

# Amavadin and Other Vanadium Complexes as Remarkably Efficient Catalysts for One-Pot Conversion of Ethane to Propionic and Acetic Acids

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**Abstract:** Synthetic amavadin  $\text{Ca}[\text{V}\{\text{ON}[\text{CH}(\text{CH}_3)\text{COO}]_2\}_2]$  and its models  $\text{Ca}[\text{V}\{\text{ON}(\text{CH}_2\text{COO})_2\}_2]$  and  $[\text{VO}\{\text{N}(\text{CH}_2\text{CH}_2\text{O})_3\}]$ , in the presence of  $\text{K}_2\text{S}_2\text{O}_8$  in trifluoroacetic acid (TFA), exhibit remarkable catalytic activity for the one-pot carboxylation of ethane to propionic and acetic acids with the former as the main product (overall yields up to 93%, catalyst turnover numbers (TONs) up to  $2.0 \times 10^4$ ). The simpler V complexes  $[\text{VO}(\text{CF}_3\text{SO}_3)_2]$ ,  $[\text{VO}(\text{acac})_2]$  and  $\text{VOSO}_4$  are less active. The effects of various factors, namely,  $\text{C}_2\text{H}_6$  and CO pressures, time, temperature, and amounts of catalyst, TFA and  $\text{K}_2\text{S}_2\text{O}_8$ , have been investigated, and this allowed optimisation of the process

and control of selectivity.  $^{13}\text{C}$ -labelling experiments indicated that the formation of acetic acid follows two pathways, the dominant one via oxidation of ethane with preservation of the C–C bond, and the other via rupture of this bond and carbonylation of the methyl group by CO; the C–C bond is retained in the formation of propionic acid upon carbonylation of ethane. The reactions proceed via both C- and O-centred radicals, as shown by experi-

ments with radical traps. On the basis of detailed DFT calculations, plausible reaction mechanisms are discussed. The carboxylation of ethane in the presence of CO follows the sequential formation of  $\text{C}_2\text{H}_5\cdot$ ,  $\text{C}_2\text{H}_5\text{CO}\cdot$ ,  $\text{C}_2\text{H}_5\text{COO}\cdot$  and  $\text{C}_2\text{H}_5\text{COOH}$ . The  $\text{C}_2\text{H}_5\text{COO}\cdot$  radical is easily formed on reaction of  $\text{C}_2\text{H}_5\text{CO}\cdot$  with a peroxo V catalyst via a  $\text{V}\{\eta^1\text{-OOC}(\text{O})\text{C}_2\text{H}_5\}$  intermediate. In the absence of CO, carboxylation proceeds by reaction of  $\text{C}_2\text{H}_5\cdot$  with TFA. For the oxidation of ethane to acetic acid, either with preservation or cleavage of the C–C bond, metal-assisted and purely organic pathways are also proposed and discussed.

**Keywords:** carboxylation • density functional calculations • homogeneous catalysis • reaction mechanisms • vanadium

## Introduction

The search for expedient processes for utilising light alkanes in synthesis is a current challenge to chemistry. Considerable efforts have been directed<sup>[1,2]</sup> towards the functionalization, under mild conditions, of methane to give more valuable

products, for example, acetic acid,<sup>[3]</sup> but undeservedly less attention has been paid to the carboxylation of ethane,<sup>[4]</sup> the least reactive hydrocarbon (after methane) and the second most abundant alkane (in natural gas). Direct transformation of ethane into the synthetically (and commercially) important<sup>[5]</sup> propionic and acetic acids could become an attractive way of functionalising alkanes. The current methods for preparing  $\text{C}_2\text{H}_5\text{COOH}$ , such as carbonylation of ethylene, oxidation of propanal and direct oxidation of naphtha,<sup>[5a]</sup> normally exhibit low selectivities and require harsh conditions, multistage processes, difficult work-up of the product mixture and, in some cases, considerable costs for reagents. The preparation of acetic acid by the Monsanto or Cativa processes also has some limitations, for example, the requirement for three separate stages (high-temperature steam reforming, further conversion of the synthesis gas to methanol and carbonylation of methanol with Rh or Ir catalysts).

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Homogeneous catalyst systems for the conversion of ethane to propionic and acetic acids have been reported only scantily. They exhibit low selectivities and yields, and the mechanisms of the reactions have not been established. One of the first examples of ethane carbonylation in aqueous medium<sup>[4b]</sup> uses  $K_2S_2O_8$  at 105–115 °C to give acetic and propionic acids (the latter only in the presence of CO) with a maximum TON of 0.4 relative to  $K_2S_2O_8$ . The oxidative functionalization of ethane by perfluorocarboxylic acid anhydrides to propionic acid and its mixed anhydride<sup>[4c]</sup> exhibit a low propionic acid yield (maximum of ca. 1 % based on the alkane) and forms various by-products.

The reaction of ethane with CO in trifluoroacetic acid (TFA)/ $K_2S_2O_8$  has been studied by Fujiwara et al., who pioneered the use of this system in alkane functionalization,<sup>[1f,i]</sup> using  $Pd^{II}$  and/or  $Cu^{II}$  acetates as catalysts.<sup>[4d]</sup> The maximum yield of propionic acid was about 18 % (based on ethane) and a TON (moles of product per mole of metal catalyst) of 11 was achieved ( $Co^{II}$  acetate led to only 0.4 % yield with a TON of 0.3).<sup>[4f]</sup> Recently, some of us found that a  $Re^V$  oxo complex containing an N,O-picolinate ligand, that is,  $[ReOCl_2(C_5H_4NCOO)(PPh_3)]$ , reaches an overall yield of propionic and acetic acids of 29 % (TON of 45),<sup>[4g]</sup> whereas Re complexes with pyrazole or tris(pyrazolyl)methane ligands catalyse the oxidation of ethane mainly to acetic acid with a maximum yield of about 40 % (carboxylation to propionic acid proceeds to a lesser extent, with ca. 8 % yield).<sup>[4h]</sup> Systems based on V-containing polyphosphomolybdates/ $H_2O_2$ ,<sup>[6a]</sup> chromic acid/ $H_2O_2$  (or  $tBuOOH$ ),<sup>[6b]</sup>  $Co^{II}$ / $N,N'$ -dihydroxypyromellitimide/ $O_2$ <sup>[6c]</sup> or  $Pd-C/H_2O_2$  (generated in situ)<sup>[4a]</sup> are also known to catalyse homogeneously the oxidation of ethane to acetic acid, although with low activities. Some heterogeneous systems have also been studied, for example, mixed metal oxides such as  $Mo_1V_{0.25}Nb_{0.12}Pd_{0.0005}O_x$ , at high temperature.<sup>[6d]</sup>

Other more effective catalyst systems for the conversion of ethane to propionic and acetic acids should be searched for, and the still-unknown mechanisms elucidated, and these are two main aims of the current study. Vanadium compounds appear promising since they are convenient catalyst precursors for various reactions of alkanes and aromatic compounds,<sup>[3e,6a,e-j,7]</sup> in particular amavadin, present in some amanita fungi, and its model (see below). They catalyse 1) peroxidative halogenation, hydroxylation and oxygenation of alkanes to the corresponding organic halides, alcohols and ketones,<sup>[6e]</sup> 2) carboxylation of methane,<sup>[7a,c]</sup> propane<sup>[7d]</sup> and of  $C_5$  and  $C_6$  alkanes,<sup>[7b]</sup> 3) the oxidation of certain thiols<sup>[8]</sup> and 4) decomposition of  $H_2O_2$ .<sup>[9]</sup> Use of amavadin for alkane functionalization has thus been limited to liquid alkanes, methane and propane (carboxylation), and a third main aim of the current work is to extend its catalytic activity to functionalization of

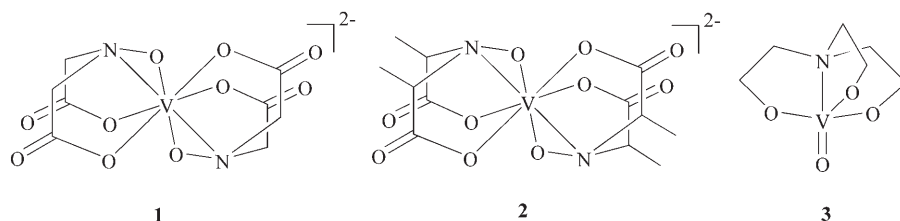
another gaseous alkane, that is, ethane. A fourth objective is to broaden the application of V compounds in catalysis,<sup>[10]</sup> which is still an underdeveloped field of research.

We now report highly effective carboxylation of ethane to propionic and acetic acids in the presence of  $K_2S_2O_8$  and in TFA, catalysed by amavadin and its model or other V complexes with N,O or O,O ligands, with overall yields (based on ethane) of carboxylic acids of up to 93 % and TONs of up to  $2.0 \times 10^4$  (the yield based on  $K_2S_2O_8$  reaches 64 %). This is, to our knowledge, the most efficient functionalization system for a gaseous alkane, under mild conditions, so far reported. Possible mechanisms are suggested on the basis of some experiments, for example, with radical traps and  $^{13}C$ -labelled reagents, and DFT calculations. These include the analysis of the most plausible pathways for the radical-formation and carboxylation processes, the study of the role of TFA in the carboxylation in the absence of CO, the investigation of both metal-assisted and purely organic routes for the oxidation of ethane to acetic acid with and without C–C bond cleavage and the roles of catalyst, oxidant and solvent.

In contrast to the extensive theoretical studies that have been undertaken to elucidate the mechanisms of various alkane reactions (hydroxylation,<sup>[11]</sup> halogenation,<sup>[12]</sup> dehydrogenation,<sup>[13]</sup>  $CH_4$  oxidation in sulfuric acid<sup>[14]</sup> and on an Fe-exchanged zeolite,<sup>[15]</sup> C–H bond activation by Re,<sup>[16]</sup> Pt,<sup>[17]</sup> Ti,<sup>[18]</sup> lanthanides,<sup>[19]</sup> and Rh<sup>[20]</sup> complexes, by unsaturated Al ions,<sup>[21]</sup>  $Sc^{+}$ <sup>[22]</sup> or metal oxides,<sup>[23]</sup> etc.), only a few papers propose plausible mechanisms of alkane carboxylation,<sup>[3a,b,d,g,4b,c,d,24]</sup> and only two, to our knowledge, report detailed theoretical studies, one of them for a quite different system<sup>[25]</sup> from ours, and the other one (studied by some of us)<sup>[7c]</sup> concerning methane.

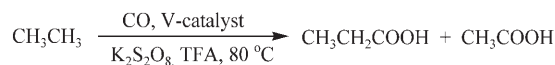
## Results and Discussion

**Catalysis studies:** The following vanadium compounds were used as catalyst precursors:  $Ca[V\{ON(CH_2COO)_2\}_2]$  (**1**;  $ON-(CH_2COO)_2$ =basic form of 2,2'-(hydroxyimino)diacetic acid (HIDA)<sup>3-</sup>; amavadin model),  $Ca[V\{ON[CH(CH_3)COO]_2\}_2]$  (**2**;  $ON[CH(CH_3)COO]_2$ =basic form of 2,2'-(hydroxyimino)dipropionic acid (HIDPA)<sup>3-</sup>; <sup>[26]</sup> synthetic amavadin)  $[VO\{N(CH_2CH_2O)_3\}]$  (**3**; Scheme 1),  $[VO(CF_3SO_3)_2] \cdot 2H_2O$  (**4**),  $[VO(acac)_2]$  (**5**; acac=acetylacetonate) and  $VOSO_4 \cdot 5H_2O$  (**6**). Each of them, in the presence of  $K_2S_2O_8$



Scheme 1.

and in TFA, exhibits high catalytic activity for carboxylation of ethane with carbon monoxide to give propionic acid as the main product (Scheme 2, Table 1 and Table S1 in the



Scheme 2.

Supporting Information). Acetic acid is also formed as a result of partial oxidation of ethane by peroxodisulfate. Blank tests were performed at different CO pressures and indicated no formation of propionic acid unless the vanadium catalyst was added.

The most active systems are provided by amavadin (**2**) and its models **1** and **3** which can lead to overall yields of carboxylic acids of up to 93% and/or TONs of up to  $2.0 \times 10^4$  (Table 1 and Tables S1–S4 in the Supporting Information). Under the same conditions, the simpler V complexes **4–6** and oxides such as  $\text{V}_2\text{O}_5$  and  $\text{V}_2\text{O}_4$  are less active but still provided yields of about 40–75% (Table 1, entries 9–11). The impact of various factors on the activity of **1–3** was investigated in detail (see the Supporting Information) with the aim of optimising conditions and gaining mechanistic information.

At low ethane pressure (up to 3 atm) oxidation to acetic acid proceeds more effectively than carboxylation to propionic acid (Figure 1a), but the latter reaction becomes dominant at higher pressures, and the best selectivity towards propionic acid is achieved at about 10 atm at a reaction time of about 20 h (Figure 1b), and at a temperature of  $80^\circ\text{C}$  (Figure 1c), above which a considerable drop in yield occurs, possibly due to further oxidation of the acid and thermal decomposition of the oxidant  $\text{K}_2\text{S}_2\text{O}_8$ , which occurs at about  $100^\circ\text{C}$ .<sup>[27a]</sup>

The carboxylation of ethane to propionic acid proceeds even in the absence of CO (albeit in low yields of ca. 3%, Figure 2), whereby the carbonyl group is then derived from TFA, as observed<sup>[3b,7]</sup> for methane carboxylation. The reaction is promoted by increasing  $p(\text{CO})$  (in accord with its role, when present, as a carbonylating agent), up to about 20–30 atm, at which propionic acid yields are about 73–78% (Figure 2, and Figure S1 in the Supporting Information). The maximum yield of propionic acid corresponds to the minimum yield of acetic acid, that is, there is competition between the two processes, which is also consistent with the predominant oxidation of ethane to acetic acid in the absence of CO.

Decreasing the amount of catalyst leads to an increase in TON, albeit with a decrease in product yield; for example, for amavadin and its model **1**, TONs of  $1.53 \times 10^4$  and  $2.0 \times 10^4$  are reached for an  $\text{C}_2\text{H}_6/\text{catalyst}$  molar ratio of  $78 \times 10^3$  (Figure 3, and Table S2 in the Supporting Information). Such high TONs, which still correspond to considerable acid yields (ca. 26–20%), are quite remarkable in the field of alkane functionalization under mild conditions and, to our knowledge, have not been previously reached.

Trifluoroacetic acid has been used as solvent in various alkane functionalization reactions,<sup>[1f,i,3b–d,g,4a,d–g]</sup> but its complete role still remains unclear. It can act as a carbonylating agent<sup>[3b,4c,7]</sup> (with possible formation of  $\text{CHF}_3$ <sup>[3b]</sup>) and is also a relatively strong acid [ $K_a=0.59$  ( $\text{p}K_a=0.2$ )].<sup>[27b]</sup> Its replacement by another strong acid such as trichloro- or tribromoacetic acid, sulfuric or nitric acid, or by acetonitrile or a fluorinated solvent like trifluorotoluene or 1,1,2-trichlorotrifluoroethane results in suppression of the catalytic activity. An optimum amount of TFA (see Table S3 in the Supporting Information) leads to the highest overall yield of 92.5%, as a balance between the solubilising and carbonylating roles of TFA on the one hand, and the decreased concentrations of reacting species on the other.

Table 1. Conversion of ethane into propionic and acetic acids (selected results).<sup>[a]</sup>

| Entry            | Catalyst | $n(\text{C}_2\text{H}_6)/n(\text{catalyst})$ | $p(\text{C}_2\text{H}_6)$ [atm] <sup>[b]</sup> | $p(\text{CO})$ [atm] <sup>[b]</sup> | Yield [%] <sup>[c]</sup> |             | Total | TON <sup>[d]</sup> |
|------------------|----------|----------------------------------------------|------------------------------------------------|-------------------------------------|--------------------------|-------------|-------|--------------------|
|                  |          |                                              |                                                |                                     | Propionic acid           | Acetic acid |       |                    |
| 1                | <b>1</b> | 306                                          | 5                                              | 15                                  | 47.0                     | 25.8        | 72.8  | 55.7               |
| 2                | <b>1</b> | 153                                          | 10                                             | 25                                  | 74.5                     | 4.6         | 79.1  | 121                |
| 3                | <b>1</b> | $78.3 \times 10^3$                           | 10                                             | 25                                  | 22.7                     | 2.9         | 25.6  | $20.0 \times 10^3$ |
| 4 <sup>[e]</sup> | <b>1</b> | 53                                           | 5                                              | 20                                  | 63.5                     | 29.0        | 92.5  | 46.0               |
| 5                | <b>2</b> | 153                                          | 10                                             | 30                                  | 78.4                     | 4.8         | 83.2  | 127                |
| 6                | <b>2</b> | $78.3 \times 10^3$                           | 10                                             | 30                                  | 17.0                     | 2.5         | 19.5  | $15.3 \times 10^3$ |
| 7                | <b>3</b> | 153                                          | 10                                             | 22                                  | 45.5                     | 6.5         | 52.0  | 79.6               |
| 8                | <b>3</b> | $77.7 \times 10^3$                           | 10                                             | 30                                  | 18.1                     | 2.2         | 20.3  | $15.8 \times 10^3$ |
| 9                | <b>4</b> | 153                                          | 10                                             | 22                                  | 68.6                     | 6.6         | 75.2  | 115                |
| 10               | <b>5</b> | 153                                          | 10                                             | 25                                  | 59.6                     | 7.5         | 67.1  | 103                |
| 11               | <b>6</b> | 153                                          | 10                                             | 25                                  | 64.2                     | 5.2         | 69.4  | 106                |

[a] Reaction conditions (unless stated otherwise): metal-complex catalyst (0.04–20.00  $\mu\text{mol}$ ),  $\text{K}_2\text{S}_2\text{O}_8$  (4.00 mmol),  $\text{CF}_3\text{COOH}$  (5.0 mL),  $80^\circ\text{C}$ , 20 h, in an autoclave (13 mL capacity). [b] Measured at  $25^\circ\text{C}$  (amounts of  $\text{C}_2\text{H}_6$  or CO gases correspond to  $0.306 \text{ mmol atm}^{-1}$ , except for run 4, for which amounts of those gases correspond to  $0.212 \text{ mmol atm}^{-1}$ ). [c] Molar yield [%] based on  $\text{C}_2\text{H}_6$ , that is, moles of products per 100 moles of ethane (determined by GC or GC-MS); molar yields [%] based on  $\text{K}_2\text{S}_2\text{O}_8$ , if required, can be estimated (except for runs 1 and 4) as total yield  $\times 0.765$ , for example, 64% for run 5; for runs 1 and 4, molar yields [%] based on  $\text{K}_2\text{S}_2\text{O}_8$  are 28 and 23%, respectively. [d] Turnover number (moles of acetic and propionic acids per mole of metal catalyst precursor) after 20 h. [e]  $\text{CF}_3\text{COOH}$  (7.3 mL).

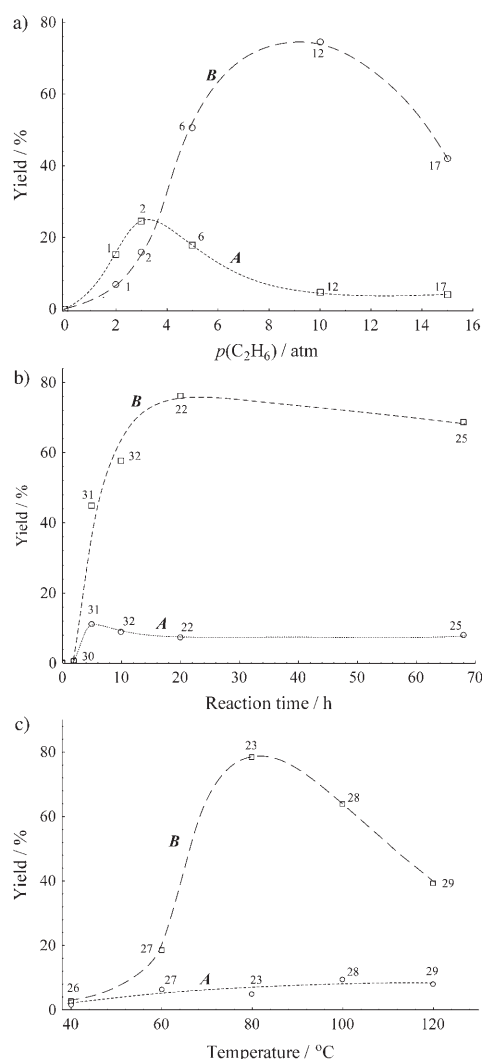


Figure 1. Effects of a)  $\text{C}_2\text{H}_6$  pressure, b) reaction time and c) temperature on the yields of acetic (curve A) and propionic (curve B) acids in ethane carboxylation catalysed by amavadin **2** (b, c) or its model **1** (a).  $p(\text{CO}) = 25$  (a, b) or 30 atm (c);  $p(\text{C}_2\text{H}_6) = 10$  atm (b, c);  $80^{\circ}\text{C}$  (a, b); 20 h (a, c). Point numbers correspond to entries in Table S1 in the Supporting Information.

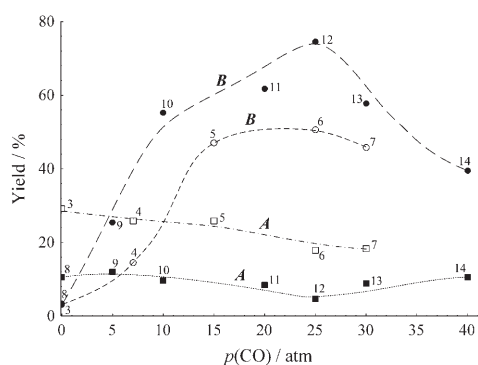


Figure 2. Effect of CO pressure on the yields of acetic (curve A) and propionic (curve B) acids in ethane carboxylation catalysed by amavadin model **1**.  $p(\text{C}_2\text{H}_6) = 5$  atm (open points), 10 atm (filled points);  $80^{\circ}\text{C}$ ; 20 h. Point numbers correspond to entries in Table S1 in the Supporting Information.

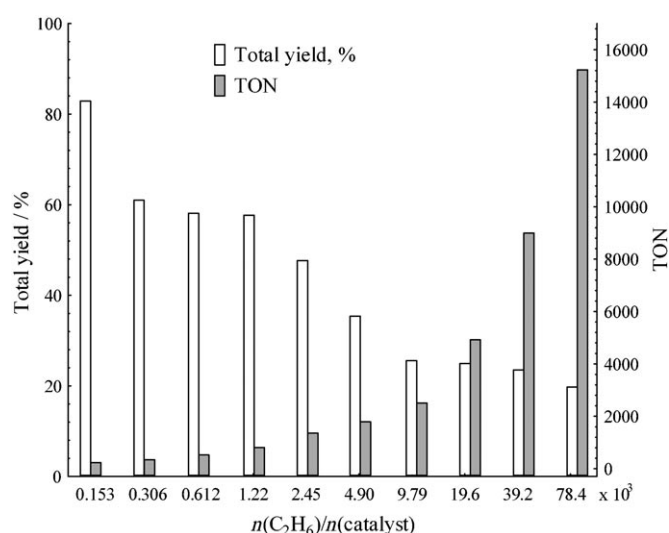
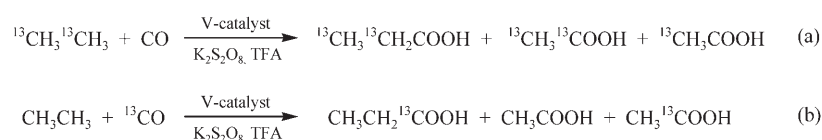


Figure 3. Effect of the amount of catalyst on the total yield of carboxylic acids and TON of catalyst in ethane carboxylation catalyzed by amavadin (**2**).  $p(\text{C}_2\text{H}_6) = 10$  atm;  $p(\text{CO}) = 30$  atm;  $80^{\circ}\text{C}$ ; 20 h. For full reaction conditions see Table S2 in the Supporting Information.

$\text{K}_2\text{S}_2\text{O}_8$  is essential, and the yield of propionic acid increases with its amount up to a maximum, beyond which a pronounced decrease occurs (see Table S4 and Figure S2 in the Supporting Information), possibly due to the increasing amount of solid (the oxidant has limited solubility) with resulting poor stirring. The yields of carboxylic acids based on  $\text{K}_2\text{S}_2\text{O}_8$  are usually rather high, in many cases exceed 50% (Table 1, and Tables S1–S4 in the Supporting Information) and reach 64% under appropriate reaction conditions.

**Mechanistic discussion:** To clearly establish the origin of the alkyl and carbonyl groups in the propionic and acetic acids,  $^{13}\text{C}$ -labelling experiments were performed with  $^{13}\text{CH}_3^{13}\text{CH}_3$  and  $^{13}\text{CO}$ , and the products identified by  $^{13}\text{C}\{^1\text{H}\}$  NMR spectroscopy. Thus, from the reaction of  $^{13}\text{CH}_3^{13}\text{CH}_3$  and  $\text{CO}$ , catalysed by complex **1**, the main products (Scheme 3a) are  $^{13}\text{CH}_3^{13}\text{CH}_2\text{COOH}$  (d,  $J(^{13}\text{C},^{13}\text{C}) = 34$  Hz, at  $\delta = 8.5$  and 28.3 ppm) and  $^{13}\text{CH}_3^{13}\text{COOH}$  (d,  $J(^{13}\text{C},^{13}\text{C}) = 56$  Hz, at  $\delta = 20.4$  and 182.8 ppm), that is, the ethyl group of propionic acid and both the methyl and carbonyl moieties of acetic acid are derived from ethane, which thus undergoes carboxylation to propionic acid and oxidation to acetic acid, both with preservation of the ethane C–C bond. However, a smaller amount (ca. 6% of the total amount of acetic acid) of singly labelled  $^{13}\text{CH}_3\text{COOH}$  (s,  $\delta = 20.4$  ppm) was also detected, that is C–C cleavage of ethane also occurred as a competitive process, and the resulting methyl group underwent carboxylation.

These results were confirmed by performing the reaction of  $\text{CH}_3\text{CH}_3$  with  $^{13}\text{CO}$  (Scheme 3b), which leads not only to  $\text{CH}_3\text{CH}_2^{13}\text{COOH}$  but also to the singly labelled acetic acid  $\text{CH}_3^{13}\text{COOH}$  (the  $\text{CH}_3^{13}\text{COOH}$ /propionic acid molar ratio is ca. 0.06) in accord with the occurrence, to some extent, of ethane C–C bond rupture. At the low  $^{13}\text{CO}$  pressure (2 atm)



Scheme 3.

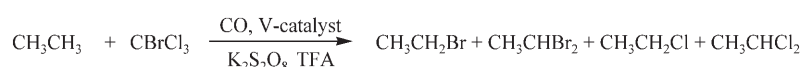
used, unlabelled  $\text{CH}_3\text{COOH}$  is formed in relatively large amounts (see also Figure 2; the  $\text{CH}_3\text{COOH}$ /propionic acid molar ratio is 1.2) due to oxidation of ethane, whereas carbonylation by TFA to afford  $\text{CH}_3\text{CH}_2\text{COOH}$  is also observed, although only to a slight extent (the  $\text{CH}_3\text{CH}_2\text{COOH}/\text{CH}_3\text{CH}_2^{13}\text{COOH}$  molar ratio is ca. 0.08).

Although under typical reaction conditions very high selectivity towards propionic and acetic acids is observed, at lower gas pressures (e.g., 2 atm) the ethyl and methyl esters of trifluoroacetic acid are also detected as reaction products, although in much lower yields than the acids. Ethane was confirmed as their carbon source by using  $^{13}\text{CH}_3^{13}\text{CH}_3$ , which affords  $\text{CF}_3\text{COO}^{13}\text{CH}_2^{13}\text{CH}_3$  (d,  $J(^{13}\text{C}, ^{13}\text{C}) = 38 \text{ Hz}$ , at  $\delta = 13.5$  and  $67.3 \text{ ppm}$ ) and  $\text{CF}_3\text{COO}^{13}\text{CH}_3$  (s,  $\delta = 55.9 \text{ ppm}$ ), again proving a considerable extent of alkane C–C cleavage. In the absence of CO, the main products are acetic acid and the ester  $\text{CF}_3\text{COOCH}_2\text{CH}_3$ , which do not involve carbonylation of ethane, although propionic acid is also detected on account of a carbonylating role of TFA.

**Radical formation:** The reactions leading to the carboxylic acids are believed to proceed mainly via both carbon- and oxygen-centred radicals, since the yields of these products sharply drop (especially that of propionic acid, formation of which can be fully suppressed; see Table S5 in the Supporting Information) in the presence of a C-radical trap,<sup>[28a–c]</sup> like 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) or  $\text{CBrCl}_3$ , or an O-radical trap<sup>[28a–c]</sup> such as  $\text{Ph}_2\text{NH}$ . Butylated hydroxytoluene (BHT),  $\text{O}_2$ , benzoyl peroxide and  $\text{PbEt}_4$ , the latter group known<sup>[4c]</sup> to be possible radical initiators, also strongly inhibit propionic acid formation, but oxidation of ethane to acetic acid can be significantly promoted by such species.

The formation of ethyl radicals has been proved by the detection, by  $^1\text{H}$  (see Figure S3 in the Supporting Information) and  $^{13}\text{C}$  NMR spectroscopy, of  $\text{CH}_3\text{CH}_2\text{Br}$  and  $\text{CH}_3\text{CHBr}_2$  as the main products (ca. 11 and 3% yield based on ethane; Scheme 4) when the reaction is carried out in the presence of  $\text{CBrCl}_3$  ( $\text{CH}_3\text{CH}_2\text{Cl}$ ,  $\text{CH}_3\text{CHCl}_2$ , and propionic and acetic acids are also detected in small amounts).

In contrast to the V catalyst,  $\text{K}_2\text{S}_2\text{O}_8$  has a decisive role in radical formation, since without it no products (in particular no organic halide when the reaction is performed in the presence of  $\text{CBrCl}_3$ ) are observed, whereas when the reaction is carried out in the absence of the metal catalyst but in



Scheme 4.

the presence of  $\text{K}_2\text{S}_2\text{O}_8$ , the organic halides  $\text{CH}_3\text{CH}_2\text{X}$ ,  $\text{CH}_3\text{CHX}_2$  and  $\text{CH}_3\text{CX}_3$  ( $\text{X} = \text{Br}, \text{Cl}$ ) are formed. The involvement of  $\text{K}_2\text{S}_2\text{O}_8$  as an oxidant is suggested by the isolation from the reaction solution in high yield of  $\text{KHSO}_4$  as a col-

ourless crystalline material (identified by IR, elemental and single-crystal X-ray diffraction analyses, the last-named of which was in accord with that already reported<sup>[29]</sup>). This salt, however, is also formed upon refluxing TFA/ $\text{K}_2\text{S}_2\text{O}_8$ .

Nevertheless, no carboxylic acid is detected in the absence of the V catalyst. We have not yet succeeded in isolating and fully characterizing any V intermediate, but amavadin and its model ( $\text{V}^{\text{IV}}$  complexes **2** and **1**, respectively) are oxidised<sup>[6e,9]</sup> by  $\text{H}_2\text{O}_2$  to the corresponding  $\text{V}^{\text{V}}$  compounds, which are related to bis-peroxo  $\text{V}^{\text{V}}$  complexes, since the deprotonated hydroxyimine(1–) group  $\eta^2\text{-ON}$  of the ligands (Scheme 1) is comparable to peroxide(2–). Moreover, V species can readily undergo peroxidation to give peroxo or hydroperoxo complexes<sup>[10,30]</sup> and compounds of these types have been proposed<sup>[6a,g]</sup> as active species in peroxidations of hydrocarbons. Hence, the involvement, in our system, of a peroxo  $\text{V}^{\text{V}}$  complex such as  $[\text{V}(\text{OO})\{\text{N}(\text{CH}_2\text{CH}_2\text{O})_3\}]$ , the peroxo analogue of oxo complex **3**, or a related species is a reasonable assumption.

On the basis of the above, one can propose that the ethane reactions are initiated by hydrogen-atom abstraction from RH by the sulfate anion radical  $\text{SO}_4^{\cdot-}$  (or its protonated form  $\text{HSO}_4^{\cdot}$ )<sup>[7c,28c]</sup> formed upon thermolytic decomposition of  $\text{S}_2\text{O}_8^{2-}$  (or the protonated form  $\text{HS}_2\text{O}_8^-$  in acidic TFA medium).<sup>[3c,28d]</sup> Quantum chemical calculations indicate that exothermic interactions of  $\text{SO}_4^{\cdot-}$ , and particularly  $\text{HSO}_4^{\cdot}$  radicals, with  $\text{C}_2\text{H}_6$  occur with a low activation barrier (the activation enthalpy in solution  $\Delta H_s^\ddagger$  is 7.61 and  $0.12 \text{ kcal mol}^{-1}$ , respectively; see reactions 2 in Table 2 and Scheme 5; the complete version of Table 2 is given in the Supporting Information as Table S6). Selected transition states (TS) are presented in Figure 4, whereas a wider view is given in Figure S4 in the Supporting Information.

In contrast, direct H abstraction from ethane (homolytic C–H bond cleavage to yield the ethyl radical) by an oxo or a peroxo vanadium complex, for example,  $[\text{V}(\text{OO})\{\text{N}(\text{CH}_2\text{CH}_2\text{O})_3\}]$  or  $[\text{V}(\text{OOH})\{\text{N}(\text{CH}_2\text{CH}_2\text{O})_3\}]^+$ , as well as heterolytic C–H bond cleavage leading to an ethyl V species are thermodynamically highly unfavourable (reactions 3–6 in Table S6 in the Supporting Information).

**Carboxylation:** The mechanism of further conversion of  $\text{C}_2\text{H}_5^{\cdot}$  to propionic acid includes carbonylation of the former by CO to form the acyl radical  $\text{C}_2\text{H}_5\text{CO}^{\cdot}$  (reaction 3, Scheme 5). The latter may then be converted by three routes (I–III) similar to those described for methane carboxylation.<sup>[7c]</sup> Route I (Scheme 5), which is the most favourable for formation of propionic acid

Table 2. Energetic characteristics [kcal mol<sup>-1</sup>] of the reactions involved in the proposed mechanisms at the CPCM-B3LYP/6-31 + G\*\*//gas-B3LYP/6-31G\* and CPCM-B3LYP/6-311 + G\*\*//gas-B3LYP/6-311 + G\*\* (in parentheses) levels of theory.<sup>[a]</sup>

| No.                  | Reaction                                                                                                                                                                                                                                            |                    | $\Delta H_s^\ddagger$ | $\Delta H_s$    | $\Delta G_s$    |
|----------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------|-----------------------|-----------------|-----------------|
| Radical formation    |                                                                                                                                                                                                                                                     |                    |                       |                 |                 |
| 1                    | $\text{HS}_2\text{O}_8^- \rightarrow \text{HSO}_4^\cdot + \text{SO}_4^{\cdot-}$                                                                                                                                                                     |                    |                       | +24.86 (+24.31) |                 |
| 2a                   | $\text{SO}_4^{\cdot-} + \text{C}_2\text{H}_6 \rightarrow \text{HSO}_4^- + \text{C}_2\text{H}_5^\cdot$                                                                                                                                               | (via <b>TS1a</b> ) | 9.82 (7.61)           | -2.31 (-6.87)   | -4.56 (-8.70)   |
| 2b                   | $\text{HSO}_4^\cdot + \text{C}_2\text{H}_6 \rightarrow \text{H}_2\text{SO}_4 + \text{C}_2\text{H}_5^\cdot$                                                                                                                                          | (via <b>TS1b</b> ) | -0.28 (+0.12)         | -9.19 (-12.74)  | -10.18 (-13.76) |
| Carboxylation        |                                                                                                                                                                                                                                                     |                    |                       |                 |                 |
| 3                    | $\text{C}_2\text{H}_5^\cdot + \text{CO} \rightarrow \text{C}_2\text{H}_5\text{CO}^\cdot$                                                                                                                                                            | (via <b>TS2</b> )  | 2.72 (3.35)           | -14.12 (-12.43) |                 |
| 4a                   | $[\text{VO}[\text{N}(\text{CH}_2\text{CH}_2\text{O})_3]] + \text{HS}_2\text{O}_8^- \rightarrow [\text{V}(\text{OO})[\text{N}(\text{CH}_2\text{CH}_2\text{O})_3]] + \text{HS}_2\text{O}_7^-$                                                         |                    |                       | +8.16           | +7.88           |
| 4b                   | $\text{HS}_2\text{O}_8^- + \text{CF}_3\text{COOH} \rightarrow \text{H}_2\text{SO}_5 + \text{CF}_3\text{C}(\text{O})\text{OSO}_3^-$                                                                                                                  |                    |                       | +7.66 (+7.59)   | +2.61 (+5.63)   |
| 4c                   | $\text{HS}_2\text{O}_8^- + \text{H}_2\text{O} \rightarrow \text{H}_2\text{SO}_5 + \text{HSO}_4^-$                                                                                                                                                   |                    |                       | +1.57 (-1.57)   | +1.46 (-0.86)   |
| 4d                   | $[\text{VO}[\text{N}(\text{CH}_2\text{CH}_2\text{O})_3]] + \text{H}_2\text{SO}_5 \rightarrow [\text{V}(\text{OO})[\text{N}(\text{CH}_2\text{CH}_2\text{O})_3]] + \text{H}_2\text{SO}_4$                                                             |                    |                       | +2.49           | +2.60           |
| 5a                   | $[\text{V}(\text{OO})[\text{N}(\text{CH}_2\text{CH}_2\text{O})_3]] + \text{C}_2\text{H}_5\text{CO}^\cdot \rightarrow [\text{V}(\text{OOC}(\text{O})\text{C}_2\text{H}_5)[\text{N}(\text{CH}_2\text{CH}_2\text{O})_3]]$                              | (via <b>TS3a</b> ) | 4.51                  | -57.32          |                 |
| 5b                   | $[\text{V}(\text{OOC}(\text{O})\text{C}_2\text{H}_5)[\text{N}(\text{CH}_2\text{CH}_2\text{O})_3]] \rightarrow [\text{V}(\text{O})[\text{N}(\text{CH}_2\text{CH}_2\text{O})_3]] + \text{C}_2\text{H}_5\text{COO}^\cdot$                              | (via <b>TS3b</b> ) | 5.53                  | -15.42          |                 |
| 6                    | $\text{C}_2\text{H}_5\text{COO}^\cdot + \text{CF}_3\text{COOH} \rightarrow \text{C}_2\text{H}_5\text{COOH} + \text{CF}_3\text{COO}^\cdot$                                                                                                           | (via <b>TS4</b> )  | 1.50 (1.10)           | +9.42 (+9.56)   | +9.71 (+9.95)   |
| 7                    | $\text{C}_2\text{H}_5\text{COO}^\cdot + \text{C}_2\text{H}_6 \rightarrow \text{C}_2\text{H}_5\text{COOH} + \text{C}_2\text{H}_5^\cdot$                                                                                                              | (via <b>TS5</b> )  | 5.53 (4.93)           | -3.82 (-7.15)   | -4.27 (-7.45)   |
| 8                    | $[\text{V}(\text{OOH})[\text{N}(\text{CH}_2\text{CH}_2\text{O})_3]]^\cdot + \text{C}_2\text{H}_5\text{CO}^\cdot \rightarrow [\text{V}(\text{OOH})[\text{N}(\text{CH}_2\text{CH}_2\text{O})_3]] + \text{C}_2\text{H}_5\text{CO}^+$                   |                    |                       | -13.66          | -13.98          |
| 9                    | $\text{C}_2\text{H}_5\text{CO}^+ + \text{CF}_3\text{COO}^- \rightarrow \text{CF}_3\text{C}(\text{O})\text{OC}(\text{O})\text{C}_2\text{H}_5$                                                                                                        |                    |                       | -36.71 (-34.16) |                 |
| 10                   | $\text{C}_2\text{H}_5\text{CO}^+ + \text{HSO}_4^- \rightarrow \text{C}_2\text{H}_5\text{C}(\text{O})\text{OSO}_2\text{OH}$                                                                                                                          |                    |                       | -32.96 (-29.54) |                 |
| 11                   | $\text{HS}_2\text{O}_8^- + \text{C}_2\text{H}_5\text{CO}^\cdot \rightarrow \text{SO}_4^{\cdot-} + \text{C}_2\text{H}_5\text{C}(\text{O})\text{OSO}_2\text{OH}$                                                                                      | (via <b>TS8b</b> ) | 4.49 (4.18)           | -56.80 (-57.18) | -56.18 (-56.61) |
| 12                   | $\text{C}_2\text{H}_5^\cdot + \text{CF}_3\text{COOH} \rightarrow \text{C}_2\text{H}_6 + \text{CF}_3\text{COO}^\cdot$                                                                                                                                | (via <b>TS12</b> ) | 12.06 (17.99)         | +13.23 (+16.70) | +13.96 (+17.40) |
| 13                   | $\text{HSO}_4^\cdot + \text{CF}_3\text{COOH} \rightarrow \text{H}_2\text{SO}_4 + \text{CF}_3\text{COO}^\cdot$                                                                                                                                       | (via <b>TS13</b> ) | 13.32 (12.85)         | +4.05 (+3.96)   | +3.78 (+3.64)   |
| 14                   | $\text{C}_2\text{H}_5^\cdot + \text{CF}_3\text{COO}^\cdot \rightarrow \text{CF}_3\text{COOC}_2\text{H}_5$                                                                                                                                           |                    |                       | -87.76 (-86.19) |                 |
| Carboxylation by TFA |                                                                                                                                                                                                                                                     |                    |                       |                 |                 |
| 15                   | $\text{C}_2\text{H}_5^\cdot + \text{CF}_3\text{COOH} \rightarrow \text{CF}_3\text{C}(\text{OH})(\text{C}_2\text{H}_5)\text{O}^\cdot$                                                                                                                | (via <b>TS14</b> ) | 9.66 (10.56)          | +6.45 (+8.21)   |                 |
| 16                   | $\text{CF}_3\text{C}(\text{OH})(\text{C}_2\text{H}_5)\text{O}^\cdot \rightarrow \text{CF}_3^\cdot + \text{C}_2\text{H}_5\text{COOH}$                                                                                                                | (via <b>TS15</b> ) | 6.53 (5.94)           | -8.62 (-9.79)   |                 |
| 17                   | $\text{CF}_3^\cdot + \text{C}_2\text{H}_6 \rightarrow \text{CF}_3\text{H} + \text{C}_2\text{H}_5^\cdot$                                                                                                                                             | (via <b>TS21</b> ) | 8.36 (6.77)           | -7.91 (-8.53)   | -8.67 (-9.44)   |
| 18                   | $\text{CF}_3^\cdot + \text{CF}_3\text{COOH} \rightarrow \text{CF}_3\text{H} + \text{CF}_3\text{COO}^\cdot$                                                                                                                                          | (via <b>TS22</b> ) | 16.30 (17.31)         | +5.33 (+8.17)   | +5.30 (+7.96)   |
| 19                   | $\text{CF}_3^\cdot + \text{H}_2\text{SO}_4 \rightarrow \text{CF}_3\text{H} + \text{HSO}_4^\cdot$                                                                                                                                                    | (via <b>TS23</b> ) | 15.10 (16.25)         | +1.29 (+4.21)   | +1.52 (+4.33)   |
| Oxidation            |                                                                                                                                                                                                                                                     |                    |                       |                 |                 |
| 20                   | $\text{C}_2\text{H}_5^\cdot + \text{HSO}_4^\cdot \rightarrow \text{C}_2\text{H}_5\text{OSO}_2\text{OH}$                                                                                                                                             |                    |                       | -81.42 (-80.80) |                 |
| 21                   | $\text{C}_2\text{H}_5\text{OSO}_2\text{OH} + \text{CF}_3\text{COOH} \rightarrow \text{C}_2\text{H}_5\text{OH} + \text{CF}_3\text{COOH} + \text{SO}_3$                                                                                               | (via <b>TS31</b> ) | 7.09 (5.84)           | +22.33 (+21.06) |                 |
| 22                   | $[\text{VO}[\text{N}(\text{CH}_2\text{CH}_2\text{O})_3]] + \text{CF}_3\text{COOH} \rightarrow [\text{V}(\text{OH})[\text{N}(\text{CH}_2\text{CH}_2\text{O})_3]]^\cdot + \text{CF}_3\text{COO}^-$                                                    |                    |                       | +13.67          | +12.91          |
| 23                   | $[\text{V}(\text{OH})[\text{N}(\text{CH}_2\text{CH}_2\text{O})_3]]^\cdot + \text{C}_2\text{H}_5^\cdot \rightarrow [\text{V}(\text{HOC}_2\text{H}_5)[\text{N}(\text{CH}_2\text{CH}_2\text{O})_3]]^\cdot$                                             |                    |                       | -44.26          |                 |
| 24                   | $[\text{V}(\text{HOC}_2\text{H}_5)[\text{N}(\text{CH}_2\text{CH}_2\text{O})_3]]^\cdot + \text{CF}_3\text{COO}^- \rightarrow [\text{V}(\text{OC}(\text{O})\text{CF}_3)[\text{N}(\text{CH}_2\text{CH}_2\text{O})_3]] + \text{C}_2\text{H}_5\text{OH}$ |                    |                       | -8.71           | -6.17           |
| 25                   | $[\text{V}(\text{OO})[\text{N}(\text{CH}_2\text{CH}_2\text{O})_3]] + \text{C}_2\text{H}_5^\cdot \rightarrow [\text{V}(\text{OOC}_2\text{H}_5)[\text{N}(\text{CH}_2\text{CH}_2\text{O})_3]]$                                                         | (via <b>TS32</b> ) | 7.21                  | -47.93          |                 |
| 26                   | $[\text{V}(\text{OOC}_2\text{H}_5)[\text{N}(\text{CH}_2\text{CH}_2\text{O})_3]] \rightarrow [\text{V}(=\text{O})[\text{N}(\text{CH}_2\text{CH}_2\text{O})_3]] + \text{CH}_3\text{CH}_2\text{O}^\cdot$                                               | (via <b>TS33</b> ) | 8.00                  | -13.02          |                 |
| 27                   | $\text{CH}_3\text{CH}_2\text{OH} + \text{HSO}_4^\cdot \rightarrow \text{CH}_3\text{CH}_2\text{O}^\cdot + \text{H}_2\text{SO}_4$                                                                                                                     | (via <b>TS34</b> ) | -1.28 (-5.30)         | -6.69 (-7.04)   | -6.39 (-6.68)   |
| 28                   | $\text{CH}_3\text{CH}_2\text{O}^\cdot + \text{HSO}_4^\cdot \rightarrow \text{CH}_3\text{CHO} + \text{H}_2\text{SO}_4$                                                                                                                               | (via <b>TS35</b> ) | -7.46 (-4.52)         | -88.53 (-92.40) | -87.74 (-91.36) |
| 29                   | $\text{CH}_3\text{CH}_2\text{OH} + \text{HSO}_4^\cdot \rightarrow \text{CH}_3\text{CHOH}^\cdot + \text{H}_2\text{SO}_4$                                                                                                                             | (via <b>TS36</b> ) | -7.55 (-6.42)         | -14.93 (-18.61) | -15.30 (-18.82) |
| 30                   | $\text{CH}_3\text{CHOH}^\cdot + \text{HSO}_4^\cdot \rightarrow \text{CH}_3\text{CHO} + \text{H}_2\text{SO}_4$                                                                                                                                       | (via <b>TS37</b> ) | 4.88 (4.07)           | -80.28 (-80.83) | -78.83 (-79.24) |
| 31                   | $\text{CH}_3\text{CHO} + \text{HSO}_4^\cdot \rightarrow \text{CH}_3\text{C}=\text{O}^\cdot + \text{H}_2\text{SO}_4$                                                                                                                                 | (via <b>TS38</b> ) | -6.68 (-4.51)         | -17.21 (-20.76) | -17.57 (-21.01) |
| 32                   | $[\text{V}(\text{OOH})[\text{N}(\text{CH}_2\text{CH}_2\text{O})_3]]^\cdot + \text{C}_2\text{H}_5^\cdot \rightarrow [\text{V}(\text{OOH})[\text{N}(\text{CH}_2\text{CH}_2\text{O})_3]] + \text{C}_2\text{H}_5^+$                                     |                    |                       | +5.93           | +6.06           |
| 33                   | $\text{C}_2\text{H}_5^+ + \text{HSO}_4^- \rightarrow \text{CH}_2=\text{CH}_2 + \text{H}_2\text{SO}_4$                                                                                                                                               |                    |                       | -37.60 (-39.33) | -37.01 (-38.14) |
| 34                   | $\text{C}_2\text{H}_5^+ + \text{CF}_3\text{COO}^- \rightarrow \text{CH}_2=\text{CH}_2 + \text{CF}_3\text{COOH}$                                                                                                                                     |                    |                       | -44.31 (-46.96) | -43.52 (-45.20) |
| 35                   | $[\text{V}(\text{OO})[\text{N}(\text{CH}_2\text{CH}_2\text{O})_3]] + \text{C}_2\text{H}_4 \rightarrow [\text{V}(=\text{O})[\text{N}(\text{CH}_2\text{CH}_2\text{O})_3]] + \text{CH}_3\text{CHO}$                                                    |                    |                       | -82.76          | -83.17          |

Table 2. (Continued)

| No.               | Reaction                                                                                                                                                                                                                 |                    | $\Delta H_s^\ddagger$ | $\Delta H_s$    | $\Delta G_s$  |
|-------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------|-----------------------|-----------------|---------------|
| C–C bond cleavage |                                                                                                                                                                                                                          |                    |                       |                 |               |
| 36                | $[\text{VO}[\text{N}(\text{CH}_2\text{CH}_2\text{O})_3]] + \text{C}_2\text{H}_5^\cdot \rightarrow [\text{V}(\text{OC}_2\text{H}_5)[\text{N}(\text{CH}_2\text{CH}_2\text{O})_3]]$                                         |                    |                       | –35.18          |               |
| 37                | $[\text{V}(\text{OC}_2\text{H}_5)[\text{N}(\text{CH}_2\text{CH}_2\text{O})_3]] + \text{HSO}_4^\cdot \rightarrow [\text{V}(\text{OCH}_2)[\text{N}(\text{CH}_2\text{CH}_2\text{O})_3]] + \text{CH}_3\text{OSO}_2\text{OH}$ | (via <b>TS46</b> ) | 17.96                 | –18.89          | –18.55        |
| 38                | $[\text{V}(\text{OCH}_2)[\text{N}(\text{CH}_2\text{CH}_2\text{O})_3]] + \text{CO} \rightarrow [\text{V}(\text{OCH}_2\text{CO})[\text{N}(\text{CH}_2\text{CH}_2\text{O})_3]]$                                             | (via <b>TS47</b> ) | 15.18                 | +9.29           |               |
| 39                | $[\text{V}(\text{OCH}_2\text{CO})[\text{N}(\text{CH}_2\text{CH}_2\text{O})_3]] \rightarrow [\text{V}(=\text{O})[\text{N}(\text{CH}_2\text{CH}_2\text{O})_3]] + \text{CH}_2=\text{C}=\text{O}$                            | (via <b>TS48</b> ) | 17.39                 | –18.60          |               |
| 40                | $\text{CH}_2=\text{C}=\text{O} + \text{CF}_3\text{COOH} \rightarrow \text{CF}_3\text{C}(\text{O})\text{OC}(\text{O})\text{CH}_3$                                                                                         | (via <b>TS49</b> ) | 11.77 (11.36)         | –20.15 (–14.25) |               |
| 41                | $\text{CF}_3\text{C}(\text{O})\text{OC}(\text{O})\text{C}_2\text{H}_5 + \text{CF}_3\text{COOH} \rightarrow \text{CF}_3\text{C}(\text{O})\text{OC}(\text{O})\text{CF}_3 + \text{C}_2\text{H}_5\text{COOH}$                | (via <b>TS9</b> )  | 26.06 (25.64)         | +6.74 (+7.14)   | +7.23 (+6.89) |
| 42                | $\text{CH}_3\text{CH}=\text{O} + \text{C}_2\text{H}_5^\cdot \rightarrow \text{CH}_3\text{CH}(\text{C}_2\text{H}_5)\text{O}^\cdot$                                                                                        | (via <b>TS50</b> ) | 6.59 (7.24)           | +1.85 (–0.22)   |               |
| 43                | $\text{CH}_3\text{CH}(\text{C}_2\text{H}_5)\text{O}^\cdot \rightarrow \text{C}_2\text{H}_5\text{CH}=\text{O} + \text{CH}_3^\cdot$                                                                                        | (via <b>TS51</b> ) | 9.81 (12.74)          | +1.96 (+4.02)   |               |
| 44                | $\text{CH}_3\text{CH}=\text{O} + \text{HSO}_4^\cdot \rightarrow \text{CH}_3\text{CH}(\text{OSO}_2\text{OH})\text{O}^\cdot$                                                                                               | (via <b>TS52</b> ) | 0.51 (–3.29)          | –8.76 (–7.35)   |               |
| 45                | $\text{CH}_3\text{CH}(\text{OSO}_2\text{OH})\text{O}^\cdot \rightarrow \text{CH}_3^\cdot + \text{HOSO}_2\text{OCH}=\text{O}$                                                                                             | (via <b>TS53</b> ) | 17.50 (15.56)         | +10.56 (+8.00)  |               |
| 46                | $\text{HOSO}_2\text{OCH}=\text{O} \rightarrow \text{H}_2\text{SO}_4 + \text{CO}$                                                                                                                                         | (via <b>TS54</b> ) | 22.78 (20.00)         | –1.18 (–5.16)   |               |
| 47                | $\text{HOSO}_2\text{OCH}=\text{O} + \text{CF}_3\text{COOH} \rightarrow \text{H}_2\text{SO}_4 + \text{CO} + \text{CF}_3\text{COOH}$                                                                                       | (via <b>TS55</b> ) | 21.45 (16.91)         | –1.18 (–5.16)   |               |
| 48                | $\text{CH}_3\text{COOH} + \text{C}_2\text{H}_5^\cdot \rightarrow \text{CH}_3\text{C}(\text{OH})(\text{C}_2\text{H}_5)\text{O}^\cdot$                                                                                     | (via <b>TS56</b> ) | 16.21 (17.26)         | +13.82 (+15.62) |               |
| 49                | $\text{CH}_3\text{C}(\text{OH})(\text{C}_2\text{H}_5)\text{O}^\cdot \rightarrow \text{C}_2\text{H}_5\text{COOH} + \text{CH}_3^\cdot$                                                                                     | (via <b>TS57</b> ) | 6.38 (5.74)           | –7.44 (–9.16)   |               |
| 50                | $\text{CH}_3\text{COOH} + \text{HSO}_4^\cdot \rightarrow \text{CH}_3\text{C}(\text{OH})(\text{OSO}_2\text{OH})\text{O}^\cdot$                                                                                            | (via <b>TS58</b> ) | 17.80 (20.18)         | +17.48 (+18.31) |               |
| 51                | $\text{CH}_3\text{C}(\text{OH})(\text{OSO}_2\text{OH})\text{O}^\cdot \rightarrow \text{CH}_3^\cdot + \text{HOSO}_2\text{OCOOH}$                                                                                          | (via <b>TS59</b> ) | 7.82 (6.78)           | –8.56 (–10.28)  |               |
| 52                | $\text{HOSO}_2\text{OCOOH} \rightarrow \text{H}_2\text{SO}_4 + \text{CO}_2$                                                                                                                                              | (via <b>TS19</b> ) | 10.39 (8.27)          | –16.18 (–19.61) |               |
| 53                | $\text{HOSO}_2\text{OCOOH} + \text{CF}_3\text{COOH} \rightarrow \text{H}_2\text{SO}_4 + \text{CO}_2 + \text{CF}_3\text{COOH}$                                                                                            | (via <b>TS20</b> ) | 13.67 (9.86)          | –16.18 (–19.61) |               |
| 54                | $\text{CF}_3\text{C}(\text{O})\text{OC}(\text{O})\text{CH}_3 + \text{CF}_3\text{COOH} \rightarrow \text{CF}_3\text{C}(\text{O})\text{OC}(\text{O})\text{CF}_3 + \text{CH}_3\text{COOH}$                                  |                    | 27.09 (26.87)         | +5.43 (+5.86)   | +5.51 (+5.56) |

[a]  $\Delta G_s$  values are indicated only for the processes which preserve the total number of molecules during reaction.

and operates in the presence of the metal catalyst, involves oxygenation of  $\text{C}_2\text{H}_5\text{CO}^\cdot$  with  $[\text{V}(\text{OO})\{\text{N}(\text{CH}_2\text{CH}_2\text{O})_3\}]$  to give  $\text{C}_2\text{H}_5\text{COO}^\cdot$  via formation of the intermediate  $[\text{V}\{\text{OOC}(\text{O})\text{C}_2\text{H}_5\}\{\text{N}(\text{CH}_2\text{CH}_2\text{O})_3\}]$  (Figure 4). The peroxo V species is derived from reaction of **3** with  $\text{HS}_2\text{O}_8^-$  (reaction 4a) or with  $\text{H}_2\text{SO}_5$  (peroxomonosulfuric acid) formed upon reaction of  $\text{HS}_2\text{O}_8^-$  with TFA or hydrolysis with traces of water<sup>[27c]</sup> (reactions 4b–d).  $\text{C}_2\text{H}_5\text{COO}^\cdot$  abstracts a hydrogen atom from, for example, excess  $\text{CF}_3\text{COOH}$  or  $\text{C}_2\text{H}_6$  (reactions 6 and 7) to afford propionic acid.

Alternative pathways II and III (Scheme 6) involve oxidation of  $\text{C}_2\text{H}_5\text{CO}^\cdot$  either by a protonated peroxo  $\text{V}^{\text{V}}$  complex such as  $[\text{V}(\text{OOH})\{\text{N}(\text{CH}_2\text{CH}_2\text{O})_3\}]^+$  (reaction 8) or by peroxodisulfate (reaction 11). Mixed anhydrides such as  $\text{CF}_3\text{C}(\text{O})\text{OC}(\text{O})\text{C}_2\text{H}_5$  and  $\text{C}_2\text{H}_5\text{C}(\text{O})\text{OSO}_2\text{OH}$  are easily formed (reactions 9–11) but they are thermodynamically more stable than  $\text{C}_2\text{H}_5\text{COOH}$ . Thus, formation of propionic acid via routes II and III is less favourable than via catalytic route I. A more detailed discussion is given in the Supporting Information.

The presence in the reaction mixture of species such as  $\text{C}_2\text{H}_5^\cdot$ ,  $\text{HSO}_4^\cdot$  and  $\text{CF}_3\text{COOH}$  provides for several side reac-

tions (reactions 12–14) leading to ethyl trifluoroacetate  $\text{CF}_3\text{COOC}_2\text{H}_5$ , and formation of this by-product was confirmed experimentally (see above).

**Carboxylating role of TFA:** In the absence of CO, the main products are acetic acid and the ester  $\text{CF}_3\text{COOC}_2\text{H}_5$ , which do not involve carboxylation of ethane. However, propionic acid was also detected on account of the carboxylating role of TFA, which possibly involves attack by  $\text{C}_2\text{H}_5^\cdot$  on the electrophilic carboxyl C atom of  $\text{CF}_3\text{COOH}$ <sup>[4c,31]</sup> to give an oxo radical intermediate (reaction 15, Scheme 7 and Scheme S2 in the Supporting Information). This intermediate undergoes a known  $\beta$ -bond cleavage reaction<sup>[32]</sup> to give  $\text{CF}_3^\cdot$  and  $\text{C}_2\text{H}_5\text{COOH}$  (reaction 16), and the former product is converted to trifluoromethane (reactions 17–19). Another less favourable mechanism, involving attack of  $\text{HSO}_4^\cdot$  on the carbonyl C atom of TFA and formation of  $\text{CO}_2$  (Scheme 8), is discussed in the Supporting Information.

**Oxidation:** Oxidation of ethane to acetic acid without C–C bond cleavage may occur via ethanol and acetaldehyde as intermediates. Indeed, alcohols are oxidised by our systems

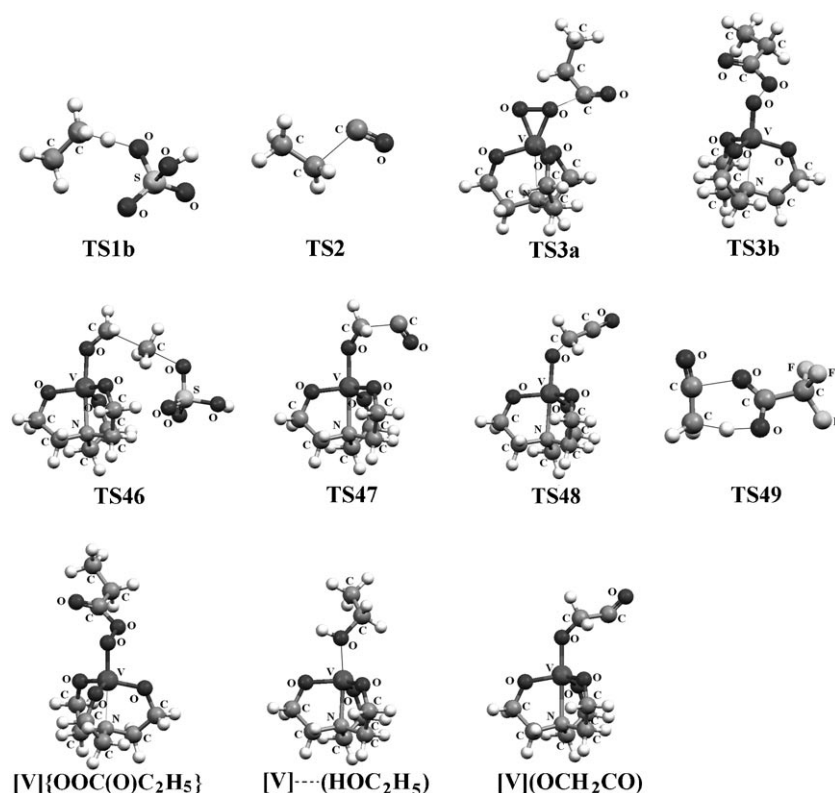


Figure 4. Equilibrium structures of selected TSs and intermediates (H atoms are not labelled for clarity). For a wider view see Figure S4 in the Supporting Information.

under typical conditions to the corresponding carboxylic acids, without appreciable carbonylation (Table 3), that is, ethanol leads to acetic acid (22% yield) with only traces of propionic acid, and propanol forms propionic acid, with a smaller amount of acetic acid, without detection of any butyric acid. The 15% yield of propionic acid from propanol is much lower than that of 78% obtained from ethane under identical conditions, and thus free propanol conceivably is not involved in the carboxylation of ethane to propionic acid. However, since the yield of acetic acid from ethanol (22%) is much higher than that from ethane (5%), we cannot rule out the possible involvement of some free ethanol in the oxidation of ethane to this acid.

Moreover, acetaldehyde is oxidised to acetic acid in a much higher yield (ca. 40%) than ethanol (22%) or ethane (5%), and this suggests possible involvement of the aldehyde in the conversion of ethane to acetic acid. Hence, the oxidative route to acetic acid with preservation of the alkane C–C bond can involve the sequential catalytic oxidations  $\text{C}_2\text{H}_6 \rightarrow \text{CH}_3\text{CH}_2\text{OH} \rightarrow \text{CH}_3\text{CHO} \rightarrow \text{CH}_3\text{COOH}$ . Acetic acid is almost unreactive under our typical reaction conditions (98% of its initial amount still remains after 20 h).

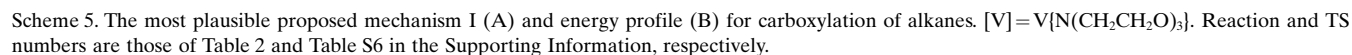
For conversion of the  $\text{C}_2\text{H}_5^\bullet$  radical to ethanol and acetaldehyde, several purely organic and metal-assisted mechanisms were theoretically investigated (Scheme 9). Among the most favourable are 1) formation of the ester  $\text{C}_2\text{H}_5\text{OSO}_2\text{OH}$  upon interaction of  $\text{C}_2\text{H}_5^\bullet$  with  $\text{HSO}_4^\bullet$  (reac-

tion 20) followed by solvolysis with  $\text{CF}_3\text{COOH}$  (reaction 21); 2) interaction of  $\text{C}_2\text{H}_5^\bullet$  with OH of the protonated form of **3**, that is,  $[\text{V}(\text{OH})\{\text{N}(\text{CH}_2\text{CH}_2\text{O})_3\}]^+$ , to give ligated ethanol (reactions 22 and 23, Figure 4) which can be liberated upon exothermic substitution by  $\text{CF}_3\text{COO}^-$  (reaction 24); 3) interaction of  $\text{C}_2\text{H}_5^\bullet$  with the peroxo V complex to give an ethylperoxo species (reaction 25) which, upon O–O bond cleavage, transforms into  $\text{C}_2\text{H}_5\text{O}^\bullet$  and regenerates **3** (reaction 26). (See Supporting Information for details and discussion of other less favourable routes.)

The oxidation of ethanol (or of the ethoxy radical) to acetaldehyde and further to acetic acid can occur easily by mechanisms involving abstraction of H atoms by radicals to form the acetyl radical  $\text{CH}_3\text{CO}^\bullet$  (reactions 27–31).<sup>[33]</sup> Plausible mechanisms for transformation of  $\text{CH}_3\text{CO}^\bullet$  into  $\text{CH}_3\text{COOH}$  were described previously.<sup>[7c]</sup> Other processes leading to  $\text{CH}_3\text{CHO}$  (reactions 60–67 in Table S6 in the Supporting Information) require significantly higher energy.

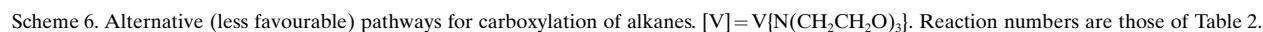
Another possible route to acetaldehyde involves oxidation of  $\text{C}_2\text{H}_5^\bullet$  by a hydroperoxo  $\text{V}^{\text{V}}$  complex, for example,  $[\text{V}(\text{OOH})\{\text{N}(\text{CH}_2\text{CH}_2\text{O})_3\}]^+$  (see above) to give  $\text{C}_2\text{H}_5^+$  (reaction 32) which, being a protonated ethylene, readily undergoes deprotonation (reactions 33 and 34). Recently, it was shown<sup>[34]</sup> that cation-radical vanadium clusters  $(\text{V}_2\text{O}_5)_n^+$  ( $n=1, 2$ ) oxidize  $\text{C}_2\text{H}_4$  to  $\text{CH}_3\text{CHO}$ . A peroxo  $\text{V}^{\text{V}}$  complex such as  $[\text{V}(\text{OO})\{\text{N}(\text{CH}_2\text{CH}_2\text{O})_3\}]$  may also be involved in ethylene oxidation. The  $\Delta G_s$  value for the corresponding overall reaction 35 is strongly negative ( $-83.17 \text{ kcal mol}^{-1}$ ). Detailed investigations of the possibility of this reaction and its mechanism are underway.

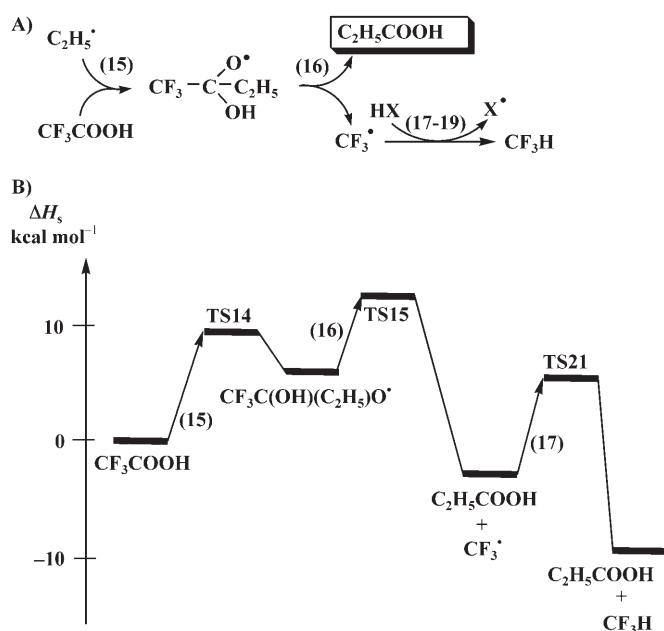
**C–C bond cleavage:** A point that deserves further analysis is the path for oxidation of ethane to acetic acid via C–C bond cleavage. A plausible mechanism (Scheme 10A) for this reaction is based on interaction of  $\text{C}_2\text{H}_5^\bullet$  with an oxo vanadium catalyst, for example,  $[\text{VO}\{\text{N}(\text{CH}_2\text{CH}_2\text{O})_3\}]$  (**3**), to give the  $\text{V}^{\text{IV}}$  species  $[\text{V}(\text{OC}_2\text{H}_5)\{\text{N}(\text{CH}_2\text{CH}_2\text{O})_3\}]$  (reaction 36). The latter may react with  $\text{HSO}_4^\bullet$  to yield the triplet structure  $[\text{V}^\bullet(\text{OC}_2\text{H}_5)\{\text{N}(\text{CH}_2\text{CH}_2\text{O})_3\}]$  (reaction 37), which interacts with CO to give the parent **3** and ketene  $\text{CH}_2=\text{C}=\text{O}$  via  $[\text{V}^\bullet(\text{OCH}_2\text{C}=\text{O})\{\text{N}(\text{CH}_2\text{CH}_2\text{O})_3\}]$  (reactions 38 and 39, Figure 4). Reaction of ketene with solvent



Cleavage of the C-C bond may also occur at later stages of ethane oxidation (Scheme 10C), that is, after formation of  $\text{CH}_3\text{CHO}$  or even  $\text{CH}_3\text{COOH}$ . Their electrophilic carbonyl C atoms may undergo attack by  $\text{C}_2\text{H}_5^\bullet$  or  $\text{HSO}_4^\bullet$  to give oxo radical intermediates (reactions 42, 44, 48, 50). As a

result of  $\beta$ -bond cleavage (reactions 43, 45, 49, 51),  $\text{CH}_3^{\cdot}$  is formed and reacts with CO to give the singly labelled acetic acid  $^{13}\text{CH}_3\text{COOH}$  (if  $^{13}\text{CH}_3^{13}\text{CH}_3$  and CO were starting materials).  $\text{HOSO}_2\text{OCHO}$  and  $\text{HOSO}_2\text{OCOOH}$ , upon decomposition into CO or  $\text{CO}_2$  and  $\text{H}_2\text{SO}_4$ , respectively (reactions 46, 47, 52, 53), are additional sources of the carbonyl

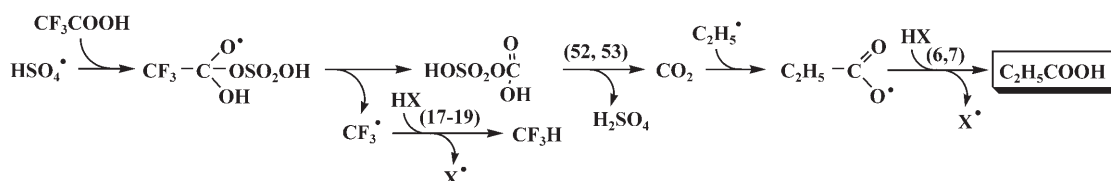




Scheme 7. Proposed mechanism (A) and energy profile (B) for carboxylation of  $\text{C}_2\text{H}_5^\bullet$  by TFA. Reaction numbers correspond to those of Table 2.  $\text{X} = \text{CF}_3\text{COO}^\bullet$ ,  $\text{C}_2\text{H}_5^\bullet$  or  $\text{HSO}_4^\bullet$ . TS numbers are those of Table S6 in the Supporting Information.

group. Other less favourable mechanisms of C–C bond cleavage are discussed in the Supporting Information.

**Role of the vanadium catalyst:** The role of the V centre in the carboxylation processes can be envisaged as promoting any of the following possible reactions: 1) oxygenation of the acyl radical  $\text{EtCO}^\bullet$  by a peroxo  $\text{V}^{\text{V}}$  complex, which provides the most preferable catalytic route for propionic acid (reactions 5–7); 2) oxidation of  $\text{EtCO}^\bullet$  to  $\text{EtCO}^+$  (reaction 8) by a hydroperoxo  $\text{V}^{\text{V}}$  species in the carboxylation process; 3) oxidation processes forming acetic acid via ethanol and acetaldehyde without C–C bond cleavage, namely, by oxidation of  $\text{Et}^\bullet$  to  $\text{Et}^+$  (reaction 32) by a hydroperoxo  $\text{V}^{\text{V}}$  species, by O transfer from a peroxo  $\text{V}^{\text{V}}$  species (with formation of the corresponding oxo  $\text{V}^{\text{V}}$  species)<sup>[6f]</sup> to give  $\text{Et}^\bullet$  (reaction 25) or  $\text{C}_2\text{H}_4$  (reaction 35) or by HO transfer from a hydroxo  $\text{V}^{\text{V}}$  species to give  $\text{Et}^\bullet$  (reaction 23); 4) carbonylation process leading to acetic acid with C–C bond cleavage via  $\text{V}^{\text{IV}}\text{--OC}_2\text{H}_5$  and  $\text{V}^{\text{IV}}\text{--OCH}_2^\bullet$  intermediates (reactions 36–39).



Scheme 8. Alternative (less favourable) pathways for the carboxylating role of TFA. Reaction numbers are those of Table 2.  $\text{X} = \text{CF}_3\text{COO}^\bullet$ ,  $\text{C}_2\text{H}_5^\bullet$  or  $\text{HSO}_4^\bullet$ .

Table 3. Comparative carboxylation of different substrates.<sup>[a]</sup>

| Entry | Substrate <sup>[b]</sup>              | $p(\text{CO})$ [atm] <sup>[c]</sup> | Yield [%] <sup>[d]</sup> |                  | Total | TON <sup>[e]</sup> |
|-------|---------------------------------------|-------------------------------------|--------------------------|------------------|-------|--------------------|
|       |                                       |                                     | Propionic acid           | Acetic acid      |       |                    |
| 1     | $\text{C}_2\text{H}_6$ <sup>[f]</sup> | 30                                  | 78.4                     | 4.8              | 83.2  | 127                |
| 2     | $\text{C}_2\text{H}_5\text{OH}$       | 30                                  | 0.3                      | 22.0             | 22.3  | 34                 |
| 3     | $\text{C}_3\text{H}_7\text{OH}$       | 30                                  | 14.5                     | 5.8              | 20.3  | 31                 |
| 4     | $\text{CH}_3\text{CHO}$               | 30                                  | 0.4                      | 40               | 40.4  | 61                 |
| 5     | $\text{CH}_3\text{COOH}$              | 30                                  | 0.0                      | — <sup>[g]</sup> | —     | —                  |

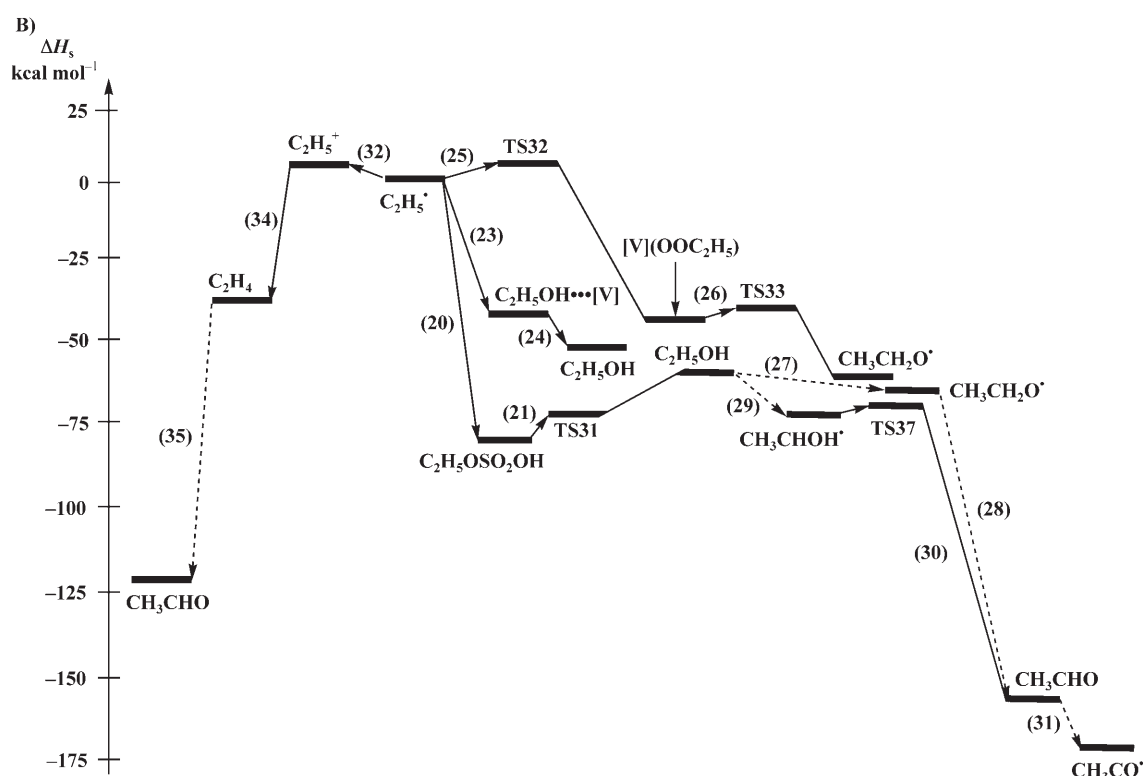
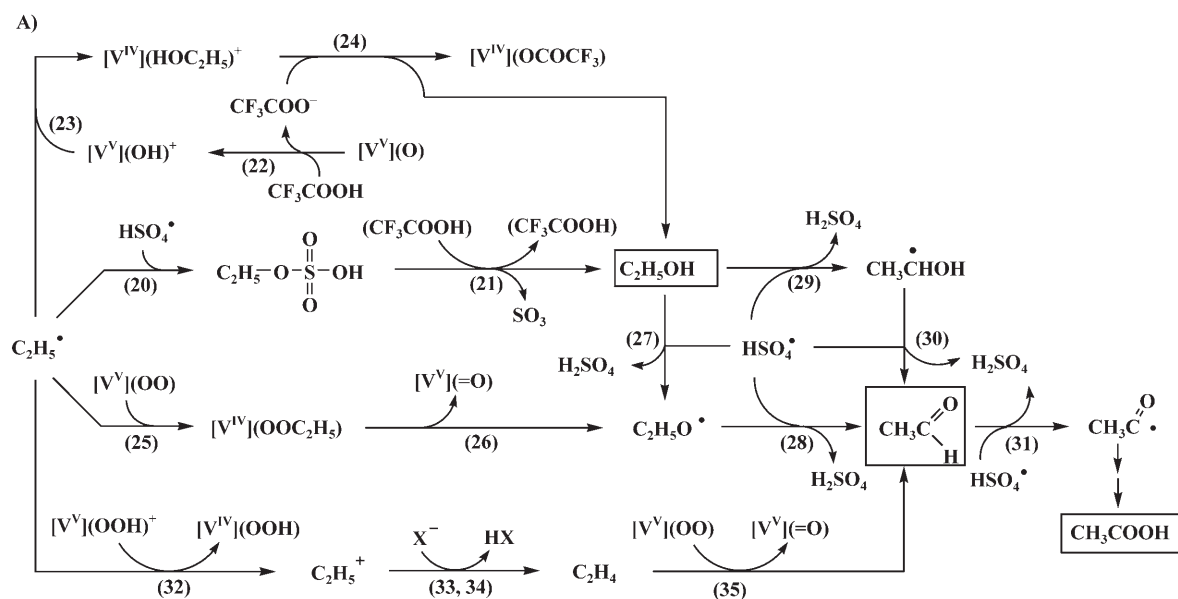
[a] Catalyst **2** (0.0200 mmol),  $\text{K}_2\text{S}_2\text{O}_8$  (4.00 mmol, i.e., 200:1 molar ratio of oxidant to metal catalyst),  $\text{CF}_3\text{COOH}$  (5.0 mL), 80 °C, 20 h, in an autoclave (13 mL capacity). [b] 3.06 mmol. [c] Measured at 25 °C (amounts of CO correspond to 0.306 mmol atm<sup>−1</sup>). [d] Molar yield [%] based on the substrate, that is, moles of product per 100 moles of the corresponding substrate. [e] Turnover number (moles of acetic and propionic acids per mole of metal catalyst). [f] 10 atm, measured at 25 °C (i.e., 3.06 mmol). [g] The amount of acetic acid at the end of the reaction is 97.8 % of its initial amount, that is, it is essentially unreactive.

## Conclusions

This work has extended to ethane the catalytic activity of amavadin and related vanadium complexes in functionalization of alkanes. It has shown that they can act as remarkably active catalysts for the direct one-pot carboxylation of ethane to give mainly propionic acid and, to a smaller extent, acetic acid, under mild conditions (the overall yield, based on the alkane, can reach 93 %). The catalysts remain active even at very low concentrations and unprecedented high TONs are obtained (up to  $2.0 \times 10^4$ ), still with good yields. The catalyst activities are much higher than those we have previously observed<sup>[7]</sup> for methane carboxylation to acetic acid and appear to be the highest so far reported in the field of alkane functionalization under mild conditions.

Optimisation and control of selectivity of the process have been achieved by studying the effects of a variety of factors that require adjustments within particular ranges, namely the ethane pressure (optimal of ca. 10 atm for propionic acid or ca. 3 atm for acetic acid), the CO pressure (ca. 15–20 atm for propionic acid and absence of CO for acetic acid), temperature (80 °C for propionic acid, whereas the effect, above ca. 50 °C, is small for acetic acid), time (ca. 20 h for propionic acid and ca. 5 h for acetic acid), and the amounts of TFA and  $\text{K}_2\text{S}_2\text{O}_8$  (e.g., 4 mmol for propionic acid under the typical conditions used).

The mechanisms involve both C- and O-centred radicals, as indicated by the inhibiting effect of radical traps, and for-

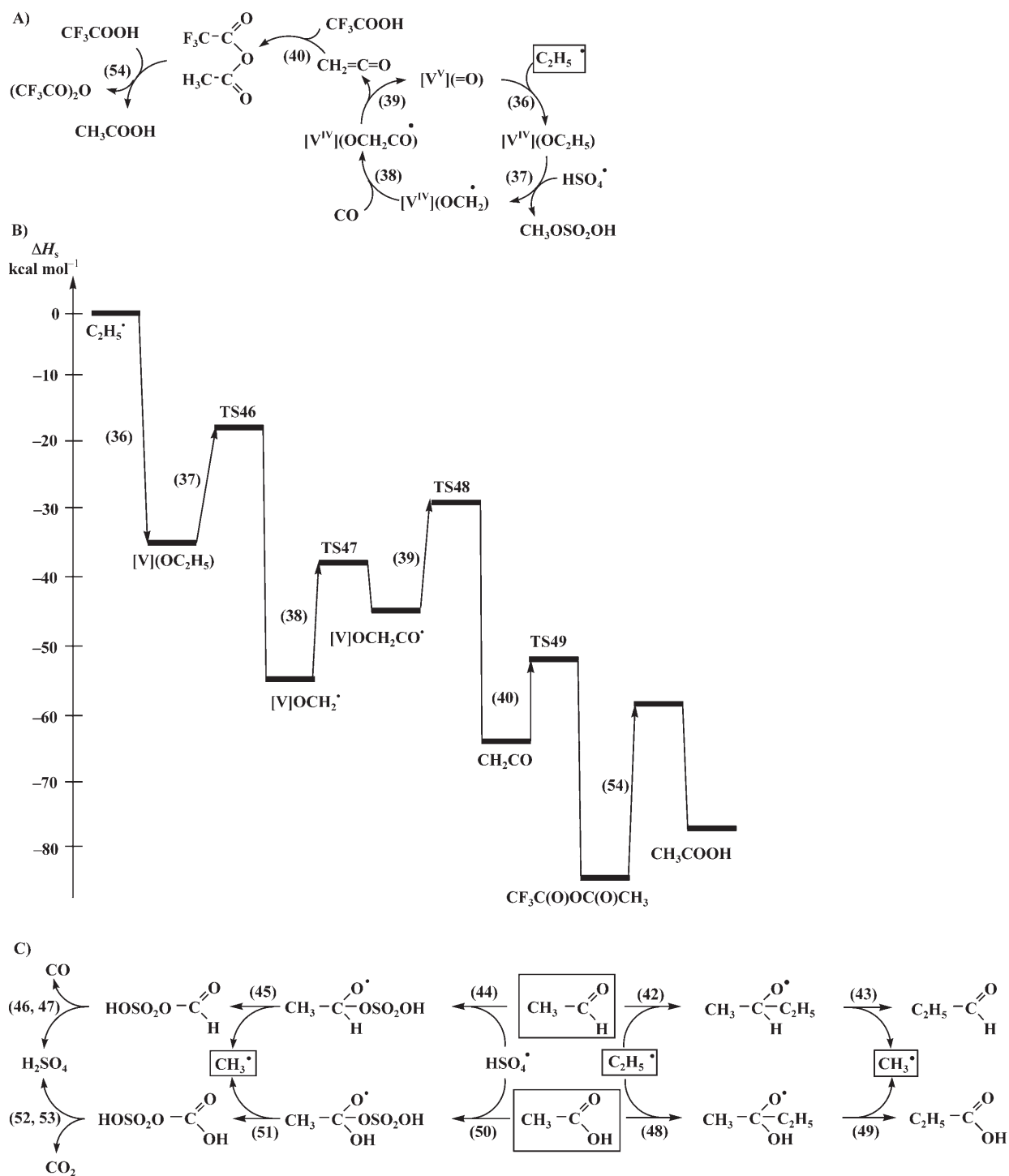


Scheme 9. Proposed mechanisms (A) and energy profile (B) for oxidation of ethane to acetic acid (via ethanol and acetaldehyde).  $[V] = V\{N-(CH_2CH_2O)_3\}$ .  $X = HSO_4$  or  $CF_3COO$ . Reaction and TS numbers are those of Table 2 and Table S6 in the Supporting Information, respectively.

mation of ethyl halides in the presence of  $\text{CBrCl}_3$ , and evidence has been presented for a key role of the oxidizing agent  $\text{K}_2\text{S}_2\text{O}_8$  as a source of radicals ( $\text{SO}_4^{\cdot-}$ ,  $\text{HSO}_4^{\cdot}$ ) suitable for H abstraction from the alkane. The thus-formed ethyl radical reacts with CO, and the resulting acyl radical  $\text{C}_2\text{H}_5\text{CO}^{\cdot}$  interacts further with the catalyst to yield the carboxyl radical  $\text{C}_2\text{H}_5\text{COO}^{\cdot}$  which, upon H abstraction from the alkane or TFA, is converted to propionic acid. In the ab-

sence of a catalyst, two alternative routes are operative, but both lead to thermodynamically stable mixed anhydrides instead of  $C_7H_5COOH$ .

A role of the TFA solvent as a carbonylating agent has also been recognised, by performing experiments in the absence of CO and theoretical calculations. Under such conditions, TFA reacts with the ethyl radical to yield an oxo radical intermediate which, upon  $\beta$ -bond cleavage, directly af-



Scheme 10. Proposed mechanisms (A, C) and energy profile for mechanism A (B) for ethane C–C bond cleavage. [V] = V[N(CH<sub>2</sub>CH<sub>2</sub>O)<sub>3</sub>]. Reaction and TS numbers are those of Table 2 and Table S6 in the Supporting Information, respectively.

fords C<sub>2</sub>H<sub>5</sub>COOH, albeit in comparatively low yield due to competitive side reactions.

Experiments with <sup>13</sup>C-enriched gases confirmed that the ethyl group of propionic acid originates from ethane and the carbonyl group from CO, whereas the formation of acetic acid follows two pathways: a dominant one via ethane oxidation with preservation of the C–C bond, and a less exten-

sive one via cleavage of this bond with carbonylation of a methyl group. The formation of acetic acid via the former route conceivably involves sequential (both purely organic and metal-assisted) oxidation of ethane to ethanol and/or acetaldehyde and further to acetyl radical with low activation barriers. The formed CH<sub>3</sub>CO\* undergoes peroxo-V-catalysed conversion to CH<sub>3</sub>COOH. However, propanol is not

expected to be an intermediate to propionic acid. For the oxidation of ethane to acetic acid with C–C bond cleavage, several metal-assisted and organic pathways were also considered.

The studies also suggest that ethane can become a promising raw material for the synthesis of propionic and acetic acids, in the presence and absence of CO, respectively, under mild conditions. However, in view of the appreciable cost of TFA, its recycling and the search for a cheaper solvent (and cheaper oxidant) are advisable, as well as establishing an easy method of separating the acid products.

Although the biological role of amavadin has not yet been ascertained, its ability to catalyse the formation of hydrophilic carboxylic acids and esters from hydrophobic hydrocarbons like alkanes could possibly be used by organisms not only for the elimination of noxious hydrocarbons but also for biosynthetic purposes, although under reaction conditions different from ours, which are not found in nature.

## Experimental Section

Catalysts **1**,<sup>[26b]</sup> **2**,<sup>[26b]</sup> **3**<sup>[40]</sup> and **4**<sup>[41]</sup> were prepared according to published methods. [VO(acac)<sub>3</sub>] (**5**; Aldrich), VOSO<sub>4</sub>·5H<sub>2</sub>O (**6**; Merck), V<sub>2</sub>O<sub>5</sub> (**7**; Aldrich) and V<sub>2</sub>O<sub>4</sub> (**8**; Merck) were obtained from commercial sources and used as received. Ethane (AlphaGaz), <sup>13</sup>C-enriched ethane (Aldrich), carbon monoxide (Air Products), <sup>13</sup>C-enriched carbon monoxide (Aldrich) and dinitrogen gases (Air Liquid Portugal), potassium peroxodisulfate (Fluka), trifluoroacetic acid (Aldrich), CBrCl<sub>3</sub> (Fluka), 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO, Aldrich), Ph<sub>2</sub>NH (Fluka), 2,6-di-*tert*-butyl-4-methylphenol (BHT, Aldrich), benzoyl peroxide (Fluka), tetraethyllead (50% xylene solution, Aldrich), ethanol (Panreac), propanol (Panreac), acetic acid (Merck), acetaldehyde (Fluka) and *n*-butyric acid (Aldrich) were obtained from commercial sources and used as received. The reaction mixtures were prepared as follows: K<sub>2</sub>S<sub>2</sub>O<sub>8</sub> (1.08 g, 4.00 mmol) and TFA (5.0–7.3 mL) were added to 0.04–20.00 μmol of catalyst, either in solid form, as a fine solid mixture with K<sub>2</sub>S<sub>2</sub>O<sub>8</sub> (K<sub>2</sub>S<sub>2</sub>O<sub>8</sub>:catalyst 100:1) or as a 0.0020 M solution in TFA, in a 13.0 mL stainless steel autoclave, equipped with a Teflon-coated magnetic stirring bar. Then the autoclave was closed and flushed with dinitrogen three times to remove the air and finally pressurised with ethane (0–15 atm) and carbon monoxide (0–40 atm). The reaction mixture was vigorously stirred for 2–20 h at 80 °C using a magnetic stirrer and an oil bath. After the selected reaction time, the autoclave was cooled in an ice bath, then degassed and opened. Diethyl ether (5 mL) and *n*-butyric acid as internal standard (90 μL) were added to 1 mL of the reaction mixture. The resulting mixture was stirred, filtered and analysed by gas chromatography (internal standard method) on a Fisons Instruments GC 8000 series gas chromatograph with a DB WAX fused-silica capillary column and the Jasco-Borwin v.1.50 software. In some cases products were also identified by GC-MS and <sup>1</sup>H and <sup>13</sup>C{<sup>1</sup>H} NMR techniques on a Trio 2000 Fisons spectrometer with a coupled Carlo Erba (Auto/HRGC/MS) gas chromatograph and a Varian UNITY 300 NMR spectrometer, respectively.

Blank experiments were performed in the absence of the metal complex catalyst or of K<sub>2</sub>S<sub>2</sub>O<sub>8</sub>. Propionic acid was never detected, and only traces of acetic acid were observed without the metal complex.

The experiments with <sup>13</sup>C-enriched ethane were performed at *p*(<sup>13</sup>C<sub>2</sub>H<sub>6</sub>) = 1.5–2.0 atm in the absence or in the presence of CO, that is, *p*(CO) = 0 or 25 atm, respectively, with catalyst **1** (0.020 mmol) and K<sub>2</sub>S<sub>2</sub>O<sub>8</sub> (4.0 mmol) in CF<sub>3</sub>COOH (5.0 mL) at 80 °C (20 h reaction time).

The experiments with <sup>13</sup>C-enriched carbon monoxide were performed at *p*(<sup>13</sup>CO) = 2.0 atm and *p*(C<sub>2</sub>H<sub>6</sub>) = 10 atm with catalyst **1** (0.020 mmol) and K<sub>2</sub>S<sub>2</sub>O<sub>8</sub> (4.0 mmol) in CF<sub>3</sub>COOH (5.0 mL) contained in a 13 mL stainless

steel autoclave equipped with a Teflon-coated magnetic stirring bar at 80 °C (20 h reaction time).

**Computational details:** Full geometry optimisation of all transition-state structures was carried out at the DFT level of theory using Becke's three-parameter hybrid exchange functional<sup>[42]</sup> in combination with the gradient-corrected correlation functional of Lee, Yang and Parr<sup>[43]</sup> (B3LYP) with the help of the Gaussian 98<sup>[44]</sup> program package. Restricted approximations were employed for the structures with closed electron shells, and unrestricted methods for the structures with open electron shells. For purely organic reactions, the 6-31G\*<sup>[45]</sup> and 6-311+G\*\*<sup>[46]</sup> basis sets were applied. For reactions involving vanadium species, a relativistic Stuttgart pseudopotential described 10 core electrons, and the appropriate contracted basis set (8s7p6d1f)/[6s5p3d1f]<sup>[47]</sup> was used for the vanadium atom, and the 6-31G\* basis set for other atoms. This level is also denoted as B3LYP/6-31G\* despite the use of the other basis set on the V atom. Symmetry operations were not applied for all structures.

The Hessian matrix was calculated analytically for all optimised structures in order to prove the location of correct minima (no imaginary frequencies) or saddle points (only one negative eigenvalue), and to estimate the thermodynamic parameters, which were calculated at 80 °C and 10 atm. The nature of all transition states was investigated by analysis of vectors associated with the imaginary frequency and, in some cases, by intrinsic reaction coordinate (IRC)<sup>[48]</sup> calculations. The entropic terms and therefore the Gibbs free energies of activation and reaction calculated by using the standard expressions for an ideal gas are overestimated or underestimated for reactions occurring in solution and proceeding with a change in number of molecules. Hence, the Δ*G*<sub>s</sub> values are indicated only for processes that retain the total number of the molecules during reaction. For the same reason, the Δ*G*<sub>s</sub><sup>‡</sup> values are indicated only for unimolecular reactions.

Solvent effects were taken into account in the single-point calculations on the basis of the gas-phase geometries at the CPCM-B3LYP/6-31+G\*\*/gas-B3LYP/6-31G\* and CPCM-B3LYP/6-311+G\*\*/gas-B3LYP/6-311+G\*\* levels of theory by using the polarizable continuum model<sup>[49]</sup> in the CPCM version.<sup>[50]</sup> This method has been recognised as quite appropriate for consideration of the solvent effects of neutral and charged species.<sup>[51]</sup> The trifluoroacetic acid solvent was approximated by values of dielectric constant and solvent radius of 8.55 and 2.18 Å, respectively. The enthalpies and Gibbs free energies in the solution (*H*<sub>s</sub> and *G*<sub>s</sub>) were estimated by addition of the solvation energy Δ*G*<sub>solv</sub> to gas-phase enthalpies and Gibbs free energies (*H*<sub>g</sub> and *G*<sub>g</sub>).

For some structures, several possible conformations or coordination modes have been calculated, and only the most stable ones are discussed.

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