

A Synthesis of 2,3-Dimethylpentanal.

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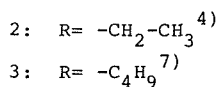
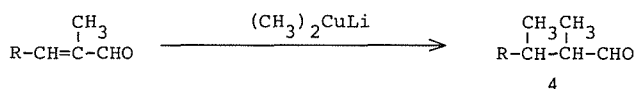
Abstract

In the presence of copper (I) salts, the reaction of 2-methyl-2-pentanal (2) with methylmagnesium iodide led to the formation of the mixture of 1,4- and 1,2-adducts. For example, 1,4-addition of methylmagnesium iodide to 2 varies in yield with the copper catalyst: CuCl (38–48%); CuBr (35–70%); CuI (40–80%).

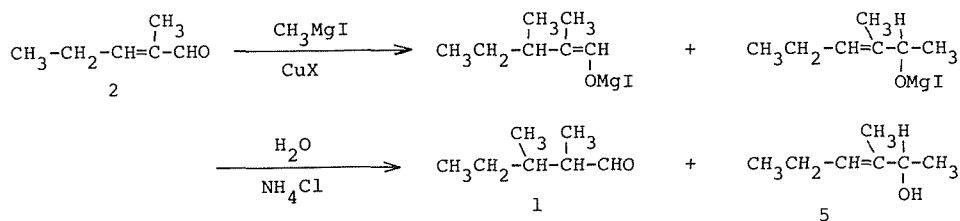
Introduction.

2,3-Dimethylpentanal (1) is employed as an intermediate of pharmaceutic product.¹⁾ The aldehyde 1 has been synthesized by the acid hydrolysis of 2,3-dimethyl-1-methoxypentan-2-ol,²⁾ by the decarboxylation of 2,3-epoxy-3,4-dimethylhexanoic acid,³⁾ and the reaction of lithiumdimethylcuprate with 2-methyl-2-pentanal (2).⁴⁾ In the presence of copper (I) salts, α,β -unsaturated carbonyl compounds react with organomagnesium compounds to give usually 1,4-adduct.⁵⁾ However, in the similar conditions, the reaction of ethylenic aldehydes with organomagnesium compounds have not been widely studied, presumably because of their well-established

tendency to undergo 1,2-addition with most reactive organometallic reagents.⁶⁾ Nevertheless, the α,β -disubstituted acroleins (2 and 3) reacted with lithiumdimethylcuprate at -78°C to give 1,4-adduct (4) only slightly contaminated by the expected 1,2-addition product.^{4,7)} Although Grignard reagents in the presence of copper (I) salt are claimed to give magnesium cuprates,⁸⁾ Whitesides *et al*⁹⁾ do not consider them to be convenient precursor. However, a general method for the preparation of organocopper compounds of the type RCu is the reaction of a Grignard or lithium reagent with an excess of a copper (I) salt. For this reason, we have studied the reaction of 2 with methylmagnesium iodide



in the presence of copper (I) halides. The yields and product compositions were determined with suitably calibrated gas chromatographic equipment. Table 1 summarized



Scheme 2

Table 1 The reaction of 2-methyl-2-pentenal with methylmagnesium iodide in the presence of copper (I) halide.

run	CuX	CuX/CH ₃ MgI (moles)	yields of products (%)		total yields (%)
			1	5	
1	—	—	0	82	76
2	CuCl	0.015	38.0	45.5	83.5
3	CuCl	0.5	40.5	44.5	85.0
4	CuCl	1.0	45.7	42.0	87.7
5	CuCl	2.0	48.0	40.0	88.0
6	CuBr	0.015	35.0	42.3	77.3
7	CuBr	0.5	49.6	34.4	84.0
8	CuBr	1.0	60.5	27.0	87.5
9	CuBr	2.0	70.3	17.5	87.8
10	CuI	0.015	40.5	45.5	86.0
11	CuI	0.5	45.4	37.0	82.4
12	CuI	1.0	60.9	20.5	81.4
13	CuI	2.0	80.2	6.2	86.4

the results of these studies. In absence of a copper (I) halide, methylmagnesium iodide ordinarily added to the carbonyl group to give the secondary alcohol, 3-methyl-3-hexen-2-ol (5). The presence of even a catalytic amount of copper (I) salt in reaction medium markedly enhanced the proportion of the conjugated 1,4-addition product (ran 2,3,6,7,10, and 11), and the product distribution of 1,4-adduct increases in order of CuI > CuBr > CuCl. Moreover, the presence of an excess amount of copper (I) salt (2 mole per CH₃MgI) allowed effective conjugated 1,4-addition

(run 5, 9, and 13).

Experimental

Materials. 2-Methyl-2-pentenal, secured from Tokyo Kasei Co., was carefully fractionated through a 25cm Vigreux column under ordinary pressure; bp 136–137°C. The copper (I) chloride¹⁰, copper (I) bromide¹⁰, and copper (I) iodide¹¹ were freshly prepared by the literatures. The gas chromatography equipment¹² was calibrated with known mixtures prepared from authentic samples and weighed samples of cumene

were added as internal standards to permit yield calculations.

The reaction of 2 with methylmagnesium iodide without copper (I) salt. To a cold (0°C) solution of 19.6g (0.20 mole) of the 2 in 100cm³ of ether was added, dropwise and with vigorous stirring over a 1.5h period, a solution of 0.35 mole of methylmagnesium iodide in 200cm³ of ether. The resulting solution was stirred for an additional 12h and then added to cold, aqueous ammonium chloride. The organic layer was separated, combined with the ether extract of the aqueous phase, dried, and concentrated to leave 17.35g (76% yield) of the crude alcohol 5 as a colorless liquid. Bp 92–94°C/165mmHg. IR (neat) : 3400 (OH), 1650, 850cm⁻¹ (-CH=C-). ¹H-NMR (CDCl₃, δ) : 0.96 (t, 3H, CH₃), 1.28 (d, 3H, -C-CH₃), 1.67 (s, 3H, -C=C-^{CH₃}), 2.24 (m, 2H, -CH₂-), 3.27 (s, 1H, -OH), 4.03 (q, 1H, -^{CH}-), 5.68 (t, 1H, -CH=C-). Found : C, 73.58; H, 12.25%; M⁺, 114. Calcd for C₇H₁₄O : C, 73.63; H, 12.36%; M, 114.

The reaction of 2 with methylmagnesium iodide in the presence of copper (I) salt. To a suspended solution of a weighed amount of copper (I) salt in ether (120cm³) was added at -10–-20°C, an ethereal solution containing 130mmole of methylmagnesium iodide. After stirring for 20min. a solution of 2 (6.86g, 70mmole) and a weighed amount of cumene (approximately 26mg as an internal standard) in ether (30cm³) was added over 1h at -10°C, the reaction mixture was stirred at room temperature for 20h and then was added to aqueous ammonium chloride. Upon working up the reaction product, the yields and product compositions were determined with gas chromatographic equipment (Hitachi gas chromatography K-53). For the separation of a pure 1, the reaction product in run 13 (see Table 1)

was fractionately distilled through a 46cm Vigreux column under an ordinary pressure. Bp 138–139°C. IR (neat) : 2750, 1730cm⁻¹ (-CHO). ¹H-NMR (CDCl₃, δ) : 0.82 (t, 3H, CH₃), 0.89 (d, 3H, CH₃), 0.98 (d, 3H, CH₃), 1.20–1.38 (m, 2H, -CH₂-), 1.80–2.30 (m, 2H, -H-), 9.60 (d, 1H, -CHO). Found : C, 73.55; H, 12.31%; M⁺, 114. Calcd for C₇H₁₄O : C, 73.63; H, 12.36%; M, 114.

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