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Synthesis of 11,12-disubstituted 9,10-anthraquinodimethanes: the first dehydroxylation reaction by active magnesium

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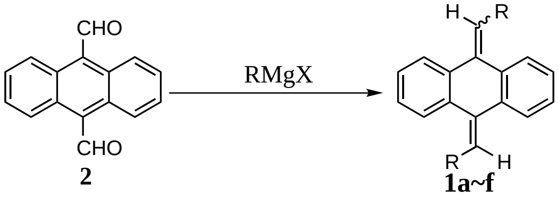
Abstract—The reaction of 9,10-diformylanthracene with Grignard reagents gave 11,12-disubstituted 9,10-anthraquinonemethane (**1**) in quantitative to excellent yields. The formation of these quinodimethanes caused by the active magnesium generated from the Grignard reagents was revealed. © 2002 Elsevier Science Ltd. All rights reserved.

9,10-Anthraquinodimethane and its derivatives have been widely and actively investigated from the viewpoint of organic superconductors and as the synthetic intermediate of [2.2]cyclophanes.[1] Although 11,12-diaryl substituted 9,10-anthraquinodimethanes have been synthesized as stable compounds,[2] the parent 11,12-dialkyl substituted quinodimethanes have been left unknown so far because of their highly reactive properties to polymerize.[3] Only 1,4,11,12-tetramethyl-9,10-anthraquinodimethane has been synthesized and isolated.[3] During the course of our research on the synthesis of new conjugated aromatic compounds containing an anthracene moiety, we found a new method for the first synthesis of 11,12-dialkyl and 11,12-diaryl substituted 9,10-anthraquinodimethanes (**1a**–**f**) in one step by the reaction of 9,10-diformylanthracene (**2**) with the Grignard reagent (RMgX) under ambient conditions in quantitative to excellent yields. Also, we succeeded in the first isolation of 11,12-dimethyl and 11,12-diethyl compounds at ambient temperature. Furthermore, the diol (**3a**) with the Grignard reagent (MeMgI) also gave the corresponding 11,12-disubstituted 9,10-anthraquinodimethanes under similar conditions. The mechanistic experiments revealed that the formation of quinodimethanes by dehydroxylation took place by the action of the active magnesium generated not only from the Grignard reagents but also from other methods.

The reaction of **2** with freshly prepared methylmagnesium iodide (60 equiv.) in dry THF–ether (ca. 1:1 in volume) solution at 40°C for 8 h gave **1a** quantitatively. Some preliminary experiments revealed that the complete quinodimethane formation requires a large excess amount of the Grignard reagent and reaction temperature above 40°C; otherwise, the reaction gave diols (**3a**–**f**) or their mixture at under that temperature. The reaction of **2** with other Grignard reagents (R = Et, Ph, etc.) also afforded the corresponding 11,12-disubstituted quinodimethanes in excellent to reasonable yields as shown in Table 1.

Table 1. The results of one-pot synthesis of **1** from **2**



Entry	Products	Yield[a] (%)	Ratio (*E*/*Z*)[c]
1	**1a**: R = Me	98[b]	1:1
2	**1b**: R = Et	90[b]	1:1
3	**1c**: R = Ph	61	1:1.29
4	**1d**: R = *o*-MeC_6H_4	47	1:1.96
5	**1e**: R = *p*-MeC_6H_4	42	1:1.04
6	**1f**: R = *p*-$MeOC_6H_4$	40	1:1.28

[a] Yields after chromatographic purification.

[b] Yields were determined by ^{1}H NMR analysis.

[c] Ratio refers to the isomer mixture characterized by ^{1}H NMR spectrum.

Keywords: Grignard reagent; dehydroxylation; active magnesium.

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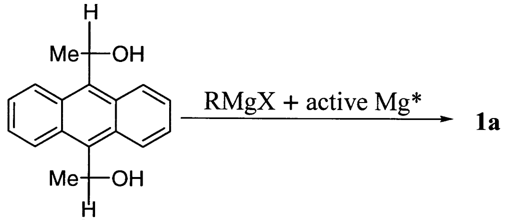
The structures of these new compounds were confirmed by their physical properties. The stereochemistry between the substituents of these quinodimethanes was determined by the ^{1}H NMR spectra. The ^{1}H NMR spectrum of **1a** showed that the methine protons appeared at δ 6.19 and 6.16 ppm as quartets ($J=7.19$ Hz), and the methyl groups at δ 2.12 and 2.13 ppm as two doublets, indicating a mixture of *syn* and *anti* forms. The structure of **1b** was determined in a similar way,[4] and the other known compounds (**1c**–**f**) were identified by comparison of the physical properties.[2] To examine the effects of the solvent and the molar ratios of the reagents, the reactions were performed under various conditions by using MeMgI as a typical Grignard reagent. The reaction does not depend upon the solvent, either THF or ether. The reaction of **2** with the use of a lesser molar ratio than 60 equiv. of the Grignard reagent gave a mixture of diol and quinodimethane depending on the ratio. Furthermore, treatment of diol (**3a**) with 60 equiv. of methylmagnesium iodide under the same conditions also gave **1a** quantitatively. The reaction of **2** and **3a** with the use of the same equiv. of filtered MeMgI or that of commercially available MeMgI (Aldrich Chemical Co.) gave only diol (**3a**) and no quinodimethane (**1a**) was obtained. These results suggested that the formation of quinodimethane was due to the active magnesium metal generated from the MeI or the MeMgI in solution.[5] This was confirmed by the use of active magnesium prepared by alternative methods as follows (Table 2). The entrainment reagent,[6] that is, the reaction of 1,2-dibromoethane with Mg (20 equiv.), of **3a** exclusively gave quinodimethane in 94% yield, entry 4. Furthermore, entries 5–7 show that less molar of reagents effective for dehydroxylation, e.g. the treatment of 5 equiv. of active Mg* generated by the reaction of Li$^+$[naphthalene]$^-$ with MgCl$_2$, also gave quinodimethane quantitatively.

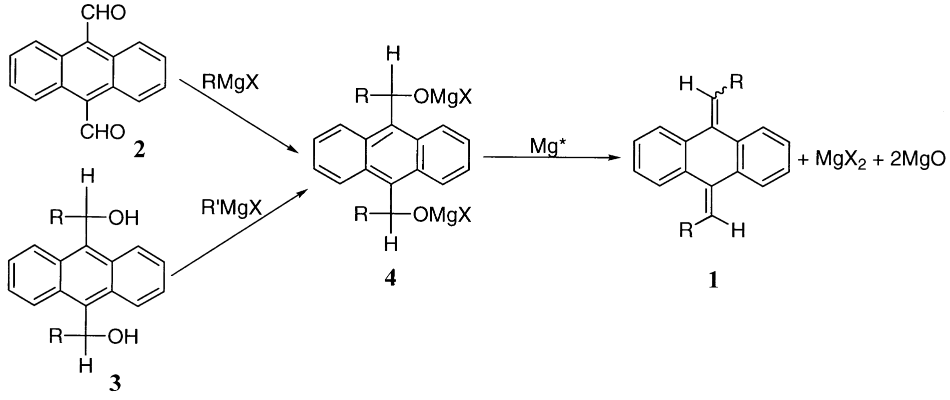
Based upon the above results, this reaction path is proposed to proceed as follows. The reaction of Grignard reagents with **2** gave halomagnesium salt of the corresponding diols (**4**), which were also generated by the reaction of **3** with any R′MgX. These complexes were dehydroxylated by the action of an excess of active magnesium, as shown in Scheme 1.

Table 2. The actions of the Grignard reagents and active Mg* on **3a** to formation of **1a**



3a

Entry	Reagents and conditions	Molar ratio (equiv.)	Ratio (%)		Total yield (%)
			3a	1a	
1	MeMgI, THF–ether, 8 h, 40°C	30	58	42	90
2	MeMgI, THF–ether, 8 h, 40°C	60	–	100	98
3	Br(CH$_2$)$_2$Br, Mg, THF–ether, 8 h, 40°C	10	21	75	95
4	Br(CH$_2$)$_2$Br, Mg, THF–ether, 8 h, 40°C	20	–	100	94
5	Naphthalene–Li, MgCl$_2$, THF, 8 h, 40°C	0.5	81	19	98
6	Naphthalene–Li, MgCl$_2$, THF, 8 h, 40°C	2	19	81	99
7	Naphthalene–Li, MgCl$_2$, THF, 8 h, 40°C	5	–	100	98



Scheme 1.

Acknowledgements

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4. General procedure: A solution of alkyl halide (60 equiv.) in dry ether (10 mL) was added dropwise under argon to stirred magnesium turnings (0.51 g, 0.02 g atoms) suspended in dry ether (4 mL) for 1.5 h, and stirring was continued for 1.5 h at room temperature. Then, to this resulting reagent, a solution of **2** (0.075 g, 0.32×10^{-3} mol) in dry THF (12 mL) was added dropwise (slowly), and stirring was continued for 8 h (24 h for aryl substituents) at 40°C. Then, the reaction mixture was poured into aqueous NH_4Cl and extracted with ether (3×80 mL). The combined organic layer was washed with brine and dried over anhydrous $MgSO_4$. The solvent was evaporated and chromatographed on silica gel (eluting with benzene/hexane, 2:1) and gave **1a**–**f**, respectively.
   Compound **1a**: Colorless oil, ^{1}H NMR (400 MHz, $CDCl_3$–TMS) δ 7.58–7.54 (m, 2H), 7.52–7.49 (m, 2H), 7.31–7.22 (m, 4H), 6.19 (q, $J=7.19$ Hz, 2H, methine–H, E or Z), 6.16 (q, $J=7.19$ Hz, 2H, methine-H, Z or E), 2.13 (d, $J=8.39$ Hz, 6H, CH_3, E or Z), 2.12 (d, $J=8.39$ Hz, 6H, CH_3, Z or E); ^{13}C NMR (100 MHz, $CDCl_3$–TMS) δ 139.47, 136.97, 135.92, 135.89, 134.85, 132.49, 127.69, 127.20, 127.07, 126.73, 126.03, 125.61, 123.86, 123.81, 123.53, 123.11, 16.01; UV–vis (MeOH) ν_{max}/nm (log ε) 213 (4.65), 227 (4.48), 261 (4.21), 283 (4.30); IR (film) 1632, 1600 cm^{-1} (C=C); MS (EI, 70 eV): m/z (%) = 232 (M^+, 100), 217 (77), 202 (58), 101 (21); HRMS calcd for $C_{18}H_{16}$: 232.1252, found 232.1265.
   Compound **1b**: Colorless oil, ^{1}H NMR (400 MHz, $CDCl_3$–TMS) δ 7.58–7.45 (m, 4H), 7.30–7.23 (m, 4H), 6.03 (t, $J=7.59$ Hz, 2H, methine-H, E or Z), 6.01 (t, $J=7.59$ Hz, 2H, methine-H, Z or E), 2.58 (quin., $J=7.19$ Hz, 4H, CH_2, E or Z), 2.56 (quin, $J=7.59$ Hz, 4H, CH_2, Z or E), 1.15 (t, $J=7.19$ Hz, 6H, CH_3, E or Z), 1.146 (t, $J=7.59$ Hz, 6H, CH_3, Z or E); ^{13}C (100 MHz, $CDCl_3$–TMS) δ 139.37, 137.02, 135.06, 134.37, 134.33, 132.87, 131.75, 131.47, 127.50, 127.10, 127.03, 126.74, 126.11, 125.65, 123.85, 123.15, 23.33, 14.79; UV–vis (MeOH) ν_{max}/nm (log ε) 211 (4.71), 252 (4.18), 261 (4.19), 285 (4.22); IR (film) 1633, 1593 cm^{-1} (C=C); MS (EI, 70 eV): m/z (%) = 260 (M^+, 64), 245 (25), 231 (100), 215 (41), 203 (50); HRMS calcd for $C_{20}H_{20}$: 260.1565, found 260.1584.
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