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OXIDATION OF ALKENES TO ENONES USING tert-BUTYL HYDROPEROXIDE IN THE PRESENCE OF CHROMIUM CARBONYL CATALYSTS

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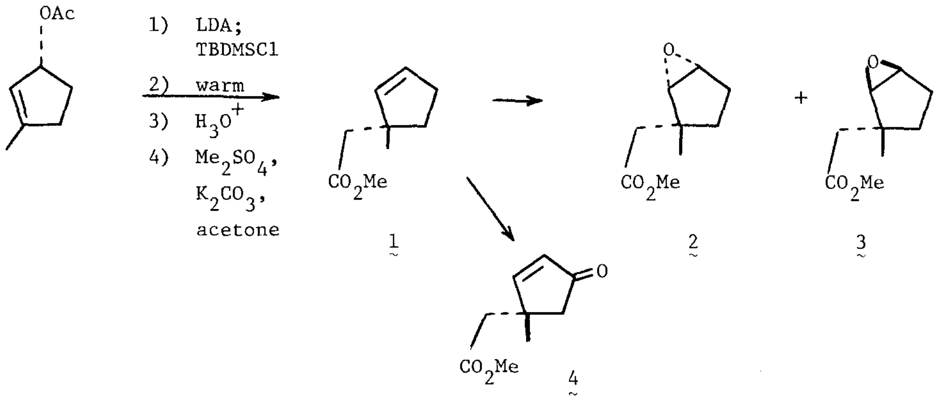
Abstract. Treatment of alkenes with t-butyl hydroperoxide in the presence of $Cr(CO)_6$ or $Cr(CO)_x(CH_3CN)_y$ species results in oxidation of allylic methylene groups to give α,β-unsaturated ketones, selectively in the presence of certain alcohols, and in moderate to excellent yields.

Oxidation of alkenes to epoxides,[1] diols,[2] allylic alcohols,[3] and α,β-unsaturated ketones,[4] forms a major part of modern synthetic method. Allylic oxidation to give enones is an extremely useful transformation, but currently available methods are inconvenient, and do not allow selective allylic methylene oxidation in the presence of, e.g. secondary alcohols.

During the course of another investigation, we had occasion to study the epoxidation of the unsaturated ester 1, readily prepared from 3-methyl-2-cyclopentenyl acetate via Ireland-Claisen rearrangement.[5]



Treatment of 1 with m-chloroperbenzoic acid (1.2 equiv., CH_2Cl_2, Na_2HPO_4, 20°C, 15h) gave a mixture[6] of α- and β-epoxides 2 and 3 in a ratio of 1.5:1. On the other hand, iodohydrin formation (N-iodosuccinimide, DMSO,H_2O[7]), followed by base treatment (DBU, CH_2Cl_2, 20° C, 1h) gave a 1:1.9 mixture of 2 and 3. In an attempt to improve this ratio in favour of 3 we subjected 1 to epoxidation using t-BuOOH in the presence of $Mo(CO)_6$ catalyst (benzene, reflux, 15h) which surprisingly, gave a 5:1 mixture of 2 and 3. Use of freshly prepared $Mo(CO)_3(CH_3CN)_3$[8] as catalyst gave a similar mixture, but when an aged sample of $Mo(CO)_3(CH_3CN)_3$ was employed, we observed appreciable formation of enone 4. Use of a $Mo(CO)_x(CH_3CN)_y$ catalyst prepared by prolonged boiling of $Mo(CO)_6$ in acetonitrile, and containing appreciable amounts of $Mo(CO)_2(CH_3CN)_4$[8], we were able to produce enone 4 as the major product in this reaction, but this required extended reaction times (ca. 38h).

We next turned our attention to the use of previously untested chromium carbonyls as catalysts in the above reactions. Treatment of 1 with t-BuOOH in refluent benzene, under N_2 atmosphere, and in the presence of a catalytic amount of $Cr(CO)_6$ (0.05 equiv.) gave a mixture containing 75% of enone 4 and 25% of epoxides 2 and 3 (ratio not determined) in a combined yield of ca. 98%. Use of 0.5 equiv. of $Cr(CO)_6$ allowed use of shorter reaction times but did not affect the product ratio. Bearing in mind the above observations with $Mo(CO)_x(CH_3CN_3)$ catalysts, we performed the oxidation in boiling acetonitrile, which produces $Cr(CO)_3(CH_3CN)_3$ *in situ*,[10] and obtained exclusively the enone 4 in 83% yield after purification by flash chromatography. No epoxides were detected in the 200 MHz NMR spectrum of crude product.

Several other alkenes have been tested in this reaction, as summarized in the Table. All oxidations are moderately superior in yield to the more traditional methods, are very much more convenient in terms of work-up procedure, and utilize a small excess of oxidant, allowing potentially greater selectivity and ready adaptation to large scale work. Of particular interest is entry 8 (Table) which shows that the alkene to enone oxidation can be performed selectively in the presence of *certain* secondary alcohols. It may be noted that the oxidation of cyclohexanol to cyclohexanone is quite sluggish under these conditions, whereas treatment of compound 5 with excess Collins reagent caused rapid oxidation of the alcohol to ketone, with very little allylic oxidation even after prolonged reaction.

The mechanism of this interesting reaction remains to be explored. However, in view of the selectivity during oxidation of 5, it is unlikely that catalytic amounts of chromium oxides are responsible for the oxidation. Further support for this comes from the following observations: (a) IR spectra of reaction mixtures indicate no loss of $Cr(CO)_x(CH_3CN)_y$ or $Cr(CO)_6$ (Table, entry 1) throughout the reaction; (b) the catalyst may be recovered almost quantitatively after completion; (c) addition of t-BuOOH to a catalytic amount of CrO_3 in benzene gives a deep blood-red solution, whereas the chromium carbonyl - t-BuOOH mixtures are yellow-orange throughout the oxidation.

Typical Procedure: Oxidation of cholesteryl acetate

To a suspension of cholesteryl acetate (1.0 g, 2.33 mmole) in acetonitrile (10 ml) was added chromium hexacarbonyl (0.26 g, 1.17 mmole), followed by 90% t-butyl hydroperoxide (0.7 ml). The reaction mixture was boiled gently under reflux and under N_2 atmosphere for 15 h, cooled to room temperature, then filtered. The filtrate was diluted with ether (100 ml), washed with water (3 x 20 ml) and saturated brine (2 x 10 ml) and dried ($MgSO_4$). The solvent was evaporated and the residue was subjected to flash chromatography (20% ethyl acetate in hexane) to yield the enone (0.82 g, 80%) as a white solid, m.p. 153-154°C (lit.[11] m.p., 155-156°C).

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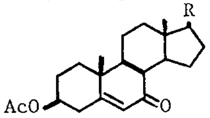
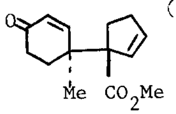
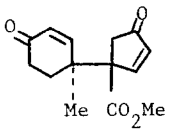
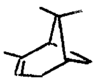
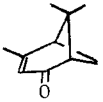
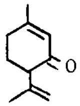
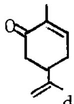
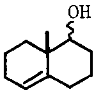
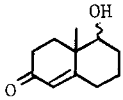
TABLE

Chromium Carbonyl-catalyzed Oxidation of Alkenes to Enones

Entry	Starting Material (% recovered)	$Cr(CO)_6$ (equiv.)	t-BuOOH (equiv.)	Reaction Time (h)	Products (Yield, %)^a
(1)	1 (0)	0.05	1.2	38	4 (75)^{b,c}
	1 (0)	0.50	1.2	18	4 (78)^{b,c}
	1 (0)	0.50	1.2	18	4 (83)
(2)	Cycloheptene^e (12)	0.50	2.0	18	cycloheptenone (30)^b
	Cycloheptene (5)	0.50	2.0	15	cycloheptenone (23)^d
(3)	Cholesteryl acetate (0)	0.50	3.0	20	 (80)^b
	" (0)	0.50	3.0	15	(80)^d
	" (0)	16.2 equiv.	CrO_3.Py.	24	(74)^f
(4)	 (g) (45)	0.50	2.0	39	 (55)^b
	" (25)	0.50	2.0	22	(60)^d
(5)	 (h) (11)	0.50	3.0	24	 (54)^b
	(24)	0.50	3.0	18	(65)^d
	(19)	6.8 equiv.	CrO_3.py.	24	(48)^f
(6)	 (48)	0.50	2.0	18	 (26)  (39)^d
	(16)	16.5 equiv.	CrO_3.Py.	24	(31) (36)^f
(7)	Cyclohexanol (0)	0.20	3.0	15	Cyclohexanone (51)^e
(8)	 (i) 5 (0)	0.5	1.2	12	 (60)^d

a) Yield based on recovered starting material; b) in benzene solvent; c) Epoxides 2 & 3 (25%) were also formed; d) in acetonitrile solvent; e) Technical grade from Aldrich Chemical Co. was used without further purification; f) From: W. G. Dauben, M. Lorber and D. S. Fullerton, J. Org. Chem., 1969, 34, 3587; g) Prepared using cyclohexadienyl-$Fe(CO)_3$ complexes, details of which will be given elsewhere; for related compounds see: A. J. Pearson and C. W. Ong., J. Am. Chem. Soc., 1981, 103, 6686; h) α-Pinene from Aldrich Chemical Co. was used without further purification; i) Prepared as a mixture of epimers from 9-methyl-$\Delta^{5(10)}$octaline-1,6-dione in two steps: (1) $NaBH_4$, EtOH; (2) $LiAlH_4$, $AlCl_3$, THF.

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3. See, for example: J. P. Schaefer, B. Horvath, and H. P. Klein, J. Org. Chem., 1968, 33, 2647; E. N. Trachtenberg and J. R. Carver, ibid., 1970, 35, 1646; E. N. Trachtenberg, C. H. Nelson, and J. R. Carver, ibid., 1970, 35, 1653; N. Rabjohn, Org. Reactions, 1976, 24, 261. Also ref. 4, pp. 335-348.
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5. See for example: R. E. Ireland and J. P. Daub, J. Org. Chem., 1981, 46, 479; R. E. Ireland and J. P. Vevert, ibid., 1980, 45, 4260.
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