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THE OXIDATION RATES OF 2-CYCLOHEXEN-1-OLS WITH CHROMIC ACID

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The chromic acid oxidation of 5- and 6-substituted 2-cyclohexen-1-ols was investigated. The relative rates of oxidation are reasonably interpreted by considering steric and stereoelectronic effects and also conformational equilibria.

Many investigations have been reported on the chromic acid oxidation of cyclohexanols and it is well known that the axial alcohols are oxidized faster than the equatorial ones and that the bulky substituent adjacant to the hydroxyl group accelerates the reaction.[1)]

In the previous communication,[2)] we have reported that the oxidation rates of chroman-4-ols with chromic acid can be explained on the basis of conformational consideration.

Since 2-cyclohexen-1-ols (CYHEs) are considered to be the most fundamental unsaturated system, it may be expected that the investigation on these compounds would provide the most pertinent approach for comparing the accelerating factor between saturated and allylic alcohols. From this point of view, the systematic investigation was carried out on CYHEs; the results are summarized in the Table.

In general, the oxidation rates of CYHEs are considerably larger than those of cyclohexanols[1)]; under the same condition CYHE (IX) is oxidized faster than cyclohexanol (X) by a factor of 40, implying that the stereoelectronic effect acts as an important accelerating factor for CYHEs.

In 5-methyl- (I,II) and 5-t-butyl-CYHEs (III, IV), the rates are little affected with an increase in the size of the respective substituent, and the ratios of k_{cis} to k_{trans} (2.5; 2.9) are the reverse of those of the corresponding 3-substituted cyclohexanols (0.23; 0.16).[1)] Because of the unfavored axial position of

Table 1. Oxidation Rates of Substituted 2-Cyclohexen-1-ols

Compound	Av. rate[a)]	cis/trans	Preferred conformation of OH[b)]
cis-5-Me-CYHE (I)[c)]	135	2.47	e'
trans-5-Me-CYHE (II)	54.6		a'
cis-5-t-Bu-CYHE (III)	130	2.86	e'
trans-5-t-Bu-CYHE (IV)	45.4		a'
cis-6-Me-CYHE (V)	134	1.36	a'
trans-6-Me-CYHE (VI)	97.9		e'
cis-6-t-Bu-CYHE (VII)	173	2.36	a'
trans-6-t-Bu-CYHE (VIII)	73.6		a'
CYHE (IX)	86.2		d)
Cyclohexanol (X)	2.18		e

a) 1/mol·sec × 10^2 in 85.5% HOAc, 25 ± 0.1°C. Rates are followed spectrophotometrically at 380 mμ. $[CrO_3]$ 3.00×10^{-4} M; $[ROH]$ 2.25×10^{-4} M. All data average of 2~4 runs.

b) The conformations of these compounds were determined by NMR.

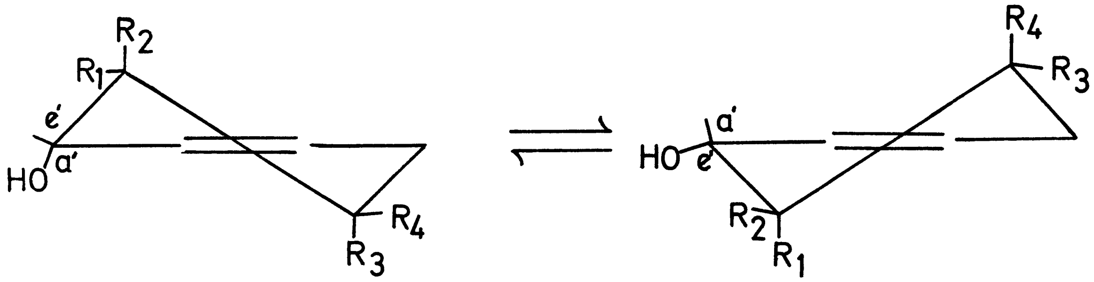
c) CYHE: 2-Cyclohexen-1-ol.

d) There seems to be no remarkable conformational preference between a' and e' conformers. See the discussion described below.

the alkyl groups (Me, t-Bu), cis- (I, III) and trans-5-CYHEs (II, IV) tend to exist mainly in the conformations (Ie', IIIe') and (IIa', IVa') respectively and, therefore, the stereoelectronic effect on cis-isomer is considered to be larger than that on trans-ones.

The smaller rate ratios of cis to trans (2.5; 2.9) for 5-CYHEs compared with those of the corresponding chromanols (11; 12)[2)] would be attributable to the relief of the relatively small $A^{(1,2)}$ strain in CYHEs.

It has been reported that the conformational energy for the acetoxyl group in 3-acetoxy-5-t-butyl-1-cyclohexene is almost zero,[3)] while that in 4-acetoxychroman is 0.8 kcal/mol[2)] favorable for axial position of the acetoxyl group. Therefore,



Ia'	$R_1 = R_2 = R_4 = H$;	$R_3 = Me$	Ie'
IIa'	$R_1 = R_2 = R_3 = H$;	$R_4 = Me$	IIe'
IIIa	$R_1 = R_2 = R_4 = H$;	$R_3 = t\text{-}Bu$	IIIe'
IVa'	$R_1 = R_2 = R_3 = H$;	$R_4 = t\text{-}Bu$	IVe'
Va'	$R_2 = R_3 = R_4 = H$;	$R_1 = Me$	Ve'
VIa'	$R_1 = R_3 = R_4 = H$;	$R_2 = Me$	VIe'
VIIa'	$R_2 = R_3 = R_4 = H$;	$R_1 = t\text{-}Bu$	VIIe'
VIIIa'	$R_1 = R_3 = R_4 = H$;	$R_2 = t\text{-}Bu$	VIIIe'
IXa'	$R_1 = R_2 = R_3 = R_4 = H$		IXe'

it is reasonable to consider that the $A^{(1,2)}$ strain [repulsion between 1-OH(e') and 2-H] in CYHEs is fairly smaller than the $A^{(1,3)}$ strain [repulsion between 4-OH (e') and 5-H] in chromanols.

It is well known[4,5] that the values obtained by kinetic and NMR methods for 4-t-butylcyclohexanols may be used to evaluate the conformational equilibrium, while those for 3-t-butyl derivatives do not afford the satisfactory results because of the effects of the t-butyl group. In CYHEs, however, there is a plausible reason[6] to permit the application of the rates of 5-t-butyl-CYHEs (III, IV) as the standard values. The result evaluated by the equation

$$k_{IX} = k_e N_e + k_a N_a$$

(where k_e and k_a are the oxidation rates of III and IV, respectively) indicates that IX consists of IXa' (50%) and IXe' (50%) in the conformational equilibrium.

Accordingly, it is reasonable to consider that the magnitude of the $A^{(1,2)}$ strain would be almost equal to that of the 1,3-diaxial (1-OH~5-H) repulsion in CYHEs and that the rate ratio of cis- (III) to trans-5-t-butyl-CYHE (IV) would indicate only the difference in the stereoelectronic effect between e' and a' conformers of CYHEs because the conformation of III and IV are almost fixed to IIIe' and IVa'.

In cis- (V) and trans-6-methyl-CYHE (VI) the rate ratio (k_V/k_{VI}) is small (1.36) compared to that of 3-methylchromanol (3.55).$^{2)}$ The compound (V), similar to cis-3-methylchromanol, exists mainly in conformation Va', whereas VI exists in VIe' because of the syn-axial repulsion (4-H~6-Me) and of the relatively smaller A strain than that of chromanols. Consequently, taking into consideration that the stereoelectronic effect is more favorable for VI than for V and there are no remarkable differences of the strain relief effect between V (a'-OH) and VI (e'-OH), the order of the rates should be $k_{VI} > k_V$, as opposed to the observed values.

The discrepancy between the expected and the observed result may be explained by considering the following factor; there is greater steric compression between adjacent e,a substituents (cis) as compared to adjacent e,e substituents (trans) in 1,2-substituted cyclohexanols, and this factor plays an important role in the chromic acid oxidation.$^{7)}$ This compression anticipated in V would become much greater than that of cyclohexanols because of increasing$^{8)}$ of eclipsed conformation of adjacent substituent.

In 2-substituted cyclohexanols the bulky group adjacent to the hydroxyl group accelerates the reaction ($k_{t\text{-}Bu}/k_{Me} = 11$),$^{1)}$ whereas the same group on 3-substituted chromanols markedly reduce the reaction ($k_{t\text{-}Bu}/k_{Me} = 0.27$) indicating that in cis-3-t-butylchromanol the esterification step is concerned to some extent with the rate-controlling step because of its sterically hindered situation.$^{2)}$ Since the hydroxyl group in CYHEs are not subjected to larger A strain as that in chromanols, it can be expected that the esterification step would be no longer so much concerned in regulating the reactivity of cis-6-t-butyl-CYHE (VII) and the rate ratio would become larger than that of 3-substituted chromanols. The experimental finding ($k_{t\text{-}Bu}/k_{Me} = 1.3$) is consistent with the above consideration.

In spite of the anticipated large accelerating effect by the adjacent t-butyl group, the rate of trans-6-t-butyl-CYHE (VIII) is still smaller than that of trans-6-methyl-CYHE (VI), contrary to the results observed in cyclohexanols.

The small $J_{1,6}$ value (2.6 Hz) for trans-6-t-butyl-CYHE (VIII) suggests that VIII, as well as trans-3-t-butyl-4-hydroxycyclohexanone,$^{9)}$ seems to exist mainly in non-chair conformation because of the large gauche interaction between the t-butyl and the hydroxyl groups.

Consequently, it can be considered that the t-butyl group has little effect on the steric compression and, furthermore, the repulsion between the t-butyl group and the developing carbonyl group is much larger than that of trans-6-methyl-CYHE (VI); VIII should have the larger activation free energy than VI.

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6) The conformational equilibrium of chroman-4-ol (a'-OH, 85%) estimated by the kinetic method using the rates of 2-t-butylchromanols as the standard values is also in fair agreement with that obtained by NMR study (a'-OH, 82%). The agreement is believed to be due to the fact that the major accelerating factor in 2-substituted chromanols is not the effects of the substituent but the stereoelectronic effect. Since the stereoelectronic effect is also the major accelerating factor in 5-substituted CYHEs, the application of the rates of 5-t-butyl-CYHEs would afford the satisfactory result.
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