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Assessing the utility of $HAlCl_2$ derived vinylalanes for Michael addition

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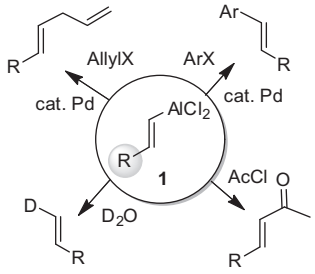
ABSTRACT

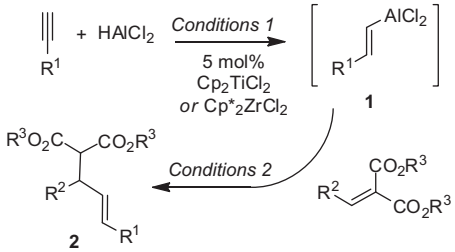
Rare alkenylalanes are prepared by Cp_2TiCl_2 or $Cp^*_2ZrCl_2$ (Cp = η-C_5H_5; Cp* = η-C_5Me_5) catalysed addition of $HAlCl_2{\cdot}(THF)_2$ to terminal alkynes ($R^1C{\equiv}CH$; R^1 = alkyl). Use of minimum head-volume sealed vials maximises the hydroalumination yields of volatile alkynes. Facile 1,4-addition of the resultant alkenylalanes to unsaturated malonates $R^2CH{=}C(CO_2R^3)_2$ (R^2 = alkyl, aryl, R^3 = alkyl) is observed providing rapid and convenient access to the addition products.

Dichlorovinylalanes (**1**) are rare, but potentially quite useful, organometallics the past application of which is limited to only four publications covering the transformations shown in Scheme 1.[1–4] First prepared in 1961[1] by the reaction of $CH_2{=}CHMgCl$ with $AlCl_3$ they have lain dormant in the literature for over 50 years. This was largely due to the fact that their only selective preparation was by $AlCl_3$ addition to Cp_2Zr(alkenyl)Cl (Cp = η-C_5H_5).[2] As the latter are simple Schwartz alkyne hydrozirconation products[5] already of high utility in subsequent couplings, the additional transmetallation was deemed pointless by most potential users. Recently, we have far easier access to **1** through terminal alkyne hydroalumination with $HAlCl_2{\cdot}(THF)_2$ under either Cp_2TiCl_2 or $Cp^*_2ZrCl_2$ (Cp* = η-C_5Me_5) catalysis (2–5 mol %).[4] As $HAlCl_2{\cdot}(THF)_2$ is readily available on at least 50 g scale (and has the useful feature that it can be handled in air for brief periods), alanes **1** warrant further investigation in their own right.

Our success in cross-coupling[4] using **1** caused us to consider other potential metal-promoted transformations, in particular 1,4-additions to Michael acceptors. In the absence of any prior literature we considered additions to alkylidene malonates **2** as initial substrates to screen alkenylalane additions, especially those derived from more problematic volatile alkynes (Scheme 2). Alkylidene malonates are powerful acceptors for (among other reagents) allyl organometallics[6] and cyclopentadienyl anions.[7]



Scheme 1. Only known reactivity of dichloroalkenylalanes **1** (1961–2013) prior to this study.



Scheme 2. Hydroalumination–Michael chemistry of this study.

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Table 1
Optimisation of *t*-BuC≡CH hydroalumination (conditions 1)[a]

Run	Cat.[a]	Conditions[b]	Yield of **1**[c] (%)	Alk.[c] (%)
1	Ti	THF, 1.0 M, 1.4 Eq. 80 °C, Schk	34–93[d]	2–7
2	Zr	THF, 1.0 M, 1.4 Eq. 80 °C, Schk	30–45[d]	2–3
3	Ti	THF, 2.0 M, 1.4 Eq. 50 °C, Schk	31	3
4	Ti	Toluene, 1.0 M, 1.4 Eq. 70 °C, vial	85	1
5	Ti	DME, 1.0 M, 1.4 Eq. 70 °C, vial	63	2
6	Ti	THF, 1.0 M, 1.4 Eq. 70 °C, vial	94	3
7	Ti	THF, 1.0 M, 1.1 Eq. 70 °C, vial	53	6

[a] Reactions carried out on 1.00 mmol (distilled) *t*-BuC≡CH in 0.5–1.0 mL solvent; Ti = Cp_2TiCl_2 (5 mol %), Zr = $Cp^*_2ZrCl_2$ (5 mol %).
[b] Data in form: solvent, [alkyne], equivalents $HAlCl_2(THF)_2$, temperature, carried out in either a 5 mL volume Schlenk tube (Schk) or a 1.5 mL vial (vial).
[c] Yield of **1** determined by GC after quench (HCl, 0 °C); Alk. = *t*-BuEt; mass balance is *t*-BuC≡CH.
[d] A range of yields was obtained.

Table 2
Optimisation of the 1,4-addition (conditions 2)[a]

Run	Eq. of **1**	Time (h)	[Malonate] (M)	Conv. to **2a**[b] (%)
1	1.0	2	0.5	16
2	1.0	2	0.7	61
3	3.0	1	0.5	58
4	3.0	2	0.5	97
5	2.0	2	0.5	98 (84)

[a] Reactions carried out on 1 mmol **1** (prepared in THF, 1.0 mL followed by solvent removal) and subsequent addition of diethyl 2-methylpropylidenemalonate (0.33–1.0 mmol) in THF (0.5–1 mL).
[b] Determined by GC versus internal standard, isolated yield in parentheses.

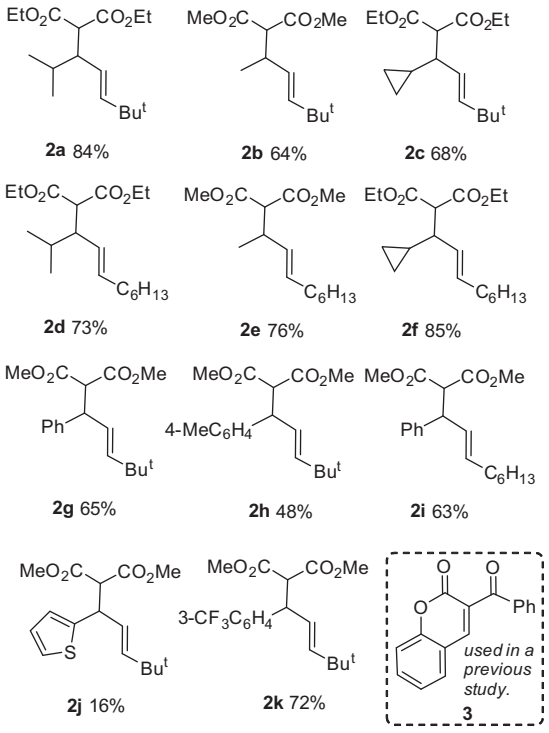

Figure 1. Isolated yields of 1,4-addition products (1 mmol scale).

Volatile *t*-BuC≡CH (bp 37 °C) can be capricious under hydroalumination[4] at smaller scales (<5 mmol). Over vigorous initial heating can cause significant escape of alkyne leading to variable yields in normal Schlenk-ware under either Cp_2TiCl_2 or $Cp^*_2ZrCl_2$ catalysis (Table 1, Runs 1 and 2). Reducing the reaction temperature and using higher concentrations are not effective (Run 3) and little reaction occurs at room temperature. Fortunately, these difficulties could be overcome using septa equipped GC vials as minimum headspace 'microreactors' (see Supporting information) (Runs 4 and 7). Optimum results were attained in THF but slight excesses of $HAlCl_2$ were required (Runs 6 and 7). Additionally, the GC vial approach worked well for other alkynes (volatile or otherwise) on 1 mmol scales (>90% yields).

Additions of **1** (R^1 = *t*-Bu) to diethyl 2-(2-methylpropylidene)malonate to afford **2a** (R^2 = *i*-Pr, R^3 = Et) were used for optimisation (Conditions 2, Table 2). Conversions into **2a** were determined by ^{1}H NMR spectroscopy. Preliminary studies revealed that ethereal solvents were optimal and chemoselectivity was optimised at 0 °C (no C=O reduction through the slight excesses of alane present in **1**).

The conditions of Tables 1 and 2 were applied to a range of substrate combinations leading to the isolated yields in Figure 1. The 1,4-addition products were isolated in moderate to good yields (16–85%) reflecting the electronic donor/acceptor properties of the R^2 groups. All additions to alkylidene malonates were spontaneous needing no catalytic copper source, as has been found previously for the acylcoumarins **3**.[8] Attempts at enantioselective additions were not successful with a range of ligands due to these fast background reactions. Conversely, analogous 1,4-additions to less activated substrates (cyclohexenone, nonenone, β-nitrostyrene) only proceeded in the presence of Cu^I catalysts, but not at practical yields (<5%) under the present conditions.[9]

In summary, these 1,4-additions provide a simple one-pot approach to addition products **2** as an alternative to palladium-catalysed additions of malonates to allylic electrophiles.[10]

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Supplementary data

Supplementary data (full experimental and spectroscopic data for compounds **2**) associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2014.01.105.

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