traditional methodology. In fact, the results shown in Table 1 indicate that the surfactant–β-CD complexes fundamentally display a stoichiometric ratio of 1:1. From data in Table 1 we can derive the concentration of complexed β-CD in the presence of OTACl as $c_{\text{surfactant}-\beta\text{-CD}} = 6.65 \times 10^{-3}$M ($c_{\beta\text{-CD,tot}} = c_{\beta\text{-CD,f}} + c_{\text{surfactant}-\beta\text{-CD}}$). Because cmc_{app} is smaller than $c_{\text{surfactant}-\beta\text{-CD}}$ we can suggest that there are OTACl–β-CD complexes with stoichiometries of both 1:1 and 1:2. Therefore one of the main conclusions to be drawn from this study is the necessity to revise the stoichiometries of the existing surfactant–CD complexes referred to in the library, derived from the values of cmc_{app}.

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[9] In mixed surfactant–CD systems the critical micellar concentration can be defined as: $\text{cmc}_{\text{app}} = c_{\text{surfactant-CD}} + c_{\text{surfactant monomer}} = c_{\text{surfactant-CD}} + \text{cmc}_{\text{real}}$, where cmc_{real} represents the concentration of free surfactant monomers in equilibrium with the micellar system and $c_{\text{surfactant-CD}}$ is the concentration of surfactant monomers complexed with the CD.
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Domino Michael Aldol and Domino Michael Mannich Reactions: Highly Stereoselective Synthesis of Functionalized Cyclohexanes**

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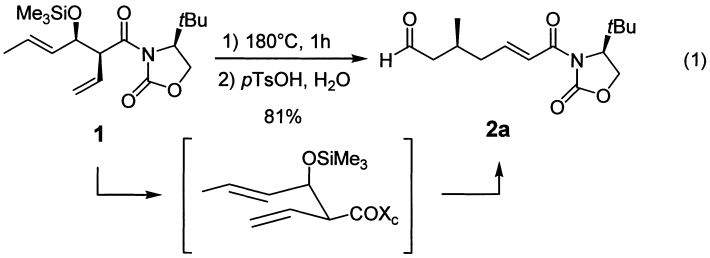
Efficiency and elegance are valued characteristics of domino transformations.[1] Even more appealing are those domino processes which form carbon–carbon bonds and thereby generate new chiral centers stereoselectively. We report here on domino Michael aldol and domino Michael Mannich reactions which in a single step give rise to highly substituted and functionalized cyclohexanes with very high stereocontrol.[2] The 7-oxo-2-enimides **2** used as substrates for the domino reactions were easily obtained in good yields and stereoselectivity by a thermal [3.3]-sigmatropic rearrangement of silylated *syn*-aldols **1** [Eq. (1)].[3] Compounds **2** have been sucessfully employed by us in syntheses of enantiopure tetrahydropyrans,[4] piperidines,[5] terpenols,[6] and polyol structures.[7]



(1)

We have already been able to show that chemoselective nucleophilic additions to the aldehyde moiety in **2a** are feasible and lead to oxygen and nitrogen heterocycles by intramolecular hetero Michael additions.[4, 5] We have now found that this sequence can be reversed when organocopper and -aluminum reagents are employed. Thus, the Lewis acid assisted addition of monoorganocuprates (Yamamoto cuprates)[8] to **2a** gave rise to the cyclohexanol **3a**[9] in moderate yield but complete stereocontrol (Table 1). The reaction is assumed to proceed by an initial, highly stereoselective Michael addition[10] of the cuprate reagent to the aluminum chelate complex **A**[11] and then formation of an imide enolate which is trapped intramolecularly by the aldehyde. The homogenous *syn*-stereochemistry of the aldol reaction results from the intramolecular transposition of the metal ion from the enolate oxygen atom to the aldehyde oxygen atom in the presumed transition structure **B**. As principal side product we

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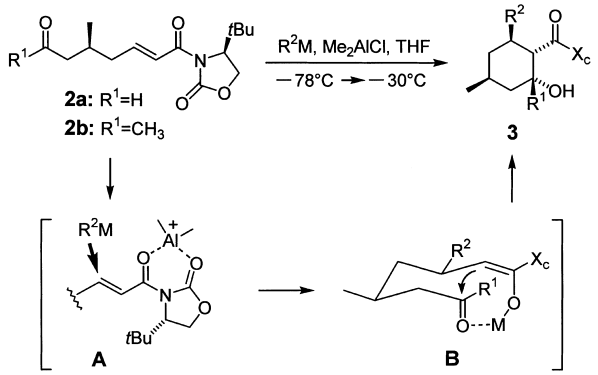
Table 1. Domino Michael aldol reactions.[a]



Compound	R^2M	Product (R^2)	Yield [%]
2a	*n*BuCu/LiI	**3a** (*n*Bu)	41
2b	*n*BuCu/LiI	**3b** (*n*Bu)	83
2b	EtCu/$MgBr_2$	**3c** (Et))	71
2b	allylCu/$MgBr_2$	**3d** (allyl)	81
2a	Me_2AlSPh[b]	**3e** (SPh)	77
2a	Me_2AlSEt[b]	**3f** (SEt)	57
2b	Me_2AlSPh[b]	**3g** (SPh)	76
2b	$Me_2AlNC_5H_{10}$[b]	**3h** (piperidinyl)	40

[a] The stereoselectivity in all cases was > 20:1. This value was determined by ^{1}H NMR (300 MHz) spectroscopy, and means that no other signal of an additional stereoisomer was detected in the ^{1}H NMR spectrum. X_c = chiral auxiliary. [b] Without additional Lewis acid Me_2AlCl.

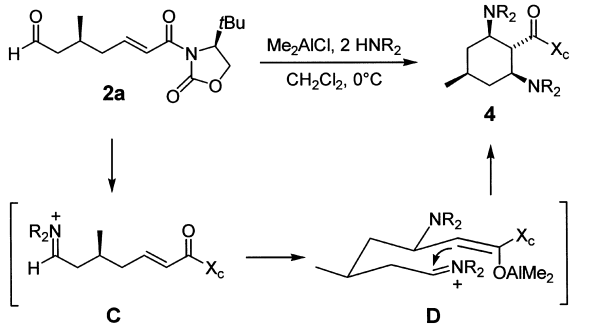
isolated the product of the double addition of the organocuprate to the aldehyde and the conjugate double bond in 15–20% yield. The chiral auxiliary was cleaved with lithium benzylate.[12]

When the reactivity of the carbonyl group was attenuated through conversion to the ketone **2b**,[13] the yields of the domino Michael aldol reactions increased substantially. A competing nucleophilic addition to the ketone did not occur here and the tertiary cyclohexanols **3b–d** were obtained in good to very good yields and high stereoselectivity (Table 1). The use of Grignard reagents as cuprate precursors broadened the scope of the method considerably.[14]

Hetero-substituted cyclohexanols **3e–h** were prepared easily by using aluminum thiolates and amides. In particular, the aluminum thiolates Me_2AlSPh and Me_2AlSEt introduced by Nozaki et al.[15] furnished sulfur-substituted cyclohexanols **3e–g** in good yields as single stereoisomers. Considering the high oxophilicity of aluminum these reagents presumably attack the aldehyde moiety of **2a** reversibly giving rise to aluminum *S*,*O*-hemiacetales which are known to be good in situ protecting groups for aldehydes.[16]

In an extension of this work we envisioned the synthesis of amino-substituted cyclohexanols by reaction of **2a** with aluminum amides. Instead of the expected cyclohexanols we obtained diamino cyclohexanes **4a–d** in good yields as single stereoisomers (Table 2). Evidently, aluminum *N*,*O*-hemiacetals[16] were initially formed, and these collapsed to the iminium salts **C** which after the Michael addition of a second equivalent Me_2AlNR_2 were trapped by the imide enolate in a Mannich reaction.[17] A complete reversal of stereoselectivity was observed compared to the aldol reaction. Because the iminium nitrogen atom cannot coordinate to the aluminum ion due to the lack of vacant coordination sites, the intramolecular transposition of the metal ion as in **B** is prohibited here. Thus, the large iminium group occupies the sterically more favorable proequatorial position in the transition structure **D**, which eventually results in the *anti* configuration of the Mannich products.

Table 2. Domino Michael Mannich reactions.[a]



Product	Amine	Yield [%]
4a	morpholine	69
4b[b]	piperidine	57
4c	$(Bn)_2NH$	65
4d	Et_2NH	46

[a] The stereoselectivity in all cases was > 20:1. This value was determined by ^{1}H NMR (300 MHz) spectroscopy, and means that no other signal of an additional stereoisomer was detected in the ^{1}H NMR spectrum. X_c = chiral auxiliary. [b] The 5-phenyl-substituted 7-oxo-2-enimide was used as substrate.

We have reported two very efficient and highly stereoselctive domino transformations for the synthesis of functionalized cyclohexanes. Just three synthetic operations (aldol reaction, Cope rearrangement, domino reaction) are necessary to prepare the enantiopure carbocycles from simple precursors. This substantiates the synthetic value of the silyloxy-Cope rearrangement of chiral *syn*-aldols for organic synthesis.

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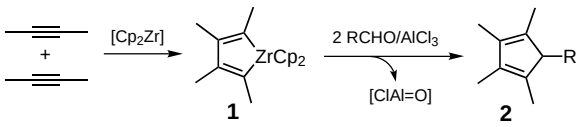
Deoxygenative Cycloaddition of Aldehydes with Alkynes Mediated by $AlCl_3$ and Zirconium: Formation of Cyclopentadiene Derivatives**

Zhenfeng Xi* and Pixu Li

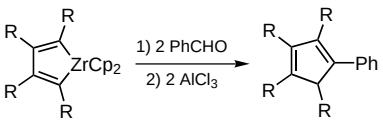
Cleavage or deoxygenation of C–O double bonds in carbonyl compounds is of significant general interest for organic transformations.[1–4] Metal-promoted cycloaddition of unsaturated organic substrates has attracted much attention, because such reactions provide a straightforward route to useful cyclic compounds.[5] Although novel methods for constructing cyclic compounds could be developed by cycloaddition of an aldehyde with alkynes and deoxygenation of the carbonyl group, to the best of our knowledge, such reactions are unprecedented.

Although aldehydes are among the most common unsaturated substrates, transition metal-mediated cycloaddition reactions of aldehydes with alkynes are rare.[6] Tsuda, Saegusa et al. reported the first cycloadditions of diynes with aldehydes to give six-membered oxacycles such as pyrans with catalysis by Ni^0.[6a] The reaction proceeded with a formal [2+2+2] pattern. Here we report the first cyclization of two alkyne molecules with an aldehyde and deoxygenation of the C=O bond to give multiply substituted cyclopentadiene derivatives; the reactions are mediated by $AlCl_3$ and zirconocene compounds [Eq. (1); $Cp = \eta^5\text{-}C_5H_5$].



(1)

Two molecules of the same or different alkynes readily underwent cycloaddition on a low-valent zirconocene complex to afford zirconacyclopentadienes **1**.[7, 8] Addition of two equivalents of benzaldehyde and two equivalents of freshly sublimed $AlCl_3$ to a solution of **1a**, prepared in situ in toluene, led to a rapid reaction [Eq. (2)]. Gas chromatographic (GC) analysis showed that the reaction was complete within 30 min



(2)

1a-c **2a-c**

a: R = *n*Pr 89% (65%)
b: R = Me (45%)
c: R = Ph (47%)

and **2a** was formed in 89% yield (yield of isolated product: 65%). Similarly, **2b** was isolated in 45% yield from the reaction of **1b** with benzaldehyde in the presence of $AlCl_3$. Different regioisomers of cyclopentadiene derivatives can be obtained, depending on the reaction conditions and work-up procedures, but under our reaction conditions, only the isomer shown in Equation (2) was obtained. The reaction of **1c** with benzaldehyde proceeded comparatively slowly at room temperature to give **2c** as colorless crystals in 47% yield. The NMR spectroscopic data and m.p. of **2c** are consistent with those reported earlier.[9] Reactions of metallacyclopentadienes with C_1 units or C_1 unit equivalents to form cyclopentadiene derivatives are rare.[10] Reaction (2) is the first of this kind in which an aldehyde behaves formally as a C_1 unit. It is noteworthy that, when zirconacyclopentadienes were prepared from $[Cp_2ZrCl_2]$/EtMgBr/alkynes,[11] the above reaction was not observed, even at an elevated temperature.

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