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SYNTHESIS OF UNSATURATED CARBONYL COMPOUNDS VIA A CHROMIUM-MEDIATED ALLYLIC OXIDATION BY 70% TERT.BUTYLHYDROPEROXIDE

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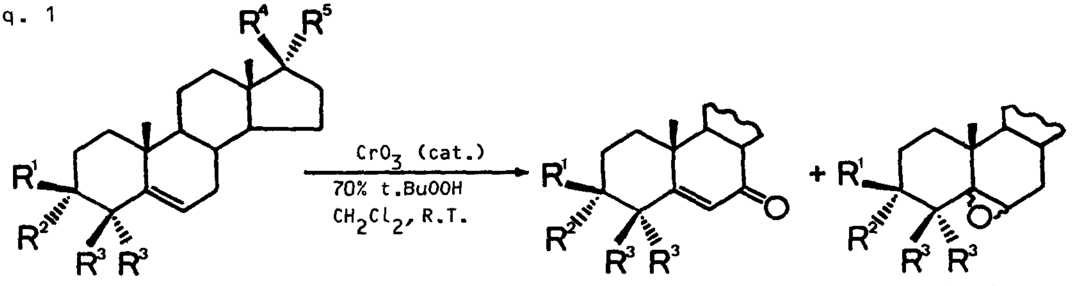
***Summary** : Alkenes were converted into α , β -unsaturated carbonyl compounds using excess of tert.butylhydroperoxide and catalytic amounts of chromium^{VI} oxide at room temperature. Fair yields and conversions were obtained from Δ^5-steroids while allylic oxidation of acyclic alkenes was less efficient. Epoxidation of the double bond, sometimes observed, remained a minor reaction pathway.*

Allylic oxidation of cycloalkenes into enones represents a stimulating challenge since efficient catalytic methods are uncommon (1). Large excess over stoichiometry of chromium^{VI} oxide or related high oxidation state chromium species are most frequently used (1-4) ; these procedures led to considerable amounts of tarry chromium residues which are environmentally hazardous and often provide trouble in carrying out the work-up.

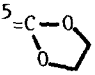
For a few years, we have been concerned by allylic oxidation of alkenes (5, 6) and in this paper, we present a new catalytic method using inexpensive commercial reagents: CrO_3 and aqueous 70% t.BuOOH in CH_2Cl_2 (eq. 1-4). Recently, the same system was employed to catalytically oxidise alcohols and benzylic methylene groups into ketones (7).

Eq. 1



1 2 (major) 3 (minor)

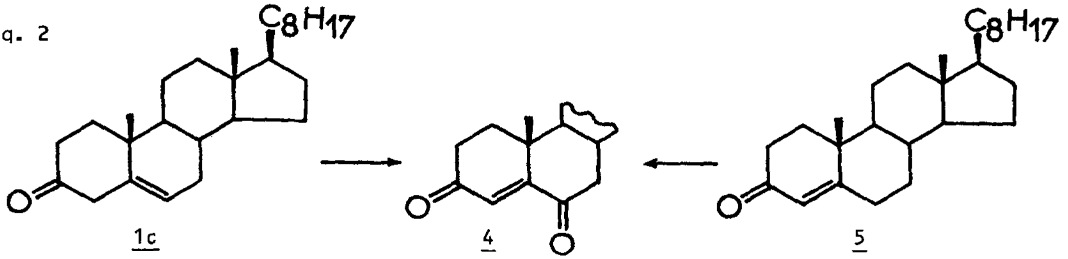
a : R^1=OAc. R^2,R^3,R^5=H. $R^4=C_8H_{17}$
b : R^1=OCOPh. R^2,R^3,R^5=H. $R^4=C_8H_{17}$
c : CR^1R^2=CO. R^3,R^5=H. $R^4=C_8H_{17}$
d : R^1=OCOPh. R^2,R^5=H. $R^3=CH_3$. $R^4=C_8H_{17}$
e : CR^1R^2=CO. $R^3=CH_3$. $R^4=C_8H_{17}$.R^5=H
f : R^1=OAc. R^2,R^3=H. CR^4R^5=CO
g : R^1=OAc. R^2,R^3=H. CR^4R^5=C



In a preliminary experiment (table, run 1), 70% t.BuOOH (0.5 ml, 3.5 mmol) was added to methylene chloride (2 ml) containing CrO_3 (2.5 mg, 0.025 mmol) then, a solution of 3β-acetoxy-5-cholestene 1a (214 mg, 0.5 mmol) was introduced at once. Stirring was maintained at room temperature during 5.5 h. The mixture was filtered through a pad of alumina (8) and evaporated under reduced pressure. T.L.C. using 10% of ethyl acetate in petroleum ether as eluent afforded starting alkene 1a (33 mg, 15%), corresponding epoxides 3a (45 mg, 20%, $\alpha/\beta \simeq 0.6$) and 3β-acetoxy-5-cholesten-7-one 2a (103 mg, 46%). Increasing the amount of catalyst to 0.1 equiv. led to close yields (run 2) while use of 0.4 equiv. of CrO_3 inhibited the formation of epoxides (run 3).

To replace the acetoxy group in C-3 position by a benzyloxy group gave similar compounds (run 4) but the presence of a keto group in C-3 induced migration of the Δ^5-double bond with formation of 4-cholesten-3,6-dione 4 (run 5). This γ-diketone was also produced from 4-cholesten-3-one (run 10, eq. 2).

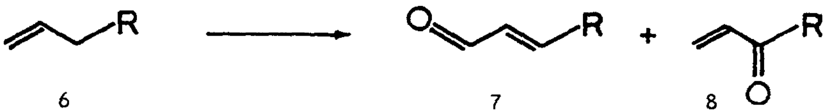
Eq. 2



Disubstitution of the methylene in C-4 position led to better yields in α,β-enones and lower quantities of epoxides (runs 6, 7). 3β-Acetoxy-5-androsten-17-one 1f and its ketal derivative 1g were principally oxidised into the expected enones 2f and 2g (runs 8, 9).

In contrast with unsaturated steroids, oxidation of acyclic alkenes by CrO_3-t.BuOOH gave poor yields in conjugated carbonyl compounds (runs 11, 12, eq. 3). Oxidation of 1-eicosene 6 gave partial conversion of the starting material and a mixture of products from which small quantities of enal 7 and enone 8 were isolated (run 11). Full conversion of allylbenzene was observed under similar conditions but the selectivity of this oxidation remains low (run 12). Such difference between polycylic and aliphatic alkenes vis a vis to efficiency of their allylic oxidation has been precedently reported, particulary when chromium ^{VI} derivatives were used as oxidants (1,2).

Eq. 3



R = $C_{17}H_{35}$:	6	7	8
R = Ph :	9	10	11

Yields of enones obtained by the catalytic method described herein are often lower than those reported in using the traditional chromium methods (1-4, 11) but formation, with our system, of minute amounts of chromium residues easily removed from the reaction mixture, must be taken in account. Comparison could also be made with the efficient allylic oxidation of cycloalkenes carried out with $Cr(CO)_6$ associated to 90% t.BuOOH (12). However, this procedure requires prolonged heating at 80-85°C and uses generally 0.25-0.5 equiv. of the relatively expensive and toxic chromium hexacarbonyl (13). Otherwise, mechanisms involved with CrO_3 or $Cr(CO)_6$ as catalysts are probably differents : chromium^{VI} peroxo species formed *in situ* seem to participate in the oxidation process with the former (7, 14) while the formal oxidation state Cr° would be maintained with the latter (12, 15).

Table : Oxidations by CrO_3 (0.05-0.4 equiv.) and 70% t.BuOOH (7 equiv.) in CH_2Cl_2 at room temperature

Run	Starting material	CrO_3 Equiv.	Time h	Isolated products, % yields[a]		
				S.M.	enone	epoxide[b]
1	1a	0.05	5.5	1a : 15	2a : 46	3a : 20
2		0.1	4	18	40	15
3		0.4	5.5	20	44	<2
4	1b	0.05	14	1b : 20	2b : 49	3b : 14
5	1c	0.05	14	1c : 6[c]	4 : 46	
6	1d	0.05	13.5	1d : 15	2d : 59	3d : <5
7	1e	0.05	16	1e : 21	2e : 61	3e : <5
8	1f	0.05	24	1f : 0	2f : 52	3f : 8
9	1g	0.05	13	1g : 30	2g : 32	3g : 11
10	5	0.05	14	5 : 64	4 : 25	
11	6	0.05	13	6 : 47	7 : 3 8 : 12	
12	9	0.05	15.5	9 : 0	10 : 14 11 : 11	

a) Yields were calculated on the quantity of starting material (S.M.) introduced. b) a mixture of α- and β-epoxides was generally obtained. c) traces of 4-cholesten-3-one were also observed.

Formation of epoxides as side reaction of cycloalkenes in the presence of CrO_3-t.BuOOH is not surprising ; in fact, such byproducts have been previously observed in oxidations with oxochromium reagents (1,2,16) and furthermore, metals catalyse epoxidation of olefins by hydroperoxides (9, 16-18).

In conclusion, we think that the Cr^{VI}-catalysed allylic oxidation presented in this paper is a useful method in terms of cost of reagents, operational simplicity and yields ; further investigations of the reaction conditions will undoubtedly lead to its improvement (19).

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