The Oxidation of Chroman-4-ols with Chromic Acid

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With regard to the oxidation rates with chromic acid of epimeric cyclohexanols(CYHs), it is well known[1] that the axial alcohols are oxidized faster than the equatorial ones and that the bulky substituent adjacent to the hydroxyl group accelerates the reaction. Although isolated studies of the oxidation rates of allyl alcohols are on record,[2] no systematic investigation has yet been reported. We wish to report the oxidation of chroman-4-ols; the results are summarized in the table. Only the most interesting results different from those in the saturated series can be discussed here.

TABLE 1. OXIDATION RATES OF SUBSTITUTED CHROMAN-4-OLS

Compound	Av. rate[a]	k_H/k_D	Preferred conformation of OH[b]	*cis*/*trans*
CR(I)[c]	29.5	5.44	ax′ [3]	
cis-2-Me-CR(II)	116	5.30	eq′	10.6
trans-2-Me-CR(III)	10.9		ax′	
cis-2-*i*-Pr-CR(IV)	129		eq′	9.21
trans-2-*i*-Pr-CR(V)	14.0		ax′	
cis-2-Ph-CR(VI)	96.9	4.99	eq′	3.30
trans-2-Ph-CR(VII)	29.4		ax′	
cis-2-*t*-Bu-CR(VIII)	133		eq′	12.1
trans-2-*t*-Bu-CR(IX)	11.0		ax′	
cis-3-Me-CR(X)	61.4	5.12	ax′	3.55
trans-3-Me-CR(XI)	17.3		ax′[3]	
cis-3-Ph-CR(XII)	42.9	5.11	eq′	3.43
trans-3-Ph-CR(XIII)	12.9	5.87	eq′[3]	
cis-3-*t*-Bu-CR(XIV)	16.7	4.11	ax′	3.65
trans-3-*t*-Bu-CR(XV)	4.58		ax′	

a) l/mol sec$\times 10^2$ in 85.5% (by volume) HOAc, 25°C. Rates followed spectrophotometrically at 380 mμ. $[CrO_3]3.00\times10^{-4}$M; $[ROH]2.25\times10^{-4}$M. All data average of 2—4 runs.
b) The conformation of these compounds were determined by NMR.
c) CR: Chroman-4-ol

In this series of compounds, the rates of *cis*-2-substituted chroman-4-ols (2-CRs) are markedly larger, and in *cis*-2- and *trans*-2-CRs the rates are little affected with an increase in the size of the respective substituent. Both *cis*-2- and *cis*-3-CRs react more rapidly than the corresponding *trans* isomers. In all the 2-CRs except 2-Ph-CRs, the ratios of the rates of *cis*/*trans* (9—12) are larger than those of 3-CRs and CYHs. Since the 2-CRs are almost conformationally homogeneous, as is indicated in the table, the above results can be explained to some extent by the fact that the acceleration by the strain relief in the *cis*-2-CRs ($A^{(1,3)}$ strain, *ca.* 1.0 kcal/mol)[3] is greater than that of *trans* ones (*ca.* 0.35 kcal/mol).[4] However, the rate ratio of *cis*/*trans* (*ca.* 3.8), as calculated[4] from the free energy difference (*ca.* 0.65 kcal/mol) between the two isomers, is not so large as the observed value (9—12); consequently, the observed ratio should be attributed to both the stereoelectronic effect[5] and the strain relief.

It is a striking fact that *cis*- and *trans*-3-*t*-Bu-CRs (XIV, XV) show the smallest rates of all the 3-isomers. In the 2-substituted CYHs, the rate ratios of *t*-Bu/Me are 9.3(*trans*)—11(*cis*)[1] due to the presence of a bulky adjacent group. Although similar effects can be expected for the 3-CRs, the ratios are markedly reversed. Since XV exists mostly in the diaxial conformation, it is considered that the *t*-Bu group has little effect on the steric compression of the hydroxyl group, and the ground state can be assumed to be similar to that of *trans*-3-Me-CR(XI). In the transition state, however, the repulsion[4] between the developing carbonyl group and the *t*-Bu group is much larger than that of XI; consequently, XV has the larger activation free energy. This assumption is also supported by the fact that the rates decrease with an increse in the size of the substituent in *trans*-3-CRs.

Contrary to the reactivity anticipated from its preferred conformation, the rate of XIV is quite small compared to that of *cis*-3-Me-CR(X) and *cis*-2-*t*-Bu-CYH ($k=79.7\times10^{-2}$). In the case of strongly hindered alcohols, it has been reported[6] that the formation of the ester is concerned in the rate-controlling step and the rate decreases. In the initial stage of the reaction of XIV, an induction period characteristic of a successive reaction and a smaller isotope effect is observed. These results suggest that the esterification step is connected to some extent with the rate-determining step because of its sterically-crowded situation, in which the hydroxyl group is surrounded by the *t*-Bu group and the hydrogen in a peri-position.

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