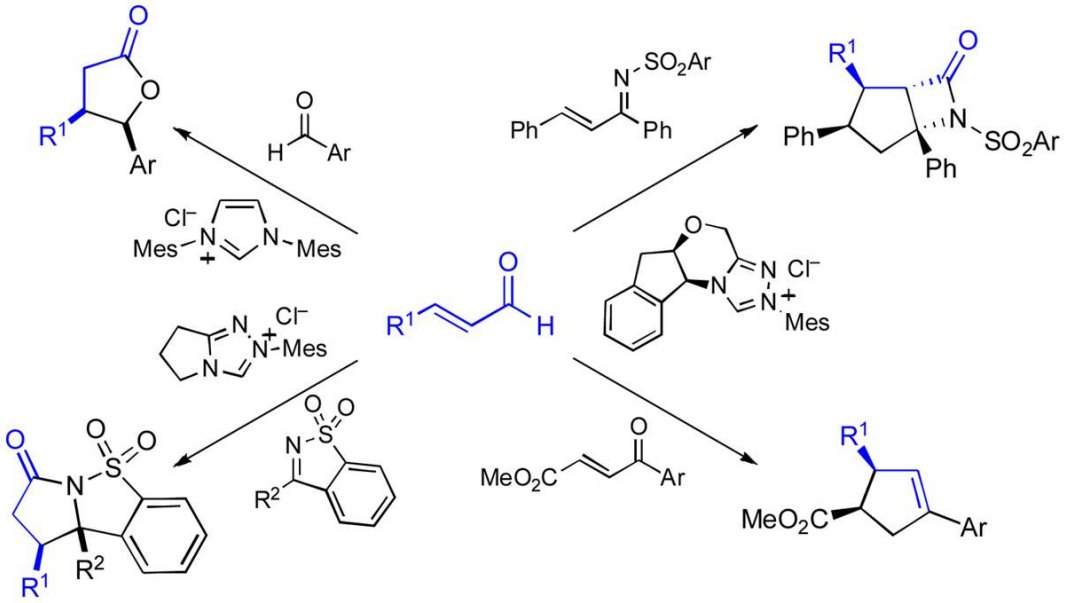
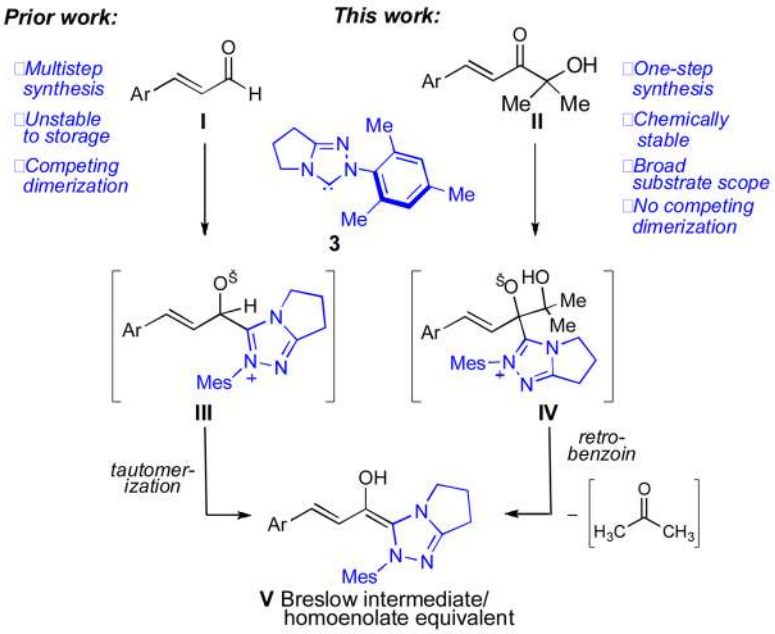
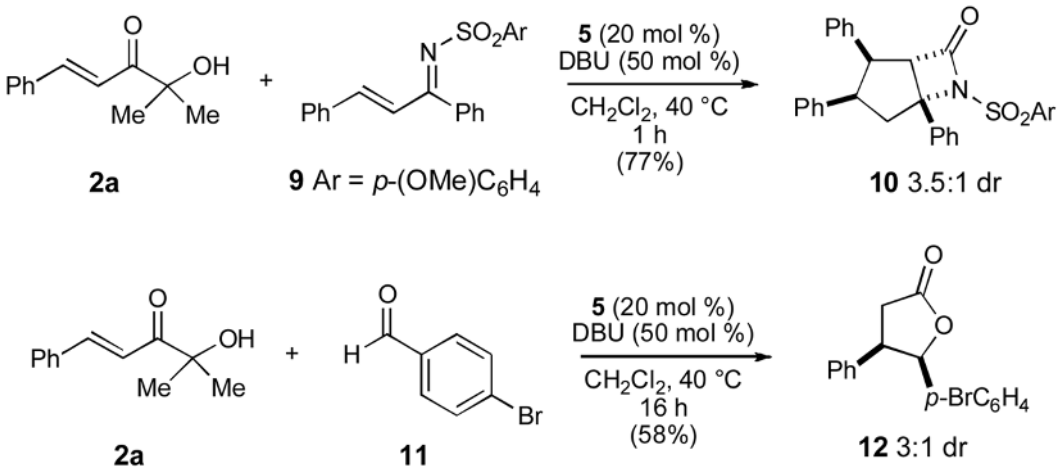


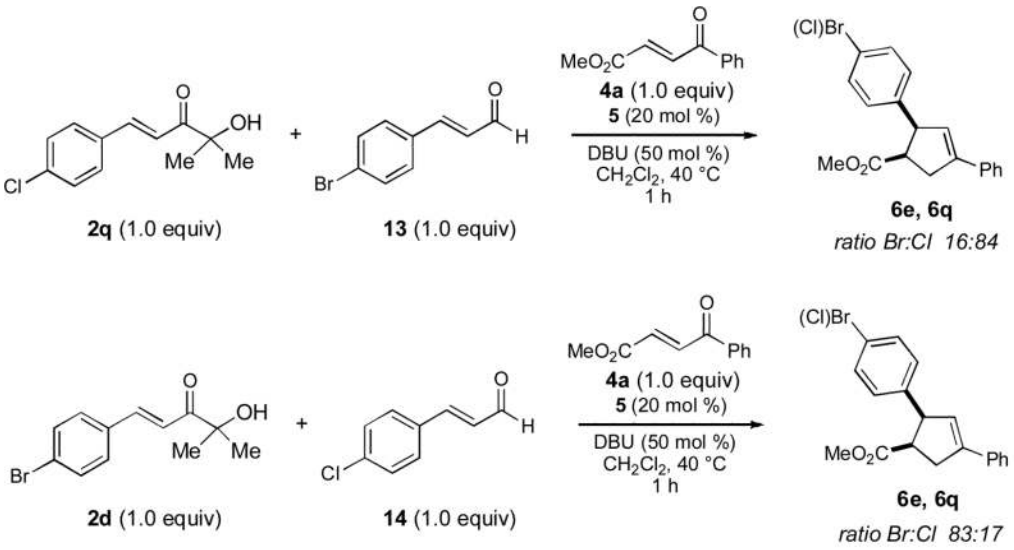
Figure 1.
Selected N-heterocyclic carbene-catalyzed annulation reactions of α,β-unsaturated aldehydes.



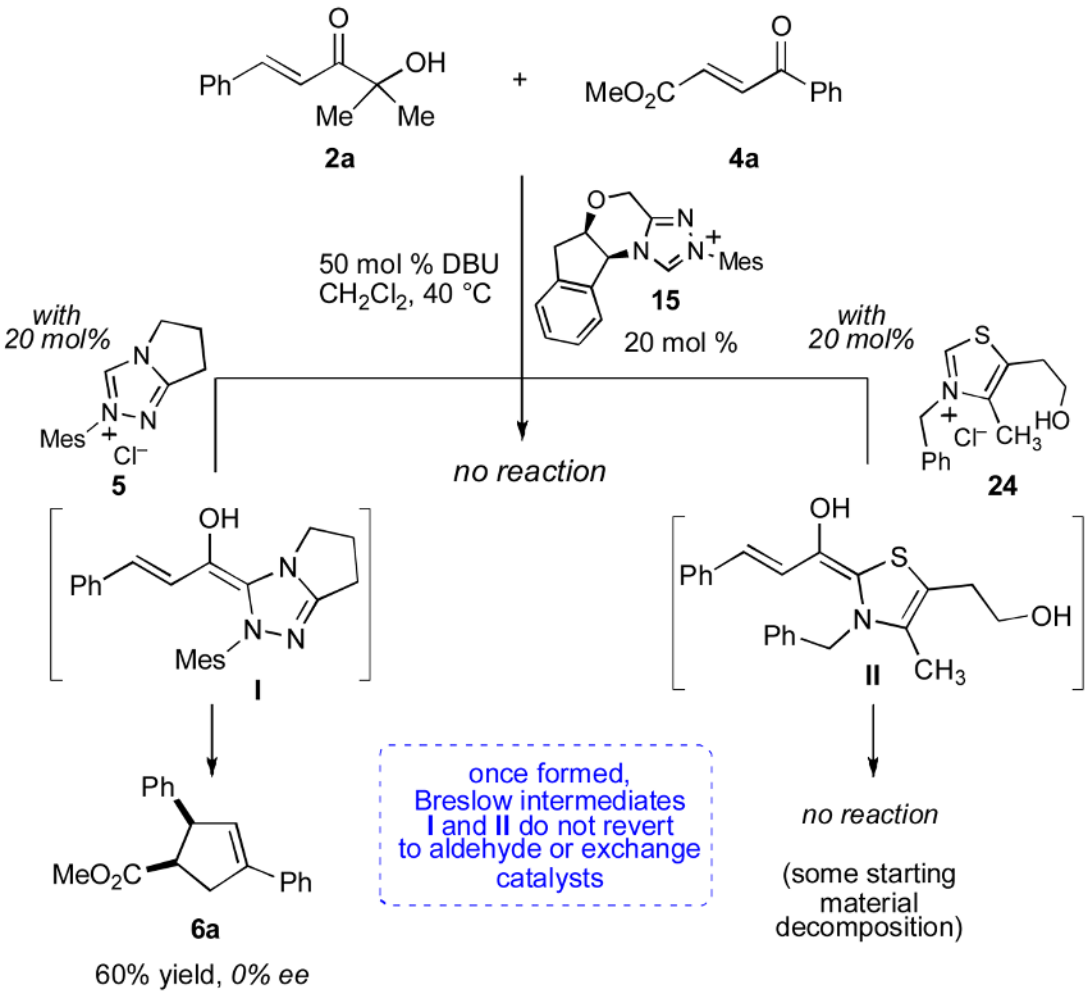
Scheme 1.



Scheme 2.
Application of α′-hydroxyenones to other azolium-catalyzed annulations reactions.



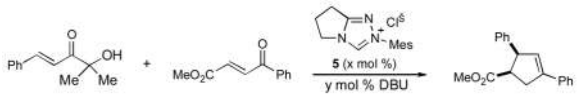
Scheme 3.
Comparison of relative reactivities of α,β-unsaturated aldehydes and α′-hydroxyenones in azolium-catalyzed reactions.



Scheme 4.
Formation of the Breslow intermediate from α′-hydroxyenones is irreversible.

Table 1

Optimization of cyclopentene-forming annulations with α′-hydroxyenones.



2a (1.2 equiv) **4a** (1.0 equiv) **6a**

entry	Catalyst/(x mol %)	DBU/(y mol %)	Solvent	Temp/°C	Time/h	Conversion[a]/%
1	15	20	0.05 M $C_2H_4Cl_2$	0–>25	16	23
2	15	20	0.05 M $C_2H_4Cl_2$	40	16	19
3	15	20	0.05 M THF	40	16	2
4	15	20	0.05 M Toluene	40	16	4
5	15	20	0.05 M EtOAc	40	16	13
6	15	20	0.05 M CH_2Cl_2	40	16	27
7	15	50	0.05 M CH_2Cl_2	40	16	74
8	15	500	0.05 M CH_2Cl_2	40	16	35
9	20	50	0.05 M CH_2Cl_2	40	16	94
10	20	50	0.05 M CH_2Cl_2	40	1	74

[a] As measured by the disappearance of **4a** by ^{1}H NMR analysis of unpurified reaction mixtures. In some cases, decomposition of **4a**, in addition to cyclopentene formation, was observed.

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Table 2

NHC-catalyzed synthesis of cyclopentenes by direct annulations with α′-hydroxyenones **2a-r**.

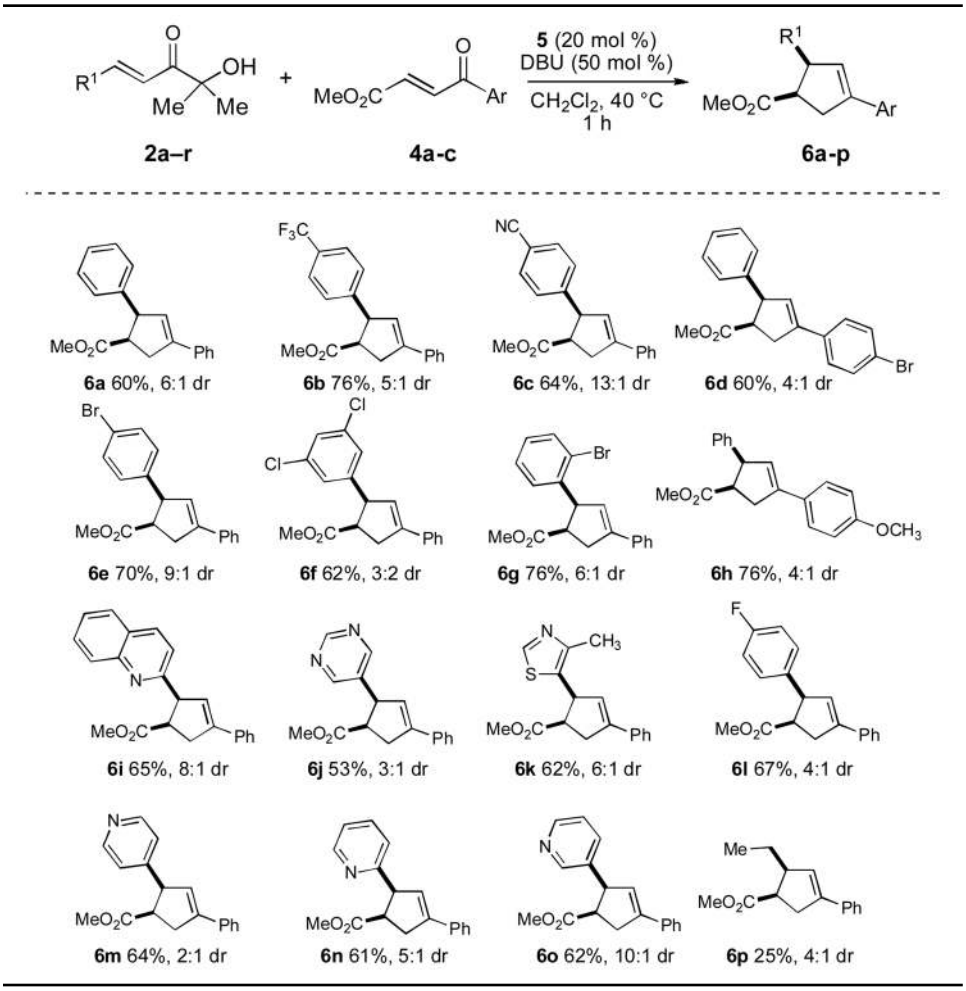
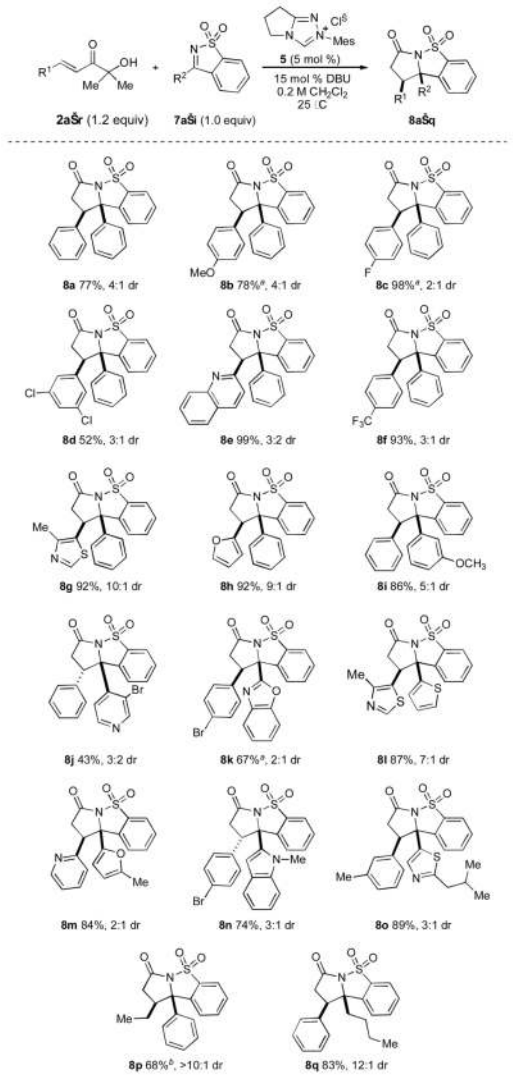


Table 3

Application of α′-hydroxyenones for γ-lactam formation with saccharin-derivatives.



[a] Reaction at 40 °C.

[b] With 20 mol % **5** and 50 mol % DBU.

Table 4

Effect of catalyst structure and steric effects on cyclopentene-forming annulations.