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Vanadium-catalyzed carboxylation of linear and cyclic C_5 and C_6 alkanes

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Abstract

Cyclopentane, cyclohexane, pentane, and hexane are carbonylated in single-pot processes and under mild conditions to carboxylic acids (highest yields of 54–33% and turnover numbers [TONs] of 76–50) by vanadium (IV) and (V) complexes in TFA. These complexes present N,O- or O,O-ligands, namely basic forms of aminoalcohols and of (hydroxyimino)dicarboxylic acids, trifluoroacetate, or triflate. The effects of various parameters (e.g., catalyst type, oxidizing agent, CO pressure, temperature, reaction time, type of solvent) were investigated. The use of either too low or too high CO pressures is discouraged, because the former promote the formation of trifluoroacetate esters and the latter, above a certain level, do not result in higher yields or TONs of the carboxylic acids. Carbon- and oxygen-centered radical mechanisms are suggested by experiments with radical traps and by acid product distribution.

Keywords: Vanadium catalyst; Carboxylation; Homogeneous catalysis; Alkane; Carbon monoxide

1. Introduction

Functionalization of saturated hydrocarbons (alkanes) is attracting great attention, and their conversion into more valuable products, like carboxylic acids, is a matter of current interest. Alkanes are unreactive by most conventional synthetic methods, and their partial oxidation with homogeneous metal catalysts has been recognized as one of the most promising approaches [1–12]. The most important general commercial methods of producing carboxylic acids include aldehyde oxidation, carboxylation of olefins (Koch synthesis), paraffin oxidation, and alkali fusion of alcohols [13]. However, saturated hydrocarbons, the main components of petroleum oil, are abundantly available and cheaper, and their direct conversion to carboxylic acids constitutes one of the most promising routes for the synthesis of the latter.

Fujiwara's group has already reported the catalytic carboxylation of alkanes by CO using such catalysts as $Pd(OAc)_2$ [14–17], $Cu(OAc)_2$ [14,15,17], Mg [18,19], $CaCl_2$ [20], and $Co(OAc)_2$ [21,22], but the yields or turnover numbers (TONs) and selectivities toward carboxylic acids are usually modest. Hence a main aim of the current work is to find a more active homogeneous catalytic system for an alkane-based synthetic method of carboxylic acids. Another objective is to provide a contribution toward the expansion of the still-underdeveloped field of catalysis with vanadium coordination compounds [23,24].

For such purposes, we have addressed some vanadium (IV) or (V) complexes (like Amavadine and related models) with N,O ligands, which we have previously found to be active, under mild conditions, for the single-pot conversion of methane into acetic acid [25] with and without the presence of CO, and for the peroxidative halogenation, hydroxylation, and oxygenation of alkanes into organohalides, alcohols, and ketones, respectively [26,27]. Here we report the results of the extension of the methane carboxylation reaction to liquid alkanes. We show that such vanadium (IV) and (V) complexes and related complexes, using $K_2S_2O_8$ as an oxidizing agent and trifluoroacetic acid (TFA) as a solvent, in mild conditions, catalyze the conversion of linear (pentane and hexane) and cyclic (cyclopentane and cyclohexane) C_5 and C_6 alkanes, in the presence of CO, into carboxylic acids with good yields (up to 50%).

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2. Experimental

2.1. Materials

The following compounds were used as received from the supplier: carbon monoxide (Air Products), dinitrogen (Air Liquid Portugal), cyclopentane (Fluka), cyclohexane (Aldrich), pentane (Lab-Scan), hexane (Fluka), potassium peroxodisulfate (Fluka), ammonium peroxodisulfate (Fluka), *tert*-butyl hydroperoxide solution, 70% in water (Fluka), TFA (Aldrich), *n*-butyric acid (Aldrich), and diethyl ether (Lab-Scan). The following complexes, applied as catalysts, were prepared according to published methods: $[VO\{N(CH_2CH_2O)_3\}]$ **1** [28,29], $Ca[V(HIDA)_2]$ (HIDA = basic form of 2,2′-(hydroxyimino)diacetic acid) **2** [30], $Ca[V(HIDPA)_2]$ (HIDPA = basic form of 2,2′-(hydroxyimino)dipropionic acid) **3** [30], $[VO(ada)(H_2O)]$ (ada = basic form of *N*-2-acetamidoiminodiacetic acid) **4** [31], $[VO(Hheida)(H_2O)]$ (Hheida = dibasic form of 2-hydroxyethyliminodiacetic acid) **5** [31], and $[VO(CF_3SO_3)_2] \cdot 2H_2O$ **8** [32]. Complexes $[VO\{N(CH_2COO)(CH_2CH_2O)(CH_2CH_2OH)\}]$ **6** and $[VO(CF_3COO)_2] \cdot 2H_2O$ **7** were prepared as described below, whereas $VOSO_4 \cdot 5H_2O$ **9** (Merck), V_2O_4 **10** (Merck), and V_2O_5 **11** (Aldrich), the other catalysts, were used as received.

2.1.1. Complex *6*

N,*N*-bis(2-hydroxyethyl)glycine (bicine) (0.82 g, 5.0 mmol) and $Ba(OH)_2 \cdot 8H_2O$ (1.58 g, 5.00 mmol) were dissolved in deionised water (20 mL) under dinitrogen. The solution was heated and stirred for 30 min, after which $VOSO_4 \cdot 5H_2O$ (1.26 g, 5.00 mmol) was added and the reaction mixture stirred for another 30 min. The formed solid of $BaSO_4$ was separated by filtration, and the filtered dark-blue solution was concentrated under vacuum to yield an oily residue, which was washed with diethyl ether by the freeze-thaw technique to give a dark-blue solid that was filtered off, washed with diethyl ether, and dried under vacuum. Yield 0.662 g (58%). IR (KBr): 951(m) ν(V=O), 1442(m), 1647(w), 3385 cm^{-1}(w,br) ν(OH). MS (FAB^+): m/z: 228 [M^+]; elemental analysis: calcd (%) for $C_6H_{11}O_5NV \cdot 0.5(CH_3CH_2)_2O$ (228): C 36.0, H 6.2, N 6.0; found: C 35.6, H 6.7, N 6.5.

2.1.2. Complex *7*

The synthesis was performed in two steps. In the first step, the salt $Ba(CF_3COO)_2$ was synthesized by the reaction of $Ba(OH)_2 \cdot 8H_2O$ (204.7 mg, 0.65 mmol) with TFA (CF_3COOH) (0.10 mL, 1.3 mmol) in water under dinitrogen (yield 89%). This salt (144.8 mg, 0.58 mmol) was then dissolved in methanol (2 mL), and the solution was added to a methanol solution (2 mL) of $VOSO_4 \cdot 5H_2O$ (146.4 mg, 0.58 mmol). The formed precipitate of $BaSO_4$ was subsequently filtered off, and the filtered bright-blue solution was concentrated under vacuum to give a brown solid, which was dried for a few hours at 120 °C in an oil bath. Yield 122 mg (72%); IR (KBr): 728 (s), 991(m) ν(V=O), 1151(m), 1205(m), 1439(m), 1676(w) ν(C=O), 3400 cm^{-1}(w,br) ν(OH); elemental analysis: calcd (%) for $C_4O_5F_6V \cdot 2H_2O$ (329): C 14.6, H 1.2; found: C 14.5, H 0.9.

2.2. Instrumentation

C, H, and N elemental analyses were carried out by the Microanalytical Service of the Instituto Superior Técnico. Positive-ion FAB mass spectra were obtained on a Trio 2000 instrument by bombarding 3-nitrobenzyl alcohol (NBA) matrices of the samples with 8 keV (ca. 1.18×10^{15} J) Xe atoms. Mass calibration for data system acquisition was achieved using CsI. Infrared spectra (4000–400 cm^{-1}) were recorded on a Jasco FT/IR–430 instrument in KBr pellets. ^{13}C-$\{^1H\}$ and ^{19}F nuclear magnetic resonance (NMR) spectra were recorded at 22 °C on a Varian UNITY 300 spectrometer using TMS as internal standard (for ^{13}C) and $CFCl_3$ (for ^{19}F).

Gas chromatography (GC) measurements were carried out on a Fisons model 8160 equipped with a flame ionisation detector and a capillary column (DB-WAX; column length, 30 m; i.d., 0.32 mm). Helium was used as the carrier gas. GC-mass spectroscopy (MS) measurements were carried out in a Fisons Trio 2000 mass spectroscope with a coupled gas chromatograph (Carlo Erba Instruments, Auto/HRGC/MS).

2.3. Typical carboxylation procedures and products analysis

The reaction mixtures were prepared as follows. To 0.0625 mmol of the metal complex contained in a 39.0 mL AISI 316 stainless steel autoclave equipped with a Teflon-coated magnetic stirring bar was added the oxidant [either $K_2S_2O_8$ (12.5 mmol), $(NH_4)_2S_2O_8$ (12.5 mmol), or *t*-BuOOH (12.5 mmol)], the substrate [cyclopentane (0.90 mL, 9.58 mmol), cyclohexane (1.00 mL, 9.26 mmol), pentane (1.00 mL, 8.68 mmol), or hexane (1.10 mL, 8.42 mmol)] and 22.0 mL of TFA. Then the autoclave was closed and flushed with dinitrogen three times for replacing the air inside and finally pressurized with 0–60 atm of carbon monoxide. The reaction mixture was vigorously stirred using a magnetic stirrer for 2–20 h at 40–150 °C with an oil bath. After the reaction was complete, the autoclave was cooled using an ice bath, then degassed and opened. To 2.5 mL of the filtered reaction solution was added 6.5 mL of diethyl ether (which led to further precipitation) and 90 µL of *n*-butyric acid (as an inner standard). The obtained mixture was stirred, then filtered off and analyzed by gas chromatography. The reaction products (carboxylic acids) were quantitatively analyzed by GC (1 µL samples) using the inner standard method. The injection temperature was 240 °C, and the column temperature was initially 100 °C for 1 min, then increased by 10 °C/min (or 5 °C/min for the analysis of the hexane products) to 250 °C and held at this value for 1 min.

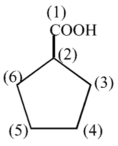
In some cases, products were also identified by GC-MS and ^{13}C-$\{^1H\}$ NMR of the final reaction solutions. The carboxylic acids of all hydrocarbons were determined by both GC and ^{13}C-$\{^1H\}$ NMR (in $CDCl_3$) spectroscopy, and the esters were identified by ^{13}C-$\{^1H\}$ and ^{19}F NMR spectroscopy. Genuine samples of the esters were synthesized in our laboratory by the reaction of TFA with the corresponding alcohols and their NMR spectra, as well as those of the carboxylic acids, were compared with those of the reaction solutions to identify the products:

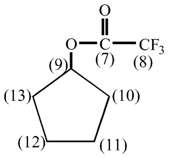
C_5H_9COOH ^{13}C-$\{^1H\}$ NMR (δ): 25.7 ($C4+C5$), 30.1 ($C3+C6$), 43.9 ($C2$), 186.2 ($C1$).

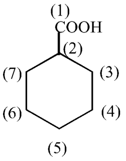
$C_5H_9OCOCF_3$ ^{13}C-$\{^1H\}$ NMR (δ): 23.4 ($C11+C12$), 32.4 ($C10+C13$), 84.0 ($C9$), 114.5 ($C8$) (buried under the CF_3COOH quartet), 161.9 ($C7$) (buried under the CF_3COOH quartet). ^{19}F NMR (δ): −79.3.

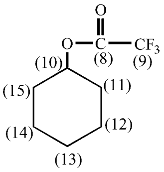
$C_6H_{11}COOH$ ^{13}C-$\{^1H\}$ NMR (δ): 25.2 ($C4+C6$), 25.5 ($C5$), 28.8 ($C3+C7$), 43.4 ($C2$), 185.3 ($C1$).

$C_6H_{11}OCOCF_3$ ^{13}C-$\{^1H\}$ NMR (δ): 23.2 ($C12+C14$), 25.0 ($C13$), 30.9 ($C11+C15$), 79.6 ($C10$), 128.5 ($C9$), 162 ($C8$) (buried under the CF_3COOH quartet). ^{19}F NMR (δ): −79.0.









The catalytic TONs and yields were expressed by the molar ratio of product/V-catalyst precursor and the molar ratio (%) of product/substrate, respectively. Blank tests demonstrated that no product was obtained without the presence of the substrate, the V compound, the oxidizing agent (peroxodisulfate salt), and carbon monoxide.

3. Results and discussion

3.1. Carboxylation of cyclopentane and cyclohexane

Both cyclopentane and cyclohexane, in TFA and in the presence of $K_2S_2O_8$ as an oxidizing agent, under the conditions described earlier, undergo carboxylation by CO to the corresponding carboxylic acids, that is, cyclopentanoic and cyclohexanecarboxylic acids (Scheme 1, Tables 1 and 2). The respective trifluoroacetate esters (i.e., cyclopentyltrifluoroacetate and cyclohexyltrifluoroacetate) were also formed, mainly in the absence of CO. However, the formation of esters does not involve carboxylation by CO and has not been investigated in detail, in contrast with alkane carboxylation to the corresponding carboxylic acids, the process on which we have focused our attention.

Table 1
Carboxylation of cyclopentane into cyclopentanecarboxylic acid[a]

Entry	Catalyst	p(CO)[b] (atm)	TON[c]	Yield[d] (%)
1	1	15	15.8	10.2
2	1	30	27.2	17.8
3	1	45	33.6	21.9
4	1	60	35.2	23.0
5	2	15	14.1	9.2
6	2	22.5	18.7	12.2
7	2	26	40.3	26.3
8[e]	2	30	49.8	32.5
9	2	34	42.6	27.8
10	2	37.5	37.7	24.6
11	2	45	29.2	19.4
12	2	60	33.7	22.0
13[f]	2	30	44.0	28.8
14[g]	2	30	18.4	12.0
15	3	30	19.0	12.4
16	4	30	21.8	14.2
17	5	30	27.8	18.2
18	6	30	21.6	14.1
19	7	30	23.0	15.4
20	8	30	42.8	28.0
21	9	30	29.3	19.5
22	10	30	24.0	15.6
23	11	30	14.4	9.6

[a] Reaction conditions (unless otherwise stated): metal complex catalyst (0.0625 mmol), $K_2S_2O_8$ (12.5 mmol, i.e., 200:1 molar ratio of oxidant to metal catalyst), cyclopentane (0.9 mL, 9.58 mmol, i.e., 150:1 molar ratio of substrate to metal catalyst), CF_3COOH (22 mL), 80 °C, 20 h reaction time, in an autoclave (39 mL capacity). Amounts of CO gas correspond to 0.575 $mol\,atm^{-1}$ with the pressure measured at 25 °C.

[b] Measured at 25 °C.

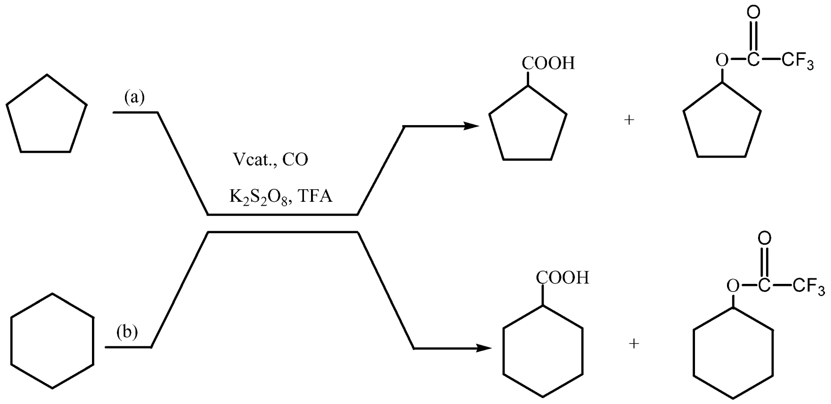
[c] Turnover number expressed by the number of moles of cyclopentanecarboxylic acid (product) per mol of metal catalyst.

[d] Molar yield (%) based on cyclopentane, i.e. number of moles of cyclopentanecarboxylic acid (product) per 100 moles of cyclopentane (substrate).

[e] Replacement of $K_2S_2O_8$ for t-BuOOH results in complete loss of activity. For a lower amount of cyclopentane (0.40 mL, 1.02 mmol) and a higher amount of CF_3COOH (23 mL), one obtains TON = 3.7, yield = 2.4.

[f] $(NH_4)_2S_2O_8$ used instead of $K_2S_2O_8$, in the same amount.

[g] More $K_2S_2O_8$ was used (15.6 mmol, i.e. 250:1 molar ratio of oxidant to metal catalyst).



Scheme 1. Carboxylation of cyclopentane (a) or cyclohexane (b) to the corresponding carboxylic acids and trifluoroacetate esters.

Table 2
Carboxylation of cyclohexane into cyclohexanecarboxylic acid[a]

Entry	Catalyst	$K_2S_2O_8$/ catalyst (molar ratio)	Cyclohexane/ catalyst (molar ratio)	p(CO)[b] (atm)	T (°C)	t (h)	TON[c]	Yield[d] (%)
1[e]	1	200	150	15	80	20	50.7	34.2
2	1	200	150	30	80	20	46.9	31.6
3	1	200	150	40	80	20	48.9	33.0
4	1	200	150	15	40	20	5.3	3.5
5	1	200	150	15	120	20	50.9	34.4
6	1	200	150	15	80	2	28.6	19.3
7	1	200	150	15	80	4	43.4	29.3
8	1	200	150	15	80	7	48.5	32.8
9	1	200	150	15	80	14	48.4	32.6
10	1	100	150	15	80	7	35.8	24.2
11	1	280	150	15	80	7	3.7	2.5
12	1	200	35	30	80	20	0.1	0.3
13	1	200	740	30	80	20	117	15.8
14	2	200	150	7.5	80	20	43.4	29.3
15	2	200	150	15	80	20	71.4	48.2
16	2	200	150	30	80	20	73.8	49.8
17	3	200	150	15	80	7	43.6	29.5
18	5	200	150	15	80	20	38.0	25.6
19	7	200	150	15	80	20	20.3	14.0
20	8	200	150	15	80	20	15.6	10.7
21	9	200	150	15	80	20	35.8	24.2
22	10	200	150	15	80	20	7.8	5.6
23	11	200	150	15	80	20	23.3	16.6

[a] Reaction conditions (unless otherwise stated): metal complex catalyst (0.0625 mmol), $K_2S_2O_8$ (12.5 mmol, i.e., 200:1 molar ratio of oxidant to metal catalyst), cyclohexane (1.0 mL, 9.26 mmol), CF_3COOH (22 mL), 80 °C, 20 h, in an autoclave (39 mL capacity). Amounts of CO gas correspond to 0.575 mol atm^{-1} with the pressure measured at 25 °C.

[b] Measured at 25 °C.

[c] Turnover number expressed by the number of moles of cyclohexanecarboxylic acid (product) per mol of metal catalyst.

[d] Molar yield (%) based on cyclohexane, i.e. number of moles of cyclohexanecarboxylic acid (product) per 100 moles of cyclohexane (substrate).

[e] Replacement of TFA by acetic acid or ethanol results in complete loss of activity, whereas replacement by acetonitrile leads to TON ≈ 2.1, yield ≈ 1.4% (p(CO) = 15 or 30 atm) (even lower values of TON = 1.1, yield = 0.7% at 120 °C). At 150 °C, decomposition occurs with formation of an insoluble solid and volatiles (pressure increase).

The most active system is provided by the Amavadine model catalyst Ca[V(HIDA)$_2$] **2**, leading to a maximum yield of 33% and a maximum TON of 50 for the cyclopentane carboxylation to cyclopentanecarboxylic acid (entry 8, Table 1), and 50% and 74 for the cyclohexane carboxylation to cyclohexanecarboxylic acid (entries 15 and 16, Table 2). (For the particular meanings of the yields and TONs, see the appropriate footnotes in the tables.) Higher TONs can be achieved for higher alkane:catalyst ratios than those normally used (e.g., TON = 117 for a 740:1 ratio, for the formation of cyclohexanecarboxylic acid [entry 13, Table 2]), although with an yield drop.

The other V-complexes form less active systems, which nevertheless can also exhibit quite considerable catalytic activities. Hence, for instance, the triethanolaminate complex [VO{N(CH$_2$CH$_2$O)$_3$}] **1** also provides an effective catalyst, with yields of 23% (entry 4, Table 1) and 34% (entry 5, Table 2) (corresponding TONs of 35 and 51) for the carboxylation of cyclopentane and cyclohexane, respectively, to the acids. The triflate complex [VO(CF$_3$SO$_3$)$_2$] **8** is also quite active (e.g., 28% yield, TON of 43 [entry 20, Table 1] for the carboxylation of cyclopentane). A lower activity is displayed by $VOSO_4$ **9** (e.g., 20% yield of cyclopentanecarboxylic acid [entry 21, Table 1] and 24% yield of cyclohexanecarboxylic acid [entry 21, Table 2]).

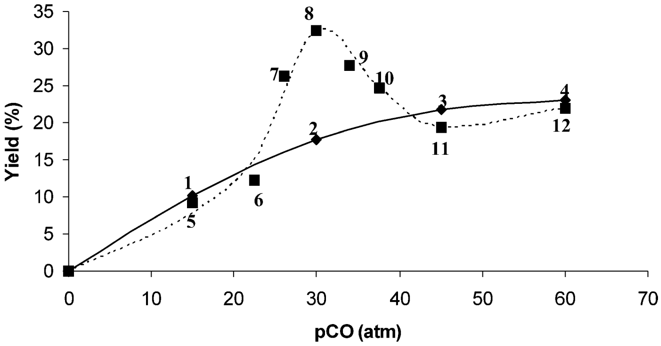


Fig. 1. Effect of CO pressure (atm) on the yield (%) of cyclopentanecarboxylic acid, using catalyst **1** (◆) or **2** (■), for the carboxylation of cyclopentane. Point numbers correspond to those of entries in Table 1.

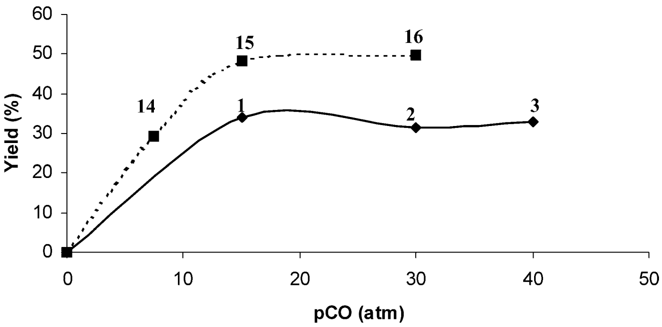


Fig. 2. Effect of CO pressure (atm) on the yield (%) of cyclohexanecarboxylic acid, using catalyst **1** (◆) or **2** (■), for the carboxylation of cyclohexane. Point numbers correspond to those of entries in Table 2.

The catalytic activity depends on the CO pressure, as shown in Figs. 1 and 2 for the catalysts [VO{N(CH$_2$CH$_2$O)$_3$}] **1** and Ca[V(HIDA)$_2$] **2**. Without CO, the trifluoroacetate esters are the only observed products and no carboxylation occurs, in contrast with the case of methane [25], for which the TFA solvent could behave as the carbonylating agent.

Usually the yield of the carboxylic acid product increases with increasing CO pressure up to a limit (15 atm for the formation of cyclohexanecarboxylic acid Fig. 2 using catalysts **1** and **2** and 30 or ca. 50 atm for the formation of cyclopentanecarboxylic acid using catalysts **2** and **1**, respectively (Fig. 1)), beyond which it becomes roughly constant or even decreases, the latter case occurring for the carboxylation of cyclopentane with catalyst **2** (Fig. 1). Hence the pressure of CO should not exceed a certain limit, depending on the particular catalyst used.

The nature of the oxidizing agent is also relevant for this reaction. Hence, although replacement of $K_2S_2O_8$ by $(NH_4)_2S_2O_8$ affects the TON and yield values only slightly (compare entries 13 and 8, Table 1), a complete loss of activity results when using t-BuOOH instead of a peroxodisulfate salt. Maximum TONs and yields are obtained for $S_2O_8{}^{2-}$: V-catalyst molar ratios of 180–200, beyond which a drop in

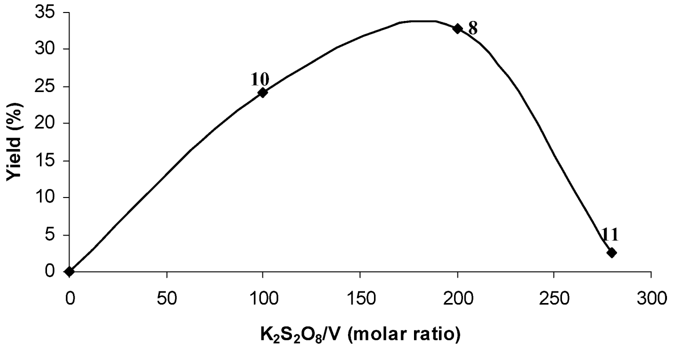


Fig. 3. Effect of the oxidant amount on the yield (%) of cyclohexanecarboxylic acid, using catalyst **1**, for the carboxylation of cyclohexane. Point numbers correspond to those of entries in Table 2.

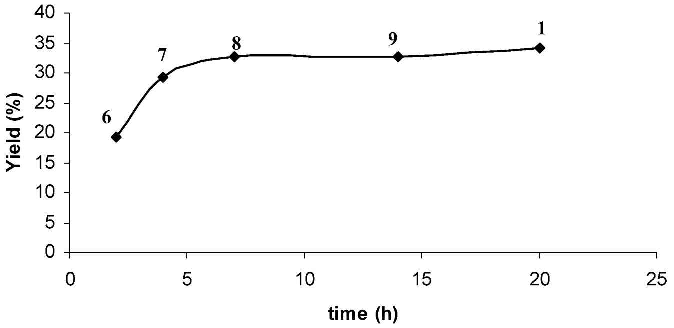


Fig. 4. Effect of time (h) on the yield (%) of cyclohexanecarboxylic acid, using catalyst **1**, for the carboxylation of cyclohexane. Point numbers correspond to those of entries in Table 2.

activity is observed (Fig. 3), conceivably resulting from the limited solubility of the peroxodisulfate salt, which leads to poor stirring of the reaction mixture.

Temperature has also a pronounced effect, with the best conversions occurring at 80–120 °C (entries 1 and 5, Table 2). Further temperature increases up to 150 °C should be avoided due to decomposition. Although a typical reaction time of 20 h is normally used, the final yields can be achieved in much shorter times (e.g., 6 h), as shown in Fig. 4. The use of TFA still remains a drawback of these processes due to its cost, but our attempts to substitute other, cheaper solvents (e.g., ethanol, acetic acid and acetonitrile) have not proven successful (Table 2, footnote e).

3.2. Carboxylation of pentane and hexane

The carboxylation of pentane gives three carboxylic acids (2-methylpentanoic acid, 2-ethylbutanoic acid, and hexanoic acid), whereas two carboxylic acids (2-ethylpentanoic acid and heptanoic acid) are formed in the carboxylation of hexane (Scheme 2). The results are summarized in Tables 3 and 4.

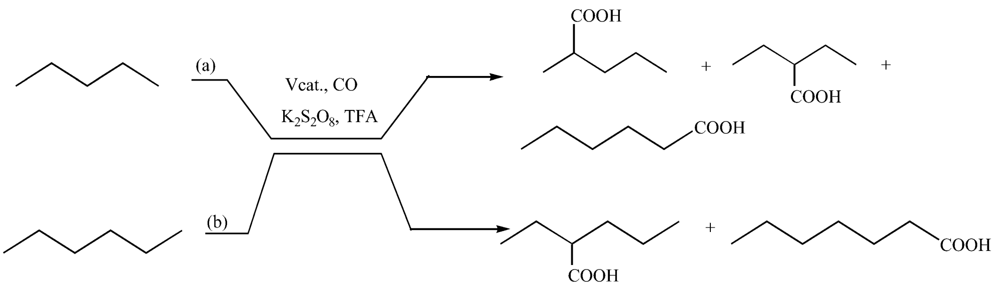
The most effective catalyst precursors are the Amavadine model **2**, the triethanolaminato complex **1**, and, in the case of hexane, the vanadyl sulfate **9**. Maximum yields of 54% and TONs of 76 for the carboxylation of pentane (entry 3, Table 3) and 46% and 63 for the carboxylation of hexane (entry 8, Table 4) have been achieved.

Replacement of the alkoxide arms of the triethanolaminato ligand in the metal catalyst **1** by carboxylates results in a decrease in catalytic activity in the case of pentane carboxylation to carboxylic acids (compare entries 3 and 13 in Table 3 for complexes **1** and **5**, respectively), but the opposite effect occurs for the formation of carboxylic acids by hexane carboxylation (compare entries 3 and 10 in Table 4 for catalysts **1** and **5**, respectively). This shows a ligand effect on catalytic activity, but generalizations cannot be made at this stage.

As for the cycloalkanes, the presence of CO is required for carboxylation to occur, and the yields and TONs are dependent on the pressure of this gas (Figs. 5 and 6). Hence, they increase with p(CO) until ca. 15 atm and remain roughly constant (in the case of pentane) or tend to decrease (in the case of hexane) in the 15–30 atm interval, beyond which further activity enhancement is observed until ca. 45–50 atm. No further significant increase occurs for higher CO pressures.

Interestingly, the main carboxylic acid products (i.e., 2-methylpentanoic acid and 2-ethylbutanoic acids in the case of pentane and 2-ethylpentanoic acid in the reaction of hexane) are formed by carboxylation of a secondary carbon atom, whereas the acids derived from carboxylation of a primary carbon (i.e., hexanoic and heptanoic acids, respectively) are obtained in much lower yields (Figs. 5 and 6). These results are in accordance with a radical mechanism involving formation of an intermediate radical ($R^{\cdot}$) by homolytic cleavage of an alkane C–H bond. In effect, hydrogen abstraction of, for example, pentane $C(1)H_3C(2)H_2C(3)H_2C(2)H_2C(1)H_3$ at either of the two carbons in position (2) or the internal carbon in position (3) leads to a radical ($R^{\cdot}$) with a secondary carbon that is more stable than the radical obtained on hydrogen abstraction of the primary carbon C(1). Moreover, 2-methylpentanoic acid is formed from pentane with the double yield of 2-ethylbutanoic acid, in agreement with the presence of two C(2) atoms and only one C(3) atom in the pentane molecule.

Nevertheless, in the carboxylation of hexane, the formation of 2-methylhexanoic acid, derived from the expected hydrogen



Scheme 2. Carboxylation of pentane (a) or hexane (b) to the corresponding carboxylic acids.

Table 3
Carboxylation of pentane into 2-ethylbutanoic acid, 2-methylpentanoic acid and hexanoic acid[a]

Entry	Catalyst	Pentane/catalyst (molar ratio)	p(CO)[b] (atm)	t (h)	Partial TONs[c] 2-Ethylbutanoic acid	Partial TONs[c] 2-Methylpentanoic acid	Partial TONs[c] Hexanoic acid	Overall TON	Partial yields (%)[d] 2-Ethylbutanoic acid	Partial yields (%)[d] 2-Methylpentanoic acid	Partial yields (%)[d] Hexanoic acid	Overall yield (%)
1	1	140	10	20	8.8	15.3	5.4	29.5	6.3	11.0	3.9	21.2
2	1	140	30	20	10.1	15.7	7.8	33.6	7.3	11.3	5.6	24.2
3	1	140	45	20	24.2	44.8	6.6	75.6	17.4	32.2	4.6	54.2
4	1	140	60	20	21.6	41.2	6.6	69.4	15.5	29.7	4.8	50.0
5	1	140	45	2	11.2	23.1	5.6	39.9	8.1	16.6	4.0	28.7
6	1	140	45	4	16.7	33.9	7.1	57.7	12.0	24.4	5.1	41.5
7	1	735	15	20	20.0	36.5	17.6	74.1	2.7	5.0	2.4	10.1
8	2	140	15	20	14.4	25.2	6.2	45.8	10.4	18.2	4.5	33.1
9	2	140	30	20	17.0	31.0	5.7	53.7	12.2	22.3	4.1	38.6
10	2	140	45	20	22.9	44.1	6.0	73.0	16.5	31.7	4.4	52.6
11	2	140	60	20	23.4	46.4	5.0	74.8	16.8	33.4	3.6	53.8
12	3	140	45	20	21.5	40.6	6.9	69.0	15.5	29.3	5.0	49.8
13	5	140	45	20	12.3	21.6	0.0	33.9	8.8	15.6	0.0	24.4
14	8	140	45	20	5.8	9.9	3.5	19.2	4.3	7.3	2.6	14.2
15	9	140	45	20	13.1	23.5	0.0	36.6	9.4	17.0	0.0	26.4

[a] Reaction conditions (unless otherwise stated): metal complex catalyst (0.0625 mmol), $K_2S_2O_8$ (12.5 mmol, i.e., 200:1 molar ratio of oxidant to metal catalyst), pentane (1.0 mL, 8.68 mmol), CF_3COOH (22 mL), 80 °C, 20 h, in an autoclave (39 mL capacity). Amounts of CO gas correspond to 0.575 mol atm^{-1} with the pressure measured at 25 °C.

[b] Measured at 25 °C.

[c] Turnover number expressed by the number of moles of 2-ethylbutanoic acid, of 2-methylpentanoic acid or of hexanoic acid per mol of metal catalyst.

[d] Molar yield (%) based on pentane, i.e. number of moles of 2-ethylbutanoic acid, of 2-methylpentanoic acid or of hexanoic acid per 100 moles of pentane.

Table 4
Carboxylation of hexane into 2-ethylpentanoic acid and heptanoic acid[a]

Entry	Catalyst	p(CO)[b] (atm)	Partial TONs[c] 2-Ethylpentanoic acid	Partial TONs[c] Heptanoic acid	Overall TON	Partial yields (%)[d] 2-Ethylpentanoic acid	Partial yields (%)[d] Heptanoic acid	Overall yield (%)
1	1	15	12.4	2.2	14.6	9.2	1.7	10.9
2	1	30	9.1	0.8	9.9	6.7	0.6	7.3
3	1	45	10.7	0.4	11.1	7.9	0.3	8.2
4	1	60	49.3	3.5	52.8	36.6	2.6	39.2
5	2	15	18.2	2.6	20.8	13.5	2.0	15.5
6	2	30	12.4	0.5	12.9	9.2	0.4	9.6
7	2	45	51.7	3.8	55.5	38.4	2.8	41.2
8	2	60	58.5	4.1	62.6	43.4	3.0	46.4
9	3	15	19.8	2.4	22.2	14.6	1.8	16.4
10	5	45	43.5	3.0	46.5	32.3	2.2	34.5
11	8	45	15.1	1.8	16.9	11.4	1.4	12.8
12	9	45	56.0	3.0	59.0	41.6	2.2	43.8

[a] Reaction conditions (unless otherwise stated): metal complex catalyst (0.0625 mmol), $K_2S_2O_8$ (12.5 mmol, i.e., 200:1 molar ratio of oxidant to metal catalyst), hexane (1.1 mL, 8.42 mmol, i.e., 135:1 molar ratio of substrate to metal catalyst), CF_3COOH (22 mL), 80 °C, 20 h, in an autoclave (39 mL capacity). Amounts of CO gas correspond to 0.575 mol atm^{-1} with the pressure measured at 25 °C.

[b] Measured at 25 °C.

[c] Turnover number expressed by the number of moles of 2-ethylpentanoic acid or of heptanoic acid per mol of metal catalyst.

[d] Molar yield (%) based on hexane, i.e., number of moles of 2-ethylpentanoic acid or of heptanoic acid per 100 moles of hexane.

abstraction of a secondary C(2) carbon, was not detected. In any case, for both the linear and cyclic alkanes, the involvement of carbon- and oxygen-centered radical mechanisms is suggested by the suppression of the catalytic activity when the reaction is carried out in the presence of either a carbon–radical trap like $CBrCl_3$ or the oxygen–radical trap Ph_2NH. A conceivable oxygen-centered radical involved in our systems is the sulfate $SO_4^{\bullet}$ derived from peroxodisulfate $S_2O_8^{2-}$ either by thermal decomposition or a product of its reduction (together with sulfate) when it behaves as a single-electron oxidant.

Carboxylation can occur via more than one mechanism, as suggested by the plots of the yield versus CO pressure (Figs. 5 and 6) which exhibit two distinct relationships, one below and the other above ca. 30 atm, possibly corresponding to the predominance of one mechanism at lower CO pressures and of another one at higher pressures. This is more clearly observed for hexane carboxylation (Fig. 6) and also appears to hold for cyclopentane when using catalyst **2** (Fig. 1). It can also be accounted for by the observed hindrance of ester formation, relative to the acids, for higher CO pressures, which favor the

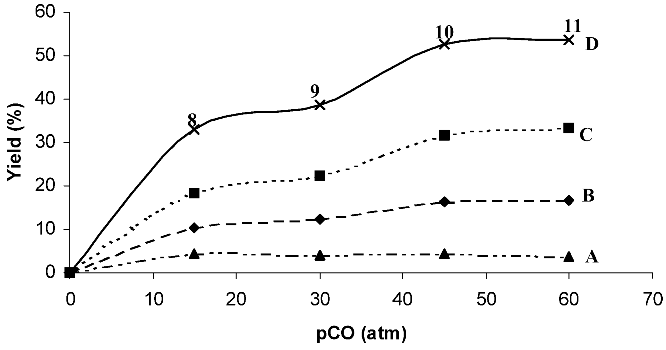


Fig. 5. Effect of CO pressure (atm) on the yields (%) of carboxylic acids, using catalyst **2** for the carboxylation of pentane. Point numbers correspond to those of entries in Table 3. (A) hexanoic acid; (B) 2-ethylbutanoic acid; (C) 2-methylpentanoic acid; (D) overall yield.

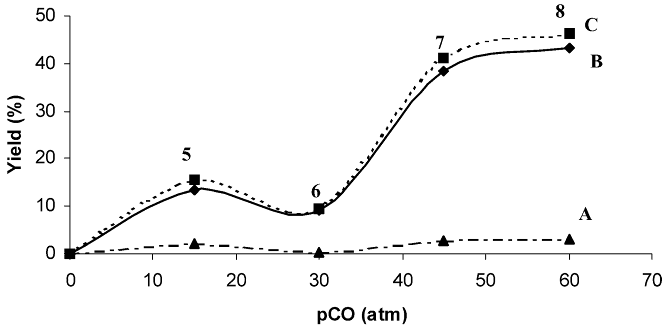


Fig. 6. Effect of CO pressure (atm) on the yields (%) of carboxylic acids, using catalyst **2** for the carboxylation of hexane. Point numbers correspond to those of entries in Table 4. (A) heptanoic acid; (B) 2-ethylpentanoic acid; (C) overall yield.

carboxylation pathway in comparison with that leading to the esters, which does not involve carboxylation by CO and can occur via reductive elimination from an intermediate alkyl–trifluoroacetate–vanadium complex.

The radical mechanism of carboxylic acid formation from the corresponding alkanes RH conceivably involves the acyl radical RCO$^{\bullet}$ (formed on carbonylation of R$^{\bullet}$), which, by oxidation and reaction with TFA, can lead to the mixed anhydride $CF_3COOCOR$. Further reaction of this anhydride with TFA would form the carboxylic acid RCOOH and trifluoroacetic anhydride $CF_3COOCOCF_3$, as has been suggested for methyl radical carboxylation [15].

4. Conclusions

The direct single-pot carboxylation of linear and cyclic alkanes into carboxylic acids by using the foregoing vanadium complexes with N,O- or O,O- ligands as catalysts proceeds under relatively moderate conditions. For cyclic alkanes (cyclopentane and cyclohexane), a marked selectivity is observed toward the formation of a main single acid product (cyclopentanecarboxylic acid and cyclohexanecarboxylic acid, respectively). Cyclohexane is more reactive than cyclopentane, giving higher TONs and yields for almost all catalysts used. However, as expected, the linear alkanes originate more acid products than the cyclic ones in processes with a lower selectivity.

For each case, the presence of CO beyond a certain limit does not lead to higher yields or TONs, and therefore the use of excessive $p(\mathrm{CO})$ is discouraged. The two distinct dependencies of the yield on CO pressure observed in a number of cases, below and above a certain $p(\mathrm{CO})$ (ca. 30 atm in the case of the linear alkanes and above this value for cyclopentane) suggest the possible involvement of two mechanisms, with the lower CO pressures promoting the formation of esters and disfavoring that of the acids. The product distribution in the case of the linear alkane carboxylation is indicative of a radical pathway, which is also corroborated by studies in the presence of radical traps that suggest the involvement of both carbon- and oxygen-centered radicals for both linear and cyclic alkanes.

The Amavadine model $Ca[V(HIDA)_2]$ **2** and/or the related N,O-complex $[VO\{N(CH_2CH_2O)_3\}]$ **1** are the best catalyst precursors, but simpler O,O-complexes like $[VO(CF_3SO_3)_2]$ **8** or $VOSO_4{\cdot}5H_2O$ **9** can also exhibit high activity in certain cases. Although for pentane carboxylation, for instance, catalytic activity is noticeably dependent on the type of N,O-ligand of the catalyst (with replacement of ligating alkoxide arms by carboxylate groups having an inhibitory effect), such a dependency is not observed for the other alkanes, and thus generalizations must be made very cautiously.

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