Effective Method for the Conjugate Addition of γ-Acetoxy-αβ-unsaturated Ketones with RCu-AlCl$_3$

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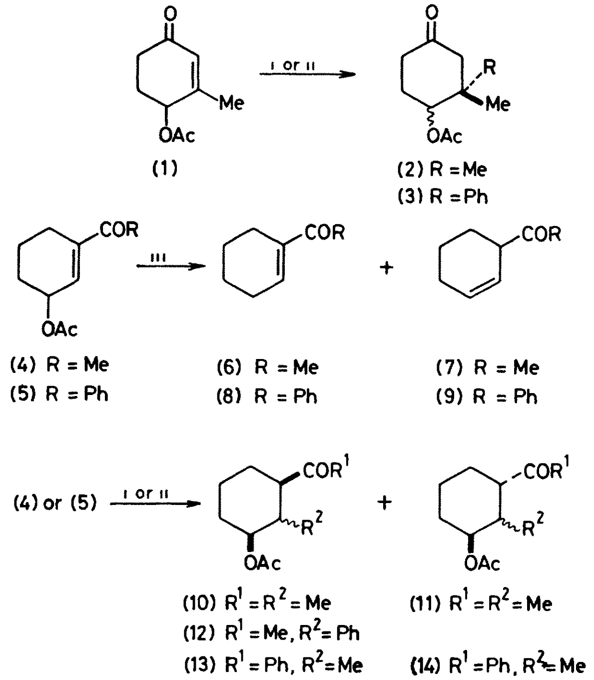
Summary An efficient procedure for the conjugate addition of γ-acetoxy-αβ-unsaturated ketones with RCu–AlCl$_3$ is described.

DESPITE the successful use of organocopper(I) reagents such as R$_2$CuLi in synthetic chemistry, considerable current interest is centred around the development of an effective method for conjugate addition as well as substitution reactions because of several drawbacks of the ordinary organocopper(I) reagents. By using lithium dimethylcuprate (Me$_2$CuLi), it has been reported that γ-acetoxy-αβ-unsaturated ketones were reduced to give αβ- and/or βγ-unsaturated ketones.[1,2,3] Unfortunately, no successful conjugate addition reaction of γ-acetoxy-αβ-unsaturated

TABLE. Yields of products in the reaction of γ-acetoxy-αβ-unsaturated ketones with Me$_2$CuLi and RCu-AlCl$_3$.[a]

Expt.	Substrate	Reagent	1,4-Adduct yield/%		Reduction product yield/%	
1	(**4**)	Me$_2$CuLi	[b]	—	(**6**) 14	(**7**) 25
2	(**5**)	Me$_2$CuLi	—	—	(**8**) 75	(**9**) 16
3	(**4**)	MeCu–AlCl$_3$	(**10**) 69,	(**11**) 4	—	—
4	(**4**)	PhCu–AlCl$_3$	(**12**) 87	—	—	—
5	(**5**)	MeCu–AlCl$_3$	(**13**) 76,	(**14**) 5	—	—

[a] The following procedure for a 1,4-addition reaction is typical. To a stirred suspension of MeCu (11·25 mmol) in dry ether (13·5 ml) under Ar at −70 °C was added dropwise a solution of AlCl$_3$ (11·25 mmol) in ether (3 ml) followed by a solution of the keto-acetate (**1**) (252 mg, 1·5 mmol) in dry ether (2 ml), and the temperature then raised to −25 °C. After each step the solution was stirred for 30 min. After the usual work-up, the product was purified by silica gel column chromatography to yield the pure adduct (**2**) (226 mg, 82% yield). [b] Though not isolated, gas chromatographic analysis of the reaction mixture showed the presence of $< 0{\cdot}75\%$ of the conjugate adduct (**10**).



Scheme Reagents, i, MeCu–AlCl$_3$ ii PhCu–AlCl$_3$ iii Me$_2$CuLi

ketones has been reported, so we describe here our results with MeCu–AlCl$_3$ and PhCu–AlCl$_3$

It has been reported that the keto-acetate (**1**) was reduced with lithium dimethylcuprate to afford a mixture of 3-methylcyclohex-2-enone and 3-methylcyclohex-3-enone [1] In contrast, treatment of (**1**) with 5—7 5 mol equiv of an equimolar mixture of methylcopper(i) and aluminium trichloride (MeCu–AlCl$_3$) and phenylcopper(i) and aluminium trichloride (PhCu–AlCl$_3$) in ether at −70 to −25±5 °C gave the conjugate adducts (**2**) and (**3**) in 82 and 95% yields, respectively (Scheme) † In these reactions, we did not detect any reduction product by gas chromatographic analysis

As shown in the Table, though the enones (**4**) and (**5**) were reduced with Me$_2$CuLi to afford $\alpha\beta$- and $\beta\gamma$-unsaturated ketones (**6**) and (**7**), and (**8**) and (**9**), respectively (expts 1 and 2), use of MeCu–AlCl$_3$ and PhCu–AlCl$_3$ provided the conjugate adducts in satisfactory yields (expts 3, 4, and 5) Application of the RCu–AlCl$_3$ system to a biologically active alkaloid is currently in progress

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† All new compounds exhibited satisfactory spectroscopic and analytical data consistent with the structures

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