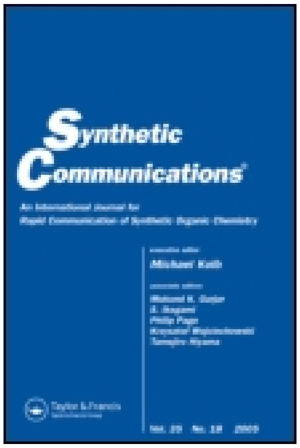

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Alkene and Alkyne Oxidative Cleavage Catalyzed by RuO_4 in Environmentally Acceptable Solvents

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ABSTRACT

The application of CCl_4, C_6H_{12}, EtOAc, and Me_2CO as solvents for biphasic systems has been compared for oxidative cleavage of alkenes and alkynes by RuO_4 to carboxylic acids, using the $RuCl_3 \cdot nH_2O$–$IO(OH)_5$ reagent for which an improved procedure is described. Cyclohexane is an effective and economic replacement for the environmentally unfriendly CCl_4; acetone and ethyl acetate are less effective.

Key Words: Alkenes; Alkynes; Carbon tetrachloride; Cyclohexane; Ruthenium tetroxide.

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Ruthenium tetroxide (RuO_4) is used in organic synthesis principally for oxidative alkene and alkyne cleavage and for the oxidation of secondary alcohol functions in sugars.[1,2] Since it is toxic and volatile it is usually made in situ from $RuCl_3 \cdot nH_2O$ or $RuO_2 \cdot nH_2O$ with a cooxidant, normally sodium periodate, $NaIO_4$.[3] A biphasic system is often used: $RuCl_3 \cdot nH_2O$ or $RuO_2 \cdot nH_2O$ is reacted with $NaIO_4$ in water and the RuO_4 is extracted into CCl_4, currently the most commonly used solvent for such oxidations. The efficiency of such systems is improved by addition of a little CH_3CN.[4]

The use of carbon tetrachloride (CTC) as a solvent is becoming increasingly untenable owing to CFC regulations.[5] There is therefore a real need for an acceptable organic solvent for such reactions, one in which RuO_4 is soluble but not attacked by it. There are few such solvents because RuO_4 is so reactive, but attempts have been reported using materials other than CCl_4, principally acetone[6,7] or ethyl acetate.[8,9] Dichloromethane, chloroform, and acetone are inferior to CCl_4 for RuO_4-catalysed oxidations of hydrobenzoin and sugars;[10] 1,2-dichloroethane has recently been used for oxidation of alkenes to aldehydes using $RuCl_3 \cdot nH_2O/NaIO_4$.[11]

We have shown that $RuCl_3 \cdot nH_2O$ with periodic acid, $IO(OH)_5$ as cooxidant, generating RuO_4 in situ, is effective for the oxidative cleavage of alkenes and alkynes to carboxylic acids.[12] Here we describe an improved procedure for using this reagent, and show that it may effectively be used with the more eco-friendly and much cheaper cyclohexane replacing CCl_4 as the organic solvent.

RESULTS AND DISCUSSION

In our method[12] we used $RuCl_3 \cdot nH_2O$ and $IO(OH)_5$ in CCl_4–CH_3CN–H_2O, extracting the products with dichloromethane. We find that better results are achieved by using diethyl ether as the extractant (see Table 1); Nuñez and Martín[13] used a similar method for oxidizing 1-hexene to pentanoic acid.

Use of Various Solvents

CCl_4

This is currently the solvent of choice for most RuO_4-catalyzed oxidations. In the table oxidations of alkenes, alkynes, and hydrobenzoin using AnalaR CCl_4 are reported. For such oxidations, addition of

Table 1. Oxidation of alkenes and alkynes to carboxylic acids with RuO_4 generated from $RuCl_3{\cdot}nH_2O$-$IO(OH)_5$ in various solvents.

		Solvent				
Substrate	Product	CCl_4	C_6H_{12}	EtOAc	Me_2CO	Time/h
Styrene	Benzoic acid	84 [14]*	72 [15]	81 [15]	10 [2]	1
cis-Cyclooctene	Suberic acid	83 [15]	97 [18]	92 [15]	78 [13]	1.5
Cycloheptene	Pimelic acid	72 [16]	77 [15]	57 [12]	59 [12]	2
Cyclohexene	Adipic acid	84 [18]	74 [19]	83 [21]	31 [7]	1.5
Cyclopentene	Glutaric acid	66 [20]	67 [18]	–	–	2
1-Dodecene	Undecanoic acid	58 [7]	58 [7]	64 [7]	–	2
Phenylacetylene	Benzoic acid	90 [17]	86 [15]	43 [9]	53 [11]	2
Diphenylacetylene	Benzoic acid	76 [17]	80 [18]	72 [15]	66 [13]	2
Hydrobenzoin	Benzoic acid	86 [15]	88 [15]	47 [8]	80 [13]	0.5

*TO = turnover (moles of product/moles catalyst).

CH_3CN is desirable:[4] in its absence the yield of benzoic acid from styrene, for example, dropped from 84% in 1 h to 14% in 3 h. AnalaR or Spectrosol[15] CCl_4 must be used since impurities rapidly degrade RuO_4. The sensitivity of even AnalaR CCl_4 to RuO_4 is shown by our electronic spectra: RuO_4 extracted into it showed the two typical peaks of the tetroxide[14] at 310 and 385 nm for only 30 min, by which time the solution had perceptibly darkened, due to traces of oxidizable material in the solvent.

Cyclohexane

There has been no reported systematic study on the use of cyclohexane as a solvent for oxidations with RuO_4. In the table we show its utility as a replacement for CCl_4 in a 1:1:2 C_6H_{12}:CH_3CN:H_2O mixture. Being less dense than water, C_6H_{12} forms the upper layer of the biphasic system, but this presents no practical problems. Oxidations using HPLC grade (99.9%+) C_6H_{12} gave essentially the same yields and turnovers as normal grade C_6H_{12}, so specially purified cyclohexane is not needed. As with CCl_4, CH_3CN enhances the yield: for oxidation of styrene to benzoic acid the yield of the latter dropped from 72% in 1 h to 12% in 2 h in the absence of CH_3CN.

Electronic spectra of RuO_4 extracted into C_6H_{12} showed the tetroxide peaks centered on 312 and 382 nm with attendant fine structure;

Raman spectra also show the presence of RuO_4 by the appearance[12] of the 881 cm^{-1} $\nu_s(Ru{=}O)$ peak. After 30 min there is only a slight darkening of the solution; there was essentially no difference if 99.9 + % HPLC-grade solvent was used.

Ethyl Acetate

Ethyl acetate has been used with RuO_4 for oxidations of 1,6-dienes to *trans*-2,6-bis(hydroxymethyl)-tetrahydropyrandiols[8] and of cyclic α-amino acids to α-aminodicarboxylic acids.[9] Like cyclohexane EtOAc is less dense than water and so lies above the aqueous layer. For oxidative cleavage we find that yields are lower than those obtained from CCl_4 and C_6H_{12}, although use of high-purity HPLC (99.8%+) reagent gave better results for oxidations of cycloheptene and of phenylacetylene. Whereas RuO_4 extracted into EtOAc darkens within the first 15 min for the normal purity reagent, the electronic spectral peaks appearing at 309 and 385 nm, with 99.95% HPLC grade darkening sets in only after 45 min.

Acetone

Acetone–water mixtures have been used for the RuO_4-catalyzed oxidation of substituted monoene steroids to α-hydroxyketones and/or diols,[6] while Piatak *et al.* used a similar system for cleavage of aromatic steroids.[7] In the table we list oxidations using AnalaR acetone; results are significantly poorer than those for CCl_4, C_6H_{12} or EtOAc, and both melting point and ^1H NMR data show that the oxidation products are less pure than those obtained from CCl_4 or C_6H_{12}. Electronic spectra too show that RuO_4, while present in freshly-prepared acetone–water solutions, deteriorates significantly within half an hour.

CONCLUSIONS

Cyclohexane is an excellent replacement for CCl_4 in oxidations with RuO_4 for the cleavage of cyclic alkenes, terminal alkenes, alkynes, and hydrobenzoin to carboxylic acids. From electronic and Raman spectra it is clear that RuO_4 is relatively stable in cyclohexane and gives similar or better yields of cleavage products than does CCl_4 as a solvent. It is likely that it could be used to replace CCl_4 in other RuO_4-catalyzed reactions.

EXPERIMENTAL

Materials were obtained from Aldrich except $RuCl_3 \cdot nH_2O$ ($n \sim 2.5$) which was from Johnson, Matthey. Products were identified by melting points, IR, and ^1H NMR spectra.

Oxidations Using CCl_4 as Solvent

In our earlier procedure[12] we used dichloromethane to extract the acids formed by alkene or alkyne cleavage effected with this reagent, but find that diethyl ether is more effective. Cleavage of cyclohexene to adipic acid is typical. To cyclohexene (0.165 g, 2 mmol) was added $RuCl_3 \cdot nH_2O$ (0.024 g, 0.12 mmol) and $IO(OH)_5$ (2.4 g, 10.5 mmol) in water (10 cm^3), CCl_4 (5 cm^3) and CH_3CN (5 cm^3). The mixture was stirred for 1.5 h at room temperature and Et_2O (20 cm^3) added with further stirring for 10 min. The reaction mixture was extracted with Et_2O ($25\,cm^3 \times 3$) and the extract dried over $MgSO_4$ (2 g) for 15 min. The product was isolated by concentration with a rotary evaporator.

Oxidations with Other Solvents

In all cases our improved extraction procedure, using diethyl ether rather than dichloromethane, was used.

Cyclohexane

Cleavage of styrene to benzoic acid is typical. To styrene (0.208 g, 2 mmol) was added $RuCl_3 \cdot nH_2O$ (0.024 g, 0.12 mmol) and $IO(OH)_5$ (2.4 g, 10.5 mmol) in water (10 cm^3), C_6H_{12} (5 cm^3) and CH_3CN (5 cm^3). The mixture was stirred for 1 h at room temperature; extraction and isolation was effected as with CCl_4.

Ethyl Acetate

A procedure modified from that of Piccialli[8] was used. Thus, to cycloheptene (0.192 g, 2 mmol) was added $RuCl_3 \cdot nH_2O$ (0.024 g, 0.115 mmol) and $IO(OH)_5$ (2.4 g, 10.5 mmol) in water (10 cm^3), EtOAc (5 cm^3) and CH_3CN (5 cm^3). The mixture was stirred for 2 h at room temperature. Extraction and isolation followed the procedure outlined for C_6H_{12} above.

Acetone

A procedure modified from that of Piccialli[6] was used. Thus, to diphenylacetylene (0.36 g, 2 mmol) was added $RuCl_3 \cdot nH_2O$ (0.024 g, 0.12 mmol) and $IO(OH)_5$ (2.4 g, 10.5 mmol) in water (10 cm^3), Me_2CO (5 cm^3) and CH_3CN (5 cm^3). The mixture was stirred for 2 h at room temperature; extraction and isolation followed the procedure outlined for C_6H_{12} above.

Instrumentation

Electronic spectra were measured on a Perkin Elmer Lambda 2 UV/VIS spectrophotometer, Raman spectra on a Dilor LabRam Infinity spectrometer with He–Ne excitation at 632.8 nm, and ^1H NMR spectra on a Bruker DRX-400 instrument in ^2H_2O using 10 mm tubes.

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