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Oxidation of Aromatic Alcohols with Chromium(VI) Trioxide in the Presence of "Wet-Aluminium Oxide" in Aprotic Solvent

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Synopsis. The title oxidation resulted in a selective formation of the corresponding carbonyl compounds in excellent yields under mild conditions.

Chromic acid[1] and chromium(VI)-based reagents, viz Jones,[2] Sarett,[3] Collins,[4] Cornforth,[5] Kiliani[6] reagents, are versatile and potent oxidizing agents which have been extensively employed for a long time in both mechanistic and synthetic processes by using a modest-to-large excess of an oxidant; recently, a catalytic system for the oxidation of alcohols has been developed.[7,8] However, the inherently hazardous toxicity of a chromium(VI) reagent, laborious preparation of a chromium(VI) complex and, in some cases, the potentially dangerous nature on handling (ignition or explosion on the preparation of a complex, rapid temperature rise during the initial stage of the reaction, etc.) as well as prosaic disposal of a chromium salt reduce the utility of the reagents to a considerable extent.

We have found, however, that many of the difficulties encountered in the conventional processes can be overcomed by means of a combination of chromium(VI) trioxide and aluminium oxide (refered as Alumina) in aprotic media. This paper describes some of the experimentally remarkable aspects in the oxidation of various aromatic alcohols including benzyl and 1-phenylethyl alcohols, and diphenylmethanols. The instances cited here offer a distinctly superior and convenient procedure for the synthesis of carbonyl compounds.

Results and Discussion

In the absence of Alumina, oxidation was rather slow, and a considerable amount of an alcohol was recovered. For example, the reaction of diphenylmethanol (**1**) in hexane at ambient temperature for 24 h afforded only 17% of benzophenone (**2**); 80% of **1** remained unreacted. In the presence of commercial "dry-Alumina", though a better result was obtained (43% yield by GLC), the yield was still inferior to that (98%) in the presence of "wet-Alumina" (see Experimental) under the same conditions as mentioned above.

Oxidation was also conducted in various aprotic media (benzene, dichloromethane, and carbon tetrachloride) in the presence of "wet-Alumina". The reactions in the former two solvents gave a smaller yield of **2** (70 and 72%, respectively), and in the latter solvent afforded a comparable yield (97%) to that obtained in hexane. Thus, subsequent reactions were carried out in hexane, since the solvent is inexpensive and much less hazardous than carbon tetrachloride; moreover, its high volatility leads to easier product isolation.

Chromium(VI) trioxide was added to a suspension of Alumina in hexane; the resultant heterogeneous mixture was stirred for 10 min, during which a uniformly deep-orange coloration of the Alumina was observed, indicating that it was covered by chromium(VI). Upon the addition of an alcohol, the Alumina immediately began to turn partially brown; finally, it appeared entirely to be brown to blackish-brown, depending on the substrate used. The progress of the reaction could readily be followed by GLC analysis of the supernatant withdrawn at half-hour intervals. GLC showed that **1** was consumed as soon as the reaction started, and that **2** accumulated with the progress of the reaction. No neutral product other than **2** was formed in a detectable amount, suggesting that there was no side-reaction and/or further oxidation of the product.

Oxidation of the other alcohols was carried out in a manner similar to **1** in hexane. It should be noted that the reaction of benzyl alcohols was performed under an inert (argon) atmosphere, since the products (benzaldehydes) are highly susceptible to autoxidation. As in the case of **1**, the oxidation was commonly promoted in the presence of "wet-Alumina", leading to a selective formation of the corresponding carbonyl compound in fairly good yield. The use of less or more oxidant than the tabulated concentration led to no improvement in the yields. The results are summarized in Table 1. It might be emphasized that oxidation with the chromium(VI) trioxide-Alumina system can be carried out without suffering from the formation of an intractably tarry precipitate, which makes the isolation of the product considerably troublesome, as typically observed in a Collins oxidation of various functional groups.[9,10]

The effects of the nature and the position of the substituents on the benzene-ring on the yields of the products were investigated (Entries 2—16, 18—29, and 32—40). Interestingly, though, there was no significant difference in the yield of the products. Thus, the present procedure is clearly proven to be applicable to a wide variety of alcohols.

The present reaction has some distinct advantages in terms of simple manipulation, selective formation of carbonyl compounds in excellent yields, and easy recovery of a chromium salt. Thus, this procedure constitutes an improved alternative of various supported reagents, consisting of chromium(VI) species and inorganic materials such as silica gel,[11] celite,[12] graphite,[13] Alumina[14] etc. In addition, the reaction can be carried out efficiently in hexane, which appears to be more preferable from both economical and environmental terms than such chlorinated hydrocarbons

Table 1. Oxidation of Aromatic Alcohols with CrO_3-"wet-Alumina"a)

$X-C_6H_4-CH(OH)-R \longrightarrow X-C_6H_4-C(=O)-R$

Entry No.	Alcohols X		R	Products b) %
1	H		H	90
2	Me	*o*-	H	89
3		*m*-	H	96
4		*p*-	H	95
5	OMe	*o*-	H	93
6		*m*-	H	93
7		*p*-	H	96
8	Br	*o*-	H	89
9		*m*-	H	92
10		*p*-	H	90
11	Cl	*o*-	H	88
12		*m*-	H	92
13		*p*-	H	88
14	NO_2	*o*-	H	97
15		*m*-	H	92
16		*p*-	H	93
17	H		Me	90
18	Me	*o*-	Me	97
19		*m*-	Me	92
20		*p*-	Me	82
21	OMe	*p*-	Me	92
22	Br	*o*-	Me	89
23		*m*-	Me	96
24		*p*-	Me	90
25	Cl	*o*-	Me	91
26		*m*-	Me	90
27		*p*-	Me	93
28	F	*p*-	Me	90
29	NO_2	*p*-	Me	91
30	H		Et	90
31	H		Ph	95
32	Me	*o*-	Ph	92
33		*m*-	Ph	93
34		*p*-	Ph	90
35	OMe	*p*-	Ph	89
36	Br	*p*-	Ph	90
37	Cl	*o*-	Ph	91
38		*m*-	Ph	94
39		*p*-	Ph	98
40	NO_2	*p*-	Ph	93

a) Ambient, 24 h; 0.5 g of alcohol, 10 cm^3 of hexane, and 2.4 g of "wet-Alumina" were used in every run; $[CrO_3]/[Alcohol]=2.0$ (mole ratio). b) Isolated yield.

as dichloromethane, chloroform, or carbon tetrachloride, which are frequently used in conventional-type oxidation procedures with chromium(VI)-based reagents.

The specification of an active species, the appreciation of a functional role of aluminium oxide as a reactive site as well as an estimation of the scope and limitation of the present reaction are now under way in our laboratory.

Experimental

^1H NMR spectra were measured with a JEOL PMX-60 model spectrometer for solutions in carbon tetrachloride. IR spectra were recorded for thin films or KBr disks on a JASCO DS-403G spectrophotometer. GLC was performed on a Shimadzu GC-6A or GC-4CM instrument with a 2 m column packed with 5% PEG-20M or 1.5% OV-17, respectively, on Chromosorb GAW-DMCS, with temperature programming.

Materials. Commercial chromium(VI) trioxide was dried in vacuo. The alcohols used in Entries 1—18, 20, 27, and 31 were also commercially available. The other aromatic *s*-alcohols were synthesized by a reduction of the corresponding ketones, either with $NaBH_4$ in 90% aqueous ethanol, with $LiAlH_4$ in dry ether, or with aluminium isopropoxide in 2-propanol. All of the alcohols were purified by distillation or by recrystallization just before use. "Wet-Alumina" was prepared by rigorous shaking of commercial super-dried aluminium oxide (ICN BIOMEDICALS, Super I; 2 g) with distilled water (0.4 g).

Oxidation Procedures. The following procedures are representative. To a heterogeneous mixture of "wet-Alumina" (2.4 g) and hexane (10 cm^3) chromium(VI) trioxide (twice moles of alcohol) was added by portions with magnetic stirring; the stirring was continued for 10 min. Benzyl alcohol (0.5 g) was then added all at once and the resultant mixture was flushed with argon; the reaction was carried out at ambient temperature with stirring. After a given period, the solution was filtered through a Pyrex Buchner funnel with a fritted disk, and the residue was repeatedly washed with either a solvent or ether. Evaporation of the combined filtrate in vacuo gave benzaldehyde, the identity of which was confirmed by the NMR and IR spectra. A GLC analysis revealed that the compound was of adequate purity (nearly 100%).

When a product was contaminated with a trace of the parent alcohol, the product could be readily purified by either TLC or flush chromatography.

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