CHAPTER III

Silica-Gel Supported Chromic Acid Reagents

SILICA-GEL SUPPORTED CHROMIC ACID REAGENTS

Abstract —— Pyridinium chromate-on-silica gel, and chromic acid-on-silica gel are described and evaluated as convenient off-the-shelf reagents for efficient oxidation of a variety of secondary and primary alcohols. Pyridinium chromate-on-silica gel can be safely used for the oxidation of alcohols containing acid-labile functions.

SILICA-GEL SUPPORTED CHROMIC ACID REAGENTS*

INTRODUCTION

As distinct from reagents covalently linked to an organic polymer[1] or an inorganic support,[2] reagents simply dispersed, adsorbed or intercalated in an inorganic polymer, have come to acquire some importance in recent years. Although this concept is an obvious extension of heterogenous catalysis, and reagents such as sodium-dispersed-on-alumina,[3] N-bromosuccinimide-on-silica[4] were described in the 1950s, there has been a spurt[5] in activity in this area in recent years, possibly due to the recognition of certain novel features of such reaction systems like induced reactivity**[6] and selectivity.[7] This Chapter deals with two reagents, based on chromic acid, for convenient and facile oxidation of primary and secondary alcohols, which is in continuation of the earlier work in the area of organic reactions in a solid matrix.[8]

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**The term induced reactivity is used to describe reactions which normally would not occur or would occur poorly with the same reagent, when the reaction is carried out under the usual solution conditions or without the support.

RESULTS AND DISCUSSION

Pyridinium chromate on silica gel

Sarett *et al.*,[9] in 1953, introduced the use of chromic acid-pyridine complex[10] for oxidation of steroidal secondary alcohols containing acid-sensitive groups. A later modification,[11] using anhydrous chromic acid-pyridine complex in methylene chloride extended its scope to saturated primary alcohols. However, since the preparation of chromic acid-pyridine complex is potentially hazardous, further modifications[12,13] or useful new reagents[14,15] have been introduced. A major drawback of most of these procedures is the relative difficulty in the working up of the reaction mixture where emulsions are often encountered when the final reaction mixture is diluted with water. A solution to this problem[16] has been recently reported[17] by the introduction of chromic acid supported on a macroreticular anion exchange polymer, though the reagent has not been evaluated for alcohols containing acid-sensitive substituents. This is the report of another approach to this problem.

It has been found that pyridinium chromate[*] supported on silica gel and prepared as outlined under Experimental, is a very convenient and effective reagent for the oxidation of allylic and benzylic alcohols, saturated primary and secondary alcohols even when containing acid-sensitive groups such as a cyclopropane ring, or a ketal function (Table 1). The reagent has an excellent shelf-life as no deterioration in its activity was observed even after storage at room temp. for over 1 year. The reaction is easily carried out by stirring and shaking a methylene chloride soln. of the alcohol with 2-4 molar equivalents of the reagent (in terms of CrO_3) and 1-2 molar equivalent of acetic acid, at room temp. (25-35^{o}) for 4-12 hr(Procedure A); the reaction can be expedited (1-3 hr) by replacing methylene chloride with benzene and carrying out the reaction at reflux (Procedure B). Work-up of the reaction mixture is simple and is outlined under Experimental. No attempt was made to optimise the yields, as given in Table 1.

Since, oxidation of 1-decanol to 1-decanal has somehow

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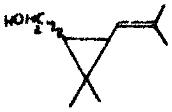
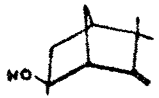
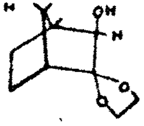
[*] From the amount of pyridine taken up by chromic acid supported on silica gel, it is clear that the salt contains pyridine and chromic acid in an approx. ratio of 1:1 and hence the reagent is considered to be essentially $C_5H_5NH_2CrO_4$ (CrO_3+H_2O+C_5H_5N; 1:1:1).

Table 1. Oxidation of alcohols with pyridinium chromate on silica gel

No	Substrate	CrO_3/substrate ratio (molar)	% Yield[a] (reaction time, hr)	
			Procedure A	Procedure B
1	Geraniol	2.0	92 (4)	83 (1)
2	Farnesol	2.0	74 (4)	78 (1)
3	Phytol	2.0	86 (4)	-
4	Cinnamyl alcohol	2.0	87 (4)	87 (1)
5	Benzyl alcohol	2.0	82 (4)	76 (1)
6	1-Decanol	2.0	67 (4)	-
7	Cyclohexanol	2.0	64 (9)	76 (3)
8	trans-Myrtanol 	2.0	80 (6)	-
9	Citronellol	2.0	69 (9)	67 (1)
10	Isopulegol	3.0	70 (12)	82 (3)
11	 (Chrysanthemol; trans/cis = 3)	2.0	75 (6)	62 (2)
12		3.8	74 (8)	71 (3)
13		2.0	56 (6)	65 (2)

[a] Corrected for 100% carbonyl content. Oxidations were run on a 1-5 mmole scale except for compound 13 which was oxidised using 0.25 mmole of the compound.

come to be used[11b,13,15] for assessing the relative merits of different varients of pyridine-chromic acid reagent, an oxidation of 1-decanol on 0.1 mole scale, using the new supported reagent was carried out to get the aldehyde in 67% yield, which compares well with results obtained by other reagents.

Sodium dichromate-aqueous sulphuric acid on silica gel

One of the simplest and most convenient methods for the oxidation of secondary alcohols to ketones is their oxidation in a two-phase system[18] by an acidic aqueous soln of chromic acid. The above results with pyridinium chromate-on-silica gel and especially the convenience of a reagent ready for use and the ease of work-up, prompted us to investigate the behaviour of a similarly supported reagent based on acidic aqueous chromic acid.

Although in two-phase oxidation systems, stoichiometric amounts of chromic acid (0.33 mole of $Na_2Cr_2O_7.2H_2O$ for 1.00 mole of the secondary alcohol) have been used with excellent results,[18e] it was necessary for us to determine first the molar equivalence of the reagent for complete conversion to the ketone, as conceivably some amount of the reagent may not be available for oxidation, because of location at sites, in the silica gel matrix, which may be inaccessible to the alcohol. Table 2 summarises the results of such a study: (-)-menthol was used as a convenient[18e] substrate and an arbitrarily chosen ratio of $Na_2Cr_2O_7.2H_2O$ to silica gel of 1:20 was employed; the reaction was carried out in ether at 25^o with stirring, and was monitored after various intervals by glc. From the results it is obvious that at least 0.8 mole equivalent of chromic acid per mole of menthol is needed for complete conversion in a reasonable time. To be sure that in Expt. No. 4 conversion after 90 min was indeed 94% and this figure is not due to any preferential retention of the alcohol (as the chromate ester?) in the silica gel matrix, in a separate duplicate experiment the reaction mixture was worked up just after 90 min to get a product (recovery on weight basis: 95%) shown by glc to be 94% menthone.

Next, it was considered desirable to reduce the silica gel/$Na_2Cr_2O_4.2H_2O$ ratio to an optimal level consistent with the need to avoid unnecessarily large volumes of the reagent (and hence of the solvent), while loading the support to a point that would not make additional amounts of the oxidant inaccessible to the substrate. Table 3 depicts the results of such a study, again using (-)-menthol as the substrate. It should be noted that the various reagent preparation (Table 3), besides varying in the silica gel/chromic acid ratio, would also vary in the water content, as with higher amounts of $Na_2Cr_2O_7.2H_2O/H_2SO_4$, the quantity of water ultimately retained by the reagent would have to be reduced to get the reagent in a free-flowing form. From the results shown in Table 3 it is clear that preparation No. 4 should be the reagent of choice.

This preparation of the reagent was next evaluated on a number of different alcohols and the results have been uniformly good (Table 4). It may be noted that during the oxidation of 2-methyloentan-2,4-diol, elimination of hydroxyl in the resulting β-hydroxyketone did not occur under the reaction conditions. Finally, the reagent was evaluated on a 0.1 molar scale by oxidation of (-)-menthol: the product which was obtained in 98.4% yield was completely devoid of any isomenthone[19] or unchanged menthol.

Oxidations with these two reagents were also carried out by packing the reagent in a chromatographic column and letting the substrate in a suitable solvent stand in contact with the reagent for an appropriate period and then finally

Table 2. Oxidation of (-)-menthol[a] at 25° by various molar equivalents of sodium dichromate - aqueous sulphuric acid supported on silica gel[b]

No.	Mole equivalents of $Na_2Cr_2O_7 \cdot 2H_2O$ per one mole of alc.	% Menthone (GLC) -reaction time in minutes- 15	30	60	90	120	% total recovery[c] (w/w)
1	0.33	54	57.5	60	61.5	63	97
2	0.40	62	68.5	69.5	71.5	73	96
3	0.60	78.5	79	82.5	85	86.5	97
4	0.80	85	88.5	92.5	94	94	94

[a] Reaction on a 5 mmole scale (details: vide experimental)

[b] 1 g of supported reagent ≡ 0.0379 g of $Na_2Cr_2O_7 \cdot 2H_2O$

≡ 0.127 mmole of $Na_2Cr_2O_7 \cdot 2H_2O$

[c] Total distilled product after 2 hr reaction period, after applying correction for samples withdrawn at different intervals.

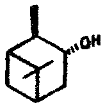
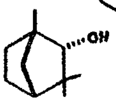
Table 3. Oxidation of (-)-menthol[a] at 25° by 0.8 mole equivalent of chromic acid supported on different amounts of silica gel.

Prep. No.	Silica gel/ $Na_2Cr_2O_7.2H_2O$ ratio	% Menthone (GLC) — reaction time in minutes 30	60	90	120	% Total recovery[b] (w/w)
1	20	90	91.5	93	94	95
2	15	100	-	-	-	96
3	10	100	-	-	-	96.5
4	5	100	-	-	-	96

[a] Reaction on a 5 mmole scale

[b] Total distilled product after 2 hr reaction period, after applying correction for samples withdrawn.

Table 4. Oxidation of some secondary alcohols by chromic acid supported on silica gel[a]

No	Substrate	Reaction time (hr)	Product recovery (w/w%)	Ketone purity by GLC (%)	Yield (%)
1	Cyclopentanol	1	93	100	93
2	Cyclohexanol	1	95	100	95
3	Cycloheptanol	1	98	100	98
4	2-Methylcyclohexanol	1	94	100	94
5	(-)-Menthol	1	98	100	98
6	Isopinocampheol 	1	98	100	98
7	α-Fenchol 	1	98	100	98
8	2-Octanol	1	97	100	97
9	2-Methylpentan-2,4-diol	1	95	100	95
10	Isopulegol	1	97	77[b]	75
		12	97	90[b]	87

[a] All oxidations using 5 mmoles of the alcohol and CrO_3/substrate molar ratio of 0.8

[b] Balance material is unreacted starting alcohol

eluting the product. This procedure is quite convenient for oxidations on a micro level and yields are comparable to those obtained by the stirring/shaking procedures. Details of one such experiment are given in the Experimental.

In view of the results obtained, the two reagents should prove useful, especially because of the convenience of a ready-for-use reagent and exceptional ease of work-up.*

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*While this manuscript was under preparation, a report describing oxidations with chromic acid absorbed on silica gel appeared.[20] These authors prepared the reagent in a different manner and their preparation has to be stored in the dark under vacuum and must be used within a week. In contrast, the preparation described here was equally active even after 1 year's storage under ordinary conditions.

EXPERIMENTAL

The following instruments were used for spectral/analytical data: Perkin-Elmer Infracord model 267; Perkin-Elmer model R32 (90 MHz) NMR spectrometer; Hewlett-Packard 5712A and 762A gas chromatographs (Al columns, 360 x 0.6 cm; support, 60-80 mesh Chromosorb W; stationary phase, 10% Carbowax 20M; carrier gas, H_2).

All reaction products described in this communication are known compounds. These compounds were distilled, purity checked by GLC and their identification established by IR and PMR.

Materials

Silica gel. The material, as supplied by Beechems, Kanpur, was sieved and the fraction -80, +200 mesh employed as the support. This material had bulk density 0.71g/ml.

Chromium trioxide, sodium dichromate dihydrate, sulphuric acid (97-99%), were all laboratory reagent grade and were supplied by Sarabhai M. Chemicals, Baroda.

Pyridine, commercial grade (Koch-Light and Co., London) was distilled over $Ba(OH)_2$ and stored over KOH pellets.

Light petroleum refers to the fraction, b.p. 60-80^0.

All other solvents were reagent grade.

Preparation of reagents

(i) Pyridinium chromate on silica gel. To a soln. of CrO_3 (50.0g; 0.5 mole) in water (300 ml), silica gel (250 g) was added and the mixture shaken mechanically for 1 hr at room temp. (30-35^0). After this, the excess water was removed on a rotary evaporator (~90^0/80 mm, 2 hr) to get 312 g of a yellow-orange free-flowing powder.

The above material (312 g) was placed in a three-necked flask and covered with light petroleum (600 ml). The mixture was cooled to 20^0 and 79.0 g (1.0 mole) pyridine was slowly introduced with stirring under anhydrous conditions, while maintaining the temp. between 20-24^0(30 min). The mixture was stirred for an additional one hr, filtered and the solid washed with light petroleum (300 ml x 2) and dried by suction to get a dark brown free-flowing powder (358 g), which was stored in a brown bottle. Analysis[21] of the total filtrate and washings for pyridine showed that the reagent has retained 45.89 g (0.58 mole) of pyridine. One gm of this preparation is equivalent to 0.0196 g of CrO_3 ($\equiv$1.396 mmole of CrO_3).

(ii) Sodium dichromate - aq sulphuric acid on silica gel.

To a soln of $Na_2Cr_2O_7$-$2H_2O$ (40 g, 0.134 mole) in water (240 ml) and sulphuric acid (97%, 30 ml), silica gel (200 g) was added and the mixture mechanically shaken for 1 hr at room temp. Excess water was then removed on a rotary evaporator ($\sim 90^\circ$/80-90 mm) to get 316 g of the supported reagent as a yellow-brown free-flowing powder, which was stored in a dark bottle at room temp. One gm of this reagent $\equiv$ 0.1263 g of $Na_2Cr_2O_7 \cdot 2H_2O$ $\equiv$ 0.424 mmole of $Na_2Cr_2O_7 \cdot 2H_2O$.

All other variants of this preparation (Tables 2,3) were prepared in a like manner, by varying the amount of silica gel and removing water to a level to get a free-flowing material.

Oxidations with pyridinium chromate-silica gel.

(i) General procedure (Procedure A). This is illustrated by the following oxidation of geraniol to geranial (citral). To a soln. of geraniol (770 mg, 5 mmole) in methylene chloride (7.5 ml), 7.2 g($\equiv$ 10 mmole of CrO_3 of pyridinium chromate-silica gel and 0.24 g (4 mmole) of acetic acid were added and the mixture mechanically shaken for 4 hr at room temp (30-35°). At the end of this period, ether (15 ml) was introduced and after shaking for another 2 min, filtered and the solids washed with ether (9 ml x 4). The combined filtrate was washed successively with 5% HCl aq (8 ml), water (5 ml x 2), 5% $NaHCO_3$ aq (8 ml), water (8 ml x 2) and brine (5 ml). The solvent layer was then passed through a small bed (0.8 cm x 4 cm) of alumina (Brockmann grade II), which was washed with ether (10 ml). From the combined filtrates, solvent was stripped off and the residue distilled to furnish 0.678 g of citral (GLC purity, 98.5%), b.p. 125^o(Bath)/ 10 mm.

(Procedure B). A mixture of geraniol (385 mg, 2.5 mmole), benzene (7 ml), acetic acid (0.125 g) and the supported reagent (3.6 g, $\equiv$ 5 mmoles of CrO_3) was refluxed (1 hr) and then worked up as detailed above to furnish 0318g (83%) of citral.

(ii) 0.1 Molar oxidation of 1-decanol. 1-Decanol (15.8 g, 0.1 mole) in methylene chloride (150 ml) and acetic acid (3.57 g) was stirred with the reagent (144 g, $\equiv$ 0.2 mole of CrO_3) at room temp ($25-27^o$) for 4 hr, and then worked up with ether (300 ml) as above. The final organic soln. was filtered through a column of alumina (grade II; 1 cm x 10 cm), which was then washed with ether (10 ml x 2). The combined filtrate and washings were freed of solvent and the crude product (14.6 g) distilled to furnish a liquid (13.9 g), b.p. 98-120°/15 mm, shown by GLC to contain 76% 1-decanal, besides unchanged starting alcohol. Separation was not carried out.

(iii) Oxidation using a column. Pyridinium chromate-silica gel (7.2 g) was loaded in a column to get a 1 cm x 10 cm bed. A soln of geraniol (770 mg) in methylene chloride (4 ml) and 0.25 ml of acetic acid was allowed to percolate through the column till it just reached the end of the bed and then closed at both ends and left aside as such for 20 hr (room temp. 20-25°). At the end of this period, the soln. was allowed to flow through and the column washed with ether (40 ml) and the material worked up as described earlier to get geranial in a yield of 85%.

Oxidations with sodium dichromate-aq. sulphuric acid on silica gel

(i) General procedure. The following oxidation of (-)-menthol to menthone is illustrative. A soln. of menthol (780 mg, 5 mmole) in ether (40 ml) was cooled to 12 ± 2° and the reagent (9.5 g, $\equiv$ 1.2 g $\equiv$ 4.02 mmole of $Na_2Cr_2O_7.2H_2O$) added in one lot with stirring. The reaction mixture was allowed to attain room temp. (~25^{0}) and then stirred for 1 hr at this temp. TLC (solvent: 10% EtOAc in benzene) indicated no starting material at this stage and hence, the reaction mixture was filtered and the solids washed with ether (10 ml x 5). The combined filtrate and washings were passed through a small bed (0.8 cm x 4 cm) of alumina (Brockman grade II), which was washed with ether (5 ml). The total soln. was freed of solvent and the residue distilled: b.p. 110^{0}(bath)/10 mm, yield 764 mg (98%); GLC indicated $>$99% menthone and the remaining isomenthone.

(ii) 0.1 Molar oxidation of (-)-menthol. (-)-Menthol (15.6 g, 0.1 mole) in ether (800 ml) was oxidised by the reagent (190 g, $\equiv$ 0.08 mole of $Na_2Cr_2O_7 \cdot 2H_2O$) during 1 hr at ~25^{0} as above and the reaction mixture worked up exactly as detailed earlier to furnish 15.5 g of the crude product. This was distilled to get a liquid (15.3 g; 98.4%), b.p. 88^{0}C/10 mm, shown by GLC to be menthone containing $<$ 1% isomenthone.

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