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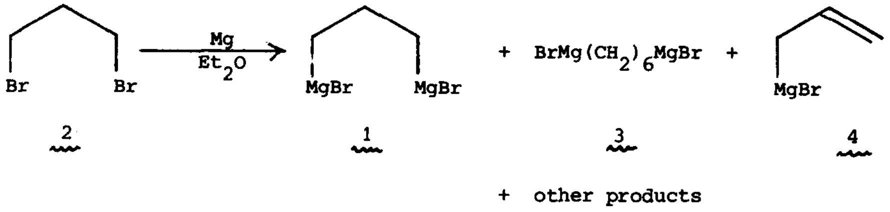
A DIRECT SYNTHESIS OF 1,3-BIS(BROMOMAGNESIO)PROPANE

J.W.F.L. Seetz, F.A. Hartog, H.P. Böhm, C. Blomberg,
O.S. Akkerman and F. Bickelhaupt*
Vakgroep Organische Chemie, Vrije Universiteit
De Boelelaan 1083, 1081 HV Amsterdam, The Netherlands

Abstract: Careful addition of 1,3-dibromopropane (2) to magnesium in Et_2O yields 1,3-bis(bromomagnesio)propane (1) which is purified via "magnesacyclobutane" (5). Reactions of 1 with H_2O, CO_2, $HgBr_2$ and Me_3SnCl are reported. $MgBr_2$ catalyzes the decomposition of 1 to allylmagnesium bromide (4).

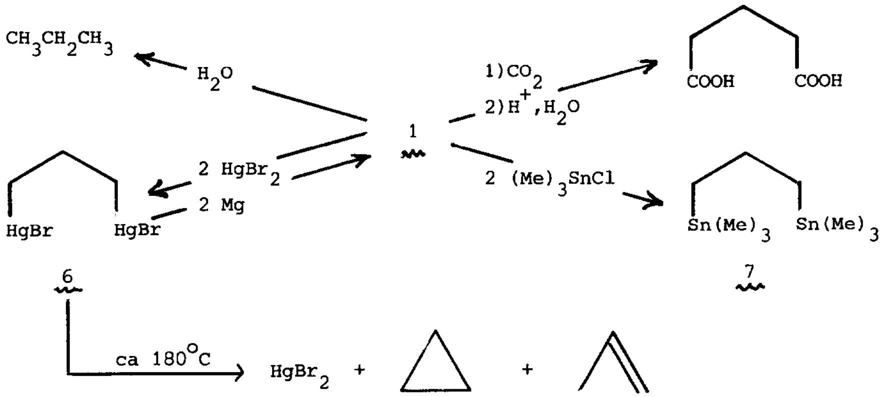
Repeated attempts to prepare a digrignard reagent from 1,3-dihalopropanes have met with failure[1]. Instead, γ-elimination occurs and cyclopropane is formed in good yield[1b]. This latter reaction has been exploited in the synthesis of many carbocyclic and heterocyclic three-membered rings[2]. There have been speculations[2a,e] and indications[2h] for the intermediate formation of mono- and diorganomagnesium compounds, but conclusive evidence is lacking.

We found that under proper reaction conditions, 1,3-bis(bromomagnesio)propane (1) can be obtained in a synthetically useful way (ca. 30% yield) by the direct reaction of magnesium with 1,3-dibromopropane (2).



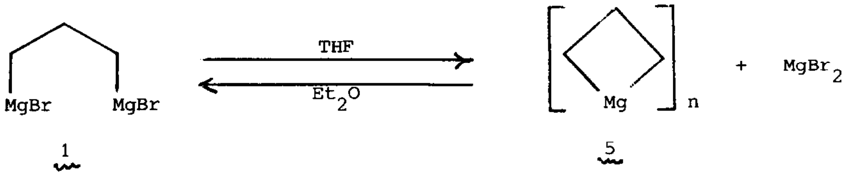
All experiments were performed in a fully sealed and evacuated glass apparatus[3], although this is not necessary for preparative purposes. At room temperature, 34.2 g 2 (170 mmol) in 200 ml Et_2O is added under stirring during 24 h to 24 g magnesium (triply sublimed; 1 mol) in 1.5 l Et_2O. After this time, 2 is completely consumed; acid/base and complexon titration show that 40-45% basic material is formed, about two thirds of which may be attributed to 1, the rest being mostly due to 3[1b] and 4.

Pure 1 was obtained from the reaction mixture via its dialkylmagnesium analog 5 (vide infra) and characterized by its NMR spectra; ^1H NMR (90 MHz, Et_2O-d_{10}, 20°C [4]): δ = -0.05 ppm (t, $^3J_{HH}$ = 6.8 Hz, 4 H), 2.12 ppm (quint., $^3J_{HH}$ = 6.8 Hz, 2 H); ^{13}C NMR (62.89 MHz, Et_2O-d_{10}, 20°C) : δ = 14.7 ppm (t, $^1J_{CH}$ = 97.9 Hz, C(α), C(γ)), 23.4 ppm (t, $^1J_{CH}$ = 122.1 Hz. C(β)). It is surprising to notice that in spite of the expected higher accumulation of negative charge in the carbon skeleton, both the ^{1}H and the ^{13}C resonances are at slightly lower field than those of n-propylmagnesium bromide[5]; the small $^1J_{CH}$ indicates rather high s-character in the carbon-magnesium bond. 1 was further characterized by reaction with water to give propane, with CO_2 to give glutaric acid, with $HgBr_2$ to give 6 and with trimethyltin chloride to give 7.



Based on 2, 6 was obtained in 30% yield[6], thus confirming the yield of 1 from 2. On heating to its melting point (177.5°C), 6 decomposed to give Hg_2Br_2 (100%), cyclopropane (76%) and propene (24%). Contrary to the experience of Costa and Whitesides with the chloro analog of 6 (1,3-bis(chloromercurio)propane)[7], 6 did react with magnesium in diethyl ether (stirring for 1 week at 25°C) to yield 70% of 1; in THF, 6 yielded 1 together with considerable amounts of 4.

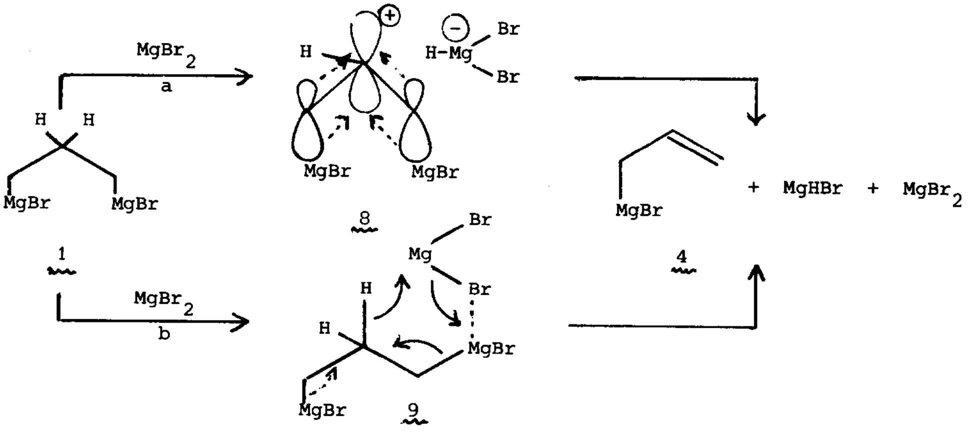
Costa and Whitesides have obtained 1 in a mixture with variable amounts of other Grignard reagents by a five-step procedure starting from allene[7]. The direct preparation of 1 from the readily available 2 in a one-step reaction may be considered as a considerable improvement; however, for the new route to be really attractive, a convenient way to purify 1 was desirable. We achieved this goal by evaporating the reaction mixture obtained from 2 and magnesium to dryness and adding THF to the residue; part of the material dissolves, while a white precipitate of pure 5 (an oligomer of magnesacyclobutane) is formed.



The mode of addition of THF is critical for success. If a large amount of THF is added, not only impurities such as 3, 4 and $MgBr_2$ dissolve , but also a considerable amount of 5, even though pure 5 is only slightly soluble in pure THF (formal concentration : 0.8 mmol/l). Apparently, an excess of $MgBr_2$ keeps 5 (or 1) in solution at a ratio of $MgBr_2$: 1 = 2 : 1 (determined by titration). We assume that complexation occurs, similar to that observed for 1,2-bis(bromomagnesio)cyclopropane[8]. This complexation leads to considerable loss of 5, but it can be avoided by adding THF in several, small portions. Under these conditions , $MgBr_2$ and other impurities dissolve rapidly, whereas complex formation between 5 and $MgBr_2$ apparently is slow; 50% of pure 5 (based on 1) can thus be obtained. When exactly 1 mol of $MgBr_2$ is added per mol of 5 in diethyl ether, the precipitate dissolves and pure 1 is quantitatively reconstituted.

Because of its slight solubility in THF, the NMR spectra of 5 were measured in HMPT-d_{18}; ^1H NMR (250 MHz) : $\delta = -0.38$ ppm (t, $^3J_{HH} = 6.5$ Hz, 4 H), 2.19 ppm (quint., $^3J_{HH} = 6.5$ Hz, 2 H); ^{13}C NMR (62.89 MHz) : $\delta = 18.2$ ppm (t, $^1J_{CH} = 104$ Hz, C(α), C(γ)), 28.3 ppm (t, $^1J_{CH} = 119$ Hz, C(β)). 5 is not stable in HMPT ($t_{1/2}$ = 4d).

Costa and Whitesides reported that 1 is unstable in THF, yielding 4 and n-propylmagnesium bromide[7]. We found that pure 1, without $MgBr_2$, is completely stable in diethyl ether; however, additional $MgBr_2$ causes decomposition to 4 (we did not observe the formation of n-propylmagnesium bromide), and the rate of decomposition increases with increasing amounts of $MgBr_2$. We rationalize these observations as follows. For simple organomagnesium species, the hydridic activation of the β-hydrogen atom is well known, e.g. in the reduction of ketones[9]. Presumably, this effect is strongly intensified in 1 by the presence of the second magnesium atom; such synergistic effects have been studied in organic 1,3-di-tin compounds[10]. With 1, the reaction may occur either in a similar fashion, i.e. by hydride abstraction by $MgBr_2$ with vertical stabilization [10,11] by the two Mg-C bonds to give the short lived carbocation 8 (pathway a). Alternatively, the reaction may proceed by cis-elimination[12] in a concerted, six-center fashion via transition state 9, in which hydride abstraction by (intramolecularly complexed) $MgBr_2$ is assisted by the second C-Mg bond (pathway b).



In conclusion, the reaction of 2 with magnesium to form 1, followed by purification makes this interesting synthon readily available. Its application in organic and organometallic chemistry is being investigated.

References and Notes.

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4. At lower temperatures, DNMR-experiments revealed coalescence phenomena which are presently being investigated.
5. n-Propylmagnesium bromide, (Et_2O-d_{10}); ^1H NMR (250 MHz) $\delta = -0.46$ ppm (t, $^3J_{HH} = 7.8$ Hz, 2 H), 0.94 ppm (t, $^3J_{HH} = 6.9$ Hz, 3 H), 1.55 ppm (m, 2 H); ^{13}C NMR (62.89 MHz) $\delta = 11.08$ ppm (t, $^1J_{CH} = 103.7$ Hz, C(α)), 22.06 (q, $^1J_{CH} = 117.9$ Hz, C(γ)), 22.25 ppm (t, $^1J_{CH} = 120.7$, C(β)).
6. **6** gave a satisfactory elemental analysis and was characterized by its NMR spectra; ^1H NMR (250 MHz, DMSO-d_6) : $\delta = 1.94$ ppm (t, $^3J_{HH} = 6.5$ Hz, $^2J_{HgH} = 214$ Hz; 4 H), 2.19 ppm (quintet, $^3J_{HH} = 6.5$ Hz, $^3J_{HgH} = 292$ Hz, 2 H); ^{13}C NMR (62.89 MHz, pyridine-d_5) : $\delta = 30.0$ ppm (t, $^1J_{CH} = 130.5$ Hz, $^2J_{HgC} = 78.1$ Hz, C(β)), 38.3 ppm (t, $^1J_{CH} = 135.2$ Hz, $^1J_{HgC} = 1645.6$ Hz, $^3J_{HgC} = 241.8$ Hz, C(α) + C(γ)).
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