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Anomalous Reactions of 2-Naphthylmethylmagnesium Bromide

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2-Naphthylmethylmagnesium bromide has been prepared with a "cyclic reactor" and its reactions with ethyl chlorocarbonate, formaldehyde, ethylene oxide and acetyl chloride have been shown to give rearrangement products. Exclusively normal products were isolated only in the reactions with carbon dioxide and tributyl borate.

Organomagnesium halides with the $-CH=CH-CH_2-MgX$ grouping often give abnormal products and since Grignard [1] himself initially conducted such a rearrangement reaction (which he did not know at that time), many investigations have been made in this field. Kharasch and Reinmuth [2] have recently summarized the situation until 1952. In connection with the preparation and study of 2-napththylmethylboronic acid as a plant growth regulator [3] it was neeessary to find out if rearrangement occurred or not and we have now further studied this and similar reactions.

The preparation of Grignard reagents from halides of the benzylic type is generally troublesome and the yields are often very low. The reason is, that under the usual conditions some metathesis will always occur between the Grignard reagent formed and the later added halide thus giving coupling products. Various strategies to avoid coupling have been tried: high dilution, excess of magnesium, etc., but the best way was introduced by Rowlands, Greenlee and Boord, who used a so called cyclic reactor [4]. By this method we have, contrary to earlier reports [3,5,6] obtained good yields of 2-naphthylmethylmagnesium bromide.

In Scheme 1, six reactions of 2-naphthylmethylmagnesium bromide are represented. 2-Naphthylmethyl bromide (I) was easily converted to the corresponding Grignard reagent (II) in the cyclic reactor (Fig. 1). In all experiments, however, small amounts of the coupling product, 1,2-di(2-naphthyl)-ethane were also isolated. The reagent II was treated with carbon dioxide, tributyl from 2-methyl-1-naphthyllithium reagent and ethylene oxide and by reduction of 2-methyl-1-naphthylacetic acid.

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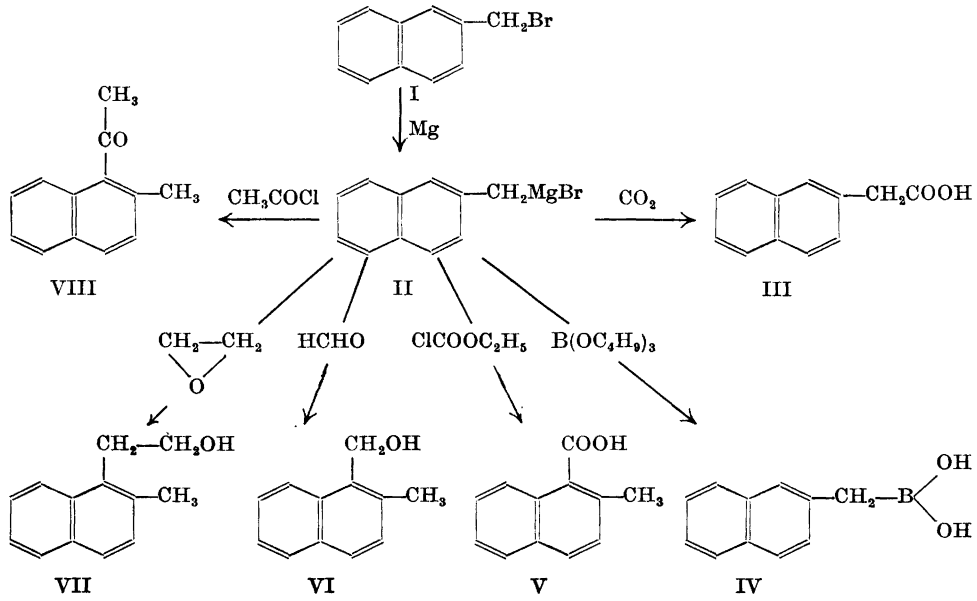

Scheme 1.

borate, ethyl chlorocarbonate, formaldehyde, ethylene oxide and acetyl chloride. "Normal" products were isolated only in the reactions with carbon dioxide and tributyl borate.

2-Naphthylacetic acid, prepared *via* the nitrile [7] was identical with III, obtained by carbonation of II. The hypothetical rearrangement product, 2-methyl-1-naphthylcarboxylic acid was shown by mixed meltingpoint test to be non-identical with III.

The non-identity of 2-naphthylmethylboronic acid [3] (IV) with the possible rearrangement product, 2-methyl-1-naphthylboronic acid [8] was confirmed by infrared investigation and by melting point differences.

The acid V was obtained if the reagent II was treated with ethyl chlorocarbonate and hydrolysis of the ester. The identity of V with 2-methyl-1-naphthylcarboxylic acid [9], was confirmed in this case by infrared analysis as well.

Gaseous formaldehyde gives with the reagent II exclusively 2-methyl-1-naphthylcarbinol (VI). The same compound was prepared from V by reduction with lithium aluminiumhydride or by treating 2-methyl-1-naphthylmagnesium bromide with gaseous formaldehyde [10]. For comparison the normal product was also prepared by reduction of 2-naphthylacetic acid with lithium aluminium hydride.

The abnormal product VII was formed by treating II with ethylene oxide. A review [11] of reactions between Grignard reagents and the oxirane (epoxide) ring was published some years ago. The compound VII was also prepared from 2-methyl-1-naphthyllithium reagent and ethylene oxide and by reduction of 2-methyl-1-naphtylacetic acid.

The product VIII was formed upon treating II with acetylchloride. Its hydrazone was shown by infrared analysis and by mixed melting point to be identical with the corresponding derivative of methyl-(2-methyl-1-naphthyl) ketone.

No rearrangement to the open 3-position has been observed in any of our experiments; consequently this constitutes another manifestation of the symmetrical bond fixation in the naphthalene nucleus. Furthermore our results agree with those of Gaertner [12] concerning the reactions of 2-thianaphthenylmethylmagnesium chloride with different substances. In both cases *exclusively* abnormal products were isolated (except with carbon dioxide) and these two examples show that rearrangement will occur more extensively to a position which is attacked preferentially in electrophilic substitution. There are exceptions, however, and our results might be only an indication.

EXPERIMENTAL

Apparatus and procedure

The cyclic reactor is sketched in Fig. 1. The condenser is topped by a funnel for slow addition of the halide. The magnesium turnings are amalgamated by mixing the magnesium and $HgBr_2$ in the column and then adding dry ether. The apparatus is then allowed to stand overnight, and after the ether has been swept down into the pot and renewed,

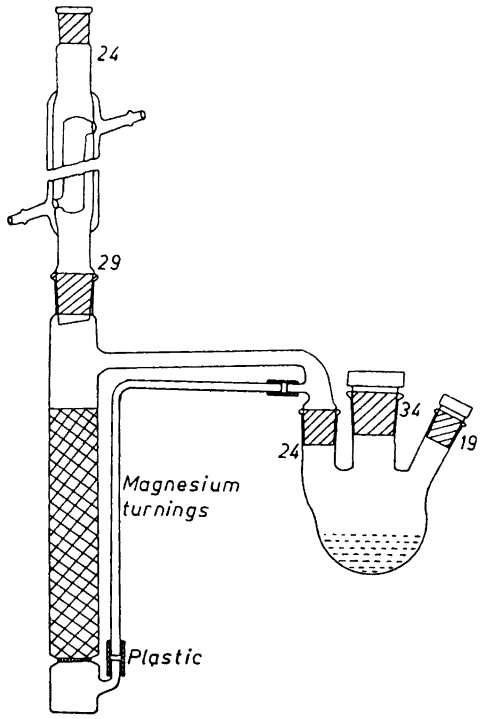

Fig. 1.

the "cycling" can start. The reactor is operated under nitrogen or at least the apparatus is swept free from oxygen before the experiment. It is furthermore important to start the column with allyl bromide or the like and then "cycle" until all the Grignard reagent is swept into the flask. Anhydrous conditions are always essential and it is also important that the addition of the halide is slow, that gentle boiling is maintained in the upper part of the Mg-column with a good ether cycling rate. High dilution must be maintained in the column (200—300 ml of ether per 0.1 mole of halide) at all times. Otherwise this method is no better than the usual pot method. Once the Grignard reagent is formed and swept into the pot it is stable against coupling.

Preparation of 2-naphthylmethylmagnesium bromide

In all experiments 0.05 mole (11 g) of I [13] was used, dissolved in 125 ml of dry ether. Hydrolysis of the Grignard reagent formed gave 2-methylnaphthalene (b.p. 108—110°C/16 mm Hg, m.p. 33—35°C) and the yield could thus be determined. The best yield was 84 % when the method of Greenlee and coworkers was used. The conventional method gave only 39 % of the theoretical, the remainder being mostly coupling products.

Carbonation of 2-naphthylmethylmagnesium bromide

The Grignard reagent II, prepared from 11 g of I, was cooled to about 0°C and then poured slowly into crushed dry ice in absolute ether. The mixture was allowed to warm to room temperature and then was hydrolyzed with water. The organic layer was separated off, the water solution extracted with ether and the combined ether layers extracted with dilute sodium hydroxide. Upon acidification of the alkaline solution, a white powder precipitated, which after recrystallisation from water-ethanol gave white needles. M.p. 140—142°C. Weight 6.9 g. Yield 74 % . With an authentitc sample [7], m.p. and mixed m.p. 139—141°. From the ether phase 0.3 g of a substance was separated, which after recrystallisation from ethanol gave white plates with m.p. 183—185°; presumably 1,2-di(2-naphthyl)-ethane [14]: m.p. 182°C.

Reaction of the Grignard reagent II with tributyl borate

The Grignard reagent, prepared from 11 g of I, was added with stirring over a two-hour period, to 15 g of tributyl borate [15] in 100 ml of dry ether at —60°C. After standing overnight it was treated with 1 M hydrochloric acid, the organic portion separated and the aqueous phase extracted with ether. The combined ether layers were extracted with 1 M sodium hydroxide. The alkaline aqueous layer was acidified with hydrochloric acid precipitating 4.5 g of the crude moist acid (Yield ≈48 %). The diethanolamine ester was prepared in the usual way [3]; m.p. 229—231°C.

Reaction of the Grignard reagent II with ethyl chlorocarbonate

The Grignard reagent, prepared from 11 g of I, was added during half an hour to a well-stirred solution of 50 ml of redistilled ethyl chlorocarbonate, cooled to —20°C in an ice-water bath. After standing with stirring overnight during which time the temperature rose to room temperature, water and 25 g of sodium hydroxide were added under gentle reflux. The alkaline solution was then acidified, liberating carbon dioxide, and then the aqueous layer was repeatedly shaken with ether. The ether was evaporated and the

residual oil was saponified by alcoholic sodium hydroxide. Upon acidifying the solution, a white powder was precipitated, which after recrystallisation from water gave fine needles. M.p. 125—127°C. Weight 6.6 g. Yield 71 %. With an authentic sample of 2-methyl-1-naphthylcarboxylic acid [9] no depression of the melting point was observed. (Found: Equiv.wt. 187.7. Calc.: Equiv.wt. 186.20.)

Reaction of the Grignard reagent II with formaldehyde

Gaseous formaldehyde [16] from 90 g of dry paraformaldehyde was carried by dry oxygen-free nitrogen into a solution of II, prepared from 11 g of I. The reaction took place at room temperature. A white precipitate was formed at once and after the solution had been cooled in an ice bath, saturated ammonium chloride was added to dissolve the magnesium compound. The solution was shaken with ether repeatedly, the organic extracts shaken free from acid and after being dried over sodium sulphate and freed from ether, the residue was distilled. The main fraction, b.p. 140—144°C/10—11 mm Hg, consisted of a heavy yellow liquid. Weight 4.4 g. Yield 51 %. The liquid was dissolved in petroleum ether and after some time faintly yellow plates were precipitated. Recrystallisation from ligroin + ether gave white plates with m.p. 114—116°C. (Found: C 84.0; H 7.24. Calc. for $C_{12}H_{12}O$(172.21): C 83.7; H 7.03.)

Reduction of 2 methyl-1-naphthylcarboxylic acid

A solution of 1.9 g of 2-methyl-1-naphthylcarboxylic acid in 50 ml of dry ether was added to an ethereal solution of lithium aluminium hydride (in excess) at such a rate that the reaction mixture boiled gently. When the reaction was over, an excess of cold water was added and then the mixture was poured into ice-cold dilute sulphuric acid. The solution was shaken repeatedly with ether, the organic layer separted, dried over sodium sulphate and evaporated. The white powder was then recrystallized from ligroin + ether, giving an almost quantitative yield of white plates. M.p. 114—116°C. Mixed m.p. with VI: 114—116°C.

Reduction of 2-naphthylacetic acid

Addition of an ethereal solution of 1.9 g of the acid to a stirred suspension of 1 g of lithium aluminium hydride in 50 ml of ether, followed by usual procedures, gave white plates of β-(2-naphthyl)-ethanol. M.p. 72—73°C. Weight 1.7 g. Yield: almost quantitative. (Found: C 83.8; H 7.00. Calc. for $C_{12}H_{12}O$ (172.21): C 83.7; H 7.03.)

Reaction of the Grignard reagent II with ethylene oxide

A solution of II, prepared from 11 g of I, was stirred in an ice-salt bath under nitrogen while excess of ethylene oxide in dry ether was added during one hour. Vigorous reaction occurred at first with each drop and a white precipitate separated. The bath was removed and stirring continued until escape of gas subsided, then ether and excess oxide were removed by distillation. Dilute hydrochloric acid was added and stirring continued until dissolution of the precipitate was complete. The ether layer was separated, the water layer shaken with ether and the organic solution combined, dried and distilled. The main fraction, boiling at 185—195°C/9 mm Hg, was a viscous colourless liquid. Weight 4.5 g. Phenylurethan, m.p. 230—232°C. (Found: C 79.1; H 6.41. Calc. for $C_{20}H_{19}O_2N$ (305.36): C 78.7; H 6.28 %.)

Preparation of β-(2-methyl-1-naphthyl)-ethanol

To 11 g of 1-bromo-2-methylnaphthalene [17], cooled to 0°C, 0.05 mole of butyllithium [18] in 50 ml of ether was added. After the spontaneous lithium-halogen exchange reaction was complete, excess of ethylene oxide in ether was added dropwise and then the usual procedure followed as above. B.p. 190–195°C/9–10 mm Hg. Weight 6.3 g. Yield 67 %. Phenylurethan m.p. 230–232°C. Mixed m.p. with the phenylurethan of VII: 230–232°C.

2-Methyl-1-chloromethylnaphthalene

This compound has been prepared before but no yields were given [19]. By repeating the experiments, low yields were obtained and mostly tarry products. A modified method is given here:

Into a 2–l flask, fitted with a reflux condenser and a teflon stirrer, were placed 65 g of 2-methylnaphthalene, 30 g of paraformaldehyde, 65 g of glacial acetic acid, 45 ml of 85 % phosphoric acid and 90 ml of concentrated hydrochloric acid. The mixture was heated at 100°C with stirring for 5 h. After the mixture had been cooled it was washed twice with cold water, then with potassium carbonate solution and finally with cold water. The organic layer was dissolved in ether, thoroughly dried over sodium sulphate and distilled. The main fraction was obtained at 165–170°C/9–10 mm Hg. Recrystallisation from ethanol gave white needles. M.p. 62–63°C. Weight 64 g. Yield 75 %.

2-Methyl-1-naphthylacetonitrile

9.5 g of 2-methyl-1-chloromethylnaphthalene and 5 g of sodium cyanide in 50 ml of aceton and 4 ml of water was refluxed for 4 h. The acetone was evaporated and water and ether were added. Excess of sodium cyanide was removed by repeated extractions with water. The ether layers were dried and the ether evaporated. The residue recrystallized from formic acid gave fine, white needles. M.p. 77–79°C. Weight 7.4 g. Yield 81 %. (Found: C 86.6; H 5.95. Calc. for $C_{13}H_{11}N$ (181.23): C 86.2; H 6.12.)

2-Methyl-1-naphthylacetic acid

a) via the nitrile. 7 g of 2-methyl-1-naphthylacetonitrile was refluxed for 12 h with excess of sodium hydroxide in a water-ethanol solution. The alcohol was distilled off and the residue extracted with ether in order to remove unsaponified nitrile. When the water solution was acidified with hydrochloric acid, the organic acid precipitated as a white powder. The acid was recrystallized from water-ethanol forming small, white needles. M.p. 176–168°C. Weight 6.5 g. Yield 84 %. (Found: Equiv.wt. 199.6; C 78.7; H 6.21. Calc. for $C_{13}H_{12}O_2$ (200.23): Equiv.wt. 200.2; C 78.0; H 6.05 %.)

b) via the Grignard reagent. 9.5 g of 2-methyl-1-chloromethylnaphthalene in 50 ml of dry ether was dropped to 1.7 g of magnesium turnings in 75 ml of ether. The reaction was initiated with a few drops of bromine. After carbonation with dry ice the reaction mixture was treated with hydrochloric acid, the ether layer was separated, the water phase extracted repeatedly with ether and the combined extracts shaken with sodium hydroxide solution. The alkaline solution was acidified with hydrochloric acid, precipitating the acid as a white powder. After recrystallisation from water-ethanol the acid was obtained as small, white needles. M.p. 176–178°C. Weight 7.1 g. Yield 71 %.

The ether phase was evaporated and the residue recrystallized, giving a white powder. M.p. 173–175°C (from ethanol). This compound seems to be 1,2-di(2-methyl-1-naphthyl)-ethane. (Found: C 93.4; H 7.15. Calc. for $C_{24}H_{22}$ (310.42): C 92.9; H 7.10.)

The same compound was formed almost exclusively when by a mistake a mechanical stirrer of *copper* was used and bromine was added as an activator. The chlorides of copper which formed apparently made the coupling product predominate and very little acid was isolated after carbonation.

Reduction of 2-methyl-1-naphthylacetic acid

The acid (2 g) was reduced with lithium aluminium hydride in the usual way. Quantitative yields. Phenyluretan, m.p. 231—233°C.

Reaction of the Grignard reagent II with acetyl chloride

The Grignard reagent (II), prepared from 11 g of I was added dropwise during one hour to a solution of 25 g of acetyl chloride in 100 ml of ether, cooled in an ice-water bath. The bath was removed and the mixture allowed to warm to room temperature, when water and ice were added to hydrolyze the excess of acetyl chloride. The water phase was shaken repeatedly with ether, the organic portions combined, washed with sodium carbonate and water, dried and distilled. The main fraction boiled at 160—170°/10 mm Hg. This was a yellow, heavy liquid, whose 2,4-dinitrophenylhydrazone melted at 236—238°C. This derivative was identical with that of an authentic sample of methyl-2(2-methyl-1-naphthyl) ketone, prepared as above from 2-methyl-1-naphthylmagnesium bromide and acetyl chloride. (Found: C 63.0; H 4.72. Calc. for $C_{19}H_{16}O_4N_4$ (364.35): C 62.6; H 4.43.)

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