

Reaction of magnesium with benzyl halides in an optically active solvent

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Abstract

Grignard reagent formation from benzyl halides with an asymmetric centre in the presence of an optically active solvent proceeds on the magnesium surface within a solvent cage by one-electron transfer mechanism.

Keywords: Magnesium; Optical activity

1. Introduction

The application of an optically active solvent and the presence of an asymmetric centre in 1-halo-1-phenylethanes in Grignard reactions are the most important preconditions for the appearance of optical activity in organomagnesium compounds [1]. These factors can also give the information on the one-electron transfer mechanism and the influence of the solvent in this reaction. Here we report the results of reactions of 1-halo-1-phenylethanes with magnesium in the presence of optically active (–)-(R)-2-methoxypentane.

2. Experimental details

NMR spectra were recorded on a Jeol LTD FX-90 Q spectrometer in CDCl_3 solution. Specific polarized light plane rotation was measured on an A-1 EPO automatic polarimeter ($\delta = 0.01^\circ$). The quantitative analysis of liquid products was performed by GLC with a Zvet-162 instrument using a 2.5 m glass columns packed with 18% Apiezon L on Chromaton-AW and 10% PEG-20M on Chromaton N-AW with flame ionization detection. Preparative separations of the reaction products were performed by HPLC with a Zvet-304 instrument using a 0.25 m stainless-steel column packed with Silosorb 600 and hexane–diethylether (1 : 5) as the eluent.

2.1. Syntheses

Synthesis of (–)-(R)-2-methoxypentane was carried out by reduction of (+)-(R)-4-methoxy-2-pentane by $\text{PdCl}_2\text{--NaBH}_4$ in accordance with the literature [2,3]. Yield 50%, b.p. 88–89°C, $[\alpha]_D^{25} = -12.8^\circ$ ($c = 5$). ^1NMR (CDCl_3 , int. TMS): δ (ppm) 1.12 (d, 3H, CH_3), 0.7–1.6 (m, 7H, $\text{CH}_2\text{CH}_2\text{CH}_3$), 3.4 (m, 1H, CH), 3.4 (s, 3H, OCH_3). Literature data: b.p. 88–89°C, $[\alpha]_D^{25} = +9.9^\circ$ ($c = 5$) for the S-isomer with 58% optical purity [2].

Synthesis of (+)-(R)-4-methoxypent-2-ene was carried out by interaction of (–)-(R)-pent-2-en-4-ol with NaH and CH_3I in diethylether in accordance with Ref. [2]. Yield 60%, b.p. 89–91°C, $[\alpha]_D^{23} = +93.5^\circ$ ($c = 3$). ^1NMR (CDCl_3 , int. TMS): δ (ppm) 1.13 (d, 3H, CH_3), 1.75 (d, 3H, CH_3), 3.32 (c, 3H, OCH_3), 3.51 (m, 1H, CH), 5.70 (m, 2H, $-\text{CH}=\text{CH}-$). Literature data: b.p. 89–91°C, $[\alpha]_D^{23} = -54.2^\circ$ ($c = 3$) for the S-isomer with 58% optical purity [2].

Synthesis of (–)-(R)-pent-2-en-4-ol was carried out in accordance with Ref. [4]. Yield 40%, b.p. 121–122°C, $[\alpha]_D^{20} = -7.7^\circ$ ($c = 12$). ^1NMR (CDCl_3 , int. TMS): δ (ppm) 1.20 (d, 3H, CH_3), 1.65 (d, 3H, CH_3), 3.21 (s, 1H, OH), 4.20 (m, 1H, CH), 5.57 (m, 2H, $-\text{CH}=\text{CH}-$). Literature data: b.p. 121–122°C, $[\alpha]_D^{20} = -7.7^\circ$ ($c = 12$) [4].

Synthesis of 1-chloro-1-phenylethane (**1a**) was carried out in accordance with Ref. [5]. Yield 85%, b.p. 73.8–74°C/10 mmHg. Literature data: b.p. 74°C/10 mmHg [6].

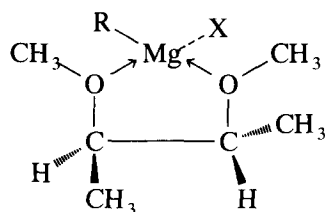
Synthesis of 1-bromo-1-phenylethane (**1b**) was car-

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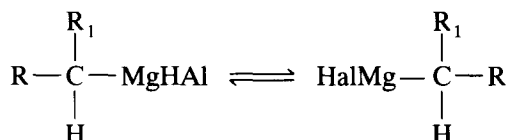
Table 1
Reactions of (*RS*)-1-halo-1-phenylethanes **1a–c** with magnesium in a benzene solution of (–)-(*R*)-2-methoxypentane

Com- pound	Yield of product (%) (quenched with ^t BuOD)	Yield of product (%) (quenched with D ₂ O)	Deuteration rate (%) (quenched with ^t BuOD)	Deuteration rate (%) (quenched with D ₂ O)
1a	76 (2)	68 (2)	97,5	90
	9 (3)	6 (3)	0	0
	5 (4)	8 (4)	0	0
	2 (5)	3 (5)	0	0
1b	75 (2)	60 (2)	95	88
	12 (3)	22 (3)	0	0
	7 (4)	12 (4)	0	0
	2 (5)	3 (5)	0	0
1c	72 (2)	46 (2)	94	82
	12 (3)	29 (3)	0	0
	8 (4)	17 (4)	0	0
	3 (5)	4 (5)	0	0

methoxypentane had any optical activity after quenching with D₂O. It is possible to assume that the main reason for this phenomenon is the radical pathway of the reaction [14–16]. The results obtained are in accordance with literature data on electrophilic substitution in benzene –(2*R*,3*R*)-(+)-dimethoxybutane solution, the latter of which forms solvates with Grignard reagents [1]:



The magnesium atom in this complex is an asymmetric centre and this solvate may exist in four stereochemically different forms in various proportions. Each form can react with a prochiral substrate at different rates and this can be the reason for the low optical activity of the reaction products in the presence of an optically active solvent (less than 5%) [1,17]. A further reason for the various reaction pathways is the stereochemical instability of the C–Mg bond and the existence of equilibrium between enantiomers:



It is known that the inversion rate of a benzylic Grignard reagent is very high [6]. Thus, Grignard reagent racemization may proceed just after its formation. If an optically active solvent takes part in the formation of intermediate complexes with Grignard reagent and reaction rate of the substrate with this reagent exceeds the

inversion rate, it is possible to expect a high reaction stereoselectivity.

We obtained clear evidence for this suggestion by carrying out the reaction of racemic 1-chloro-1-phenylethane with magnesium in benzene–(–)-(*R*)-2-methoxypentane solution with quenching by ^tBuOD. The main product of this reaction, 1-phenylethane-1D (**2**), was optically active with an optical purity of about 6%. Taking into account that the optical purity of (–)-(*R*)-2-methoxypentane was 75% and hydrocarbon **2** contained 2.5% of 1-phenylethane with an unknown deuterium site as an impurity, we can adjust the optical purity of the 1-phenylethane-1D obtained to 8.2%.

It is well known that recombination of optically active 1-phenylethyl radicals proceeds within a solvent cage 15 times more slowly than inversion and leads to partial retention configuration of the recombination products [18]. The optical purity of 1-phenylethane-1D (8,2%) a slightly exceeds that for 1-phenylethyl radical recombination within a solvent cage. Hence it is possible to assume that a phenylethyl radical recombines with an MgCl radical on the magnesium surface more rapidly than the inversion of 1-phenylethyl radicals. The reason for the increase in optical purity may be the result of partial recombination of ion–radical pairs within the solvent cage without decay to radical intermediates on the magnesium surface [14].

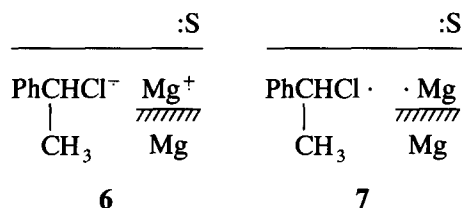
The formation of racemic 1-phenylethane-1D in the course of the reaction of **1a–c** with magnesium is reliable evidence for this suggestion and may proceed by radical pair recombination at a slower rate than that of 1-phenylethyl radical inversion on the magnesium surface within the solvent cage. Racemization may proceed either by recombination of optically inactive MgHal and PhCHCH₃ radicals in the solution or just after its return to the magnesium surface.

It was found earlier with the use of a radical trapping technique that Grignard reagent formation proceeds on the magnesium surface and the radicals obtained either recombine, giving by-products, or return to the magnesium surface. In this case only 25% of the forming radicals return to the solution [19,20].

The results presented in Table 1 show that the yields of products and the rate of deuteration are higher when ^tBuOD is added than for quenching with D₂O. These results indicate that the Grignard reagent formation probably proceeds on the magnesium surface within the solvent cage by a one-electron transfer mechanism. In this case the solvent is a reagent and an environment taking part in the transition-state formation.

The results obtained suggested that the limiting step in the course of the reaction of 1-chloro-1-phenylethane with magnesium is the formation of solvated ion–radical pairs of type **6**. In the case of the reactions of 1-bromo- and 1-iodo-1-phenylethane, the limiting step is whether the recombination of the solvated radical

pairs of type **7** formed by decay of ion–radical pairs **6** occurs or the reaction of **1b** and **c** with magnesium in the internal sphere without intermediate ion–radical pair formation takes place.



Otherwise none of the reaction products would have any optical activity and there would be a low rate of deuteration as a result of 1-phenylethyl radical disproportionation and reaction with the solvent in solution.

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