

Unprecedented Reactivity of N-Heterocyclic Carbenes toward DMAD and Aldehydes Leading to Novel Multicomponent Reactions[†]

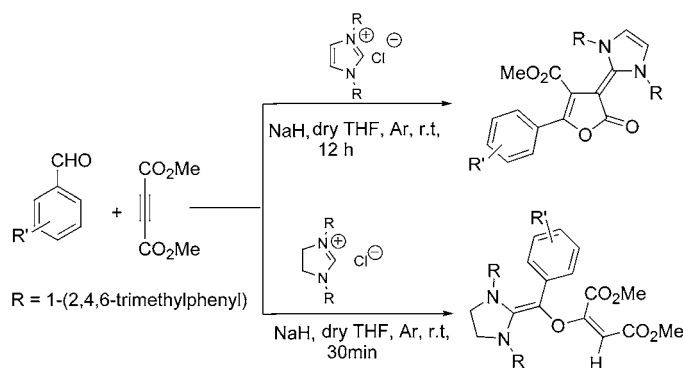
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ABSTRACT



A facile synthesis of highly functionalized 2-oxymaleate and furanone derivatives by the multicomponent reaction of 1,3-dimesityl imidazolium-2-ylidene/imidazol-2-ylidene, DMAD, and aldehydes is described.

The history of N-heterocyclic carbenes (NHCs) can be traced to the work of Wanzlick¹ in the 1960s, and the seminal contributions of Arduengo leading to the isolation and characterization of the first stable diaminocarbene in 1991 stands as a milestone in the development of the chemistry of these species.² Since then a wide range of NHCs, including the first air-stable carbene, have been prepared, and they have found impressive use as ligands, by virtue of their strong σ -donating ability, in the preparation of catalysts in orga-

nometallic chemistry.³ A general method for the synthesis of these species involves the deprotonation of the corresponding azolium salts by a suitable base.⁴ It is noteworthy that as early as 1958, Breslow recognized the role of N-heterocyclic carbenes as nucleophilic catalysts in enzymatic reactions, and in due course, different thiazolium, imidazolium, and triazolium salts were found to be excellent catalysts for various C–C coupling reactions, namely, benzoin condensation, Michael–Stetter reaction, and Formoin condensation.⁵ Asymmetric versions of these reactions have also been achieved by employing chiral azolium salts.⁶ Although the coordination and organometallic chemistry of diaminocarbenes have been extensively investigated, much

[†] Dedicated to Prof. Gilbert Stork in appreciation of his unique contributions to Organic Chemistry.

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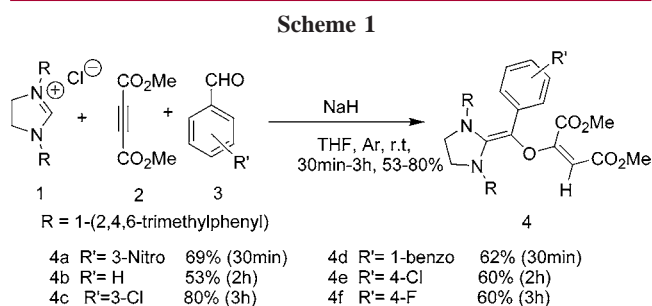
(2) Arduengo, A. J., III; Harlow, R. L.; Kline, M. K. *J. Am. Chem. Soc.* **1991**, *113*, 9704.

(3) (a) Arduengo, A. J., III. *Acc. Chem. Res.* **1999**, *32*, 913. (b) Herrmann, W. A. *Angew. Chem., Int. Ed.* **2002**, *41*, 1290. (c) Herrmann, W. A.; Köcher, C. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2162 and references therein.

(4) Arduengo, A. J., III; Krafczyk, R.; Schmutzler, R. *Tetrahedron* **1999**, *55*, 14523

of the fundamental chemistry of these species remains unexplored.⁷ In particular, the participation of NHCs in multicomponent reactions (MCRs) has not been reported so far. Herein we report the preliminary results of the first use of NHCs exemplified by **1** and **7**, generated by the deprotonation of the corresponding imidazolium or imidazolinium salt with sodium hydride following the Arduengo prescription, in multicomponent reactions.⁴

Our studies were set in motion by exposing 3-nitro benzaldehyde to dimethyl acetylenedicarboxylate (DMAD) and 1,3-dimesityl imidazolin-2-ylidene, generated in situ by the reaction of 1,3-dimesityl-imidazolium chloride with sodium hydride in THF under an argon atmosphere. A facile reaction leading to the exclusive formation of 2-oxy maleate derivative **4a** occurred. (Scheme 1)



The product was characterized by spectroscopic analysis. Final proof for the structure assigned for **4a** was derived from single-crystal X-ray analysis (Figure 1)

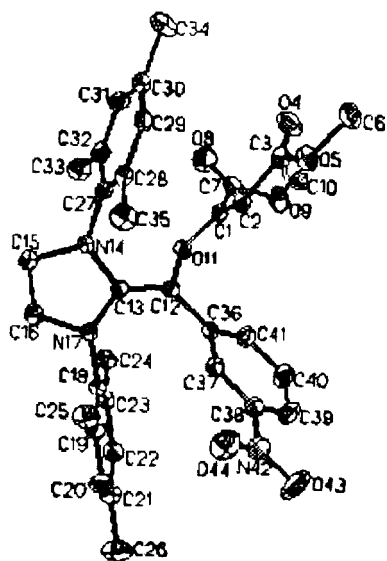
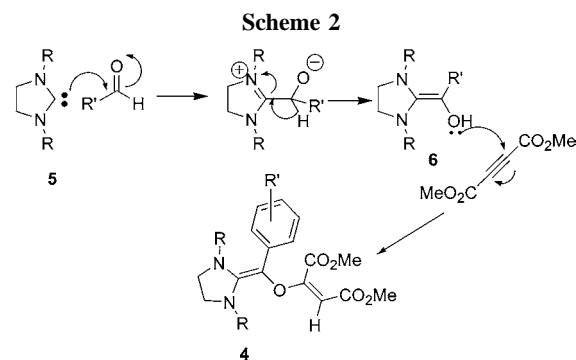


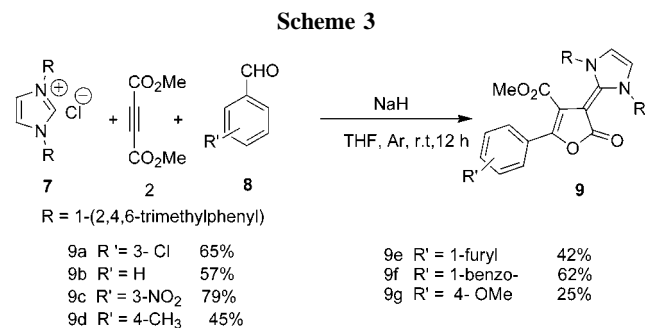
Figure 1. ORTEP diagram for **4a**.

The reaction was found to be applicable to a number of other aldehydes as shown in Scheme 1. A mechanistic



rationale for this reaction is given in Scheme 2. It is worthy of note that unlike the case of nucleophiles such as isocyanides and dimethoxycarbene, the initial event in this reaction is the addition of diaminocarbene to the aldehyde to form an electron-rich enaminol⁵ intermediate **6**. The latter, due to steric reasons, undergoes a conjugate addition on the activated alkyne through the harder oxygen atom, followed by proton abstraction to furnish the product.⁸ It is conceivable that the addition of diaminocarbene to DMAD is reversible at rt and the thermodynamic stability of **6** drives the reaction toward product formation.

A different reactivity pattern was observed with the less nucleophilic 1,3-dimesityl imidazol-2-ylidene. The latter, generated in situ from 1,3-dimesityl imidazolium chloride and sodium hydride, on reaction with 3-chloro benzaldehyde and DMAD afforded exclusively the furanone derivative **9a** in good yield (Scheme 3).



The structure of the product **9a** was ascertained by spectroscopic methods, and the final proof for the assigned structure was obtained by single-crystal X-ray analysis. (Figure 2). The reaction has been extended to other aromatic aldehydes and the furanone derivatives were obtained in moderate to excellent yields (Scheme 3). Isobutyraldehyde afforded the furanone in 27% yield.

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(6) (a) Enders, D.; Breuer, K.; Runsink, J.; Teles, J. H. *Helv. Chim. Acta* **1996**, *79*, 1899. (b) Kerr, M. S.; de Alaniz, J. R.; Rovis, T. *J. Am. Chem. Soc.* **2002**, *124*, 10298. (c) Enders, D.; Kallfass, U. *Angew. Chem., Int. Ed.* **2002**, *41*, 1743.

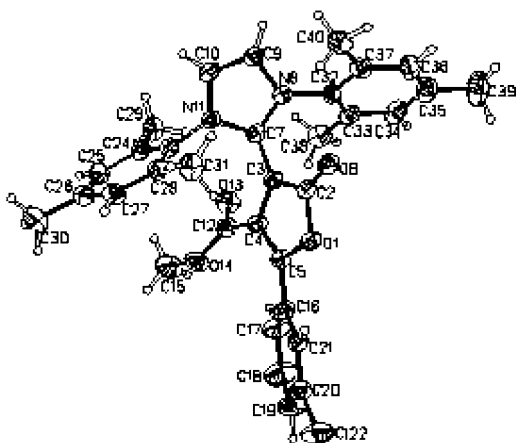


Figure 2. ORTEP diagram for **9a**.

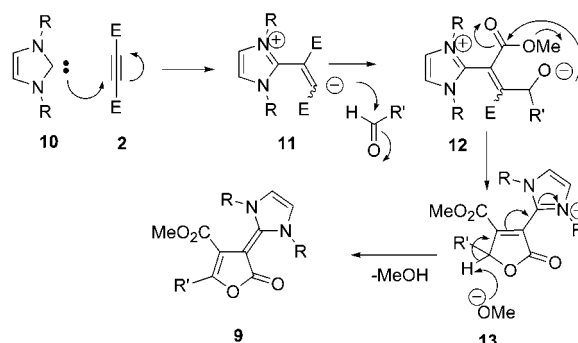
A plausible mechanism for this reaction is given in Scheme 4.

It is possible that this sequence is initiated by the formation of zwitterion **11**, from NHC and DMAD, which adds to the aldehyde to form another zwitterionic species **12**. This ion, presumably for steric reasons, adds to the ester carbonyl of DMAD in preference to the iminium ion to afford **13**, which subsequently eliminates methanol to furnish the furanone derivative **9**.

In conclusion, we have unraveled some interesting reactivity profiles of the N-heterocyclic carbenes **5** and **10**, thus

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Scheme 4



achieving novel multicomponent reactions that offer a simple and efficient route to the synthesis of highly functionalized 2-oxymaleate and furanone derivatives. It is interesting to note that a wide range of biologically active molecules contain dihydroimidazole and furanone moieties.⁹ It is anticipated that the work presented in this paper will arouse much interest in the area of NHCs. Further work to explore the reactivity profile of NHCs toward various other electrophiles in MCRs is in progress

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Supporting Information Available: General experimental procedures and IR, ¹H NMR, and ¹³C NMR data for compounds **4a–e** and **9a–e,f,g**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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