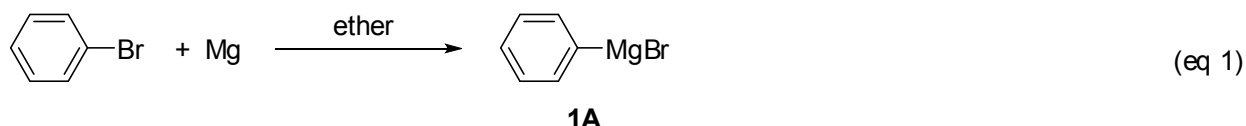


## 化学問題 I

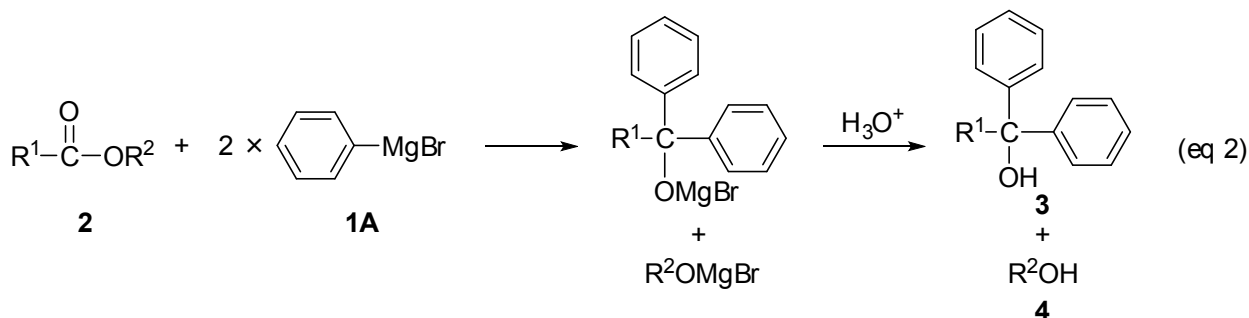
Grignard 反応剤に関する 2 つの英文 (a) および (b) を読んで問 1～9 に答えよ。解答はそれぞれ所定の解答欄に記入せよ。ただし、**1-6** は一般化合物を示し、**1A**, **1B**, **2A**, **3A**, **3B**, **4A**, **5A**, **6A** はある特定の化合物を示す。 $R^1, R^2, R^3, R^4$  は飽和炭化水素基または不飽和炭化水素基を指す。

(a) Carbon can make bonds not only with C, H, N, O, S, *etc.* but also with metals such as Li, Mg, Al, Zn and Cu. Such compounds having carbon-metal bond(s) are called *organometallic compounds*. In many cases, the carbon atom is electronically more negative than metals, thus leading to polarity of organometallic compounds. For example, the carbon atom of a carbon-lithium bond is highly electronegative, reflecting the electronegativity<sup>(1)</sup> difference between carbon and lithium. The reactivity of organometallic compounds is related to the ionic character of their carbon-metal bonds.

Formation of carbon-carbon bonds is the most important transformation in organic chemistry. Organometallic compounds can function as *carbanions* (electronically negative carbon species), useful for carbon-carbon bond formation: organometallic compounds show efficient reactivity with various types of electronically positive reaction partners, such as carbonyl compounds (having a carbon-oxygen double bond). In 1900, Victor Grignard discovered organomagnesium compounds, which are called "Grignard reagents" today. These reagents are prepared by the reaction of halogenated aliphatic<sup>(2)</sup> or aromatic<sup>(3)</sup> hydrocarbons with magnesium metal in ether. For example, the reaction of bromobenzene with magnesium in diethyl ether produces a Grignard reagent **1A** (eq 1). Grignard reagents react with carbonyl compounds including esters, aldehydes or ketones to give various types of alcohols after acid treatment. Today, Grignard reagents are widely used in organic synthesis for carbon-carbon bond formation.



**1. Reaction with esters.** As shown in eq 2, an ester **2** reacts with two molecules of the Grignard reagent **1A** to produce magnesium salts. Treatment of these salts with an acid ( $\text{H}_3\text{O}^+$ ) produces an alcohol **3** having two aromatic groups, along with the eliminated alcohol **4**.



Taro investigated the reaction of an ester **2A** with the Grignard reagent **1A**. After treatment with dilute hydrochloric acid, he obtained the alcohol **3A** (molecular formula:  $\text{C}_{17}\text{H}_{20}\text{O}$ ) and alcohol **4A** (molecular formula:  $\text{C}_3\text{H}_6\text{O}$ ).

(1) electronegativity : 電気陰性度

(2) aliphatic : 脂肪族の

(3) aromatic : 芳香族の

問 1 リチウム、炭素、マグネシウムおよび亜鉛の電気陰性度は表 1 の通りである。C-H 結合、C-Li 結合、C-Mg 結合、C-Zn 結合について、炭素原子が電氣的により陰性である順となるように、空欄に元素記号を入れなさい。

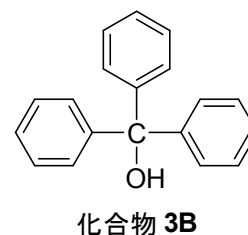
表 1 電気陰性度

Li	1.0
C	2.5
Mg	1.2
Zn	1.6

問 2 化合物 **3A** として考えられる構造を全て示せ。また、構造式中に不斉炭素があれば、その炭素に\*印を付しなさい。

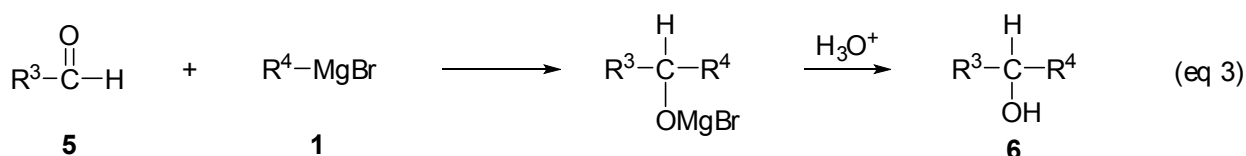
問 3 化合物 **2A** の分子式を書け。

問 4 Grignard 反応剤を使った反応を利用して化合物 **3B** (右図) を合成したい。適当な出発物質および反応剤を下の【 】内から選び、合成経路を立案して反応式を書きなさい。ただし、下記以外の出発物質および反応剤は使用できないものとし、反応式は eq 1 および eq 2 に従って書くこと。



【Mg/エーテル、ベンゼン、トルエン、KMnO<sub>4</sub>、Br<sub>2</sub>/鉄粉、塩酸、メタノール/H<sub>2</sub>SO<sub>4</sub>】

(b) **2. Reaction with aldehydes.** An aldehyde **5** reacts with a Grignard reagent **1** to produce an alcohol **6** as shown in eq 3.



The experimental protocol for the preparation of Grignard reagent **1B** and its reaction with acetaldehyde **5A** is as follows: in a 3 L three-necked flask, fitted with a mechanical stirrer, a dropping funnel,<sup>(4)</sup> and a reflux condenser<sup>(5)</sup> the upper end of which is protected by a calcium chloride tube, are placed 146 g (6 gram atoms) of dry magnesium turnings and about 250 mL of dry diethyl ether.

A solution of 600 g (4.9 moles) of isopropyl bromide<sup>(6)</sup> in 300 mL of dry diethyl ether is then added through the dropping funnel. The reaction begins after about 15 mL of the solution has been added. It should be noted that heating on the water bath to start the reaction should be unnecessary if all the apparatus and reagents are completely dry. The solution is added at such a rate that the reaction mixture refluxes gently. It is well to arrange to cool the flask with running water if the refluxing becomes too vigorous. The addition of the isopropyl bromide solution should require from three and one-half to four hours. The reaction mixture is refluxed on the water bath for forty minutes after addition of the isopropyl bromide solution is complete.

The flask is then cooled to -5 °C, and a solution of 198 g of acetaldehyde **5A** in 250 mL of dry diethyl ether is added at this temperature over a period of one hour.

After addition of the acetaldehyde solution is complete, the product is decomposed by pouring the reaction mixture onto 2 kg of cracked ice. The excess magnesium may be removed conveniently by decantation at this point. The basic magnesium halide is dissolved by addition of about 1 L of 15% H<sub>2</sub>SO<sub>4</sub>. ①The diethyl ether solution is separated, and the aqueous layer is extracted with four 150 mL portions of diethyl ether. The ether solutions are combined, dried over 25 g of calcined potassium carbonate, filtered, and fractionally distilled, using a short column. The 3-methylbutan-2-ol<sup>(7)</sup> **6A** distills at 110–111.5 °C. ②The fraction boiling at 37–109 °C should be dried and refractionated. The total yield of **6A** is 205–215 g.

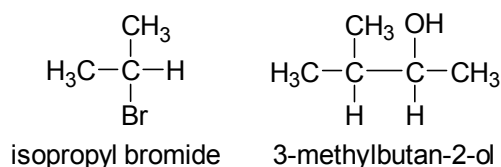
Nathan L. Drake, Giles B. Cooke, *Organic Syntheses*, **12**, 48-50 (1932) を一部改変  
"Reproduced with permission of Organic Syntheses, Inc."

(4) dropping funnel : 滴下ロート

(5) reflux condenser : 還流冷却器

(6) isopropyl bromide : 右図参照

(7) 3-methylbutan-2-ol : 右図参照



問 5 Isopropyl bromide のジエチルエーテル溶液を加える方法について、英文に記載されている内容に従って、50～100 字でまとめなさい。使用する器具、加える速さ、反応時間、温度管理に関するすべての内容を含めること。

- 問 6 反応を行う際には、よく乾燥した実験器具とジエチルエーテルを用いる必要がある。乾燥が不十分である際に起こりうる問題とその対処方法について、英文に記載されている内容に従って具体的に答えなさい。
- 問 7 下線部①の操作の意義を簡潔に述べなさい。
- 問 8 精製の過程において、ある基準に従って混合物を複数個に分割したものをフラクション (fraction) という。蒸留においては、蒸留温度により留分をいくつかのフラクションに分割することが多い。下線部②のフラクションに含まれる可能性のある化合物の名称を 2 つ挙げなさい。
- 問 9 得られる見込みの 3-methylbutan-2-ol (**6A**) の収量は、理論収量の何パーセントに相当するか。用いたアセトアルデヒドのモル数を基準として、その幅を有効数字 2 桁で表せ (例: 90–95%)。ただし、水素、炭素、酸素の原子量をそれぞれ 1, 12, 16 とする。