Benzylic Grignard Reagents: Application of [Mg(anthracene)(thf)$_3$] (thf = tetrahydrofuran) in Regioselective Grignard Formation and C–O Cleavage in Benzyl Ethers

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Benzylic Grignard reagents (2)—(4), bearing *ortho-* and *para*-halogeno ring substituents, are readily accessible by treating the corresponding benzylic halide with [Mg(anthracene)(thf)$_3$] (1) in tetrahydrofuran (thf); *o-* and *p*-chloromethyl(methoxymethyl)benzenes with (1) rapidly yield 'di-Grignards' whereas the *meta*-isomer only affords a mono-Grignard' (5), and bis(methoxymethyl)benzenes slowly undergo C–O cleavage, (6).

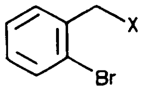
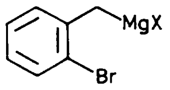
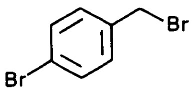
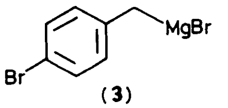
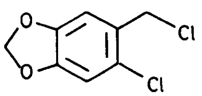
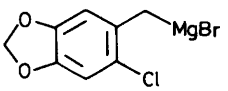
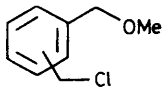
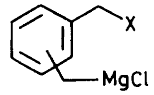
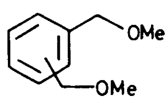
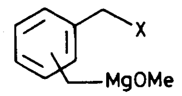
Benzylic Grignard reagents can be prepared in high yield[1] using [Mg(anthracene)(thf)$_3$] (**1**)[2] (thf = tetrahydrofuran) in place of elemental magnesium[2] in the classical method of Grignard formation. Such Grignards can be otherwise difficult to prepare or inaccessible, even using highly activated magnesium.[3] Complex (**1**) is seemingly a soluble source of magnesium and the mechanism of formation of Grignard reagents involves electron transfer processes.[1]

In further exploring the applications of (**1**) in synthesis we have studied its reactions with benzylic halides bearing halogeno and methoxymethyl ring substituents, and also benzylic ethers, and find some novel reactions, *viz*, (i) high yield, and regiospecific formation of Grignard reagents (**2**)—(**4**), (ii) generation of *ortho* and *para*-di-Grignard and *meta*-mono-Grignard reagents (**5**), from chloromethyl-(methoxymethyl)benzene, and (iii) some Grignard formation for the isomeric bis(methoxymethyl)benzenes. Results are detailed in Table 1.

Compound (**2**) is reported to be obtainable using elemental magnesium, albeit under rather critical conditions and with some coupled di-Grignard, (o-BrMgC$_6$H$_4$CH$_2$)$_2$.[4] However, we have found that stirring equimolar amounts of magnesium and o-BrC$_6$H$_4$CH$_2$Br in diethyl ether gives high yields of (**2**; X = Br), and only small amounts (<5% total) of the coupled di-Grignard and the di-Grignard (o-BrMgC$_6$H$_4$CH$_2$MgBr). None of the latter di-Grignard is evident using (**1**) [*cf.* one equivalent to generate (**2**; X = Br)], although there is *ca.* 12% of coupled product (for X = Br), (o-BrC$_6$H$_4$CH$_2$)$_2$. Bickelhaupt *et al.*[4] claim to have converted o-BrC$_6$H$_4$CH$_2$Br into a mixture of o-BrMgC$_6$H$_4$CH$_2$MgBr (82%) and the coupled di-Grignard (18%) using two equivalents of (**1**) and our published procedure.[1] In our hands this reaction, and the analogous reaction of o-BrC$_6$H$_4$CH$_2$Cl, yields a complex mixture containing *ca.* 25% of (**2**; X = Br) and *ca.* 25% of substituted anthracene arising from addition of preformed (**2**; X = Br) across the C-9/C-10 positions of anthracene in (**1**). This addition has been identified as a general reaction for aromatic bromides but chlorides fail to react.[5] Synthesis of (**4**) is more significant with respect to difficulties in preparing Grignard reagents of oxygen substituted benzylic halides.[6]

o- and p-MeOCH$_2$C$_6$H$_4$CH$_2$Cl rapidly afford 'di-Grignard reagents' (**5**), in high yield; attempts to prepare mono-Grignards gave a mixture of (**5**) and unchanged halide. Under the same conditions the *meta*-isomer, however, gave exclusively the mono-Grignard derived from insertion into the C–Cl bond. In the classical procedures using elemental magnesium, the *ortho-* and *para*-isomers give (C$_8$H$_8$)$_n$ *via* polymerization of quinodimethanes, whereas the *meta*-isomer

Table 1. Results of reactions of [Mg(anthracene)(thf)$_3$] (**1**) with benzylic halide/ether compounds at *ca.* 20 °C.[a]

Compound	Product[b,c]	% Yield[b]
	 (**2**)	X = Cl: 90 X = Br: 85
	 (**3**)	>95
	 (**4**)	>95
	 (**5**)	X = MgOMe, *ortho* and *para*:[d] >95 X = OMe, *meta*: >95
	 (**6**)	X = MgOMe, *ortho*: 70, *para*: 40 X = OMe, *meta*: 11

[a] The general procedures are given in ref. 1; a typical experiment involved the slow addition of the halide or ether to a slurry of an equimolar amount of (**1**) in thf with a target concentration of 0.1 M. [b] Products and yields were determined by quenching aliquots with 0.1 M HCl and back titrating with 0.1 M NaOH, followed by ^{1}H n.m.r. and gas chromatography–mass spectrometry of ClSiMe$_3$ derivatives. [c] Reactions were complete in *ca.* 30 min, except for the last entry where products were identified after *ca.* 16 h at *ca.* 20 °C. [d] Reaction at *ca.* 0 °C.

which is unable to form a quinodimethane gives the mono-Grignard.[7] The corresponding dimethoxy compounds all react slowly with (**1**) yielding some di-Grignard (*ortho*- and *para*-isomers) or mono-Grignard (**6**) (*meta*-isomer). Formation of di-Grignards (**5**) is rapid so that presumably formation of a mono-Grignard at the chloride centre is the primary process and this activates the methoxy group at the *ortho*- or *para*-methylene group. The same argument would account for the lack of formation of detectable amounts of mono-Grignard for the corresponding bis(methoxy) compounds. In general the insertion of Mg into C–O bonds normally requires rather forcing conditions, *e.g.* Rieke's magnesium reacts slowly with dibenzyl ether,[8] or the presence of a transition metal catalyst.[9] Since there appear to be no obvious stereoelectronic explanations for this behaviour it is possible that the quinodimethanes are formed in all reactions of the *ortho*- and *para*-isomers but are rapidly trapped by electron transfer from (**1**). In addition, it is noteworthy that (**1**) cleaves thf at 120 °C yielding butoxy substituted 9,10-dihydroanthracenes.[10]

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