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216. Steric Rate-Retardation in the Chromium Trioxide Oxidation of 4,6-Dimethyl-benzocyclobutenol[1])

by **Paul Müller**

Institut de Chimie Organique de l'Université, 1211 Genève 4

(11. IX. 70)

Summary. The rate of oxidation of 4,6-dimethyl-benzocyclobutenol[1]) (**1**) with chromium trioxide has been measured. After correction for the influence of the two methyl substituents the rate of oxidation of **1** is lower than that of 1-tetralol (**9**) and 1-indanol (**10**) by factors of 3 and 5 respectively. The lower oxidation rate of **1** as compared to **9** and **10** is interpreted in terms of a steric rate retardation arising from angle strain in the developing carbonyl function of 4,6-dimethylbenzocyclobutenone (**4**).

Rate accelerations due to steric effects are well known phenomena in the chromium trioxide oxidation of primary and secondary alcohols, and they have been discussed extensively in the literature [3] [4]. They are believed to be caused by relief of nonbonded interactions by changing the hybridization at the reacting carbon from sp^3 to sp^2, with a considerable amount of sp^2 hybridization developed in the transition state. Thus, axial hydroxyl groups on the cyclohexane ring react approximately 3 times faster than their equatorial epimers and further increase of steric ground-state interactions leads to even more impressive rate accelerations [5]. The hypothesis of a transition state resembling the carbonyl product has been challenged [6] [7] on the grounds that it requires a rate retardation in the oxidation of an alcohol leading to a strained ketone. In fact, no correlation could be established until now between oxidation rates of alcohols and strain in the resulting ketones as measured by the value of the carbonyl stretching frequency [8]. In particular, the oxidation rate of cyclobutanol is higher than that of cyclopentanol [9], although the corresponding ketone is much more strained in the 4-membered ring. Moreover, in the solvolysis reaction where, except in some isolated situations [10], the reactivity parallels the reactivity towards oxidation [3], cyclopentyl tosylate reacts faster than cyclobutyl tosylate [11]. The unexpected behaviour of cyclobutanol presents a serious problem for the understanding of the oxidation mechanism, and no satisfactory explanation has yet been found for this discrepancy.

It was therefore of interest to investigate whether benzocyclobutenol would show similar reactivity compared with 1-indanol as cyclobutanol does compared with

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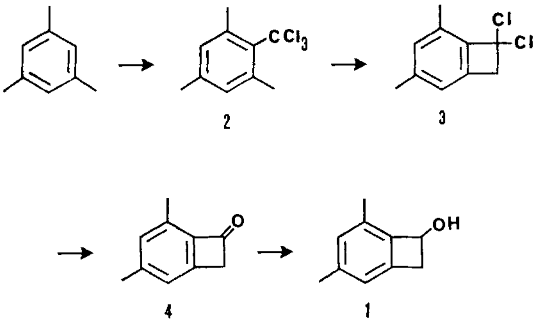
[1]) This nomenclature is preferred in the literature [1] [2] to the more systematic name (7-hydroxy-3,5-dimethyl-bicyclo[4.2.0]octa-1,3,5-triene).

cyclopentanol, or whether it constitutes an unambiguous case for a steric rate retardation.

The geometry of the benzocyclobutenyl skeleton is known from X-ray studies of several 1,2-dihalobenzocyclobutenes [12]. The molecule is essentially planar rather than skewed, with bond angles compressed to *ca.* 85° at the aliphatic carbon atoms. This deformation increases the ground state energy (in the alcohol) by a considerable amount. However, since the deviation from the ideal trigonal bond angle is more important than from the ideal tetrahedral angle, namely 35° as compared with 25°, an even higher destabilisation of the transition state could be expected with a corresponding rate retardation. The low reactivity of the benzocyclobutenyl system in nucleophilic substitution reactions has been reported [13] [14]. The main oxidation product obtained from 3,4,5,6-tetramethylbenzocyclobutenol was the ketone, isolated in 80% yield [2]. The recently published synthesis of *Hart et al.* [2] provides a simple route to methylsubstituted benzocyclobutenols from common starting materials. 4,6-Dimethylbenzocyclobutenol (**1**) was selected as a suitable model compound for oxidation with chromic acid, because it has the lowest number of substituents of all the products accessible by this method.

The synthesis (see Scheme) involves trichloromethylation of mesitylene, thermal decomposition of the intermediate trichloromethyl-mesitylene (**2**) to give 1,1-dichloro-4,6-dimethylbenzocyclobutene (**3**), which is hydrolyzed to the ketone **4** in sulfuric acid. The alcohol **1** is obtained by reduction of **4** with aluminium hydride.

Scheme of Synthesis



The rates of chromium trioxide oxidation of **1** and of some additional alcohols are given in the Table. The compounds **5**–**8** were measured in order to evaluate the effect on the rate of the two methyl substituents in **1**. Their selection is based on the similarity of the Hammett ϱ-values for the alcohol-carbonium ion equilibrium in the benzocyclobutenol and di-, as well as triphenylmethanol series, and will be justified later. The *para*-methyl group in **6** accelerates the oxidation rate as compared to phenylethanol (**5**) by a factor of 1.75. Substitution in the *ortho*-position by one methyl group results in a rate retardation. This effect has been ascribed to steric inhibition of resonance between the phenyl ring and the developing ketone [6]. A second *ortho*-substituent as in **8** leads, however, to a rate acceleration. The behaviour of **7** and **8** is apparently irregular and no conclusions can be drawn on the cyclobutenol case from these two compounds.

Rate of oxidation of alcohols with chromium trioxide in 90% acetic acid, at 25.0°, containing 0.01 M *potassium acetate*

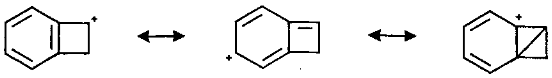
Alcohol	No.	k_2 $M^{-1} \cdot min^{-1}$	k_{rel}
1-Phenyl-ethanol	**5**	0.784	1.0
1-(4-Methylphenyl)-ethanol	**6**	1.37	1.75
1-(2,4-Dimethylphenyl)-ethanol	**7**	0.556	0.71
1-(2,4,6-Trimethylphenyl)-ethanol	**8**	3.37	4.30
4,6-Dimethylbenzocyclobutenol	**1**	4.28	5.47
1-Tetralol	**9**	4.5[a])	5.75
1-Indanol	**10**	7.27	9.27

[a]) Extrapolated from Ref. [6].

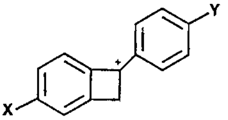
The unusual reactivities of **7** and **8** are even more striking, considering the fact that in the solvolysis of 1-phenylethyl chlorides both one and two *ortho*-substituents have rate accelerating effects [15], and it may well be that solvolysis and chromium trioxide oxidation are not as similar as is generally assumed.

Because of the steric complications in **7** and **8**, the rate accelerating effect of the methyl substituents in 4,6-dimethylbenzocyclobutenol (**1**) was assumed to be identical for both methyl groups, since resonance inhibition such as in **7** is not to be expected in a planar molecule. Using twice the value found for *para*-substitution in 1-phenylethanol (**5**), the relative rate of the oxidation of unsubstituted benzocyclobutenol is expected to be *ca.* 1.8. With this correction the rate of benzocyclobutenol oxidation is retarded by a factor of 5 as compared to 1-indanol (**10**) which is considered to be the best model, while the rate retardation in 4,6-dimethylbenzocyclobutenol (**1**) compared to **10** by a factor of 1.7 is much less convincing. The low rate of the oxidation of benzocyclobutenol is attributed to angle strain for the following reasons. It can be seen from models that in neither **9** or **10** are *van der Waals* interactions present which would have resulted in rate accelerations of **9** and **10** as compared to **1**. Torsional interactions are probably responsible for the higher oxidation rate of indanol (**10**) compared with tetralol (**9**), but they cannot accelerate **10** relative to **1**. The cyclobutane and cyclopentane rings in benzocyclobutenol and 1-indanol respectively are either completely or at least close to planar, and in both cases torsional strain between carbon atoms 1 and 2 will be freed upon oxidation. The additional trigonal carbon will lead to a further flattening of the 5-membered ring, thereby increasing strain between carbons 2 and 3, while no such effect can be present in the 4-membered ring. As a result, there is less strain release during oxidation of **10** and no reason to assume a rate acceleration of 1-indanol (**10**) as compared with benzocyclobutenol on the basis of torsional strain. A similar argument can be applied to 1-tetralol, the main difference being the absence of 1–2 interactions in the alcohol.

Steric inhibition of resonance seems to be the determining factor in the rate profile for solvolyses of 1-chlorobenzocyclenes [16]. The possibility of resonance in the benzocyclobutenyl cation has been questioned [14]. It was argued that resonance forms like **11**, with a double bond in the 4-membered ring exocyclic to the aromatic ring were energetically unfavourable. The problem was then further investigated by *Hart* & *Hartlage* [17] who could show that structures such as **11** are perfectly normal. Moreover it was found that, in cations like **13**, stabilization by the fused benzene ring is more important than stabilization by the 1-phenyl substituent. An additional factor for *meta*-substituent effects (through 1,3 π-interactions) involving structures like **12** is needed to fit the *Hammett* equation for the alcohol-carbonium ion equilibrium



11 12



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for a series of substituted 1-phenylbenzocyclobutenols corresponding to **13**, with $\varrho = -4.05$, in good agreement with other reactions involving generation of carbonium ions in solution [18]. In particular, for the pK_{R+} in the diphenyl- and triphenylmethanol series, ϱ was found to be -4.1 and -3.6 respectively[2]. On these grounds it can be safely argued that resonance is not inhibited in the benzocyclobutenyl cation and, for this reason **1** is not less reactive in the oxidation than **10**. Further, the similarity of the ϱ-values in the benzocyclobutenol and phenylmethanol series suggests that the choice of the model compounds to evaluate the influence of the methyl substituents in 4,6-dimethylbenzocyclobutenol (**1**) is not a bad one. The small differences in these values can be neglected, because the chromium trioxide oxidation is much less sensitive to electronic effects ($\varrho = -1.0$) [21] than the alcohol-carbonium ion equilibrium.

It seems therefore justified to ascribe the low rate of chromium(VI) oxidation of benzocyclobutenol to angle strain in the ketone-like transition state. This, to our knowledge, represents the first case of a steric rate retardation in chromium trioxide oxidation of alcohols, and it is in agreement with the generally accepted mechanism. Why other compounds, like cyclobutanol, do not behave in the same way can still not be explained and will require further investigation.

Support of this work by a grant of the *Fonds National Suisse de la Recherche Scientifique* (grant No. 5202.2) for the purchase of instruments is gratefully acknowledged.

Experimental. – *Alcohols.* Commercially available products (1-phenylethanol (**5**) and 1-(4-methylphenyl)-ethanol (**6**) were distilled. 4,6-Dimethylbenzocyclobutenol (**1**) was obtained by reduction of the ketone with aluminium hydride [2]; m.p. 88–89° (from petrol ether). The other alcohols were obtained by reduction of the corresponding ketones with sodium borohydride. All compounds gave satisfactory spectral and physical data[3].

Kinetic measurments. Acetic acid (*Merck, pro analysi*) was diluted to 90% (by weight) aqueous solution, and made 0.01M in potassium acetate. This solution was used to prepare stock solutions of chromium trioxide. Solid alcohols were weighed directly into a UV.-cell and diluted with 2.0 ml of solvent or added from appropriate stock solutions, and equilibrated in the cellholder of a *Perkin-Elmer* UV.-spectrophotometer, model 402, thermostatted to 25.0°. After equilibration 1.0 ml of

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[2] The now accepted σ^+ constants [18], and pK_{R+}-values [18] [19] give a somewhat different ϱ than originally reported [20].

[3] Microanalyses for **1**, **8** and **10** were carried out by Dr. *K. Eder*, Ecole de Chimie, Université de Genève.

thermostatted chromium trioxide solution was added and the mixture stirred with a glass rod. Liquid samples were added directly by means of a syringe to the chromium trioxide solution in the cell. The concentration of chromium (VI) at the beginning of all kinetic runs was ca. 5×10^{-4} M. At least a ten-fold excess of organic substrate was used for the determination of first-order rate constants.

Under the conditions employed solvent oxidation was found to be negligible. The disappearance of chromium (VI) was followed by continuously measuring the absorbance at 350 nm. Good straight lines were obtained, plotting $\log(A - A\infty)$ against time. The second-order rate constants were calculated by division of the pseudo-first-order rate constants with the initial concentration of organic substrate. The values given are averages from 3 to 6 runs and were reproducible to ± 5%.

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217. Stabilité des carboxylates de terres rares, II(1)
Bis-hydroxyméthyl-2,2-propionates

par **R. Roulet** et **T. Vu Duc**

Institut de chimie minérale et analytique de l'Université de Lausanne

(6 VIII 70)

Summary. The stability constants of 2,2-bis-hydroxymethyl-propionates of rare earths have been determined at ionic strength 0,100 ($NaClO_4$) at 25.0°C by a potentiometric method. The ligand forms 1:1 and 1:2 complexes with all the rare earths and weak 1:3 complexes with light rare earths only. In these last complexes, it binds in a unidentate way. The dissociation constant of the acid has also been measured.

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(1) I^e communication, v. [1].