SHORT PAPER

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Nickel (II) catalysed 1,4- addition reactions of functionalised organozinc reagents with enones[†]

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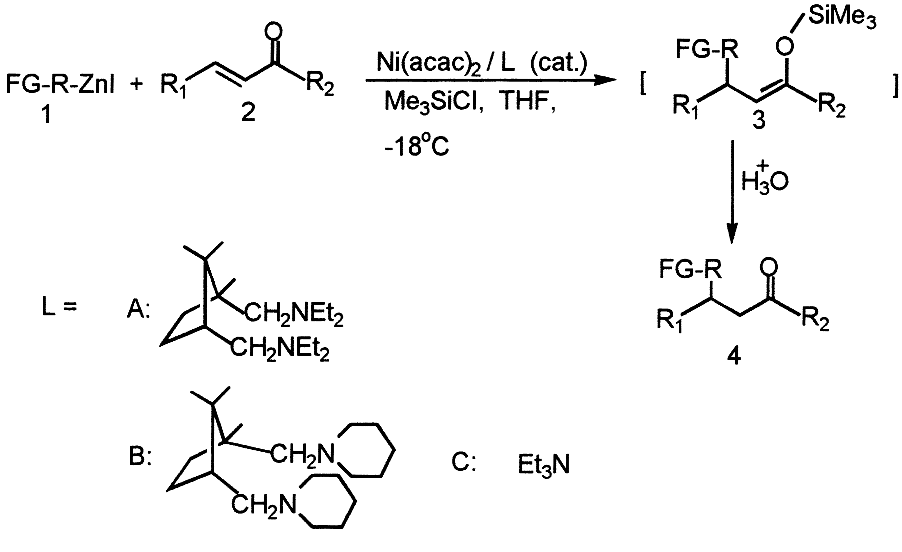
An efficient catalytic 1,4 addition reaction of functionalised organozinc reagents with enones has been developed using a nickel complex as catalyst.

Keywords: organozinc reagents, enones

Organozinc reagent are some of the earliest known organometallic compounds. Investigation of their application in organic synthesis had been completed before 1880.[1–3] However, they were replaced at the turn of the century by the more reactive organomagnesium reagent except the Reformatsky reaction,[4] because of its low reactivity toward most organic electrophiles. In 1978, Mukaiyama first reported that Et_2Zn reacted with benzaldehyde in the presence of aminoalcohol to give the 1, 2-addition product an excellent yield.[5,6] Pursuant to this report, a lot of papers about the reaction of organozinc reagents with organic electrophiles have appeared.[7–14] However, most research focussed on dialkylzinc reagents, few papers on study of organozinc halides had appeared until 1988. In 1988, P. Knochel reported that functionalised organozinc iodides (FG-RZnI) could be transmetallated into organozinc–copper reagents with the THF-soluble copper salt CuCN·2LiCl, and then used in a coupling reaction with RCOCl or a 1,4-addition reaction with enones. Many functionalities can exist on organozinc–copper reagents and remain unchanged in the reactions,[15] which make it possible to avoid the tedious protection of some functional group in organic synthesis. After this study, functionalised organozinc halides have found a broad application in organic synthesis in the presence of stoichiometric amounts of CuCN·2LiCl.[16–17] As for their 1,4-addition reactions, most of them were carried out using stoichiometric CuCN·2.LiCl, but Lipshutz reported that the functionalised alkylzinc iodides could undergo 1,4-addition reactions with enones in the presence of a catalytic amount of copper catalyst with slightly tedious procedure.[18,19] Although Rieke showed[20] that secondary and tertiary alkylzinc halides were reactive enough to add to enones in the presence of $BF_3 \cdot OEt_2$ without the use of copper(I) salts, primary alkylzinc halides did not react with enones under the same reaction conditions. In order to avoid the toxicity of CuCN and extend the application of FG-RZnI in organic synthesis, especially the asymmetric one, we also have done some research work in this field.[21–25] We previously[22] reported that in the presence of $Cu(OAc)_2$/LiCl, FG-RZnI can smoothly conduct 1,4-addition reactions, but $Cu(OAc)_2$ was still used stoichiometrically. In this paper we wish to report an effective Nickel complex catalysed 1,4-addition reactions of FG-RZnI which will be hopefully carried out asymmetrically (Scheme 1).

The present catalytic reaction is more effective than the $Cu(OAc)_2$-mediated one,[22] for example, FG-RZnI cannot react with chalcone in the presence of $Cu(OAc)_2$/LiCl, but it gives good results using $Ni(acac)_2$/diamine as catalyst (Table 1, entry 9 and 10).

In conclusion, we have developed an efficient catalytic method for the 1,4-addition reaction of FG-RZnI with enone while the functional groups in FG-RZnI can transfer to products. Because only a catalytic amount of Nickel complex is used as catalyst, it opens the door for the asymmetric 1,4-addition reaction of FG-RZnI.



Scheme 1

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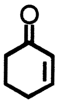
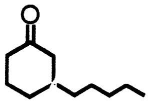
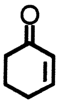
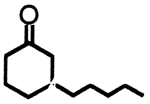
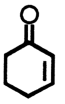
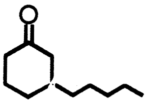
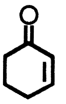
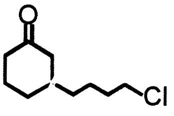
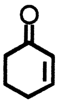
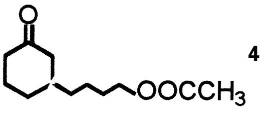
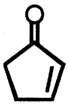
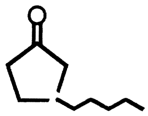
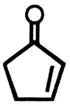
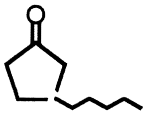
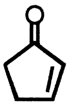
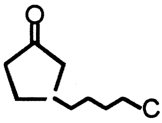
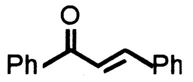
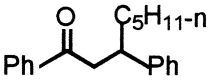
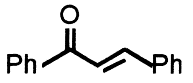
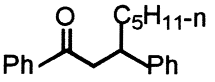
[†] This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M)*.

Table 1 1,4-Addition reaction of FG-R-ZnI with enones catalysed by $Ni(acac)_2$

No.	Enone	L	FG-R-	Product[a]		Yield/%[b]
1		A	n-C_5H_{11}–		**4a**	68
2		B	n-C_5H_{11}–		**4a**	64
3		C	n-C_5H_{11}–		**4a**	70
4		A	$Cl(CH_2)_4$–		**4b**	65
5		A	$CH_3COO(CH_2)_4$–		**4c**	54
6		A	n-C_5H_{11}–		**4d**	67
7		C	n-C_5H_{11}–		**4d**	71
8		B	$Cl(CH_2)_4$–		**4e**	65
9		A	n-C_5H_{11}–		**4f**	67
10		C	n-C_5H_{11}–		**4f**	75

[a]Structures were determined by NMR, IR and MS; [b]Isolated yield.

Experimental

Infrared spectra were measured as KBr discs (or liquid film) using a Nicolet-10DX FT-IR spectrometer. ^1H NMR spectra (80 MHz and 400 MHz) were recorded in $CDCl_3$ using Brucke AC-80 and Varian Ft-400 spectrometers. Mass spectra were obtained on a QP-1000A GC-MS spectrometer using the electron impact mode (70eV or 20eV).

General procedure for the preparation of compounds **4a–f**: A mixture of $Ni(acac)_2$ (1.2 mmol), L (2.4 mmol for A and B, 4.8 mmol for C) and 10 ml acetonitrile were put into a three-neck flask under a nitrogen atmosphere, heated to 60°C and stirred for 10 minutes. The mixture was cooled to room temperature and a solution of FG-RZnI (12 mmol) in THF was added.[21] The resulting mixture was cooled to –18°C and a solution of enone (9 mmol) and Me_3SiCl (18 mmol) in dried THF (5 ml) was added drop by drop. The reaction mixture was allowed to reach room temperature and stirred for 12 h. After completion, 10 ml 5N HCl was added and stirred for another hour. The reaction mixture was extracted with Et_2O three times. The combined organic layer was dried over $MgSO_4$, and concentrated. The product was isolated from the crude reaction mixture by chromatography on silica gel coumn using petroleum ether:diethyl ether or dichloromethane (10:1, V/V).

4a: Oil, IR υ_{max}(neat)/cm^{-1} 2955, 2988, 1714, 1458; ^{1}HNMR: δ_H(80 MHz; $CDCl_3$) 2.38–2.02(m, 4H), 1.86–1.28(m, 13H), 0.88(m, 3H); EI-MS *m*/*z* 168(M$^+$, 56%), 153(6), 139(11), 125(100), 111(24), 97(98), 83(99), 81(60), 55(98).

4b: Oil, IR υ_{max}(neat)/cm^{-1} 2953, 2930, 2860, 1712, 680; ^{1}HNMR: δ_H(80 MHz; $CDCl_3$) 3.54(t, 2H), 2.33–2.03(m, 4H), 1.85–1.37(m, 11H); EI-MS *m*/*z* 188(M$^+$, 5%), 145(22), 97(100), 69(16), 55(52).

4c: Oil, IR υ_{max}(neat)/cm^{-1} 2953, 2807, 1739, 1685, 1238, 1045; ^{1}HNMR: δ_H(80 MHz; $CDCl_3$) 4.01(t, 2H), 2.23–2.08(m, 4H), 2.02(s, 3H), 1.83–1.08(m, 11H); EI-MS *m*/*z* 212(M$^+$, 49%), 197(6), 153(4), 141(69), 125(5).

4d: Oil, IR υ_{max}(neat)/cm^{-1} 2959, 2926, 2856, 1743, 1462; δ_H(400 MHz; $CDCl_3$) 2.3–2.0(m, 4H), 1.71(q, 2H), 1.44–1.23(m, 9H), 0.82(t, 3H); EI-MS *m*/*z* 154(M$^+$, 2%), 126(4), 83(100), 70(20), 55(68), 28(42).

4e: Oil, IR υ_{max}(neat)/cm^{-1} 2957, 2933, 2864, 1739, 650; δ_H(400 MHz; $CDCl_3$) 3.54(t, 2H), 2.29–2.08(m, 3H), 1.89–1.47(m, 10H); EI-MS *m*/*z* 174(M$^+$, 36%), 145(69), 139(16), 111(6), 97(32), 83(100), 55(97).

4f: Oil, IR υ_{max}(neat)/cm^{-1} 3069, 3028, 2951, 2924, 2854, 1674, 1597, 1493, 1448, 1375, 762, 746, 698; δ_H(400 MHz; $CDCl_3$) 7.93–7.23(m, 10H), 3.30–3.10(m, 3H) 1.40–1.10(m, 8H), 0.89–0.75(t, 3H); EI-MS *m*/*z* 280(M$^+$, 5%), 209(81), 208(87), 161(13), 160(78), 131(12), 130(17), 117(22), 104(92), 105(100), 90(39), 77(23).

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