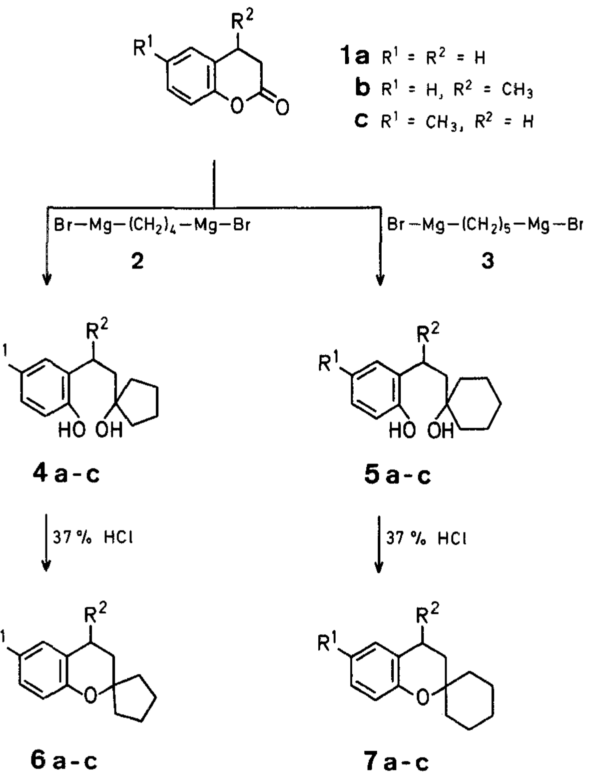
# A Facile Synthesis of Spirochromanes - 3,4-Dihydrospiro[2*H*-1-benzopyran-2,1′-cycloalkanes]

P. Cannone*, D. Bélanger, G. Lemay

Département de Chimie, Université Laval, Québec, Canada G1K 7P4

Recently, we showed that aliphatic (β-, γ-, δ-, and ε-) lactones could be converted by a one-stage procedure involving bis[bromomagnesio]alkanes to the corresponding ω-hydroxyalkylcycloalkanols[1]. In the present communication, we now report results from our study on the conversion of the dihydrocoumarins **1** to the *o*-hydroxyphenylethylcycloalkanols **4** or **5**, in very good yields, by the simple reaction of butane-1,4-diyl- and pentane-1,5-diyl-dimagnesium dibromides (**2** and **3**, respectively). The 1,ω-di-Grignard reagents **2** or **3** are obtained from the 1,ω-dibromoalkanes rather than other dihalides, and are prepared in very good yields in tetrahydrofuran, in which they are soluble[2,3], in contrast to diethyl ether[4]. The dihydrocoumarins **1** are obtained by hydrogenation[5] of the corresponding coumarins at room temperature, using Pd/C and are listed in Table 1. The 4-methylcoumarin **1b** was prepared according to Ref.[6].

In agreement with previously reported observations[7], our experiments demonstrate that the unhindered carbonyl group of dihydrocoumarin can participate in di-Grignard reactions with the same organodimagnesium compound, and this provides a useful new method for the preparation of *o*-hydroxyphenylethylcycloalkanols **4a-c** and **5a-c**. The synthesis of this type of substituted alkanol requires more than one-step by other methods.



The di-Grignard preparations are performed at room temperature with a small excess of the corresponding dimagnesium compound and the addition of the dihydrocoumarin in tetrahydrofuran solution allows a reaction temperature of 45 °C. Following the addition, the reaction mixture is stirred overnight at room temperature and hydrolysed with ammonium chloride. The diols **4** or **5** are obtained by distillation after the usual work-up.

The structures of the prepared diols were confirmed by microanalysis, I.R., and $^1$H-N.M.R. spectra and they are summarised in Table 2. The yields are calculated after distillation. By gas chromatographic analysis, results obtained were 10–15% higher.

One synthetic use of the *o*-hydroxyphenylethylcycloalkanols **4** or **5** prepared by this method is their transformation into corresponding spirochromans **6** or **7**, by simple treatment with hydrochloric acid under reflux. The cyclisation reaction for the formation of these ethers does not go to completion below 100 °C, but at this temperature, we have not observed any products arising from rearrangement due to the presence of the hydrochloric acid. The data for products **6** and **7** are indicated in Table 3 and the yields are calculated after distillation. The structures were confirmed by microanalysis, I.R., $^1$H-N.M.R., and mass spectra.

The 3,4-dihydro-spiro[2*H*-1-benzopyran-2,1′-cycloalkanes] **6** and **7** have not been previously reported. This two-step method is general and very convenient, allowing the successful preparation of this class of compound.

Melting points were determined on a Thomas-Hoover melting point apparatus and are uncorrected. The I.R. spectra were recorded on a Beckmann I.R.-12 spectrophotometer and the $^1$H-N.M.R. spectra on a Bruker HX-90 spectrometer, using TMS as internal standard. The mass spectra were obtained on a Varian M-66 spectrometer.

**Dihydrocoumarins 1a-c; General Procedure:**

A mixture of the corresponding coumarin (0.1 mol) and ethyl acetate (150 ml) is placed in a standard Parr bottle, along with 2.0 g of

Table 1. Dihydrocoumarins **1**

| Product | Yield [%] | m.p. [°C] or b.p. [°C]/torr | Molecular formula | I.R. (film) or (KBr) $\nu_{C=O}$ [cm$^{-1}$] | $^1$H-N.M.R. (CDCl$_3$) $\delta$ [ppm] |
|---|---|---|---|---|---|
| **1a** | 96 | 25;<br>148–149/20 | $C_9H_8O_2$<br>(148.2) | 1760 | 2.55–3.2 (m, 4H); 6.8–7.35 (m, 4H) |
| **1b** | 91 | 82–83/15 | $C_{10}H_{10}O_2$<br>(162.2) | 1755 | 1.2–1.5 (d, 3H); 2.35–2.9 (2 q, 2H); 3.0–3.3 (q, 1H); 6.7–7.25 (m, 4H) |
| **1c** | 94 | 78–79 | $C_{10}H_{10}O_2$<br>(162.2) | 1742 | 2.3 (s, 3H); 2.6–3.1 (m, 4H); 6.8–7.15 (m, 3H) |

Table 2. Diols **4** and **5**

| Product | Yield[a] [%] | m.p. [°C] | Molecular formula[b] | I.R. (KBr) $\nu_{max}$ [cm$^{-1}$] | (CCl$_4$)[c] $\nu_{OH}$ | $^1$H-N.M.R. (CDCl$_3$) $\delta$ [ppm] | M.S. (70 eV) *m/e* |
|---|---|---|---|---|---|---|---|
| **4a** | 90 | 95.5–96 | $C_{13}H_{18}O_2$<br>(206.3) | 3380 | 3620 (F)<br>3350 (B) | 1.3–1.9 (m, 8H); 1.9 (t, 2H); 2.8 (t, 2H); 2.7 (s, OH); 7.55 (s, OH); 6.9 (m, 2H); 7.1 (m, 2H) | 206 (4.3%, $M^+$);<br>188 (74%, $M^+ - H_2O$);<br>107 (100%, $M^+ - H_2O - C_6H_9$) |
| **4b** | 88 | 89–89.5 | $C_{14}H_{20}O_2$<br>(220.3) | 3400 | 3620 (F)<br>3345 (B) | 1.3 (d, 3H); 1.65 (m, 8H); 1.9 (m, 2H); 3.4 (q, 1H); 3.1 (s, OH); 6.7–7.3 (m, 4H); 8.1 (s, OH) | 220 (7.1%, $M^+$);<br>202 (98%, $M^+ - H_2O$);<br>121 (100%, $M^+ - H_2O - C_6H_9$) |
| **4c** | 85 | 90–90.5 | $C_{14}H_{20}O_2$<br>(220.3) | 3420 | 3620 (F)<br>3350 (B) | 1.25–2.1 (m, 10H); 2.2 (s, 3H); 2.7 (t, 2H); 3.0 (s, OH); 6.6–7.0 (m, 3H); 7.6 (s, OH) | 220 (4.0%, $M^+$);<br>202 (44%, $M^+ - H_2O$);<br>121 (100%, $M^+ - H_2O - C_6H_9$) |
| **5a** | 80 | 108.5–109 | $C_{14}H_{20}O_2$<br>(220.3) | 3360 | 3615 (F)<br>3350 (B) | 1.2–1.8 (m, 10H); 1.8 (t, 2H); 2.7 (t, 2H); 2.3 (s, OH); 7.25 (s, OH); 6.85 (m, 2H); 7.1 (m, 2H) | 220 (9.2%, $M^+$);<br>202 (100%, $M^+ - H_2O$);<br>107 (93%, $M^+ - H_2O - C_7H_{11}$) |
| **5b** | 82 | 85.5–86 | $C_{15}H_{22}O_2$<br>(234.3) | 3380 | 3620 (F)<br>3350 (B) | 1.3 (d, 3H); 1.2–1.7 (m, 10H); 1.7 (d, 2H); 3.3 (q, 1H); 3.1 (s, OH); 8.25 (s, OH); 6.75–7.3 (m, 4H) | 234 (8.2%, $M^+$);<br>216 (51%, $M^+ - H_2O$);<br>121 (100%, $M^+ - H_2O - C_7H_{11}$) |
| **5c** | 84 | 112.5–113 | $C_{15}H_{22}O_2$<br>(234.3) | 3420 | 3620 (F)<br>3350 (B) | 1.5 (m, 10H); 1.76 (t, 2H); 2.7 (t, 2H); 3.6 (s, OH); 6.65–7.0 (m, 3H); 6.75 (s, OH) | 234 (4.4%, $M^+$);<br>216 (41%, $M^+ - H_2O$);<br>121 (100%, $M^+ - H_2O - C_7H_{11}$) |

[a] Yields of isolated products.

[b] All products gaves satisfactory microanalyses (C ± 0.18%, H ± 0.18%).

[c] $c$ $0.5 \times 10^{-3}$ mol/l, (F) = free OH band, (B) = intramolecularly bonded OH band.

5% palladium on charcoal catalyst, and the hydrogenation is carried out under an initial pressure of 3.4 bar (50 p.s.i.). After the hydrogen uptake ceases, the catalyst is removed by filtration over Celite, using an ethyl acetate wash, the solvent is removed under reduced pressure, and the residue distilled (Table 1); yield: 91–96%.

**Bis[bromomagnesio]alkanes 2 or 3; General Procedure:**

The 1,ω-dibromoalkane (0.069 mol) dissolved in anhydrous tetrahydrofuran (150 ml) is added to magnesium turnings (3.5 g, 0.15 mol), under a stream of nitrogen. A small volume of the dihalide solution is added to cover the magnesium and the stirring is started. The exothermic reaction starts within a few min. The rest of the dihalide solution is added dropwise, at a rate slow enough to avoid excessive heating (40–50 °C). After the addition is completed, the clear solution is allowed to stir 4 h at room temperature. The yield of the Grignard reagent is determined by the Gilman procedure[9].

**Diols 4 or 5 from Dihydrocoumarins 1a–c; General Procedure:**

To the organomagnesium compound (0.06 mol) prepared in anhydrous tetrahydrofuran (150 ml) under nitrogen is added dropwise at room temperature the dihydrocoumarin **1** (0.04 mol) in anhydrous tetrahydrofuran (50 ml). The reaction mixture is stirred overnight under an atmosphere of nitrogen. After hydrolysis with saturated aqueous ammonium chloride, the mixture is extracted with ether, washed with water, and dried with sodium sulfate. The solvents are removed under reduced pressure and the residue is purified, either by distillation or recrystallisation (Table 2).

**Spirochromans 6 or 7 from Diols 4 or 5; General Procedure:**

A mixture of the diol **4** or **5** (10 mmol) and 37% hydrochloric acid (15 ml) is heated under reflux for 6 h. After cooling, the resulting mixture is diluted with water and extracted with ether. The extracts are washed with water and dried with sodium sulfate. The solvent is removed in vacuo and the residue distilled (Table 3).

*We thank the National Research Council of Canada and le Ministère de l'éducation du gouvernement du Québec for support of this work.*

Received: November 5, 1979

**Table 3.** Spirochromanes **6** and **7**

| Product | Yield[a] [%] | b.p. [°C]/ torr | Molecular formula[b] | I.R. (KBr) $\nu_{C=O}$ [cm$^{-1}$] | $^1$H-N.M.R. (CDCl$_3$) $\delta$ [ppm] | M.S. (70 eV) *m/e* |
|---|---|---|---|---|---|---|
| **6a** | 84 | 74–76/0.05 | $C_{13}H_{16}O$ (188.3) | 1248, 1045 | 1.45–2.1 (m, 8H); 1.8–1.95 (t, 2H); 2.7–2.9 (t, 2H); 6.95–7.3 (m, 4H) | 188 (56%, M$^+$);<br>107 (100%, M$^+$ $-C_6H_9$) |
| **6b** | 80 | 68–70/0.02 | $C_{14}H_{18}O$ (202.3) | 1240, 1035 | 1.3 (t, 3H); 1.2–2.2 (m, 10H); 6.7–7.3 (m, 4TH) | 202 (56%, M$^+$);<br>121 (100%, M$^+$ $-C_6H_9$) |
| **6c** | 84 | 78–80/0.05 | $C_{14}H_{18}O$ (202.3) | 1235, 1040 | 1.3–2.1 (m, 10H); 2.25 (d, 3H); 2.75 (t, 2H); 6.55–6.95 (m, 3H) | 202 (65%, M$^+$);<br>121 (100%, M$^+$ $-C_6H_9$) |
| **7a** | 80 | 80–82/0.05 | $C_{14}H_{18}O$ (202.3) | 1242, 1050 | 1.1–1.95 (m, 10H); 1.7–1.85 (t, 2H); 2.7–2.85 (t, 2H); 6.7–7.2 (m, 4H) | 202 (78%, M$^+$);<br>107 (100%, M$^+$ $-C_7H_{11}$) |
| **7b** | 75 | 84–86/0.02 | $C_{15}H_{20}O$ (216.3) | 1235, 1035 | 1.3 (t, 3H); 1.2–2.2 (m, 12H); 2.7–3.2 (q, 1H); 6.7–7.3 (m, 4H) | 216 (34%, M$^+$);<br>121 (100%, M$^+$ $-C_7H_{11}$) |
| **7c** | 75 | 88–89/0.05 | $C_{15}H_{20}O$ (216.3) | 1240, 1045 | 1.05–1.95 (m, 12H); 2.25 (d, 3H); 2.7 (t, 2H); 6.6–7.2 (m, 3H) | 216 (60%, M$^+$);<br>121 (100%, M$^+$ $-C_7H_{11}$) |

[a] Yield is given from the starting dihydrocoumarin **1**.

[b] All products gave satisfactory microanalyses (C ±0.23%, H ±0.18%).

---

[1] P. Canonne, G. Foscolos, G. Lemay, *J. Chem. Soc. Chem. Commun.* **1979**, 691.

[2] T. Yvernault, G. Casteignau, M. Estrade, *C. R. Acad. Sci. Ser. C* **269**, 169 (1969).

[3] H. Denise, J. Ducom, J. F. Fauvarque, *Bull. Soc. Chim. Fr.* **1972**, 990.

[4] J. Colonge, R. Falcotet, R. Gaumont, *Bull. Soc. Chim. Fr.* **1978**, 211.

[5] P. L. de Benneville, R. Conner, *J. Am. Chem. Soc.* **62**, 2830 (1940).

[6] E. C. Horning, *Org. Synth. Coll. Vol.* III, 581 (1955).

[7] P. Canonne, G. Foscolos, D. Bélanger, *J. Org. Chem.*, in press.

[8] W. E. Parham, Y. A. Sayed, *Synthesis* **1976**, 116.

[9] H. Gilman, *J. Am. Chem. Soc.* **45**, 508 (1923).

0039-7881/80/0432-0303 $ 03.00