202. Medium Effects on C, C-Bond Cleavage in the Alcohol Oxidation with Chromic Acid

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Dedicated to Professor *André Dreiding* on occasion of his 60th birthday

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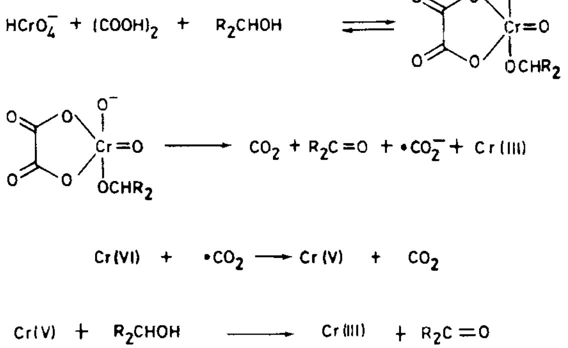
Summary

The C, C-bond cleavage which occurs during chromic acid oxidation of *t*-butylphenylmethanol (**1**) and 1,2-diphenylethanol (**2**) to the extent of up to 67% is reduced to 3% for **1** and 13% for **2** when the reaction is run in acetone, and totally suppressed upon co-oxidation of the alcohols **1** and **2** with oxalic acid. Similarly, the yield of 7-norbornanone obtained from 7-norbornanol (**7**) is raised in going from acetic acid (24%) to acetone (41%) and approaches 100% in the co-oxidation. With the co-oxidation 5-*endo*-bicyclo[2.1.1]hexanol (**3**) is converted to the corresponding ketone in 54% yield. Mechanistic implications of these results are discussed.

Introduction. - The mechanism of co-oxidation of a primary or secondary alcohol and oxalic acid by chromic acid has been investigated by *Hasan & Roček* [1]. The key step consists in the breakdown of a ternary complex containing Cr(VI), oxalic acid and alcohol *via* a three-electron oxidation *(Scheme 1)* to Cr(III), ketone, CO_2 and $\cdot CO_2^-$. The latter, in turn, is oxidized by Cr(VI) to CO_2 and Cr(V) which converts a second alcohol molecule to ketone. Alcohol oxidations by Cr(V) formed

Scheme 1



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during co-oxidation have been investigated [2] and were found to be very similar to those with Cr(VI). The co-oxidation has two aspects which are potentially relevant for preparative applications: alcohol oxidation proceeds faster in the presence of oxalic acid by a factor of up to 250 [1] and the formation of intermediate Cr(IV) is avoided *(Scheme 1)*. This is important because the Cr(IV) species is known to react with certain alcohols *via* C,C-bond cleavage rather than *via* oxidation to ketone [3]. Such cleavages take place with alcohols capable of splitting into stabilized radicals such as *t*-butylphenylmethanol (**1**) [4] and 1,2-diphenylethanol (**2**) [5] and also with strained alcohols such as cyclobutanol [6] where C,C-bond cleavage allows strain release. *Trahanovsky* [5] and *Roček* [7] have demonstrated that the cleavage is a one-electron oxidation process which can be ascribed to Cr(IV). In contrast, the oxidations of an alcohol by Cr(VI) as well as Cr(V) are two-electron processes and lead to the ketone. The C,C-bond cleavage with Cr(VI) has so far only been established for oxidation of cyclopropanol [8], 1-methyl-1-cyclobutanol [9] and triarylmethanols [10]. The co-oxidation with oxalic acid therefore represents a convenient and mild procedure for conversion of alcohols which undergo C,C-bond cleavage under conventional chromic acid oxidations, and *Krumpolc & Roček* [11] oxidized cyclobutanol to the ketone in 85-92% yield.

We wanted to oxidize 5-*endo*-bicyclo[2.1.1]hexanol (**3**) to 5-bicyclo[2.1.1]hexanone (**4**). This transformation has been reported by *Wiberg* [12] who used *Oppenauer* oxidation and obtained a yield of only 30%. After unsuccessful experiments with mild (chromic acid in a two-phase system [13] or acetone [14], $BaMnO_4$ [15]) as well as vigorous reagents (RuO_4 [16]) we decided to adapt the co-oxidation procedure of *Roček* to aqueous acetone in order to oxidize organic compounds insoluble in water.

Oxidation of *t*-butylphenylmethanol (1) and 1,2-diphenylethanol (2) *(Table)*. - Oxidation of **1** with chromic acid in aqueous acetic acid affords the ketone **5** and the cleavage products benzaldehyde and *t*-butanol *(Scheme 2)*. Similarly, 1,2-diphenylethanol leads to deoxybenzoin (**6**) and benzaldehyde. The second expected cleavage product, benzyl alcohol, was not detected, owing to its rapid oxidation to benzaldehyde [5]. For both alcohols the cleavage is completely suppressed by oxalic acid in aqueous acetone within the limits of detection (*ca.*1%). In addition, the *Table* reveals an intriguing observation: when the reaction was run in aqueous acetone without added oxalic acid, the cleavage was reduced to 6% for **1** and 16% for **2**. Similarly, with *Jones* reagent cleavage amounted to 3 and 13% respectively.

Scheme 2

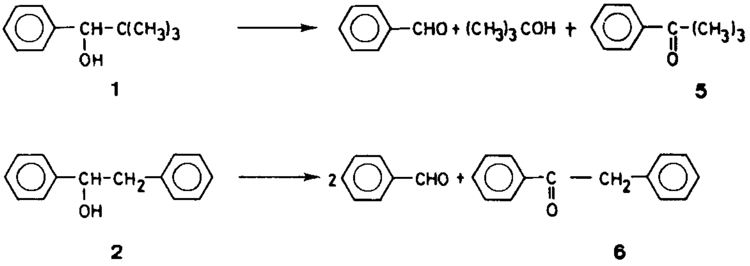

Table. *Oxidation of* t-*butylphenylmethanol* (**1**) *and 1,2-diphenylethanol* (**2**) *with chromic acid.*

Alcohol	Conditions	Yield of ketone (%)	Cleavage (%)	Comment
1	70% AcOH 0.18 M H_2SO_4	60	40	[4c]
1	85% AcOH	33	max. 67	[4a]
1	Co-oxidation: 60% acetone, 6 eq. $(COOH)_2$	100	0	
1	60% acetone	66	6	28% **1** recovered
1	*Jones* oxidation [14]	97	3	
2	85% AcOH	75	25	[5]
2	85% 0,1 M NaOAc	45	55	[5]
2	85% 0,5 M NaOAc	30-45	55-70	[5]
2	Co-oxidation	100	0	
2	60% acetone	84	16	
2	*Jones* oxidation [14]	87	13	

According to the mechanism for chromic acid oxidation the Cr(IV) promoted cleavage should account for 33 to 67% of the oxidation products [6] [7] [17].

Two possibilities should be considered. The intermediate Cr(IV) species could have different selectivity in acetone than in acetic acid and react partly by C,H-bond cleavage to give a carbon radical ultimately oxidized to the ketone. This mechanism cannot be dismissed because one-electron oxidations of ordinary alcohols proceed normally by this pathway. Although cleavage is typical for one-electron oxidants, the latter do not need to react in this way. *Trahanovsky & Cramer* [18] have investigated the reaction of **1** with Ce(IV) and found a small amount of ketone. This indicates that the two processes are in principle competitive. The same should hold with Cr(IV). Alternatively, the cleavage can be avoided if Cr(IV) is transformed to other Cr species, for example by disproportionation to Cr(III) and Cr(V) [19].

Oxidation of 7-norbornanol (7) and 5-*endo*-bicyclo[2.1.1]hexanol (3). - 7-Norbornanol has been previously oxidized with *Jones* reagent [20] and with *Sarrett* procedure [21] to give the ketone **8** in *ca.* 25 and 37% yield respectively. When **7** was oxidized with a stoichiometric amount of CrO_3 in 80% acetic acid, 10^{-2}N in H_2SO_4, **8** was obtained in 24% yield while 23% of **7** was recovered. With *Jones* oxidation the yield of **8** was 41 and 20% of **7** did not react. Thus 53 and 39% of products escaped during the isolation procedure. Since enough Cr(VI) was present to oxidize the alcohol some of it must have reacted in another way. Oxidation of **7** with Cr(IV) may proceed *via* C,C-bond cleavage and the cleavage product (probably 4-hydroxycyclohexanecarboxaldehyde) will be more reactive towards Cr(IV) than **7** itself. This hypothesis is corroborated by the observation that **7** is the least reactive alcohol whose rate is known [22]. Furthermore, with the co-oxidation procedure, quantitative conversion of **7** to **8** was obtained within the limits of the analytical procedure (3%). Since in the co-oxidation only Cr(VI) and Cr(V) are involved, the losses under normal conditions must be ascribed to Cr(IV). The trend towards reduction of cleavage in going from acetic acid to acetone is the same for

7 as for **1** and **2**, however the effect is much less pronounced. A similar reduction of cleavage has been reported by *Fürst* [23] for oxidation of *trans*-fused 8-methylhydrindanols in acetone.

Application of the co-oxidation to 5-*endo*-bicyclo[2.1.1]hexanol (**3**) was less successful. Although the yield of ketone **4** could be raised from 14% with the *Jones* reagent (19% of **3** recovered) to 54%, 13% of **3** was recovered while 33% of products could not be accounted for. This result again indicates formation of water-soluble cleavage products and products of over-oxidation which could have escaped detection. However, since in the co-oxidation Cr(IV) cannot be involved, the side reactions must be due to something else. Under kinetic conditions (80% acetic acid, 10^{-2}N H_2SO_4, 25°) the rate constant k_2 for disappearance of Cr(VI) in the presence of alcohol **3** is 0.14M^{-1} min^{-1}. Surprisingly the ketone **4**, under the same conditions, reacts 6 times faster ($k_2=0.84 M^{-1} min^{-1}$). If this higher reactivity prevails in other solvents, it should be responsible for the low yield of **4** in the co-oxidation. Although ketones are in general attacked by chromic acid, they are normally much less reactive than the respective alcohols. A typical illustration of this fact is provided by the oxidation of alcohols with *Jones* reagent in acetone. The case of 5-bicyclo[2.1.1]hexanone (**4**) is remarkable, because the normal mechanism for oxidation of ketones cannot account for its oxidation. Ketones such as cyclohexanone react with chromic acid *via* rate-determining enolization [24]. The latter reaction should be precluded for **4**. To our knowledge, the oxidation of non-enolizable ketones is not sufficiently well understood to draw analogies, however a mechanism of the *Baeyer-Villiger* type could represent a reasonable working hypothesis.

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Experimental Part

Preparation of alcohols. t-Butylphenylmethanol (**1**) [4b] and 1,2-diphenylethanol (**2**) [5] were synthesized by reduction of *t*-butylphenylketone (**5**) [25] and deoxybenzoin (**6**) *(Fluka)* with $LiAlH_4$. 5-*endo*-Bicyclo[2.1.1]hexanol (3) was obtained by reduction of 2-oxatricyclo[3.2.0.0^{3,7}]heptane with $LiAlH_4$ [26], and 7-norbornanol (7) following [27].

Oxidation of **1** *and* **2**. To the alcohol (0.80 mmol) in 5.0 ml of 60% acetone containing 30 µl of conc. H_2SO_4 at 0-5° was added with stirring the stoichiometric amount of CrO_3 (0.53 mmol) 8M in H_2O in portions. For the co-oxidation oxalic acid dihydrate (48 mmol) was added to the solvent and the amount of chromic acid was increased to 1.6 mmol. When all the Cr(VI) had reacted, a known quantity of standard (nitrobenzene for **1** and 4-methoxybenzophenone for **2**) was added. The mixture was extracted (CH_2Cl_2) and concentrated. Product analysis for oxidation of *t*-butylphenylmethanol (**1**) was carried out by GC. and yields were calculated with respect to the internal standard, using appropriate response factors for each component. No benzoic acid was present within the limits of detection. For the oxidation of **2** the products were analyzed by NMR. The yields given in the *Table* are average values of 3 determinations with an error of *ca.* 3%.

Oxidation of **3** *and* **7**. The procedure was similar to the one already described; however, owing to the volatility of the oxidation products the amount of solvent was reduced to 1-2 ml and the work-up was simplified as follows: At the end of the reaction a known amount of standard was added to the mixture (cyclohexanone for **3**, 3,3,5,5-tetramethylcyclohexanone for **7**), followed by addition of 2 ml of saturated. NaCl-solution and 2 ml of CH_2Cl_2. After stirring for 30 min the organic phase was analyzed by GC. When acetic acid was used, the reaction mixture was injected into the GC. after neutralization of the sulfuric acid with sodium acetate.

When the co-oxidation of **3** was carried out on a 1 g scale a mixture containing *ca.* 60% of ketone **4** and 7% of **3** was obtained. Pure **4** was separated by preparative GC. and identified by its spectral data [12].

Kinetic measurements. The rate of disappearance of Cr(VI) was followed spectroscopically at 350 nm as previously described [28].

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