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The effect of the *N*-mesityl group in NHC-catalyzed reactions†

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Abstract

The majority of *N*-heterocyclic carbene catalyzed reactions of α -functionalized aldehydes, including annulations, oxidations, and redox reactions, occur more rapidly with *N*-mesityl substituted NHCs. In many cases, no reaction occurs with NHCs lacking ortho-substituted aromatics. By careful competition studies, catalyst analogue synthesis, mechanistic investigations, and consideration of the elementary steps in NHC-catalyzed reactions of enals, we have determined that the effect of the *N*-mesityl group is to render the initial addition of the NHC to the aldehyde irreversible, thereby accelerating the formation of the Breslow intermediate. These studies rationalize the experimentally observed catalyst preference for all classes of NHC-catalyzed reactions of aldehydes and provide a roadmap for catalyst selection and design.

Introduction

Since the first reports in 2004 by our group,¹ Rovis,² and Glorius,³ more than 100 publications have documented the unique reactivity of the catalytically generated intermediates arisen from the combination of an α -functionalized aldehyde and an *N*-heterocyclic carbene catalyst.⁴ Multiple catalyst types including imidazolium, triazolium, and thiazolium-derived NHCs are employed but one clear trend emerges: all reactions of α,β -unsaturated aldehydes proceed more effectively with ortho,ortho-disubstituted aromatic groups on the azolium ring. It is therefore no surprise that most practitioners in this field have adopted *N*-mesityl substituted catalysts, usually *N*-mesityl substituted triazolium derivatives,⁵ for NHC-catalyzed redox reactions, oxidations, and annulations.⁶ In contrast, the majority of “simple” aldehydes employed in NHC catalyzed benzoin and Stetter-type reactions or redox reactions of α -heteroatomic aldehydes prefer *N*-pentafluorophenyl triazolium salts.⁷ Despite this repeated observation by multiple groups, no explanation for the marked superiority of *N*-mesityl substituted carbenes in NHC-catalyzed reactions of α,β -unsaturated aldehydes has appeared.⁸

The effect of the *N*-mesityl substituent is not simply one of enhancing selectivity or stereochemistry; it is responsible for dramatically enhanced rates of reaction and different outcomes from otherwise identical substrates and conditions. A striking example of its activity is the redox esterification of cinnamaldehyde with methanol to give methyl cinnamate, a prototypical NHC-catalyzed reaction of enals (Scheme 1). When performed with *N*-mesityl substituted triazolium precatalyst **1**, the reaction proceeds to completion even in the absence of added base.⁹ The corresponding *N*-C₆F₅ precatalyst **2** gives no conversion without base and slower reactions than **1** in the presence of Hünig’s base. This is surprising; the *N*-C₆F₅ precatalyst is more acidic than the *N*-mesityl precatalyst. Indeed, an

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NMR investigation on the extent of deprotonation between the two catalysts revealed that precatalyst **2** became fully deprotonated (from the observation of protonated DBU) while the *N*-mesityl precatalyst **1** was only partially deprotonated (Figure 1). This observation prompted the question of why the *N*-mesityl precatalyst **1**, which generates less of the active NHC species, is the superior catalyst¹⁰ for reactions with enals?

Results and Discussion

We have previously shown that α,β -unsaturated Breslow intermediates from *N*-mesityl substituted triazoliums do not revert to aldehyde and NHC.¹¹ We therefore hypothesized that the success of the *N*-mesityl substituted catalyst **1** lay in the irreversible formation of the Breslow intermediate, while those formed from the *N*-C₆F₅ substituted salt **2** were reversible. To test this, we examined numerous reactions, such as that of D-cinnamaldehyde (**5**, Scheme 2) in the presence of a proton source with both *N*-mesityl and *N*-C₆F₅ substituted triazoliums. In no case did we observe H/D exchange in the recovered aldehyde at any conversion. These results show that the formation of the Breslow intermediate from α,β -unsaturated aldehydes is irreversible¹² with either catalyst and contrary to the generally accepted mechanism for azolium catalyzed benzoin-type reactions.¹³

We revised our hypothesis to state that formation of the *initial adduct* between the aldehyde and the carbene is *reversible* for the *N*-C₆F₅ catalyst **2** and *irreversible* for the *N*-mesityl catalyst **1**. The resulting adduct would then undergo a proton transfer sequence that would lead to the Breslow intermediate.¹⁴ This hypothesis would explain both why less acidic *N*-mesityl chloride **1** is able to catalyze reactions with only Cl[−] as a base – because any carbene generated would react irreversibly with the enals – as well as why the reactions with the *N*-mesityl catalyst are faster than with the more acidic *N*-C₆F₅ precatalyst **2**. In order to investigate the origin of the observed reactivity, two additional catalysts were synthesized: the *N*-3,4,5-trimethoxy derivative **6**, intended to be electronically similar to *N*-mesityl but sterically closer to *N*-C₆F₅ catalyst and *N*-2,4,6-trichloro triazolium **10** with the opposite profile.

We first needed to determine which of the elementary steps in NHC-catalyzed reactions of enals was responsible for the reactivity differences. To eliminate catalyst turnover from the acyl azolium intermediate as the origin of the catalyst divergency, we examined two NHC-catalyzed redox esterification reactions, one from cinnamaldehyde^{5a} and the other from an α -chloroaldehyde (Scheme 3).¹⁵ These two reactions converge to the same acyl triazolium intermediate that serves as a catalytically generated activated carboxylate. We found that *N*-mesityl catalyst **1** is faster for cinnamaldehyde while the *N*-C₆F₅ catalyst is superior with α -chloroaldehyde **5**. This discrepancy established that the rate acceleration for catalyst **1** in the reaction with enals must come from an elementary step prior to acyl azolium formation.

This left two possible origins for the divergent reactivity: 1) the β -protonation of the Breslow intermediate and 2) the formation of the Breslow intermediate from the initial adduct. To distinguish these, we examined the oxidative esterification reaction¹⁶ of cinnamaldehyde (Scheme 4A), a reaction that requires generation of the Breslow intermediate from an α,β -unsaturated aldehyde but not its protonation. The *N*-mesityl catalyst **1** proved to be an excellent catalyst for this reaction, followed by the *N*-2,4,6-trichloro **10**, the *N*-C₆F₅ **2**, and the *N*-3,4,5-trimethoxy **9**. The identical trend was observed in the redox esterification of ynals¹⁷ – a process that passes through the same α,β -unsaturated acyl azolium intermediate¹⁸ (Scheme 4B). The observation that the more sterically hindered catalysts initiate faster reactions is most dramatically illustrated by the oxidative esterification of α -hydroxyenone.¹¹ Despite the fact that the requisite retro-benzoin reaction is very sensitive to steric hindrance, the bulkier catalysts were far superior (Scheme 4C).

The absolute rates of all of these reaction are much faster than the redox esterification of cinnamaldehyde and together rule out the oxidation of the Breslow intermediate as the rate-limiting step. This leaves the formation of the Breslow intermediate as the origin of the reactivity difference.

The success of sterically hindered catalysts **1** and **10** originates from their rapid formation of the key Breslow intermediate **II** (k_b , Figure 2) – a consequence of the irreversible addition¹⁹ of the NHC to the electrophile when sterically hindered NHCs are used. In other words, the reverse reaction (k_{-a}) has a higher activation barrier than the forward proton transfer steps (k_b) that leads to the Breslow intermediate. The situation is the opposite with less-sterically demanding catalysts **2** and **9**, which prefer to rest on the side of enal and catalyst – that is $k_b > k_{-a}$.

This assertion predicts that the combination of *N*-mesityl catalyst **1** and cinnamaldehyde, in the absence of other reagent, should give an observable adduct. In contrast, *N*-C₆F₅ catalyst **2** should favor the starting materials: aldehyde and *N*-heterocyclic carbene should be observed. Indeed, the *N*-C₆F₅ triazolium **2** was completely deprotonated by one equiv of DBU (by the detection of DBU-H⁺) but no adduct was observed upon the addition of cinnamaldehyde (Scheme 5). In contrast the *N*-mesityl variant **1** was only partially deprotonated by DBU. Upon addition of cinnamaldehyde the extent of catalyst deprotonation increased, reaching full deprotonation only after two equiv of aldehyde were added. A titration with cinnamaldehyde showed that in the absence of an oxidant, electrophile, or alcohol, the *N*-mesityl carbene forms a 2:1 adduct with cinnamaldehyde. This is a consequence of the irreversible formation of the initial adduct, which reacts with another equivalent of the starting aldehyde when no other forward pathway is available. Although in our case this gives an complex mixture, possibly the diastereomeric forms of the 2:1 NHC:aldehyde adduct recently described by Berkessel²⁰. Similar behavior was observed with triazolium **10** (see Supporting Information). The less hindered carbenes more rapidly revert to starting materials in the absence of a forward pathway.

These findings leave the question: why does the *N*-mesityl catalyst forms essentially irreversible adducts with enals while the addition of the *N*-C₆F₅ catalyst to the aldehyde is reversible? We initially believe this to be due to electronic differences. The more electron deficient *N*-C₆F₅ carbene should be a better leaving group, thereby facilitating the reverse reactions (k_{-a} , Figure 2). The fact that the *N*-trimethoxy catalyst **9** behaves similarly to the *N*-C₆F₅**2** and the *N*-trichloro catalyst **10** more like the *N*-mesityl catalyst **1** argues against this electronic effect and implicates steric argument as the key determinant. This may be the consequence of ground state destabilization of the initial adduct **I** (Figure 2); rapid formation of the Breslow intermediate **II** provides relief from this sterically congested initial adduct. The initial adduct **I** bearing *N*-C₆F₅ moiety has a relative higher activation barrier for Breslow intermediate formation than the reverse reaction to enal and catalyst – an observation consistent with Rovis' recent findings concerning the Stetter reaction.

This insight also explains one reaction of enals in which the *N*-C₆F₅ triazolium salt is superior to the *N*-mesityl variant. In 2009, Csáky reported an NHC-catalyzed oxidative esterification of aldehydes with 1,4-naphthoquinone as the stoichiometric oxidant.²² Electron-deficient catalysts **2** and **10** proved to be viable catalysts while electron-rich catalysts **1** and **9** did not lead to product (Scheme 6). The proposed mechanism is not oxidation of the Breslow intermediate but rather hydride transfer from the initial adduct **I**. This reaction is mechanistically related²³ to the Cannizzaro reaction and follows similar electronic preference for faster hydride transfer with electron-withdrawing-aryl group.²⁴ Because this reaction does not occur from electron-transfer oxidation²⁵ via the intermediacy

of the Breslow intermediate **II**, it does not follow the steric preference outlined previously. We therefore present this observation as “the exception that proves the rule.”¹⁵

Conclusion

The conclusion that the effect of the *N*-mesityl group in NHC-catalyzed reactions is to enhance the rate of formation of the Breslow intermediate is consistent with known NHC-catalyzed reactions of aldehydes.¹⁰ Less hindered azolium salts, such as the *N*-C₆F₅ derivatives, are preferred for benzoin and Stetter type reactions (i.e. Scheme 7A); the use of the *N*-mesityl catalyst is likely to change the rate-limiting step from Breslow intermediate formation to the attack of the acyl anion equivalent onto electrophile. Indeed, Rovis very recently reported an elegant enantioselective intermolecular Stetter reaction between α,β -unsaturated aldehydes and nitroalkenes using a chiral analog of **2**.^{21b} The *N*-C₆F₅ triazolium catalyst is also preferred for redox esterification reactions of α -heteroatomic and α,β -epoxy aldehydes²⁶. These reactions do not require formation of the Breslow intermediate (Figure 2),^{1a,27} and catalyst turnover is most likely the turnover-limiting step – a process facilitated by more electron deficient carbenes, which are better leaving groups. The relative ease of C–C bond cleavage during catalyst turnover of *N*-C₆F₅ catalysts is apparent in a reaction between ynal **22** and kojic acid derivative **23** in which *N*-C₆F₅ catalyst **2'** exclusively afforded the ester product **25** while *N*-mesityl catalyst **1'** gave only the Coates-Claisen rearrangement⁹ product **24** (Scheme 7D).

The *N*-mesityl triazoliums are preferred in the NHC-catalyzed hetero-Diels-Alder reaction of α -halo aldehydes (Scheme 7C) due to the increase in electron density of the enolate **IV**, which deterred tautomerization to the activated carboxylate. Similarly, annulation cascade via a formal homoenolate addition prefers catalyst **1'** due to increased electron density of the Breslow intermediate (Scheme 7B).^{10b-d} This explanation is also consistent with recent reports from Scheidt²⁸, You²⁹, and Chi³⁰ in their applications of ortho,ortho' disubstituted aromatic NHCs in formal homoenolate annulations, and Glorius on NHC-catalyzed hydroacylation reactions of olefins – a process that requires formation of the Breslow intermediate and proceeds more efficiently with *N*-mesityl substituted carbenes.³¹ These experiments, coupled with the ever-growing body of literature on NHC-catalyzed reactions, allows us to make predictions about the reactivity of the intermediates generated during NHC-catalyzed reactions of aldehydes. Figure 3 provides a roadmap for selecting the most likely azolium salt for reactions with the desired mode of reactivity. In certain cases, such as γ -lactone formation annulations of enals and aldehydes^{1b,3} and air oxidation of aldehydes,³² more electron rich imidazolium or thiazolium carbenes are preferred but the choice of *N*-aryl substituent remains the same.³³ NHC-catalyzed reactions of substrates other than aldehydes, such as esters³⁴ and ketenes,³⁵ may not follow these generalizations. For the majority of NHC-carbene catalyzed reactions, however, either the *N*-mesityl or *N*-C₆F₅ will be the most competent catalyst.

Supplementary Material

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Acknowledgments

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Notes and References

- 1 (a). Chow KY-K, Bode JW. *J. Am. Chem. Soc.* 2004; 126:8126–8127. [PubMed: 15225048] (b) Sohn SS, Rosen EL, Bode JW. *J. Am. Chem. Soc.* 2004; 126:14370–14371. [PubMed: 15521753]
2. Reynolds NT, Read de Alaniz J, Rovis T. *J. Am. Chem. Soc.* 2004; 126:9518–9519. [PubMed: 15291537]
3. Burstein C, Glorius F. *Angew. Chem., Int. Ed.* 2004; 43:6205–6208.
- 4 (a). For recent reviews on NHC catalysis, see Chiang P-C, Bode JW. *N-Heterocyclic Carbenes*. 2011:399–435. The Royal Society of Chemistry Moore JL, Rovis T. *Top. Curr. Chem.* 2009; 291:77–144. [PubMed: 21494949] Nair V, Vellalath S, Babu BP. *Chem. Soc. Rev.* 2008; 37:2691–2698. [PubMed: 19020682] Enders D, Niemeier O, Henseler A. *Chem. Rev.* 2007; 107:5606–5655. [PubMed: 17956132]
- 5 (a). For the first report of a *N*-mesityl substituted triazolium precatalyst, see Sohn SS, Bode JW. *Org. Lett.* 2005; 7:3873–3876. [PubMed: 16119920] For the first chiral variant, see He M, Struble JR, Bode JW. *J. Am. Chem. Soc.* 2006; 128:8418–8420. [PubMed: 16802805] For the synthesis of *N*-mesityl triazolium salts, see: Struble JR, Bode JW. *Org. Synth.* 2010; 87:362–376.
6. Chiang P-C, Bode JW. *TCI MAIL*. 2011; 149:2–17.
- 7 (a). The *N*-C₆F₅ triazolium catalyst **2** was first reported in Kerr MS, Read de Alaniz J, Rovis T. *J. Org. Chem.* 2005; 70:5725–5728. [PubMed: 15989360] The chiral amino alcohol-derived *N*-C₆F₅ precatalysts were first reported in Kerr MS, Rovis T. *J. Am. Chem. Soc.* 2004; 126:8876–8877. [PubMed: 15264801] For the synthesis of *N*-C₆F₅ triazolium salts, see: Vora HU, Lathrop SP, Reynolds NT, Kerr MS, Read de Alaniz J, Rovis T. *Org. Synth.* 2010; 87:350–361.
8. For a discussion regarding the effect of different aryl substitution on triazolium salts in the context of intramolecular Stetter reactions see: Rovis T. *Chem. Lett.* 2008; 37:2–7.
9. We have reported that the weak base Cl[−] counterion deprotonates the triazolium to generate the NHC species: Kaeobamrung J, Mahatthananchai J, Zheng P, Bode JW. *J. Am. Chem. Soc.* 2010; 132:8810–8812. [PubMed: 20550127]
- 10 (a). Examples include: Kaeobamrung J, Kozlowski MC, Bode JW. *Proc. Natl. Acad. Sci.* 2010; 107:20661–20665. [PubMed: 20974930] Kaeobamrung J, Bode JW. *Org. Lett.* 2009; 11:677–680. [PubMed: 19175349] He M, Bode JW. *J. Am. Chem. Soc.* 2008; 130:418–419. [PubMed: 18092785] Chiang P-C, Kaeobamrung J, Bode JW. *J. Am. Chem. Soc.* 2007; 129:3520–3521. [PubMed: 17335218]
- 11 (a). Chiang P-C, Rommel M, Bode JW. *J. Am. Chem. Soc.* 2009; 131:8714–8718. [PubMed: 19530737] (b) Chiang P-C, Kim Y, Bode JW. *Chem. Commun.* 2009:4566–4568.
12. We noted an exception to this observation in the case of α -methyl cinnamaldehyde, in which H/D exchange is observed for both catalysts **1** and **2** (with **2** being faster at exchanging than **1**, see Supporting Information). We attribute this to the reduced stability of the more sterically hindered Breslow intermediate formed in this case. This is similar to the Breslow intermediates derived from simple aldehyde such as benzaldehyde, which appeared to be formed reversibly. For example:

- 13 (a). Breslow R, Kim R. *Tetrahedron Lett.* 1994; 35:699–702. (b) Teles JH, Melder JP, Ebel K, Schneider R, Gehrer E, Harder W, Brode S, Enders D, Breuer K, Raabe G. *Helv. Chim. Acta.* 1996; 79:61–83. (c) White MJ, Leeper FJ. *J. Org. Chem.* 2001; 66:5124–5131. [PubMed: 11463265]
14. Breslow R. *J. Am. Chem. Soc.* 1958; 80:3719–3726.
15. Reynolds NT, Rovis T. *J. Am. Chem. Soc.* 2005; 127:16406–16407. [PubMed: 16305222]

- 16 (a). De Sarkar S, Grimme S, Studer A. J. Am. Chem. Soc. 2010; 132:1190–1191. [PubMed: 20055393] (b) De Sarkar S, Studer A. Org. Lett. 2010; 12:1992–1995. [PubMed: 20359171]
17. Zeitler K. Org. Lett. 2006; 8:637–640. [PubMed: 16468730]
18. Mahatthananchai J, Zheng P, Bode JW. Angew. Chem., Int. Ed. 2011; 50:1673–1677.
19. While this manuscript was under review, Mayr reported an elegant, detailed study on reaction of NHCs with various electrophiles and concluded that the observed reactivity of NHC catalysts originate from their high Lewis basicity, not their nucleophilicity. He concluded the attack of NHCs to the carbonyl group of α,β -unsaturated aldehydes occurs under kinetic control and “has a lower degree of reversibility.” Additionally, using methyl cation affinity calculation, they found an *N*-mesityl substituted triazolium NHC to be more Lewis basic than the *N*-phenyl counterpart. Maji B, Breugst M, Mayr H. Angew. Chem., Int. Ed. 2011 DOI: 10.1002/anie.201102435.
20. Berkessel A, Elfert S, Etzenbach-Effers K, Teles JH. Angew. Chem., Int. Ed. 2010; 49:7120–7124.
- 21 (a). Moore JL, Silvestri AP, de Alaniz JR, DiRocco DA, Rovis T. Org. Lett. 2011; 13:1742–1745. [PubMed: 21355598] (b) DiRocco DA, Rovis T. J. Am. Chem. Soc. 2011; 133:10402–10405. [PubMed: 21678918]
22. Molina MT, Navarro C, Moreno A, Csáky AG. J. Org. Chem. 2009; 74:9573–9575. [PubMed: 19938843]
23. Chan A, Scheidt KA. J. Am. Chem. Soc. 2006; 128:4558–4559. [PubMed: 16594677]
24. Hazlet SE, Stauffer DA. J. Org. Chem. 1962; 27:2021–2024.
- 25 (a). Castells J, Llitjos H, Moreno-Mañas M. Tetrahedron Lett. 1977; 18:205–206. (b) Inoue H, Higashiura K. J. Chem. Soc., Chem. Commun. 1980:549–550.
- 26 (a). Vora HU, Moncecchi JR, Epstein O, Rovis T. J. Org. Chem. 2008; 73:9727–9731. [PubMed: 18989930] (b) Thai K, Wang L, Dudding T, Bilodeau F, o. Gravel M. Org. Lett. 2010; 12:5708–5711. [PubMed: 21080709] (c) Jiang H, Gschwend B, Albrecht L, Anker Jorgensen K. Org. Lett. 2010; 12:5052–5055. [PubMed: 20932050] (d) Deiana L, Dziedzic P, Zhao G-L, Vesely J, Ibrahim I, Rios R, Sun J, Córdova A. Chem. Eur. J. 2011; 17:7904–7917. [PubMed: 21611987]
27. Nowak RM. J. Org. Chem. 1963; 28:1182–1187.
- 28 (a). Raup DEA, Cardinal-David B, Holte D, Scheidt KA. Nat. Chem. 2010; 2:766–771. [PubMed: 20729898] (b) Cohen DT, Cardinal-David B, Scheidt KA. Angew. Chem. Int. Ed. 2011; 50:1678–1682.
29. Li Y, Zhao Z-A, He H, You S-L. Adv. Synth. Catal. 2008; 350:1885–1890.
30. Fang X, Jiang K, Xing C, Hao L, Chi YR. Angew. Chem., Int. Ed. 2011; 50:1910–1913.
- 31 (a). Bugaut X, Liu F, Glorius F. J. Am. Chem. Soc. 2011; 133:8130–8133. [PubMed: 21520959] (b) Piel I, Steinmetz M, Hirano K, Fröhlich R, Grimme S, Glorius F. Angew. Chem. Int. Ed. 2011; 50:4983–4987. (c) Hirano K, Biju AT, Piel I, Glorius F. J. Am. Chem. Soc. 2009; 131:14190–14191. [PubMed: 19807174]
- 32 (a). Chiang P-C, Bode JW. Org. Lett. 2011; 13:2422–2425. [PubMed: 21486084] (b) Maji B, Vedachalan S, Ge X, Cai S, Liu X-W. J. Org. Chem. 2011; 76:3016–3023. [PubMed: 21449617]
33. For a side-by-side comparison of NHC-catalyzed reactions with *N*-mesityl substituted chiral triazolium and imidazolium precatalysts, see: Struble JR, Kaeobamrung J, Bode JW. Org. Lett. 2008; 10:957–960. [PubMed: 18266380]
34. Ryan SJ, Candish L, Lupton DW. J. Am. Chem. Soc. 2009; 131:14176–14177. [PubMed: 19757788]
- 35 (a). Concellon C, Duguet N, Smith AD. Adv. Synth. Catal. 2009; 351:3001–3009. (b) Wang X-N, Lv H, Huang X-L, Ye S. Org. Biomol. Chem. 2009; 7:346–350. [PubMed: 19109680]

Figure 1.

Extent of deprotonation of azolium salts **1** and **2**. A) ¹H NMR spectra of DBU in CD₂Cl₂ as reference; B) and D) ¹H NMR spectra of triazolium salts **1** and **2**; C) and E) ¹H NMR spectra of triazolium salts following addition of 1.0 equiv DBU.

Figure 2.
A proposed theory and mechanistic probes

Figure 3.
Roadmap for triazolium selection for the reaction modes available from NHC catalyzed reactions of aldehydes

Scheme 1.
Redox esterification of enal in the absence of base

Scheme 2.
Irreversible formation of the *Breslow intermediate*

A. Redox esterification reactions of cinnamaldehyde
(redox reaction via *Breslow intermediate*).

B. Redox esterification reactions of α -chloroaldehyde
(elimination via *initial adduct*).

Scheme 3.
Redox esterifications of α -functionalized aldehydes

Scheme 4.
NHC catalyzed esterifications

Scheme 5.

Titration of azoliums with DBU and cinnamaldehyde

Scheme 6. Hydride transfer oxidative esterification comparison (reaction via *initial adduct*)

A. Intramolecular Stetter reaction (via acyl anion equivalent II)

B. Cyclopentene formation (via formal homoenolate equivalent II')¹⁰⁴

C. Hetero Diels-Alder reaction (via enolate equivalent IV)

D. Claisen vs. esterification (via unsaturated acyl azolium III)

Scheme 7.

Comparison of reactions catalyzed by **1**, **1**⁺, **2**, and **2**⁺