First Reference to the Alkoxymetallation of Diisobutylaluminium and Bromomagnesium-2-vinyloxy Ethoxide to the Corresponding (1,3-Dioxolan-2-yl)methyl Organometallics

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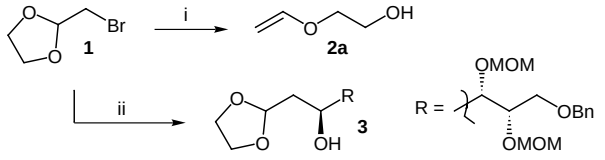
Abstract: Diisobutylaluminium and bromomagnesium-2-vinyloxy-ethoxide add at carbonyl compounds in the manner of (1,3-dioxolan-2-yl)methyl organometallics, giving the carbon-carbon addition products. It is assumed that the aluminium and magnesium compounds of 2-vinyloxy-ethoxide are in equilibrium with the corresponding (1,3-dioxolan-2-yl)methide.

Key words: carbanion, intramolecular cyclization, metallation, organometallic reagent, rearrangement

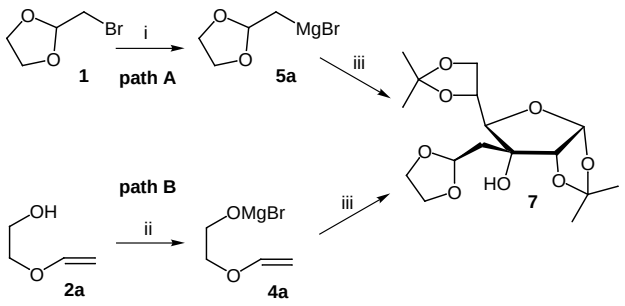
Organometallic compounds, bearing a functional group at the β-position, undergo facile β-elimination.[1] This elimination is only prevented by generating the carbanion at low temperature, with a very poor leaving group X at the β-position, or in the case of a perpendicular arrangement of lone electron pair and C-X bond. Earlier studies established that the action of sodium on 2-bromomethyl-1,3-dioxolane (**1**) in ether proceeds according to Scheme 1.[2] Similar results were obtained by Feugeas for the Grignard reagent from 2-bromomethyl-2-methyl-1,3-dioxolane. Refluxing in tetrahydrofuran yielded the corresponding β-elimination compound as the sole reaction product.[3] On the other hand, there are a few examples in the literature on the successful addition of the Grignard reagent of 2-bromomethyl-1,3-dioxolane (**1**) to carbonyl compounds. Kibayashi et al. reported the generation of **3** by addition of the organomagnesium compound of **1** to the aldehyde group of a *threo*-configurated carbohydrate derivative.[4]



Reagents and conditions: (i): Na, Et_2O, 35 °C, H_2O, 64%; (ii): Mg, THF, r.t., RCHO, NH_4Cl/H_2O, 70% (100% de).

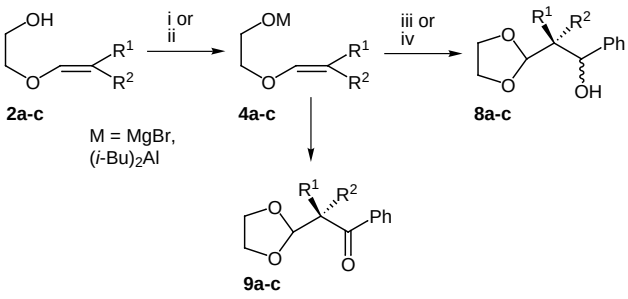
Scheme 1

In a preceding paper we described the preparation of the Grignard reagent from (**1**) and magnesium and its reaction with less reactive carbohydrate ketones in refluxing tetrahydrofuran. These uloses gave the corresponding branched chain carbohydrate derivatives in good to excellent yields (Scheme 2, path A).[5] The discrepancy in both findings caused us to approach the problem from the opposite side. Bromomagnesium-2-vinyloxy-ethoxide (**4a**), the product of β-elimination from (1,3-dioxolan-2-yl)-methylmagnesium bromide, was generated at room temperature (Scheme 2, path B), by addition of ethylmagnesium bromide in tetrahydrofuran to a solution of 2-vinyloxy-ethanol (**2a**) in tetrahydrofuran. The mixture was allowed to warm to room temperature and then a solution of ulose **6** in tetrahydrofuran was added. After refluxing for four hours the reaction was quenched.



Reagents and conditions: (i): Mg, 1.0 equiv, THF, r.t.; (ii): EtMgBr, 1.0 equiv, THF, r.t.; (iii):1,2;5,6-Di-*O*-isopropyliden-α- D-*ribo*-hexofuranos-3-ulose (**6**), 0.2 equiv, 4h, 65 °C, NH_4Cl/H_2O; A:64%, B:67%.

Scheme 2



Reagents and conditions: (i): EtMgBr, 1.1 equiv, 0 °C, THF; (ii): DIBALH, 1.1 equiv, 0 °C, THF; (iii): PhCHO, 2.0 equiv, 160 h, r.t.; NH_4Cl/H_2O; (iv): PhCHO, 2.0 equiv, 4 h, 65 °C; NH_4Cl/H_2O.

Scheme 3

Surprisingly, the magnesium alkoxide **4a** gave the carbon-carbon addition product of the Grignard reagent of 2-bromomethyl-1,3-dioxolane **5a** in a comparable yield. This unexpected result led to further examinations (Scheme 3), concerning the nature of metal and substituents. These reactions were carried out with the highly reactive benzaldehyde instead of ulose **6**.[6,7] The data shown in the Table indicate a strong enhancement of yield for the diisobutylaluminium alkoxide. Furthermore, the reaction was observed to be feasible even in the case of the substituted alkoxides **4b-c**.

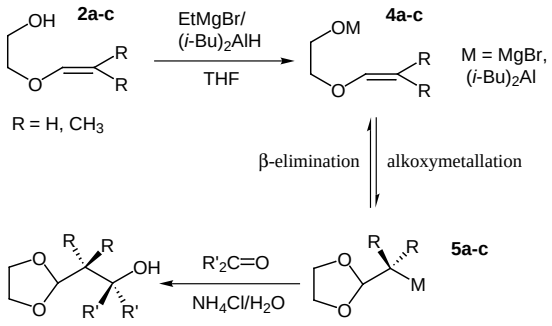
Moreover, we observed the ketones **9a-c**, generated by mono addition of **4a-c** to benzyl benzoate, as additional products. A reasonable explanation for the generation of the ester intermediate is given by the Tishenko reaction, the alkoxide catalyzed disproportionation of aldehydes to esters.[8] We also attempted, unsuccessfully, to detect the C-C addition products of the lithium, sodium or potassium derivative of **4a**, generated by deprotonation of **2a** with *n*-butyllithium, sodium hydride and potassium hydride.

Table Influence of metal and substituents

Substrat	R^1	R^2	M	Conditions	Yield **8a-c** [%]	Yield **9a-c** [%]
2a	H	H	MgBr	4h, 65°C	5	<1
2b[a)]	CH_3	H	MgBr	4h, 65°C	8[b)]	10
2c	CH_3	CH_3	MgBr	4h, 65°C	<1	10
2a	H	H	DIBAL	160 h, r.t.	25	21
2b[a)]	CH_3	H	DIBAL	160 h, r.t.	29[b)]	50
2c	CH_3	CH_3	DIBAL	160 h, r.t.	31	12

a) *E*/*Z* = 47:53, b) **8b**, *anti* (100% de).

In consideration of the resemblance to the corresponding carba-analogous carbometallations, these results can be explained by the mechanism, shown in Scheme 4. This intramolecular rearrangement of an unsaturated alkoxide to a carbanion corresponds to an alkoxymetallation. As a strong support for such a supposed anionic mechanism, Alexakis et al. already mentioned the cyclization of alkoxyallene derivatives.[9] Another description of these findings is that the examined (1,3-dioxolan-2-yl)methyl organometallics **5a-c** are in equilibrium with their products of β-elimination (**4a-c**). From the mechanistic point of view the assumed equilibrium may have some analogies to the well-known 5-hexenyl system.[10-13] However, due to the strong O-M bond in the open-chain components, the equilibria are expected to be far on the side of the alkoxide compounds.



Mechanistic conception

Scheme 4

Acknowledgement

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(6) 2-Vinyloxy-ethanol (**2a**) was obtained from Aldrich. 2-(α-propenyloxy)-ethanol (**2b**) and 2-methyl-(α-propenyloxy)-ethanol (**2c**) were prepared by the literature method: Davis, H.A.; Brown, R.K. *Can. J. Chem.* **1971**, *49*, 2563.
(7) **General Procedure** for the reactions shown in the Table. A 0.1-0.2 M solution of the alcohol (**2a-c**, typically 2.0-3.0 mmol) was cooled to 0 °C under an argon atmosphere and with stirring, 1.1 molar equiv of DIBALH in THF was added via syringe. The solution was allowed to warm to r.t. before addition of 2.0 molar equiv of benzaldehyde. After stirring for 160 h at r.t., the reaction was quenched with 1-2 mL of sat. aq NH_4Cl. The mixture was extracted with Et_2O, washed with water, dried (Na_2SO_4), filtered, evaporated and analysed by GC. Quantitative GC analyses were obtained with response corrected peak areas by using diphenylmethane as an internal standard.
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(14) All the compounds were characterized by ^{1}H and ^{13}C NMR. Data for selected products are as follows.
7; ^{1}H NMR data is identical to literature data; ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ = 25.73, 26.90, 27.14, 27.52 (4 x CH_3, $C(CH_3)_2$), 35.72 (CH_2, 2'-C), 64.80, 65.35 (2 x CH_2, dioxolane-C), 67.71 (CH_2, 6-C), 73.10 (CH, 5-C), 79.91 (C, 3-C), 84.22 (CH, 4-C), 86.41 (CH, 2-C), 103.11 (CH, 1'-C), 105.25 (CH, 1-C), 109.46, 112.63 (2 x C, $C(CH_3)_2$).
8a; ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 2.01 (1H, ddd, *J* = 3.8 Hz, 4.8 Hz, 14.4 Hz, 2a-H), 2.11 (1H, ddd, *J* = 4.8 Hz, 9.2 Hz, 14.4 Hz, 2b-H), 3.75-3.99 (4H, m, dioxolane-H), 4.93 (1H, dd, *J* = 3.8 Hz, 9.2 Hz, 1-H), 4.97 (1H, t, *J* = 4.8 Hz, dioxolane-H), 7.17-7.36 (5H, m, aryl-H); ^{13}C NMR (75 MHz, C_6D_6, TMS): δ = 43.53 (CH_2, 2-C), 64.63, 64.80 (2 x CH_2, dioxolane-C), 70.53 (CH, 1-C), 103.35 (CH, 3-C), 126.09, 127.37, 127.71 (3 x CH, aryl-C), 145.10 (C, aryl-C).
8b, *anti*; ^{1}H NMR (300 MHz, C_6D_6, TMS): δ = 0.82 (3H, d, *J* = 7.0 Hz, methyl-H), 2.20 (1H, ddq, *J* = 4.4 Hz, 7.0 Hz, 8.2 Hz, 2-H), 3.24, (2H, m, dixolane-H), 3.42 (2H, m, dioxolane-H), 4.72 (1H, d, *J* = 8.2 Hz, 1-H), 4.81 (1H, d, *J* = 4.4 Hz, dioxolane-H), 7.16 (3H, m, aryl-H), 7.33 (2H, m, aryl-H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ = 11.73 (CH_3, methyl-C), 43.27 (CH, 2-C), 64.77, 65.02 (2 x CH_2, dioxolane-C), 76.05 (CH, 1-C), 106.52 (CH, dioxolane-C), 126.88, 127.52, 128.21 (3 x CH, aryl-C), 142.59 (C, aryl-C).
8c; ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 0.76 (3H, s, methyl-H), 0.95 (3H, s, methyl-H), 2.80 (1H, s, -OH), 3.94 (4H, m, dioxolane-H), 4.70 (1H, s, 1-H), 4.74 (1H, s, dioxolane-H), 7.31 (5H, m, aryl-H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ = 15.92, 20.67 (2 x CH_3, methyl-C), 64.89, 65.14 (2 x CH_2, dioxolane-C), 78.08 (CH, 1-C), 109.69 (CH, dioxolane-C), 127.21, 127.46, 128.00 (3 x CH, aryl-C), 140.79 (C, aryl-C).

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