# Reaction of Di(bromomagnesio)alkanes with Cyclic Dicarboxylic Acid Anhydrides

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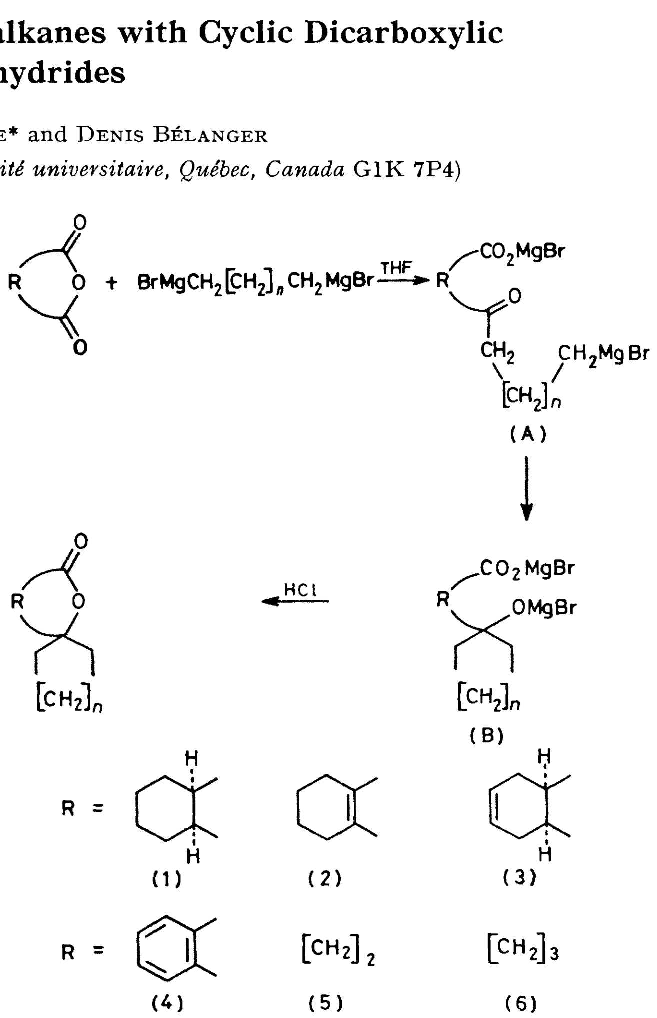
*Summary* The reaction of the di(bromomagnesio)alkanes $BrMg[CH_2]_4MgBr$ and $BrMg[CH_2]_5MgBr$ with cyclic anhydrides produces spirolactones in one step in good yield.



The preparation of spirolactones has been the subject of much study in recent years and numerous procedures have been developed, including the oxidation of bicyclic ketones.[1–8] The most general and convenient method involves oxidation of 1-(ω-hydroxyalkyl)cycloalkanols by Jones' reagent.[9,10]

We now report preliminary results on the use of the reaction of di(bromomagnesio)alkanes with cyclic anhydrides. The simplicity and efficiency of this approach which have been demonstrated already in similar reactions with lactones to afford 1-(ω-hydroxyalkyl)cycloalkanols,[11] prompted us to test its effectiveness for the preparation of spirolactones.

This reaction involves the selective addition of both nucleophilic centres in the dimagnesium compound to the same carbonyl group of cyclic dicarboxylic anhydrides.

Our main interest has been in the synthesis of spirolactones without the concomitant formation of diols. This annelation involves the initial formation of an intermediate, the ketocarboxylate (A), which immediately cyclizes to the final product (B). Careful control of the reaction temperature is required in order to prevent the formation of diols.

Extension of the present method to aromatic and unsaturated cyclic anhydrides has been demonstrated and has shown in particular that 1,4-addition in the case of compound (**2**) does not take place

The spirolactones synthesized and their yields are in the Table In all cases, the starting anhydride is commercially available Consequently, the reduction of these spirolactones provides a valuable route to the corresponding spiroethers and diols [7,8,12,13] The general procedure used for the spirolactones is similar to that previously reported for preparation of lactones with Grignard reagents [11]

TABLE

| Compound | Yield/% ($n = 2$) | M p /°C | Yield/% ($n = 3$) | M p /°C |
|---|---|---|---|---|
| (**1**) | 63[a] | 81—82 | 70[b] | — |
| (**2**) | 69 | 39—39 5 | 70[b] | — |
| (**3**) | 66 | 51—51 5 | 70 | 46 5—47 |
| (**4**) | 75[a] | — | 66[c] | — |
| (**5**) | 86[d] | — | 77[e] | — |
| (**6**) | 80[f] | — | 75[g] | — |

[a] Ref 10 [b] Refs 10—13 [c] Refs 4, 5, 10 [d] Refs 1, 2, 10 [e] Refs 2, 5, 8, 10 [f] Refs 6, 10 [g] Refs 10, 14

A solution of the anhydride in tetrahydrofuran (THF) was added to the Grignard reagent at −12 °C under nitrogen The mixture was stirred, and kept at this temperature for 3 h and then overnight at room temperature After hydrolysis with 10% HCl and work-up in the usual manner, the lactones were isolated by fractional distillation and characterized by i r , $^{1}$H-n m r , and mass spectroscopy as well as by elemental analysis in the case of new compounds (Table)

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[1] D H Aue, M J Meshishnek and D F Shellhamer, *Tetrahedron Letters*, 1973, 4799

[2] G Sturtz, B Corbel, and J P Paugam, *Tetrahedron Letters*, 1976, 50

[3] W E Parham, D C Egbey, and Y A Sayed, *J Org Chem* , 1976, **41**, 2628

[4] W E Parham and L D Jones, *J Org Chem* , 1976, **41**, 2704

[5] P E Eaton, G F Cooper, R C Johnson, and R H Mueller, *J Org Chem* , 1972, **37**, 1947

[6] H Christol, F Plenat, and C Reliaud *Bull Soc chim France*, 1968, 1566

[7] M J Bogdanowicz, T Ambelang, and B M Trost, *Tetrahedron Letters* 1973, 923

[8] B M Trost and M J Bogdanowicz, *J Amer Chem Soc* , 1973, **95**, 5321

[9] P Picard and J Moulines, *Bull Soc chim France* 1973, 3377

[10] P Canonne, G B Foscolos, and D. Belanger, *J Org Chem* , in the press

[11] P Canonne, G B Foscolos, and G Lemay, *J C S Chem Comm* , 1979, 691

[12] S W Baldwin, R J Doll and S A Hant, *J Org Chem* , 1974, **39**, 2470

[13] C G Overberger and P Kabasakalion *J Amer Chem Soc* , 1957, **79**, 3182

[14] I D Rae and B N Umbrasas, *Austral J Chem* , 1975, **28**, 2669