# Rearrangement of α-Hydroxycyclobutanes. A Facile Route towards the Carbocyclic Skeleton of Aplysin *via* an Incipient Trichothecane-like Cationic Intermediate

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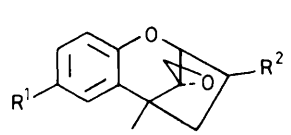
Acid-catalysed rearrangement of cyclobutachromenol (**7**) followed by oxidation furnishes the tricyclic ketone (**9**) as the major product, which possesses the carbocyclic framework of aplysin (**3**).

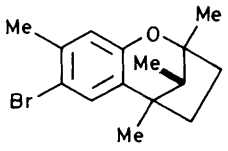
Current interest in the rearrangement of α-hydroxycyclobutane systems stems largely from their potential to lead to interesting polycyclic compounds[1] and the synthesis of complex natural products.[2] In connection with a programme directed towards the synthesis of A-ring aromatic trichothecane analogues (**1**),[3] filiformin (**2**)[4] mirroring the trichothecane ring system, and the marine natural product aplysin (**3**),[5] we have investigated the acid-catalysed rearrangement of cyclobutachromenol (**7**) with a view to obtaining the ring system(s) present in the above compounds and herein report our results.

Irradiation of a benzene solution of chromone with a continuous flow of ethylene afforded the adduct (**4**) in 65% yield. The *cis* stereochemistry has been assigned by analogy with earlier work[6] and additionally confirmed from the *X*-ray structural determination[7] of the crystalline alcohol (**5**) obtained from lithium aluminium hydride (LAH) reduction of (**4**). Similarly cycloaddition of ethylene to 3-methylchromone furnished (**6**) in 55% yield which was reduced to (**7**) (LAH, 90%). Treatment of (**7**) with toluene-*p*-sulphonic acid in boiling benzene (3 h) led to a mixture of toluene-*p*-sulphonates [$^1$H n.m.r. ($CDCl_3$, 200 MHz) δ 1.36(s), 1.54—2.36(m), 2.44(s), 3.38(d, *J* 8 Hz), 4.72—4.95(m), 6.64—7.32(m), 7.42(d, *J* 8 Hz), 7.86(d, *J* 8 Hz)], in 70% yield. This mixture could not be resolved by column chromatography or t.l.c. and was directly subjected to further transformations. Modified Kornblum oxidation[8] (dimethyl sulphoxide–$NaHCO_3$, 150 °C, 30 min) of this mixture afforded the tricyclic ketone (**9**) as the major product along with an unreacted toluene-*p*-sulphonate.† The ketone (**9**) displayed characteristic spectral features in support of the assigned structure [i.r. $\nu_{max.}$ 1740 cm$^{-1}$; $^1$H n.m.r. ($CDCl_3$, 200 MHz) δ 1.44(s, 3H), 2.14—2.56(m, 4H), 5.11(d, 1H, *J* 4.4 Hz), 6.78—7.28(m, 4H)]. This tricyclic ketone provides the carbocyclic frame-

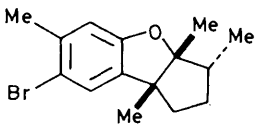
† Though these are separable with difficulty on account of close polarity, an efficacious method turned out to be reduction of the mixture with sodium borohydride, easy separation of the alcohol by p.l.c. followed by reoxidation (pyridinium chlorochromate) to give (**9**).



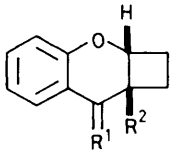
(1)



(2)



(3)

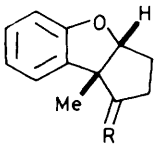


(4) $R^1$ = O, $R^2$ = H

(5) $R^1$ =  , $R^2$ = H

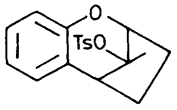
(6) $R^1$ = O, $R^2$ = Me

(7) $R^1$ =  , $R^2$ = Me



(8) R = 

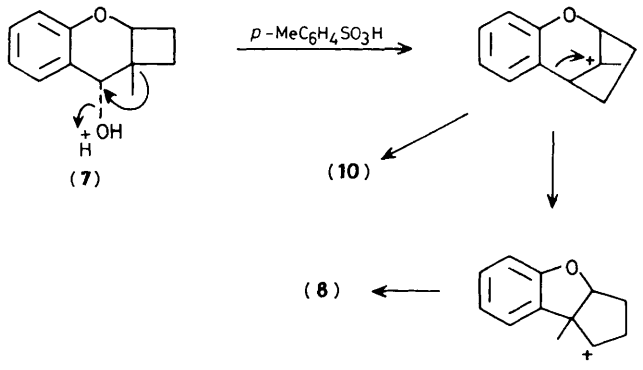
(9) R = O



(10)

Ts = $p$-$MeC_6H_4SO_2$

work of aplysin (**3**), which is thought to arise from the migration of an external bond in the cyclobutachromenol (**7**) leading to a trichothecane-like cationic intermediate, followed by an aryl migration (Scheme 1).[9] The minor unchanged toluene-*p*-sulphonate, which is resistant to oxidation, was obtained as a crystalline solid (m.p. 93 °C) and assigned structure (**10**) from spectral data [$^1$H n.m.r. ($CDCl_3$, 200 MHz) δ 1.36(s, 3H), 1.6—2.38(m, 4H), 2.44(s, 3H), 3.38(d, 1H, *J* 8 Hz), 4.78(br, 1H), 6.64—7.16(m, 4H), 7.38(d, 2H, *J* 8 Hz), 7.84 (d, 2H, *J* 8 Hz)]. However, on comparison of the $^1$H n.m.r. spectrum of pure (**10**) with the spectrum of the mixture of toluene-*p*-sulphonates mentioned earlier, the composition




**Scheme 1**

of the original mixture, in retrospect, is seen to consist of (**8**) and (**10**) in a proportion of 1.5 : 1.

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