

Rearrangement of α -Hydroxycyclobutanes. Unusual Rearrangement of Some Cyclobutachromanols to a Component of the Ring System of Averufin

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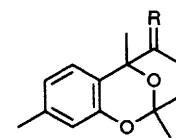
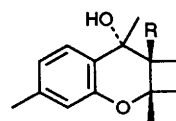
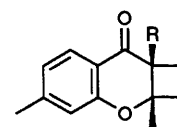
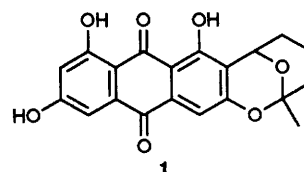
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Acid-catalysed rearrangement of cyclobutachromanols **4** and **5** furnishes the benzo-1,3-dioxane compounds **6** and **7**, respectively, arising from a de Mayo-type rearrangement.

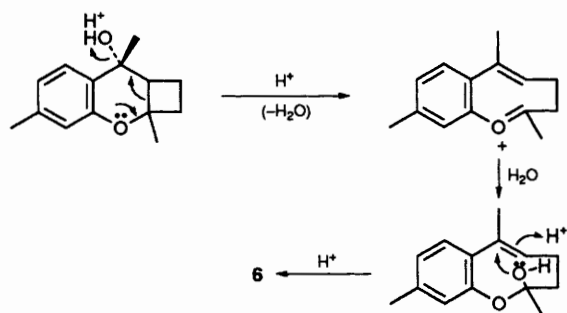
Averufin **1**,¹ the pivotal intermediate in the biogenesis of the aflatoxins, features a 2,6-epoxy-3,4,5,6-tetrahydro-2*H*-1-benzoxocine ring system. This internal ketal ensemble has been prepared by various methods resulting in the synthesis of **1**.² We now report a facile assembly of this ring system, *via* an α -hydroxycyclobutane rearrangement in the cyclobutachromanols **4** and **5**. Previously we have reported³ the rearrangement of cyclobutachromanols to provide a rapid synthesis of the marine sesquiterpenes aplysin and filiformin, and we also showed that such a rearrangement involved the primary migration of both the external and internal bonds; the use of different solvents made it possible to discriminate between the two modes of primary migration. In our continuing studies on the rearrangement of various substituted cyclobutachromanols, we now present another alternative mode of rearrangement for cyclobutachromanols such as **4** and **5**, offering a ready access to the benzo-1,3-dioxane ring system of **1**.

Irradiation of a benzene solution of 2,7-dimethylchromone with a continuous flow of ethylene furnished the cycloadduct **2**† (70%). Alkylation of the lithium enolate obtained from **2**

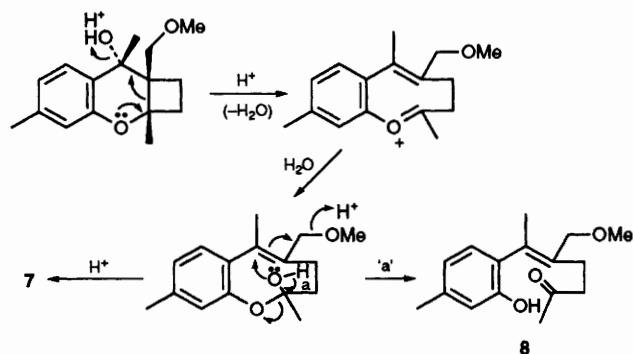
using lithium diisopropylamide with chloromethyl methyl ether afforded the methoxymethylated cyclobutachromanone **3** (65%). Reaction of **2** and **3** with methylmagnesium iodide furnished the chromanols **4** (90%) and **5** (90%), respectively. Treatment of **4** in benzene with boron trifluoride–diethyl ether at ambient temperature for 1 h resulted in complete re-



† All compounds reported here gave spectral and analytical data consistent with assigned structures.



Scheme 1



Scheme 2

arrangement to provide the benzo-1,3-dioxane **6** in 70% yield, m.p. 72–74 °C. The structure was deduced from a combination of analytical and spectral[‡] data, particularly ¹³C NMR, where the C-2 carbon atom flanked by the two oxygen atoms appeared at δ 99.16, very close to the value for the same carbon in **1**.⁴ This is deemed to arise from **4**, through a de Mayo-type fragmentation⁵ followed by hydroxy capture and internal ketalisation (Scheme 1). Similar treatment of the chromanol **5** furnished the benzo-1,3-dioxane compound **7**[‡] in 70% yield, m.p. 58–59 °C. Loss of the OMe group may be envisaged as arising from protonation at the OMe oxygen in the de Mayo intermediate followed by an intramolecular displacement (Scheme 2). Isolation of a minor amount of the ketone **8** in one experiment offered support to this hypothesis.

[‡] *Spectral data for 6*: ¹H NMR (300 MHz) δ 1.53 (s, 3H), 1.59 (s, 3H), 1.5–1.8 (m, 5H), 1.9–2.0 (m, 1H), 2.28 (s, 3H), 6.61 (br s, 1H), 6.64 (d, *J* 7.6 Hz, 1H), 6.86 (d, *J* 7.8 Hz, 1H); ¹³C NMR (75 MHz) δ 17.37, 21.14, 26.74, 28.47, 35.60, 37.35, 73.41, 99.16, 115.33, 120.32, 123.43, 137.98, 153.17; *m/z* 218.1309 (C₁₄H₁₈O₂); For **7**: ¹H NMR (300 MHz) δ 1.55 (s, 3H), 1.72 (s, 3H), 1.85–2.0 (m, 1H), 2.27 (s, 3H), 2.05–2.4 (m, 3H), 4.77 (s, 1H), 5.03 (s, 1H), 6.63 (s, 1H), 6.64 (d, *J* 6.8 Hz, 1H), 6.86 (d, *J* 8.2 Hz, 1H); ¹³C NMR (75 MHz) δ 21.13, 23.05, 27.07, 27.96, 38.03, 74.88, 98.99, 106.59, 115.86, 120.64, 123.36, 123.87, 138.26, 148.59, 152.47; *m/z* 230.1305 (C₁₅H₁₈O₂).

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