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One-pot synthetic route to homoallylketones *via* selective combination of alkyne, ethylene and aldehyde mediated by $AlCl_3$ and zirconocene†

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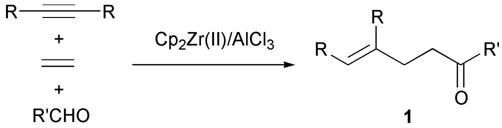
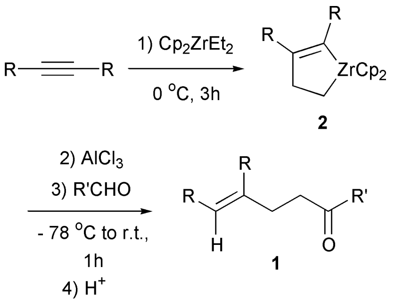
Zirconacyclopentenes generated *in situ* from alkynes and ethylene undergo selective reaction with aldehydes to afford homoallylketones in yields exceeding 70% in the presence of $AlCl_3$.

We have recently reported a deoxygenative cycloaddition reaction of one aldehyde with two alkynes mediated by $AlCl_3$ and zirconacyclopentadienes affording cyclopentadiene derivatives.[1] $AlCl_3$ played important roles in the reaction, not only as a Lewis acid increasing electrophilicity of the carbonyl carbon atom,[2] but also as a transmetallation reagent. As part of our continuous interest in Lewis acid mediated intermolecular carbon–carbon bond formation reactions involving carbonyl groups and other unsaturated components, we studied $AlCl_3$ mediated reactions of aldehydes with zirconacyclopentenes, which were generated *in situ* from alkynes and ethylene.[3] Surprisingly, totally different results from those of our previous report were obtained.[1] No deoxygenative cyclization was observed. Linear products, homoallylketones **1** were formed in good yields with excellent selectivities, as shown in Scheme 1. Acylation of alkynes and alkenes with aldehydes has been accepted as one of the most important and straightforward methods for introducing carbonyl groups into organic molecules.[4] The relevant reaction reported here represents the first example of ketone formation from three different components involving aldehydes, ethylene and alkynes.



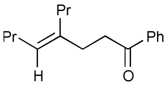
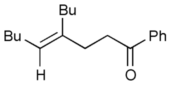
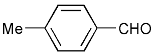
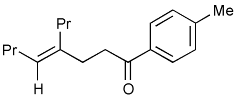
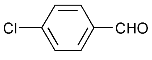
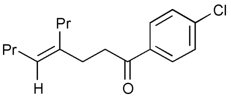
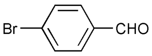
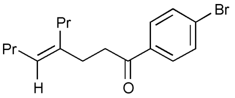
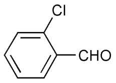
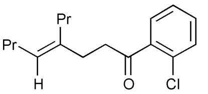
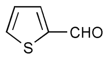
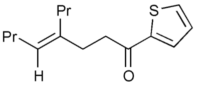
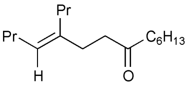
Scheme 1

Pair-selective coupling of alkynes with zirconocene–ethylene complexes generated *in situ* from Cp_2ZrEt_2 readily affords zirconacyclopentenes **2** in high yields.[3] After two equivalents of freshly sublimed $AlCl_3$ and aldehydes were added at −78 °C to the toluene solution of **2** generated *in situ*,[3] the reaction mixture was warmed up to rt and stirred for 1 h. Hydrolysis of the reaction mixture with 3 N HCl afforded a homoallyl ketone **1** as the only product in good yield (Scheme 2). Results given in Table 1 indicate that the reaction applies to a broad range of aliphatic and aromatic aldehydes and indifferently tolerates electron-donating as well as electron-withdrawing substituents.



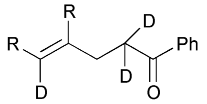
Scheme 2

Table 1 One-pot formation of homoallyl ketones from the reaction of aldehydes with zirconacyclopentenes mediated by $AlCl_3$

Aldehyde	Alkyne	Product		Yield (%)[a]
PhCHO	Pr—≡—Pr		**1a**	87 (65)
PhCHO	Bu—≡—Bu		**1b**	76 (55)
	Pr—≡—Pr		**1c**	79 (51)
	Pr—≡—Pr		**1d**	81 (53)
	Pr—≡—Pr		**1e**	78 (61)
	Pr—≡—Pr		**1f**	74 (65)
	Pr—≡—Pr		**1g**	70 (48)
$C_6H_{13}CHO$	Pr—≡—Pr		**1h**	70 (59)

[a] GC yields. Isolated yields are given in parentheses.

Significantly, when the deuterated aldehyde PhCDO was used, hydrolysis of the reaction medium with 3 N HCl produced **1a**‡ in 88% yield, with no detectable deuterium incorporation. By contrast, when PhCHO was used as a substrate, deuteriolysis of the reaction mixture with 20% DCl in D_2O afforded trideuterated **1aD**§ and **1bD** with more than 98% of deuterium incorporation in 85% and 82% yields, respectively. One deuterium was found bonding with the alkenyl carbon, while the



1aD: R = Pr, Yield: 85% (64%)
D > 98%
1bD: R = Bu, Yield: 82% (58%)
D > 98%

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† Electronic supplementary information (ESI) available: experimental details. See http://www.rsc.org/suppdata/cc/b1/b109761j/

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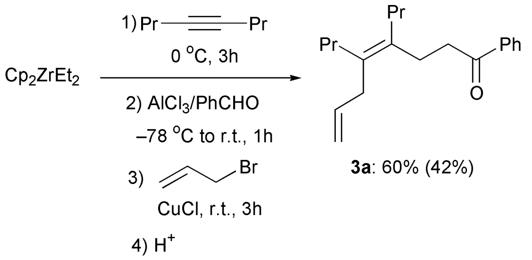
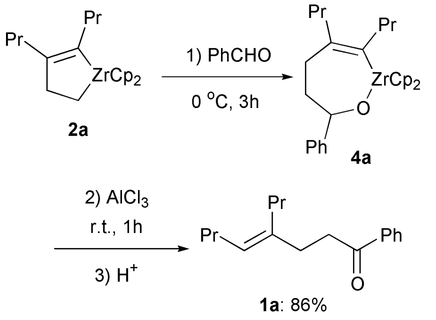


Scheme 3

other two deuterium atoms were bonded to the same sp^3 carbon atom adjacent to the carbonyl group.

These results indicate that M–C bonds still exist in the final organometallic species, thereby allowing further functionalization of the metal-bound organic fragment.[5] Effectively, when allyl bromide and CuCl were added to the above reaction mixture, allylated compound **3a** was formed in 60% yield (Scheme 3). As a whole, the starting alkyne is unsymmetrically bifunctionalized with two useful functional groups.

Insertion of aldehydes into zirconacyclopentenes has been reported to afford seven-membered oxazirconacycles.[6,7] To investigate the reaction mechanism, we firstly treated zirconacyclopentene **2a** (R = Pr) with benzaldehyde. The formation of **4a** was monitored by NMR and GC.[6] Addition of AlCl$_3$ to the reaction mixture of **4a** resulted in the formation of **1a** in 86% yield after hydrolysis (Scheme 4),[8] thereby suggesting the occurrence of the oxazirconacycloheptene species **4** as a probable intermediate *en route* to **1**.



Scheme 4

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Notes and references

‡ *Selected data* for **1a**: ^{1}H NMR (CDCl$_3$, SiMe$_4$) δ 0.89 (t, J = 7.2 Hz, 3H), 0.90 (t, J = 7.2 Hz, 3H), 1.26–1.48 (m, 4H), 1.94–2.07 (m, 4H), 2.41 (t, J = 6.6 Hz, 2H), 3.03–3.08 (m, 2H), 5.18 (t, J = 6.9 Hz, 1H), 7.41–7.56 (m, 3H), 7.94–7.97 (m, 2H); ^{13}C NMR (CDCl$_3$, SiMe$_4$) δ 13.86, 14.14, 21.63, 23.16, 29.87, 31.29, 32.43, 37.77, 125.60, 128.08, 128.56, 132.88, 137.15, 138.07, 200.29. HRMS calcd. for $C_{17}H_{24}O$ 244.1827, found 244.1822.

§ *Selected data* for **1aD**: ^{1}H NMR (CDCl$_3$, SiMe$_4$) δ 0.86–0.93 (m, 6H), 1.26–1.46 (m, 4H), 1.95–2.07 (m, 4H), 2.39 (s, 2H), 7.42–7.56 (m, 3H), 7.95 (d, J = 7.2 Hz, 2H); ^{13}C NMR (CDCl$_3$, SiMe$_4$) δ 13.88, 14.15, 21.63, 23.15, 29.77, 31.16, 32.41, 37.08–37.75 (m, CD$_2$), 125.22 (t, J = 22.9 Hz, CD), 128.09, 128.57, 132.88, 137.14, 137.96, 200.36. HRMS calcd. for $C_{17}H_{21}OD_3$ 247.2016, found 247.2010.

1 Z. Xi and P. Li, *Angew. Chem., Int. Ed. Engl.*, 2000, **39**, 2950.
2 M. Santelli and J. M. Pons, *Lewis Acids and Selectivity in Organic Synthesis*, CRC Press, Tokyo, 1996.
3 T. Takahashi, C. Xi, Z. Xi, M. Kageyama, R. Fischer, K. Nakajima and E. Negishi, *J. Org. Chem.*, 1998, **63**, 6802; T. Takahashi, M. Kageyama, V. Denisov, R. Hara and E. Negishi, *Tetrahedron Lett.*, 1993, **34**, 687; Z. Xi, R. Hara and T. Takahashi, *J. Org. Chem.*, 1995, **60**, 4444.
4 A. Yamamoto, *Adv. Organomet. Chem.*, 1992, **34**, 111; B. E. Maryanoff and A. B. Reitz, *Chem. Rev.*, 1989, **89**, 863; H. Pommer and P. C. Thieme, *Top. Curr. Chem.*, 1983, **109**, 165; H. J. Bestmann and O. Vostrowsky, *Top. Curr. Chem.*, 1983, **109**, 85.
5 T. Takahashi, M. Kotora, R. Hara and Z. Xi, *Bull. Chem. Soc. Jpn.*, 1999, **72**, 2591; T. Takahashi, Z. Xi and R. Hara, *Trends Organomet. Chem.*, 1997, **2**, 117.
6 C. Coperet, E. Negishi, Z. Xi and T. Takahashi, *Tetrahedron Lett.*, 1994, **35**, 695; P. Li, Z. Xi and T. Takahashi, *Chin. J. Chem.*, 2001, **19**, 45; see also: F. Sato, H. Urabe and S. Okamoto, *Chem. Rev.*, 2000, **100**, 2835.
7 Y. Yamamoto and K. Maruyama, *Tetrahedron Lett.*, 1981, **22**, 2895; K. Mashima, H. Yasuda, K. Asami and A. Nakamura, *Chem. Lett.*, 1983, 219; G. Erker, K. Engel, U. Dorf, J. L. Atwood and W. E. Hunter, *Angew. Chem., Int. Ed. Engl.*, 1982, **21**, 914.
8 Aluminacyclopentene formation involving zirconocenes: E. Negishi, D. Y. Kondakov, D. Choueiry, K. Kasai and T. Takahashi, *J. Am. Chem. Soc.*, 1996, **118**, 9577; E. Negishi, T. L. Montchamp, L. Anastasia, A. Elizarov and D. Choueiry, *Tetrahedron Lett.*, 1998, **39**, 2503; U. M. Dzhemilev and A. G. Ibragimov, *J. Organomet. Chem.*, 1994, **466**, 1.