Catalytic functionalization of methane†
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A mixture of sodium vanadate and pyrazine-2-carboxylic acid (pcaH) efficiently catalyses the reaction of methane with molecular oxygen (from air) and hydrogen peroxide to give methyl hydroperoxide and, as consecutive products, methanol and formaldehyde. The reaction takes place under mild conditions (25–75°C) either in aqueous or in acetonitrile solution. The complexes formed from the catalyst precursor and the co-catalyst (under the reaction conditions) have been isolated and characterized as the derivatives [VO₂(pca)₂]⁻ (1) and [VO(O₂)(pca)₂]⁻ (3). The implications of these species in the catalytic process are discussed. Copyright © 2000 John Wiley & Sons, Ltd.

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1 INTRODUCTION

Methane, the major component of natural gas, is one of the most important feedstocks for the chemical industry, although it is the least reactive organic compound.1,2 It is extremely inert, even in comparison with other aliphatic hydrocarbons.3–6 Almost all transformations of methane require high temperatures above 500°C, and only in recent years have new methods of C–H activation been reported for it.7–26 The partial oxidation of methane into valuable oxygenates (methanol, formaldehyde, formic acid) at temperatures below 100°C remains a challenging task for homogeneous catalysis.

Recently, we have shown that a catalytic system composed of vanadate ([VO₃]⁻) and pyrazine-2-carboxylic acid (pcaH) efficiently catalyses the oxidative functionalization of methane with air and hydrogen peroxide to give, as consecutive products, mainly methanol and formaldehyde.27–30 We have also demonstrated that the catalyst precursor and the co-catalyst react, under catalytic conditions, to give the anionic complexes [VO₂(pca)₂]⁻ (1) and [VO(O₂)(pca)₂]⁻ (3). In this paper we report the catalytic implications of these complexes in the catalytic functionalization of methane and other hydrocarbons.

2 RESULTS AND DISCUSSION

The oxidative functionalization of methane with air and hydrogen peroxide is catalysed by a combination of metavanadate ([VO₃]⁻) with pyrazine-2-carboxylic acid (pcaH). The primary oxidation product is methyl hydroperoxide, which slowly decomposes to give methanol and formaldehyde.

Scheme 1 Transformation of methane with molecular oxygen and hydrogen peroxide in the presence of the VO₃⁻/4 pcaH catalytic system.
After prolonged reaction, especially at higher temperature, formic and acetic acid are also formed. Methyl hydroperoxide reacts quantitatively with triphenylphosphine in acetonitrile to give triphenylphosphine oxide and methanol, which allows the GC detection of CH$_3$OOH. After 24 h, the yield of CH$_3$OOH had attained 24% (based on H$_2$O$_2$), the catalytic turnover number being 480.

The incorporation of molecular oxygen from air into the oxygenated products has been demonstrated using the analogous reaction with cyclohexane (which is liquid and allows a better dosage): in the absence of air (N$_2$ atmosphere, CH$_3$CN, [NBu$_4$][VO$_3$] $10^{-4}$ M, pcaH $4 \times 10^{-4}$ M, 40 °C, 2 h) no reaction takes place between cyclohexane and H$_2$O$_2$. However, if the reaction vessel is opened to air, the reaction starts immediately with the same rate as observed in the presence of air. Moreover, the cyclohexane oxidation under an 18O$_2$ atmosphere unambiguously leads to a high degree of 18O incorporation into the oxygenated products.

The catalytic reaction does not work with the vanadate alone, but requires a co-catalyst. Pyrazine-2-carboxylic acid is one of the best co-catalysts, pyrazine-2,3-dicarboxylic acid and picolinic acid having a comparable activity. These compounds have in common a six-membered aromatic cycle containing at least one nitrogen ring atom and one carboxylato substituent in the $\alpha$-position with respect to the nitrogen atom. The highest catalytic activity is observed for a catalyst/co-catalyst ratio of 1:4.

In order to understand the role of the co-catalyst in the oxidative functionalization of alkanes catalysed by vanadate, we studied the reaction of various co-catalysts with [NBu$_4$][VO$_3$] in acetonitrile solution. The reaction with pcaH and anthranilic acid (anaH) (Eqns [1] and [2]) leads to the disubstituted vanadate derivatives [VO$_2$(pca)$_2$]$^-$ (1) and [VO$_2$(ana)$_2$]$^-$ (2), which can be isolated as the tetrabutylammonium salts.

\[
[\text{VO}_3^- + 2\text{pcaH} \rightarrow [\text{VO}_2(\text{pca})_2]^- + \text{H}_2\text{O}] \\
(1)
\]

\[
[\text{VO}_3^- + 2\text{anaH} \rightarrow [\text{VO}_2(\text{ana})_2]^- + \text{H}_2\text{O}] \\
(2)
\]

The single-crystal X-ray structure analyses of these compounds show both anions to be pseudo-octahedral with the two oxo ligands in a cis-position. There is, however, an important difference in the coordination of the two chelating ligands which might explain the different activities of the two co-catalysts: whereas the two pca ligands (derived from the efficient co-catalyst pcaH) are coordinated through a nitrogen atom of the aromatic cycle and an oxygen atom of the $\alpha$-carboxylato function (N,O-coordination), the two ana ligands (derived from the less efficient co-catalyst anaH) are coordinated through the two oxygen atoms of the carboxylato function (O,O-coordination) (Fig. 1).

As hydrogen peroxide is present in the reaction solution of the oxidative methane functionalization catalysed by [VO$_3$]$^-$/pcaH, we studied the reaction of complex 1 with H$_2$O$_2$ which gives rise to the formation of the peroxo derivative [VO(O$_2$)(pca)$_2$]$^-$ (3) (Eqn [3]).

\[
[\text{VO}_2(\text{pca})_2]^- + \text{H}_2\text{O}_2 \rightarrow [\text{VO}(\text{O}_2)(\text{pca})_2]^- + \text{H}_2\text{O} \\
(3)
\]

With the tetrabutylammonium cation, the double salt [NBu$_4$][VO$_2$(pca)$_2$][VO(O$_2$)(pca)$_2$] crystallizes from acetonitrile. The $^{51}$V NMR spectrum of this salt in CD$_3$CN shows signals at $\delta = -537$ ppm (anion 1) and $-558$ ppm (anion 3). They are identical with the two $^{51}$V NMR signals observed in the reaction mixture of the oxidative functionalization of cyclohexane with air and hydrogen.
peroxo catalysed by [NBu$_4$][VO$_3$]/pcaH (1:4) in CH$_3$CN after a catalytic run.

In order to characterize the peroxy complex [VO(O$_2$)(pca)$_2$] (3) unambiguously, and to separate it from anion 1, with which it tends to crystallize as the tetrabutylammonium double salt, we decided to synthesize 3 in aqueous solution and to crystallize it as the ammonium salt. NH$_4$VO$_3$ was found to react in H$_2$O with pcaH and H$_2$O$_2$ to give [NH$_4$][VO(O$_2$)(pca)$_2$], which crystallizes directly from water upon addition of ethanol. The single-crystal X-ray structure analysis of [NH$_4$][VO(O$_2$)(pca)$_2$] revealed the presence of two water molecules of crystallization per molecule of complex. As found for complex 1, the vanadium atom is at the centre of an irregular octahedron, and both pca ligands are N,O-coordinated. Surprisingly, the orientation of the two N,O-pca ligands is different from that in 1 and also from that found for the same anion 3 in the double salt [NBu$_4$]$_2$[VO$_2$(pca)$_2$] [VO(O$_2$)(pca)$_2$]. Whereas for anion 3 in the double salt both pca ligands (as in 1) are found to be N,O-coordinated with the two nitrogen atoms cis with respect to each other (isomer 3a), anion 3 in the salt [NH$_4$][VO(O$_2$)(pca)$_2$] contains the two pca ligands N,O-coordinated with the nitrogen atoms trans with respect to each other (isomer 3b), as was also found by X-ray crystallography$^{32}$ for the picolinato analogue [VO(O$_2$)(pic)$_2$]$^-$ (picH = picolinic acid) (Fig. 2). The electrochemical characteristics of the vanadate complexes used for catalytic methane functionalization are not easy to understand: Whereas the cyclovoltamogram of [NBu$_4$][VO$_3$] in acetonitrile solution shows no signal in the area of −0.5 to −1.5 V (with respect to a saturated silver electrode), three reduction and oxidation peaks are observed for [NBu$_4$][VO$_2$(pca)$_2$] (anion 1) ($E_{1/2}$ = −1.11 V, cathodic $E_{pc}$ = −1.22 V, $I_{pa}$ = 1.80 µA and anodic $E_{pa}$ = −0.99 V, $I_{pa}$ = 0.30 µA; $E_{1/2}$ = −1.30 V, cathodic $E_{pc}$ = −1.36 V, $I_{pc}$ = 0.28 µA and anodic $E_{pa}$ = −1.24 V, $I_{pa}$ = 0.20 µA; $E_{1/2}$ = −1.43 V, cathodic $E_{pc}$ = −1.48 V, $I_{pc}$ = 0.48 µA and anodic $E_{pa}$ = −1.38 V, $I_{pa}$ = 0.20 µA for 2.6 × 10$^{-2}$ M). In the case of anion 3, employed as double salt [NBu$_4$]$_2$[VO(O$_2$)(pca)$_2$][VO$_2$(pca)$_2$] (anion 3a) in acetonitrile solution, only one wave is observed ($E_{1/2}$ = −0.61 V, cathodic $E_{pc}$ = −0.67 V, $I_{pc}$ = 0.05 µA and anodic $E_{pa}$ = −0.55 V, $I_{pa}$ = 0.044 µA for 1.74 × 10$^{-2}$ M), quasi-reversible for a scanning rate of 50 mV s$^{-1}$; these peaks are tentatively assigned to the vanadium(V)/vanadium(IV) transitions. In addition, complex 3a shows an oxidation wave at 1.15 V ($E_{pa} = 0.044$ A and anodic $E_{pa} = 0.33$ V) which is supposed to represent the oxidation of the peroxo ligand to give the neutral vanadium(V) complex containing a hydroperoxyl ligand. An OOH ligand has been discussed in the case of iron complexes.$^{34}$ Complex 4 could split off an OH radical to give the neutral vanadium(IV) complex 5 containing a hydroperoxyl ligand. An OOH ligand has been discussed in the case of iron complexes.$^{34}$ Complex 4 could split off an OH radical to give the vanadium(IV) complex 5 which could react with hydrogen peroxide to give 4 and another OH radical. In such a way, the reversible interconversion of 4 and 5 would catalytically transform hydrogen peroxide into two OH radicals.

For the oxidative functionalization of methane (and other alkanes) we propose the general scheme

![Figure 2](https://example.com/figure2.png)

**Figure 2** Molecular structure of anion 3 (isomers a and b).

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accepted for radical reactions (Scheme 3). The reaction is initiated by the attack of the OH radical on the methane molecule to give water and a methyl radical. The radical chain is propagated by the reaction of the methyl radical with the diradical O2 to give the CH3OO radical, which can attack a CH4 molecule to give the product CH3OOH and another methyl radical. The radical chain can be terminated by combination of two radicals. The implication of OH radicals in the oxidative functionalization of methane is supported by the fact that the reaction works best in aqueous solution, water being known to be an excellent solvent for OH radicals. 35

The oxidative functionalization of methane, catalysed by a vanadium system in aqueous solution, takes place under milder conditions (25–75 °C) than those used in the methane functionalization catalysed by mercury salts 36 or by platinum complexes (Catalytica process), 37 both requiring fuming sulfuric acid (100%) as reaction medium and temperatures between 160 and 220 °C. 36,37

### Table 1 Oxidative functionalization of cyclohexane

<table>
<thead>
<tr>
<th>Catalyst (10⁻⁴ M)</th>
<th>Co-catalyst</th>
<th>Total TONb</th>
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<tr>
<td>[NBu₄][VO₃]</td>
<td>pcaH (4 x 10⁻⁴ M)</td>
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</tr>
<tr>
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<td>pcaH (2 x 10⁻⁴ M)</td>
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</tr>
<tr>
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<td>0</td>
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<tr>
<td>[NBu₄][VO₂(pca)₂] (anion 1)</td>
<td>None</td>
<td>215</td>
</tr>
<tr>
<td>[NBu₄][VO₂(pca)₂] (anion 1)</td>
<td>pcaH (2 x 10⁻⁴ M)</td>
<td>924</td>
</tr>
<tr>
<td>[NBu₄][VO₂(pca)₂] (anion 1)</td>
<td>HClO₄ (2 x 10⁻⁴ M)</td>
<td>892</td>
</tr>
<tr>
<td>[NBu₄][VO₂(pca)₂] (anion 3b)</td>
<td>pcaH (2 x 10⁻⁴ M)</td>
<td>1120</td>
</tr>
</tbody>
</table>

### Scheme 2

Suggested role of the vanadium complexes functioning as a catalytic pump for the generation of hydroxyl radicals.

### Scheme 3

Radical mechanism proposed for the functionalization of methane catalyzed by the VO₃⁻/4 pcaH system.
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Zurich, Switzerland. Gas chromatographic analyses were recorded with a Dani 86.10 Doppler instrument (with CH₃NO₂ as internal reference) using a capillary Cp-wax 52-CB (25 m × 0.32 mm) column from Chrompack, and a Chrom Jet integrator (Spectra-Physics). Cyclic voltammetry was performed with a Metrohm VA-Scanner E612 and a Metrohm Polarecord E506 using a Hewlett-Packard 7040A X–Y recorder. A three-electrode system was employed with a platinum disc as the working electrode, an Ag/AgCl reference electrode and a platinum sheet auxiliary electrode, CH₃CN as solvent and NBu₄PF₆ (0.1 M) as supporting electrolyte. Under the conditions used, the one-electron oxidation of ferrocene occurs at +0.52 V in acetonitrile solution.

### 3.1 Synthesis of [NBu₄][VO₂(pca)₂] (anion 1)

[BR Hen]V₃O₅ (681 mg, 2 mmol) was dissolved in 20 ml of CH₃CN. After complete dissolution, pyrazine-2-carboxylic acid (492 mg, 4 mmol) was added, and the solution was stirred under reflux for 5 h. After filtration of the green solution, evaporation of the solvent gave a yellow–green powder, which was dissolved in a minimum amount of CH₂Cl₂. Addition of the same volume of cyclohexane led, after a few days, to the formation of light yellow crystals. Yield 64%. Found: C, 33.14; H, 2.71; N, 19.03; O, 30.96.

C₁₀H₁₀N₅O₇V requires C, 33.07.; H, 2.78; N, 30.84%. IR (cm⁻¹): 533s, 553s, 939s, 1668vs. ¹H NMR (acetone-d₆): δ = 1.4806 (1H, t, J = 7 Hz, H4). 31P NMR (acetone-d₆): δ = 7.5 Hz, CH₂). 

[BR Hen]V₃O₅ (681 mg, 2 mmol) was dissolved in 20 ml of CH₃CN. After complete dissolution, anthranilic acid (547 mg, 4 mmol) was added, and the solution was stirred under reflux for 4 h. After filtration, evaporation of the solvent gave a yellow–green powder, which was dissolved in a minimum amount of CH₂Cl₂. Addition of the same volume of cyclohexane led, after a few days, to the formation of light violet crystals. Yield 78%. Found: C, 60.17; H, 8.06; N, 7.08. C₃₀H₄₈N₃O₇V requires C, 60.29; H, 8.09; N, 7.03%. IR (cm⁻¹): 825s, 875s, 1623vs. ¹H NMR (acetone-d₆): δ = 0.9410 (12H, t, J = 7 Hz, CH₃). 1.4045 (8H, m, J = 6.6 Hz, CH₂₃). 1.774 (8H, m, CH₂). 3.421 (8H, m, CH₂) NBu₄⁺; 6.507 (2H, ddd, J(H₄–H₃) = 8 Hz, J(H₄–H₅) = 6.8 Hz and J(H₄–H₆) = 1 Hz, H₄). 6.7065 (2H, dd, J(H₃–H₄) = 8 Hz and J(H₃–H₅) = 0.6 Hz, H₃). 7.154 (2H, ddd, J(H₅–H₆) = 8.4 Hz, J(H₅–H₄) = 7 Hz and J(H₅–H₃) = 1.8 Hz, H₅). 7.867 (2H, dd, J(H₆–H₅) = 7.2 Hz and J(H₆–H₄) = 1 Hz, H₆) an ligand. ⁵¹V NMR (acetone-d₆): δ = −503. MS (electrospray, negative): m/z = 354.7.

### 3.2 Synthesis of [NBu₄][VO₂(ana)₂] (anion 2)

[BR Hen]V₃O₅ (681 mg, 2 mmol) was dissolved in 20 ml of CH₃CN. After complete dissolution, pyrazine-2-carboxylic acid (492 mg, 4 mmol) was added, and the solution was stirred under reflux for 4 h. After filtration, evaporation of the solvent gave a yellow–green powder, which was dissolved in a minimum amount of CH₂Cl₂. Addition of the same volume of cyclohexane led, after a few days, to the formation of light red crystals. Yield 64%. Found: C, 33.14; H, 2.71; N, 19.03; O, 30.96.

C₁₀H₁₀N₅O₇V requires C, 33.07.; H, 2.78; N, 30.84%. IR (cm⁻¹): 533s, 553s, 939s, 1668vs. ¹H NMR (acetone-d₆): δ = 1.4806 (1H, t, J = 7 Hz, H4). 31P NMR (acetone-d₆): δ = 7.5 Hz, CH₂). 

The salt [NBu₄][VO₂(ana)₂] (500 mg, 0.875 mmol) was dissolved in 5 ml of CH₃CN and, after complete dissolution, H₂O₂ (30%) (87 µl, 0.9 mmol) was added. The resulting solution was stirred at room temperature for 1 h. Slow evaporation of the solvent at room temperature to ca 2/3 of its volume and addition of the same volume of ethanol led after a few days at −18 °C to the formation of light red crystals. Yield 64%. Found: C, 33.14; H, 2.71; N, 19.03; O, 30.96. C₁₀H₁₀N₅O₇V requires C, 33.07.; H, 2.78; N, 30.84%. IR (cm⁻¹): 533s, 553s, 939s, 1668vs. ¹H NMR (CD₃OD): δ = 9.2275 (1H, d, J = 3 Hz), 9.3815 (2H, d, J = 3 Hz), 9.410 (1H, d, J = 1.2 Hz), 9.4925 (1H, d, J = 1 Hz), 9.922 (1H, m) pca ligand. ⁵¹V NMR (D₂O): δ = −600. MS (electrospray, negative): m/z = 344.9.

### 3.3 Synthesis of [NH₄][VO₂(pca)₂] (double salt containing anions 1 and 3a)

The salt [NBu₄][VO₂(pca)₂] (500 mg, 0.875 mmol) was dissolved in 5 ml of CH₃CN and, after complete dissolution, H₂O₂ (30%) (90 µl, 0.88 mmol) was added. The solution was stirred at room temperature for 1 h. After filtration of the red solution, evaporation of the solvent gave a red powder, which was dissolved in a minimum amount of acetone. Addition of the same volume of diethyl ether led, after a few days at room temperature, to crystallization of light red crystals. Yield 56%.

### 3.5 Catalytic runs

The oxidation of methane was carried out in...
cylindrical glass vessels placed in stainless steel autoclaves with intensive stirring at 50 °C (volume of the reaction solution, 30 ml; total volume of the autoclave, 100 ml). Gaseous air and methane were introduced into the autoclave (10 and 75 bar, respectively) containing the solution of H2O2 (0.193 M) and the catalyst (NaVO3 in water or NBu3VO3 in acetonitrile, 10−4 M; pKaH, 4 × 10−5 M). CAUTION: mixtures of air and H2O2 with organic compounds are potentially explosive at elevated temperatures and pressures! The reactions were stopped by cooling the autoclave with ice, and the concentration of methanol was analysed by GLC, and methyl hydroperoxide was determined spectrophotometrically after its conversion into 3,5-diacetyl-2,6-dimethyl-1,4-dihydropyridine. 39

The oxidation of cyclohexane was carried out in thermostated cylindrical glass vessels equipped with reflux condensers, with intensive stirring in air. The reagents (catalyst, co-catalyst and CH3NO2 as internal standard) were dissolved separately in acetonitrile, and these solutions were added to cyclohexane. After addition of H2O2 (30% aqueous solution), the reaction solution (total volume 10 ml) was stirred at 40 °C for 24 hours. The reaction was monitored by withdrawing aliquots (0.5 ml) and, after addition of triphenylphosphate to saturation, the samples were analysed by GLC.

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REFERENCES