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Review

An Overview of Recent Advances of the Catalytic Selective Oxidation of Ethane to Oxygenates

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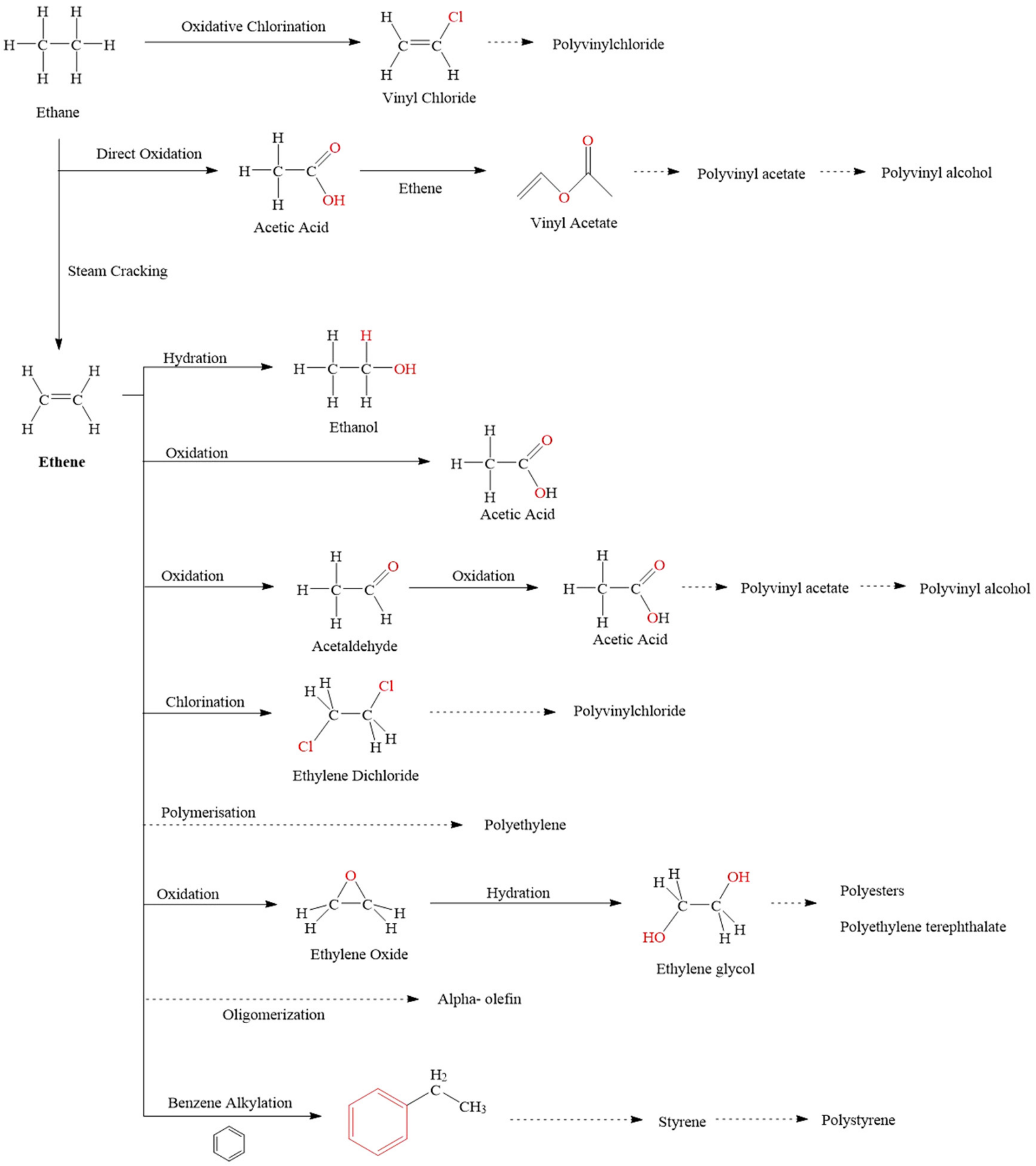
Abstract: The selective partial oxidation of short chain alkanes is a key challenge within catalysis research. Direct ethane oxidation to oxygenates is a difficult aim, but potentially rewarding, and it could lead to a paradigm shift in the supply chain of several bulk chemicals. Unfortunately, low C–H bond reactivity and kinetically labile products are just some reasons affecting the development and commercialisation of such processes. Research into direct ethane oxidation is therefore disparate, with approaches ranging from oxidation in the gas phase at high temperatures to enzyme catalysed hydroxylation under ambient conditions. Furthermore, in overcoming the barrier posed by the chemically inert C–H bond a range of oxidants have been utilised. Despite years of research, this remains an intriguing topic from both academic and commercial perspectives. Herein we describe some recent developments within the field of catalytic ethane oxidation focusing on the formation of oxygenated products, whilst addressing the key challenges which are still to be overcome.

Keywords: catalysis; ethane; partial oxidation; natural gas

1. Introduction

The increasing exploitation of traditional fossil fuels, coupled with their declining reserves has led to recent instability in the price of crude oil. Modern society is heavily dependent upon such finite reserves, not only for utilisation as energy sources, but also as feedstocks for both bulk and fine chemical synthesis. At the same time, added emphasis is being given within the developed world to environmental conscience, with legislation emerging which seeks to curtail the environmental impact associated with CO_2 and methane emissions. Burgeoning demand, coupled with dwindling oil reserves and more stringent emission controls, has created an incentive for research into the exploitation of alternate feedstocks for chemicals, with a major field of scientific research being the valorisation/catalytic upgrading of the components of natural gas.

With estimated global reserves of natural gas exceeding 190 trillion cubic meters, this is an as yet underutilised resource [1]. Although the exact composition of natural gas varies according to its source, a typical breakdown is; methane (70%–90%), ethane (1%–10%), propane/butane (1%–10%), CO_2 (0%–8%), nitrogen (0%–5%), H_2S (0%–5%) and oxygen (0%–0.02%) [2]. Due to the high abundance of methane in natural gas, and the wide uses of methanol; as a fuel additive, coolant, hydrogen carrier for fuels cells and chemical feedstock for bulk chemicals such as formaldehyde and acetic acid [3,4], the direct oxidation of methane to methanol has captivated the scientific community for over 100 years. Meanwhile, ethane (1%–10% of natural gas) is primarily utilised in the production of ethene through steam cracking [5]. This, in turn, is used in the production of polyethylene, acetic acid, ethylene oxide, acetaldehyde, vinyl chloride and ethanol [6,7].



Scheme 1. A scheme showing key industrial ethane-derived products.

On-site oxidation of the aliphatic hydrocarbons present within natural gas circumvents the key limitation to their global distribution and utilisation. Specifically the transportation of large volumes of flammable gas from their sources, which are nucleated in isolated regions of the world, incurs significant financial expense. Although developments have been made in the liquefaction and transportation of natural gas (LNG), the high energy requirements and associated safety concerns hinder its viability for application on a global scale. Natural gas has been proposed as a transitional fuel for the 21st century, allowing for continued dependence upon fossil fuels, whilst reducing greenhouse gas emissions when compared with oil or coal [4,8].

Unfortunately, in spite of the significant desire to selectively oxidise ethane under mild conditions, progress has been hampered due to its chemical inertness, which results from a high C–H bond strength of 423.29 $kJ \cdot mol^{-1}$ [9]. Another crucial limitation arises from the fact that the partial oxidation products of ethane are inherently more reactive, with deep oxidation to CO_x (CO and CO_2) a limiting factor in the viability of catalytic systems. Hence the direct oxidative conversion remains a major challenge.

2. Current Industrial Approaches to Ethane Upgrading

As mentioned previously, the main industrial use of ethane is in the production of ethene through steam cracking over zeolite catalysts [5]. This is the most energy intensive process within the petrochemical industry, accounting for *ca*. 40% of the industry's annual energy consumption, as well as a major portion of its CO_2 emissions, to achieve yields of 24%–55% depending on the gas feed. Considering the commercial uses of ethane, the most important is for production of polyethylene [10]. Other uses include the production of ethylene oxide and ethylene glycol (from ethylene oxide), preparation of ethylene dichloride (a precursor to vinyl chloride) and in the preparation of ethylbenzene, a precursor to styrene [11]. An overview of the key industrial processes for the upgrading of ethane to value- added products is shown in Scheme 1.

A key product of direct ethane oxidation is acetic acid. Global demand for acetic acid is currently around 7.8 million tonnes per annum, and growing at 3.5%–4.5% annually [12,13]. Acetic acid is primarily used as a raw material in the production of; vinyl acetate monomer, acetic anhydride and as a solvent for the synthesis of purified terephthalic acid (PTA) [13]. Acetic acid production was first commercialised in 1916 in Germany whereby acetylene was converted to acetaldehyde and subsequently oxidised through to acetic acid [13]. A number of industrial processes are currently operated to produce acetic acid through synthetic and enzymatic routes. Principally the BP Cativa Process which proceeds through methanol carbonylation using a homogeneous Iridium catalyst is one of the main routes [3]. Prior to the Cativa process, acetic acid was produced through the Monsanto process. However, due to the expense of the rhodium catalyst used ($5200 per ounce for Rh *vs.* $300 for Ir), its shorter lifetime, lower solubility and lower activity, which resulted from an oxidative MeI addition which was 150 times slower than that for the Cativa process, many plants now use the Cativa process [14]. A number of attempts have been made to immobilise the Rh catalyst of the Monsanto process, to allow for gas phase operation, thereby negating the solubility issues associated with the Monsanto catalyst, with activated carbon [15], inorganic oxides [16] and zeolites [17] having been studied as potential supports. However these showed rates which were lower by 1 or 3 orders of magnitude when compared with the homogeneous catalyst. Some progress has been reported by Chiyoda Corp however, with the development of the Acetica process [18–20]. Through complexation of Rh with a poly-vinyl pyridine ion exchange resin, operation at 160–200 °C and 30–60 bar, with low water concentrations of 3%–7% has been achieved. The catalyst has been shown to be more stable than the homogeneous anologue, with no loss in activity over 7000 h on-line and with negligible loss of Rh.

Aside from the homogeneous Cativa and Monsanto systems, acetic acid may also be derived from acetaldehyde, at 150–160 °C and 80 bar, over either cobalt or manganese acetate [13]. An additional halide- free route to acetic acid synthesis is the carbonylation of dimethyl ether over Brønsted acidic zeolite catalysts [21–24]. This reaction yields methyl acetate, which can be hydrolysed to yield methanol and acetic acid. High methyl acetate selectivity (>99%) and appreciable rates have been reported at relatively low reaction temperatures of *ca*. 150–190 °C when compared with methanol carbonylation processes [22]. This is because the catalytic cycle in methanol carbonylation requires water, which might competitively adsorb at CO binding sites, whereas dimethyl ether carbonylation is operated under anhydrous conditions and does not generate water [21,23]. This is a promising route to acetic acid synthesis, though it has been noted that reaction rates do not currently meet commercial targets [22].

3. Partial Oxidation of Ethane

The low reactivity and high stability of the C–H bond in ethane, second only to that of methane has hindered development of a viable process for the partial oxidation of ethane under mild conditions. This is further complicated by the fact that one must not only activate the relatively inert alkane substrate, but also minimise subsequent oxidation of desirable products to deep oxidation products such as formic acid and CO_2.

3.1. High Temperature Approaches

Many approaches have attempted gas phase catalytic selective oxidation of ethane at elevated temperature, and these have been reviewed extensively elsewhere [25]. Perhaps the most widely adopted approach has been the oxidative dehydrogenation of ethane to ethene [26], however, there are also a number of studies that have targeted the formation of oxygenated products. Just some example studies are highlighted here.

Following the pioneering work of Thorsteinson *et al.* Mo-V-Nb catalysts [27], specifically $Mo_{0.61}V_{0.31}Nb_{0.08}$ and variations thereof have been reported as active for the selective oxidation of ethane to ethene and acetic acid using molecular oxygen [28–38]. Indeed, a process for the direct conversion of ethane to acetic acid using molybdenum-mixed metal oxide catalysts has also been described [39,40]. In 2001 SABIC announced their plans to build a 30,000 tonne/annum plant in Saudi Arabia, using a Mo-V-Ln-Nb-Pd-*X* (*X* = Al, Ga, Ge and/or Si) catalyst for the oxidation of ethane to acetic acid in O_2 or air at operating temperatures of between 150 and 450 °C. Their patent claims the ability to oxidise ethane (C_2H_6:O_2:N_2:H_2O (40:8:32:20) P(total) = 13.8 bar, T = 280 °C) at 10% conversion, with 85% selectivity to acetic acid [30]. Such a direct oxidation of ethane (EDO) to acetic acid has been shown to be an economically and energetically viable alternative to methanol carbonylation as an industrial route to acetic acid production, with feasibility increasing from 50 kt to 200 kt/annum [41]. A cost analysis based upon a model 76.1% acetic acid selectivity (C_2H_6:O_2:CO_2 in the ratio 0.73:0.12:0.15, 16 bar total, 242 °C) showed the direct oxidation process to be favourable to current industrial practices. This is because direct ethane oxidation uses a cheaper feedstock. The product stream requires fewer separation steps and capital costs are lower, as methanol carbonylation reactors must me composed of Hastelloy to avoid corrosion, whereas ethane oxidation may be operated in stainless steel reactors [41]. These benefits offset the costs implied by the need to recirculate the ethane/CO_2 effluent in an oxidation system, which typically operates at low conversion.

Through a number of studies, a system was developed whereby; $Mo_{0.61}V_{0.31}Nb_{0.08}O_x/TiO_2$ afforded 5.4% ethane conversion to ethene (58%), acetic acid (35%) and CO_x (7%) whilst addition of 0.01 wt % Pd led to slightly lower ethane conversion (5.1%) to ethene (1%), acetic acid (82%) and CO_2 (17%). In the latter system, an unprecedented acetic acid productivity of 13.8 $\text{mol}_{\text{acetic acid}} \cdot \text{kg}_{\text{cat}}{}^{-1} \cdot \text{h}^{-1}$ was achieved [38]. Due to the array of phases present within such Mo-V-Nb oxides, elucidation of the specific function of each component has limited the system's development [37]. Kinetic studies showed that the C–H bond activation in ethane by the oxygen-saturated catalyst surfaces is the rate limiting step [37]. The initial step, ethane oxidative dehydrogenation, arises due to the interaction of ethane with lattice oxygen, which is associated with an oxidation state change in the vanadium component [32]. Through precipitation with TiO_2, leading to increased dispersion of the active mixed oxide component, a 10 fold increase in reaction rate was reported. Niobium promotes the formation and stabilisation of Mo_5O_{14} and VMo_4O_{14} in preference to MoO_3, which can catalyse total oxidation to CO_2 when present [36]. It has been shown that ethene inhibits ethane oxidation through depletion of lattice oxygen (O*). The consecutive oxidation of ethene to acetic acid is itself catalysed by the palladium oxide in a heterogeneous analogue of the Wacker process [32]. The Pd^{2+} species is proposed to bind hydroxyl groups, thereby providing a site for the conversion of ethene to acetic acid [32]. Water is also believed to increase acetic acid selectivity by promoting the desorption of acetate species as acetic acid [37]. A number of patents have been filed for this family of catalysts, for application in direct ethane oxidation [30,33,34,42,43]. One such reported that a 1:9 ethene:ethane feed could be oxidised to acetic acid (63%) and ethene (14%) at 3% ethane conversion, over a vanadium, molybdenum, niobium, antimony, calcium catalyst supported on an LZ-105 molecular sieve at 255 °C. This system showed bifunctionality to (a) partially oxidise the methyl group and (b) hydrate the ethene to ethanol or acetaldehyde.

Whilst the productivities shown by the Pd/Mo-V-Nb for acetic acid are impressive, the high CO_2 selectivities shown and complex nature of the active sites present are key limitations.

Numerous other solid catalysts have been reported as active for the direct oxidation of ethane (EDO) in the gas phase. Unsupported heteropoly compounds (both free acids and caesium salts) containing molybdenum and vanadium anions have been reported for oxydehydrogenation of ethane to ethene (60%) and CO_x [44]. Oxidation of ethane to acetaldehyde (*ca.* 25% selectivity), in addition to ethene (47%) and CO_x (18%) was reported by Moffat *et al.*, who used silica- supported HPMo at 540 °C, however, conversion was limited to 3% and no acetic acid was observed [45]. Sopa *et al.* furthered this work by supporting Keggin molybdo (vanado) phosphoric heteropolyacid ($HPMoV_x$) on oxide supports (SiO_2, TiO_2 and Al_2O_3) [46]. Activity was shown at 250–400 °C under atmospheric pressure (C_2H_6:O_2:H_2O:N_2 of 2:1:8:4). Alumina, silica and titania- supported HPAs showed acetic acid selectivities of 28%, 22% and 25% respectively at 250 °C. However the alumina and silica supported catalysts gave low ethane conversion (0.4%), increasing to 3% for titania-supported HPA. HPA/SiO_2 showed high selectivity to ethene (67%) leaving acetic acid (22%) and CO_2 (11%) as minor products [46]. Higher conversions (22%) were attainable at higher temperatures (400 °C) however this was associated with decreased acetic acid selectivity (5%) compared with ethene (50%) and CO_2 (45%). Vanadium ions were shown to be integral for ethane conversion, with acetic acid selectivity limited to <5% in their absence. Silica and titania were shown to preserve the Keggin structure *in situ*, due to their acidic surface functionality, whilst the basic centres present in alumina led to decay of the Keggin structure thereby impairing activity [46].

Partial oxidation systems based upon silica-supported vanadium oxide catalysts were reported by Erdöhelyi *et al.* with low ethane conversion (3%), but high selectivity towards acetaldehyde (45%) at 550 °C using $RbVO_3/SiO_2$ with N_2O as oxidant [47]. The same group later showed Rb_2MoO_4/SiO_2 to give higher conversion (8.9%) under the same conditions, this time affording high ethene selectivity (45.7%) and lower acetaldehyde selectivity (7.3%) [48].

Bodke *et al.* reported impressive ethane conversion (73%) to ethene (83%) using a Pt-Sn/alumina catalyst at 900–950 °C [49]. By introducing H_2 into the gas feed to give a 2:1:2 ratio for C_2H_6:O_2:H_2, deep oxidation to CO_x was largely suppressed (from 20% to 5% selectivity), as H_2 was preferentially oxidised, to H_2O. Unfortunately, safety considerations limited these system's viability upon scale up.

3.2. Low Temperature Approaches

3.2.1. Homogeneous Catalytic Approaches

Whilst a number of homogeneous catalytic systems have been reported for the activation of methane, the catalytic oxidation of ethane using homogeneous catalysts has rarely been studied [50–65].

Fujiwara *et al.* showed the conversion of ethane to *N*,*N*-dimethylpropylamine through reaction with *N*,*N*-triethylamine and N-oxide, catalysed by $Cu(OAc)_2$ [66]. Although not direct oxidation, this system was a major development in the C–H activation of ethane, as it avoided the use of highly acidic environmentally non-benign media often associated with electrophilic alkane activation. Shortly thereafter Süss-Fink *et al.* reported the selective oxidation of ethane in acetonitrile using $[PMo_{11}VO_{40}]^{4-}$ and $[PMo_6V_5O_{39}]^{4-}$ in their tetra-*n*-butylammonium salts using H_2O_2. They reported TOFs of 1.4 h^{-1} for the former at 60 °C, with selectivity favouring ethylhydroperoxide (CH_3CH_2OOH) as major product and ethanol and acetaldehyde as minor products [67]. Analogous tests under aqueous conditions gave productivities towards ethanol, acetaldehyde and acetic acid, which failed to exceed those of blank reactions. It was concluded that this process proceeded through formation of hydroxyl radicals upon interaction with a V (V) species. It was then postulated that the radical species went on to activate ethane, and a range of substrates, to form their alkylperoxide product. In spite of the selectivity shown, this system was limited by low activity and a dependence on complex organic salts. Nevertheless, it was an important development in low temperature activation of ethane, given its 60 °C operating temperature. However, a lack of analysis of the gas effluent products for CO_x raises questions as to the true selectivity of the reaction.

Shul'pin *et al.* later reported the efficient low temperature selective oxidation of ethane using H_2O_2 or *ter*-BuOOH in acetonitrile, catalysed by the complex manganese (IV) salt $[L_2Mn_2O_3](PF_6)_2$ where (L = 1,4,7-trimethyl-1,4,7-triazacyclononane) [68]. The activity of the system was dependent upon addition of a carboxylic acid to the reaction solution (typically acetic acid), with only non-productive H_2O_2 decomposition to O_2 observed in the absence of additional acid. As with the vanadium salt catalysed system described by Süss-Fink *et al.*, the primary product was believed to be ethylhydroperoxide, with acetaldehyde and ethanol shown to be secondary oxidation products. For 2 h tests a TOF of 180 h^{-1} was observed at 20 bar ethane, 25 °C, 1 M H_2O_2 with propionic acid added (0.25 M). Under these conditions, selectivities to ethylhydroperoxide (39%), acetaldehyde (33%) and ethanol (28%) were reported. At lower temperatures (5 °C) and longer reaction times (75 h) the ethylhydroperoxide selectivity reached 65% with TOFs of 5.3 h^{-1} [68]. As with previous studies, selectivity towards CO_2 was not reported. Whether this is due to the lack of deep oxidation, or of gas analysis is not stated, however, the latter is most likely given the precedent for CO_2 formation in systems containing H_2O_2 [7,69]. Shul'pin *et al.* also reported that chromic acid catalyses the oxidation of ethane using H_2O_2 in acetonitrile [70], with high rates of 620 $\text{mol}_{\text{ethane converted}} \cdot \text{mol}_{\text{chromic acid}}{}^{-1} \cdot h^{-1}$ observed at a 60 °C reaction temperature. As with their previous studies with manganese salts, reaction selectivity favoured primary reaction products, with acetaldehyde and ethylhydroperoxide as major products (52% and 23% selectivity respectively) [70]. As with previous studies by the same authors, potential formation of gaseous carbon oxide products was not explored. This trend continued when Shul'pina reported partial oxidation of ethane over $NaVO_3 + H_2SO_4$ and H_2O_2 in acetonitrile [71]. Hydroxyl radical attack was found to attack the alkane in solution, to form alkyl radicals, which reacted rapidly to generate alkyl peroxy radicals and subsequently the alkyl hydroperoxide (ethylhydroperoxide). This undergoes facile conversion to oxygenated products [71]. High rates of ethane oxidation (47.5 $\text{mol}_{\text{ethane converted}} \cdot \text{mol}_{\text{NaVO3}}{}^{-1} \cdot h^{-1}$) were achieved at the low temperature of 30 °C, with reaction selectivity favouring ethanol (51% selectivity), acetaldehyde (32%) and acetic acid (17%).

Shul'pin *et al.* later reported that a range of iron (III) species are active for the activation of ethane with H_2O_2 using acetonitrile as solvent. These include iron(III) chloride, iron(III) perchlorate and iron(III) acetate [72], with the latter two showing TOFs of 23 h^{-1} and 6 h^{-1} respectively, at 27 bar ethane and 25 °C with H_2O_2 (0.6 M). The most active Iron (III) perchlorate catalyst gave high selectivity towards ethylhydroperoxide (88%) with minor products ethanol (3%) and acetaldehyde (9%). The reactions for iron perchlorate and iron acetate were shown to proceed through a hydroxyl radical oxidant, whereas the activity of iron (III) chloride was attributed, at least partially, to the formation of a ferryl ion $(Fe^{IV} = O)^{2+}$ [72]. Such ferryl species may arise as a result of interactions between H_2O_2, hydroperoxy radicals ($\cdot$OOH) [73]. More recently Yuan *et al.* have shown a variety of transition metal chlorides to be active for the selective oxidation of ethane to oxygenates with H_2O_2 in aqueous conditions [74]. A broad range of metal chlorides were evaluated with activity for ethane oxidation following the order: $H_2PtCl_6 < PdCl_2 < FeCl_3 < HAuCl_4 < OsCl_3$. The most active, $OsCl_3$, showed a TOF of 40.8 h^{-1} for ethane oxidation at 30 bar ethane, 0.5 M H_2O_2 and 90 °C. Of the homogeneous systems cited, this was the first to quantify CO_2, with selectivities to ethanol, acetaldehyde and CO_2 of 21%, 64% and 15% respectively, at 0.56% conversion [74]. Mechanistic and radical scavengers studies showed ethane oxidation to proceed via the formation of hydroxyl and hydroperoxy radical species generated from H_2O_2 by the catalyst, as opposed to electrophilic activation of ethane.

Partial oxidation of ethane over non- heme [Fe=O] was reported by Tse *et al.* Using $[Fe^{III}(Me_3tacn)(Cl\text{-}acac)Cl]^+$ type catalysts, and oxone ($KHSO_5$) as oxidant. Using different bidentate and tridentate ligands to stabilise the active site, high C_2 oxygenate selectivity was achieved (typically 80% acetic acid, 20% ethanol). The most active catalyst $[Fe^{III}(Tp)_2]ClO_4$ (Tp = hydrotris (1-pyrazolyl1)-borate) showed a TOF of 12.0 $\text{mol}_{\text{ethane converted}} \cdot \text{mol}_{\text{catalyst}}{}^{-1} \cdot h^{-1}$ at room temperature [75].

The conversion of ethane to ethyl- esters has been recently reported by Periana and co-workers [76–78] who adopt an electrophilic activation approach, at temperatures of *ca.* 180 °C. Ethane is activated by $M^{n+}(TFA)_n$ where M = (Pb^{IV} or Tl^{III}) at 180 °C with product yields of 90% and 75% for Pb^{IV} and Tl^{III} respectively. These reactions yield the ethyl- ester products; EtTFA and $EG(TFA)_2$ at selectivities of *ca.* 70% and 30% respectively [76,78] with the Tl process proceeding according to Equation (1).

$$\mathrm{Et-H + Tl^{III}(TFA)_3 \rightarrow Tl^{I}(TFA) + TFAH + Et-TFA} \tag{1}$$

These products would of course require additional workup steps to yield the desired oxygenated products [76]. The same group also reported a high yield of EtTFA (73% yield, 91% selectivity) at a reaction temperature of 150 °C when using a perfluoroarene iodine (III) complex in TFAA/HTFA as solvent (Equation (2)) [77].

$$C_6F_5I^{III}(TFA)_2 + Et-H \rightarrow C_6F_5I^{I} + EtTFA + 1,2-Et(TFA)_2 \quad (2)$$

Whilst homogeneous catalysts have been shown to be active for the selective oxidation of ethane to oxygenated products under mild, aqueous conditions, a general dependence upon additives coupled with low turnover frequencies and the inherent disadvantages of homogeneous catalysts mean that heterogeneous catalysts are often more favourable for downstream industrial applications.

3.2.2. Enzymatic Approaches

Methane mono-oxygenase of *Methylococcus capsulatus* (MMO) is a nonspecific oxygenase, which is capable of catalysing the oxidation of a range of C_1–C_8 *n*-alkanes to corresponding primary and secondary alcohols in air at ambient conditions [79]. Colby *et al.* showed that the soluble form (sMMO) (2 mg) in a solution of KCN (0.5 nM) was active for the selective oxidation of ethane to ethanol yielding ethanol (1.64 μmol) in the presence of NADH cofactor over 12 min [79]. Tonge *et al.* later showed that purified *Methylosinus trichosporium* could catalyse the stoichiometric oxidation of ethane to ethanol at productivities of 50 μmol (ethanol) min^{-1} mg $(protein)^{-1}$ lending it the descriptor *monooxygenase* [80]. Crucially, sMMO was able to avoid production of deeper oxidation products acetic acid and CO_2. Key to the activity of sMMO is the proposed diiron μ-oxo active site (Figure 1) [81]. More recently Meinhold *et al.* have shown engineered variants of P450 BM3 to be active for the fast oxidation of ethane to ethanol, with turnover frequencies $mol_{ethanol} \cdot mol_{protein}^{-1} \cdot h^{-1}$ of 500 reported, at an NADPH oxidation rate of 31,200 h^{-1} [82]. The active site for P450 is shown in Figure 2.

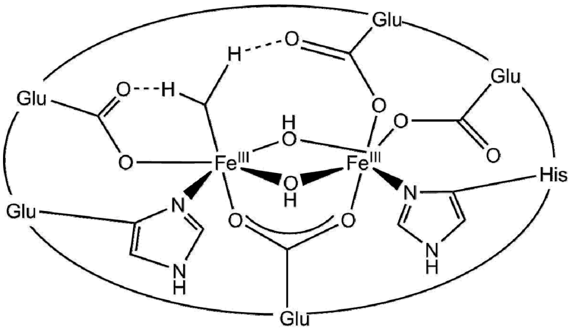


Figure 1. The active site for methane monoooxygenase (redrawn from ref. [81]).

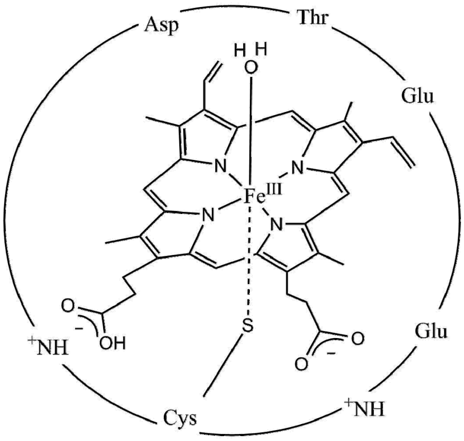
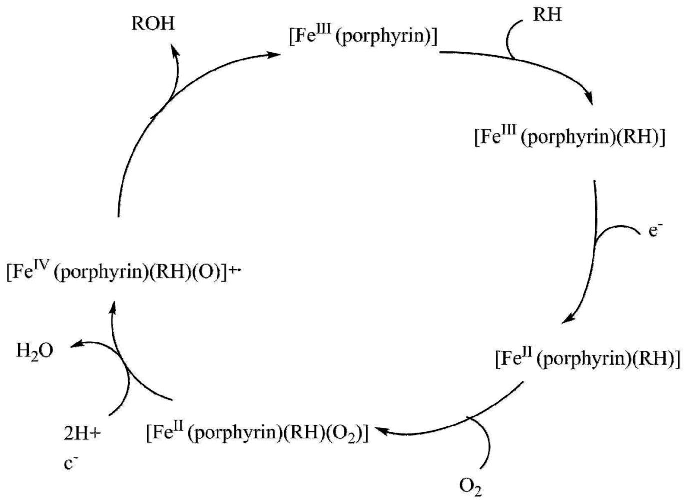


Figure 2. The active site of P450 [81].

In such systems, catalysed by heme- dependent monooxygenase P450 enzymes, the cofactor (NADPH) is required to donate two electrons to activate oxygen in order to generate a [(Porphyrin)$^+$ Fe^{IV} = O] intermediate which attacks the C–H bonds (Scheme 2) [83]. Feng *et al.* also showed selective oxidation of ethane to ethanol exclusively, with H_2O_2 and NADH with higher turnover frequencies of up to 4692 h^{-1} at an NADH oxidation rate of 44,460 h^{-1} reported [65,83]. The catalytic cycle proposed for P450 catalysed alkane oxidation with O_2 is shown in Scheme 2.



Scheme 2. The proposed catalytic cycle for alkane oxidation by O_2 catalysed by P450 [83].

Firstly the substrate (RH) coordinates to iron (III) centre. The iron (III) is then reduced and subsequently an O_2 molecule is coordinated, to form an iron (II) peroxo species. This species is then oxidised by the enzyme system to form an oxoiron (IV) radical cation [(Porphyrin)(RH) Fe^{IV}=O]$^+$. The C–H bond in RH is then cleaved, and oxygen extracted from the iron oxo species, thereby reforming P450 and generating ROH [65].

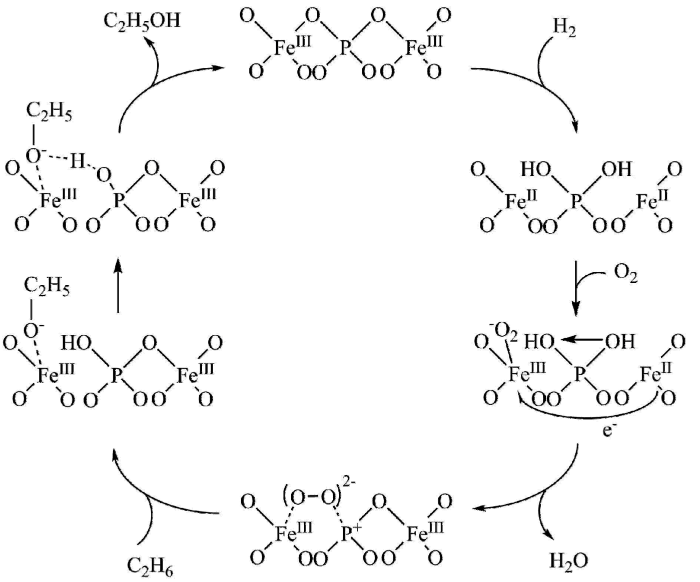
Kawakami *et al.* also reported a Cytochrome P450 BM3 enzyme system to be active for the hydroxylation of ethane to ethanol. A high reaction rate of 40 $mol_{ethane\ converted} \cdot mol_{enzyme}^{-1} \cdot h^{-1}$ and 100% ethanol selectivity was achieved through use of a perfluorocarboxylic acid decoy molecule (PFC10) and NADPH cofactor [84]. Total selectivity towards ethanol was also reported by Chen *et al.* who evolved a mutant form of Cytochrome P450 BM3 with the aim of achieving a high affinity for short chain alkane binding [85]. Using iodosylbenzene, hydrogen peroxide or 3-chloroperoxybenzoic acid as oxidant, respective ethane turnover frequencies of 15.0, 1.4 and 2.0 $mol_{ethane\ converted}\ mol_{P450}^{-1} \cdot h^{-1}$ were achieved [85].

Whilst the selective oxidation of ethane to ethanol under ambient conditions with molecular oxygen is an attractive prospect, a dependence on dilute aqueous environments, need for expensive cofactors and sensitivity to higher temperatures limits the feasibility of enzyme- catalysed ethane oxidation as an industrial process. Unfortunately, synthetic homologues of these structurally complex active enzymes and their active sites have not yet been realised, and a suitable organism for an optimised commercially applicable biocatalytic process has not yet been found.

3.2.3. Biomimetic Approaches

Due to the expense of NADH cofactors and difficulties associated with enzyme isolation, MMO and P450 are not considered to be viable for commercial ethane oxidation processes. Therefore in light of the high selectivity towards primary oxidation products afforded by enzyme catalysts, a number of approaches have been taken to synthesise biomimetic catalysts, often seeking to mimic the binuclear Fe^{III} active site ($Fe_2(\mu\text{-}O)_2$) found within methane monoxygenase.

Wang *et al.* reported that $FePO_4$ catalyses the oxidation of ethane at a rate of 0.059 $mol_{ethane\ converted}\cdot kg_{cat}^{-1}\cdot h^{-1}$ in a C_2H_6:H_2:O_2 feed to yield ethanol (22.5% selectivity) at 350 °C via a redox mechanism involving a diferric active site (Scheme 3) [86]. Whilst a higher productivity (9.8 $mol_{ethane\ converted}\cdot kg_{cat}^{-1}\cdot h^{-1}$) was attainable upon increasing the reaction temperature to 422 °C, resulting in ethanol selectivity decreasing to 8.7%, suggesting that lower temperature systems may further favour ethanol selectivity [86].



Scheme 3. Mechanism for the ethane oxidation proposed by Otsuka *et al.*

Hydrogen was shown to reduce the catalyst surface to generate Fe (II) and H^+ which is absorbed by a neighbouring phosphate group. Oxygen is activated by accepting electrons from Fe (III) to form a peroxide species. This adsorbed peroxide may be formed using a gas feed comprising of either H_2-O_2 or N_2O. Formation of ethanol from the ethoxide intermediate occurs due to the proximity of the iron sites to acidic phosphate groups which allows rapid protonation of the ethoxide, thereby preventing decomposition to CO_x [86]. When compared with earlier studies, whereby the same conditions and catalyst were used in methane oxidation, rates were 7–8 times higher [86,87].

Also seeking to emulate the diiron active site of sMMO, Nizova *et al.* prepared and tested $[Fe_2(HPTB)(\mu\text{-}OH)(NO_3)_2](NO_3)_2\cdot CH_3OH\cdot 2H_2O$ where HPTB = *N*,*N*,*N*′,*N*′-tetrakis(2-benzimidazolylmethyl)-2-hydroxo-1,3-diaminopropane) [88]. Although inactive itself, addition of pyrazinic acid led to catalytic activity when H_2O_2 was used as the oxidant. This system showed a TOF of 3.5 $mol_{ethane\ converted}\cdot mol_{catalyst}^{-1}\cdot h^{-1}$ at the low temperature of 25 °C, with ethylhydroperoxide (82% selectivity) and acetaldehyde (17%) as the major products in a free- radical driven catalytic system [88].

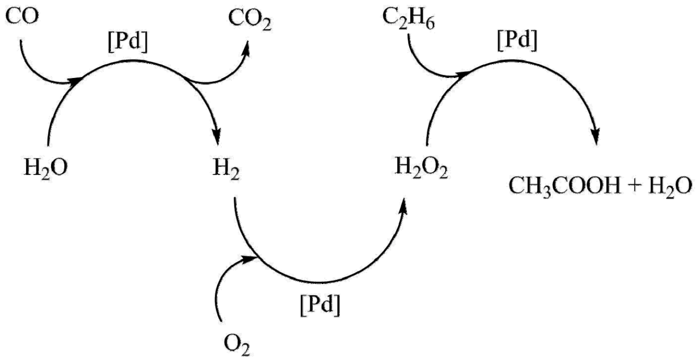
Having the target to emulate Cu- active sites found within membrane-bound particular pMMO, Nagababu *et al.* studied tricopper $[Cu^I Cu^I Cu^I$ (7-*N*-Etppz)$]^{1+}$ (7-*N*-Etppz = 3,3′-(1,4-diazepane-1,4-diyl)bis[1-(4-ethyl piperazine-1-yl)propan-2-ol) [89]. Operating at ambient temperature, in acetonitrile, this catalyst produced ethanol (100% selectivity) at a rate of 11.0 $mol_{ethanol\ converted}\cdot mol_{catalyst}^{-1}\cdot h^{-1}$ using H_2O_2 as the oxidant [89]. The authors later discuss an intention to encapsulate this catalyst within a mesoporous material, with the aim of developing a 100% selective heterogeneous catalyst for ethane hydroxylation.

A biomimetic system for alkane oxidation in the gas phase was reported by Xiao *et al.*, who employed N_2O as the oxidant for ethane conversion, catalysed by the metal organic frameworks Fe_2(dobdc) and $Fe_{0.1}Mg_{1.9}$(dobdc) where $dobdc^{4-}$ = 2,5-dioxido-1,4-benzenedicarboxylate [90].

Reaction of the high spin iron (II) centres within Fe_2(dobdc) with N_2O was proposed to form a transient iron (IV) oxo intermediate. In the absence of alkane substrate, this decayed to form $Fe_2(OH)_2$(dobdc). Using a gas composition containing N_2O:C_2H_6:Ar (10:25:65) and reaction temperature of 75 °C, Fe_2(dobdc) produced the oxygenated products; ethanol, acetaldehyde and diethyl ether, in addition to other ether oligomers under both flow and closed batch conditions [90]. Meanwhile, under the same conditions, the solid solution catalyst $Fe_{0.1}Mg_{1.9}$(dobdc) yielded ethanol and acetaldehyde in 10:1 and 25:1 ratios under flow and batch conditions respectively, with products being solvent- extracted from the catalyst post-reaction. The authors did not discount potential retention of additional products within the MOF framework.

3.2.4. Heterogeneous Approaches

Despite significant interest within the scientific community towards the oxidation of lower alkanes, there are relatively few reports regarding the low temperature, heterogeneously catalysed selective oxidation of ethane. In 1992 Lin *et al.* reported ethane oxidation over 5% Pd/Carbon and 5% Pt/Carbon catalysts [91]. They reported yields of 0.54 M acetic acid with 0.05 M mmol formic acid as a by-product under the following conditions; 24 h, 100 °C, 40 mg 5% Pd/C, 5 mL 0.1 M DCl, ethane (35 bar), oxygen (7 bar) and CO (7 bar). The assigned reaction scheme is shown in Scheme 4.



Scheme 4. Partial oxidation over Pd/C [91].

As shown in Scheme 4, the reaction proceeds through three catalytic steps and requires an acidic medium (DCl) and water due to the initial water gas shift reaction. It was also shown that through charging the system with H_2 (7 bar), O_2 (7 bar) and ethane (34 bar), a 0.002 M concentration of H_2O_2 could be prepared *in situ*. This utilised a non-aqueous environment comprising methylnitrate and trifluoroacetic acid, with acetic acid (0.1 M) and formic acid (0.05 M) formed after 12 h at 85 °C. It was also reported that the oxidation of ethane to ethanol and consecutive oxidation to acetic acid, formic acid and CO_2 occurred [91].

Shul'pin *et al.* later reported that TS-1 catalysed the partial oxidation of ethane with H_2O_2, via the formation of a reactive Ti-OOH species [92]. They reported partial oxidation to acetaldehyde (0.028 M) and ethanol (0.017 M) using H_2O_2 at 30 bar ethane, 12 h and 60 °C [92].

Another class of catalysts which have been reported as active for the partial oxidation of short chain alkanes with H_2O_2 are iron phthalocyanine complexes [50,51,93,94]. Whilst to date most research has focussed upon the partial oxidation of methane, Sorokin and co-workers have recently reported that the SiO_2 supported phthalocyanine $(FePc)_2N/SiO_2$ shown in Figure 3 affords high reaction yields (34%) with appreciable acetic acid selectivity (69%) in the aqueous phase at the low temperature of 60 °C [95]. This equated to a TON of 37 $mol_{AcOH} \cdot mol_{catalyst}^{-1}$ whilst the other major product, HCOOH, was obtained at a TON of 33 [95].

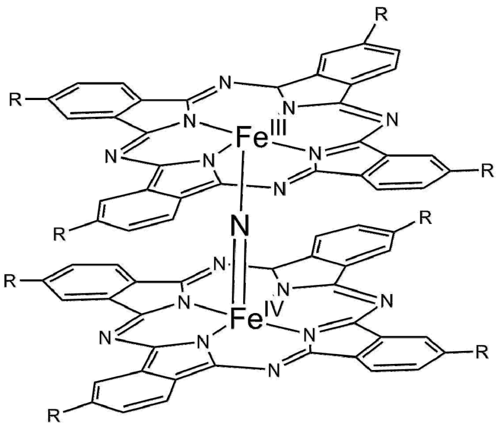


Figure 3. The μ-ntirido diiron phthalocyanine complex used by Sorokin and co-workers.

A number of studies have recently reported the selective oxidation of ethane by H_2O_2 in the aqueous phase using the MFI-type zeolite ZSM-5 [7,69,96,97]. This was first reported by Rahman *et al.*, who showed the direct oxidation of ethane to acetic acid and formic acid using ZSM-5 (1.5 g), aqueous H_2O_2 (4 M), 30 bar ethane, 120 °C, 2 h with 0.3 g of PPh_3 as an additive. Under these conditions they showed 35.1% ethane conversion with major product selectivities of acetic acid (48.5%), formic acid (36.3%) and CO_2 (11.9%) [69]. A positive effect upon ethane conversion and acetic acid selectivity was reported at increasing SiO_2/Al_2O_3 ratios, with a ratio of 23.8 shown to be the most active catalyst, giving a total productivity of 6.81 $\text{mol}_{\text{ethane converted}} \cdot \text{kg}_{\text{cat}}{}^{-1} \cdot \text{h}^{-1}$ [69]. Based upon these data, Rahman *et al.* attributed catalytic activity to the Brønsted acidic $AlO_4{}^{-}$ sites present within ZSM-5, although the nature of the active site was not extensively discussed. Based upon EPR radical trapping studies, $\cdot OH$ radicals were implicated in the proposed transformations.

$$C_2H_6 + 4 \cdot OH \rightarrow CH_3CHO + 3\,H_2O \tag{3}$$

$$CH_3CHO + \tfrac{1}{2}\,O_2 \rightarrow CH_3COOH \tag{4}$$

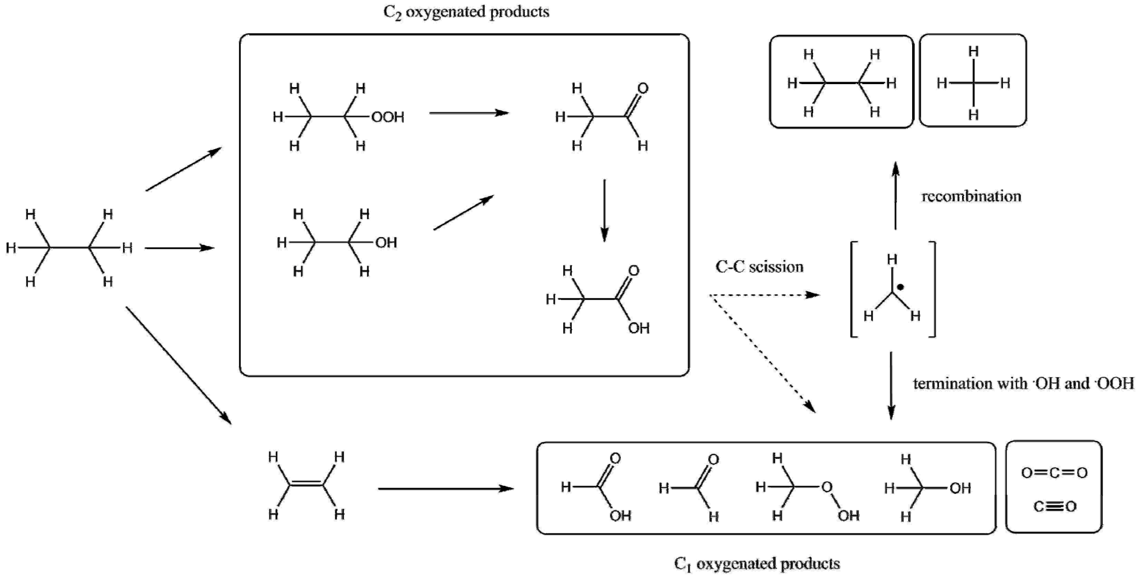
Studies of the temporal evolution of products led the authors to conclude that Equations (3) and (4) dominate, with CH_3OOH the major initial product [69]. Meanwhile, low selectivity towards CH_3CH_2OH was attributed to the competing minor reaction pathways shown in Equations (5) and (6).

$$C_2H_6 + \cdot OH \rightarrow C_2H_5OH \tag{5}$$

$$C_2H_5OH + O_2 \rightarrow CH_3COOH + H_2O \tag{6}$$

The authors also studied H^{+}β-Zeolite, the heteropolyacid H_4PVMoO_{40} and TS-1 under the same conditions. TS-1 showed the lowest catalyst productivity but highest acetic acid selectivity (84%), indeed total C_2 selectivity was higher than the other, more Brønsted acidic catalysts in the study [69].

In 2013, Forde *et al.* also reported that ZSM-5 catalysts are effective, reusable catalysts for the oxidation of ethane with H_2O_2 [7]. The system required lower operating temperatures than those reported by Rahman *et al.*, at 50 °C, lower H_2O_2 concentrations of *ca.* 0.5 M and there was no requirement for a PPh_3 additive. In line with analogous studies of the ZSM-5 catalysed oxidation of methane within the same group [98], the catalytic conversion of both ethane and H_2O_2 was attributed to extraframework iron sites. Indeed, whilst H-ZSM-5 (30) showed a rate of 2.8 $\text{mol}_{\text{ethane converted}} \cdot \text{kg}_{\text{cat}}{}^{-1} \cdot \text{h}^{-1}$, post synthesis deposition of 1.1 wt % Fe increased the rate to 47.1 $\text{mol}_{\text{ethane converted}} \cdot \text{kg}_{\text{cat}}{}^{-1} \cdot \text{h}^{-1}$ under the same conditions [7]. This constituted a decrease in TOF, from 1211.4 $\text{mol}_{\text{ethane converted}} \cdot \text{mol}_{\text{Fe}}{}^{-1} \cdot \text{h}^{-1}$ to 137.2 $\text{mol}_{\text{ethane converted}}\ \text{mol}_{\text{Fe}}{}^{-1} \cdot \text{h}^{-1}$ [7]. Comparatively low TOFs (12.9 and 66.5 $\text{mol}_{\text{ethane converted}} \cdot \text{mol}_{\text{Fe}}{}^{-1} \cdot \text{h}^{-1}$) were observed for catalysts comprising of Fe impregnated onto amorphous SiO_2 and the alumina-free MFI zeolite Silicalite-1 respectively. It was therefore determined that Fe/ZSM-5 catalysts derived their activity, to varying degrees, from multiple iron species including; extraframework dimeric μ- oxo- hydroxo species, highly dispersed surface iron species and iron species within the zeolite pores [7]. The speciation of iron sites was determined to effect catalytic activity to a greater extent than total iron loading, therefore justifying the trends in TOF. Process optimisation using a 2.5 wt % Fe/ZSM-5 (30) catalyst led to productivities of up to 65 $\text{mol}_{\text{ethane converted}} \cdot \text{kg}_{\text{cat}}^{-1} \cdot \text{h}^{-1}$ at 56% ethane conversion, with acetic acid the major product (70% selectivity, 39.1% yield) [7]. Consistent with the studies of Rahman *et al.* EPR radical trapping studies showed $\cdot$OH radicals in solution, however mechanistic studies showed the reaction scheme to differ significantly from that previously reported, being more in line with homogeneous studies discussed in Section 3.2.1. Three primary products were observed; ethanol, ethene and ethylhydroperoxide. Ethanol and ethylhydroperoxide were shown to undergo consecutive oxidations through acetaldehyde to acetic acid, with catalytic C–C scission reactions yielding C_1 products (methylhydroperoxide, methanol, formic acid and CO_x). Meanwhile, ethene was shown to undergo oxidation to acetic acid and C_1 products as shown in Scheme 5 [7].



Scheme 5. Proposed reaction scheme for ethane oxidation using ZSM-5 catalysts based on mechanistic studies [7].

The disparity between reaction schemes proposed by Rahman *et al.* and Forde *et al.* is due to the catalytic nature of consecutive oxidation reactions, and this could be a consequence of the differing reaction conditions used. Indeed, Forde *et al.* showed Fe/ZSM-5 catalysed the oxidation of ethanol under reaction conditions, with acetic acid as the major product (37.5 $\text{mol}_{\text{reacted}} \cdot \text{kg}_{\text{cat}}^{-1} \cdot \text{h}^{-1}$, 17.5% acetic acid yield). The subsequent conversion of acetic acid was then shown to proceed at a far lower rate (7.5 $\text{mol}_{\text{reacted}} \cdot \text{kg}_{\text{cat}}^{-1} \cdot \text{h}^{-1}$, 1.6% and 3.4% yield of formic acid and CO_2 respectively) [7]. Furthermore, the low temperature continuous oxidation of ethane using ZSM-5 catalysts and H_2O_2 was recently reported by Armstrong *et al.* Through optimisation of a 0.4 wt % Fe/ZSM-5 (30) catalysed trickle bed reactor system, 22% ethane conversion to acetic acid (73% selectivity, 16% yield) was achieved with low selectivity towards carbon oxides (*ca.* 1%) [96].

3.2.5. Summary of Catalyst Performance

Considering the wide range of catalytic approaches that have been employed for the direct selective oxidation of ethane, it is interesting and informative to try to summarise the performance of these catalysts. Furthermore, the wide variety of conditions that have been adopted are also noteworthy. Table 1 shows a summary of performance of some of the catalysts reviewed in this article.

Table 1. A summary of the performance of partial ethane oxidation systems.

Entry	Catalyst	Regime	Oxidant	Solvent(s)	*P* (C_2H_6)/bar	T/°C	Time/h	Major Product Selectivities/%	Mass Normalised Conversion Rate [a]	TOF [b]	Ref.
1	$[Fe^{III}(Tp)_2]ClO_4$ [c]	Batch. L/G	$KHSO_5$	$MeCN/H_2O$	6.9	RT	0.08	CH_3COOH (80), EtOH (20)	20.64	12.0	[75]
2	$[Fe^{III}(L)\text{-}(acac)Cl]ClO_4$ [d]	Batch. L/G	$KHSO_5$	$MeCN/H_2O$	6.9	RT	0.5	CH_3COOH (83), EtOH (17)	13.01	6.0	[75]
3	$[Fe^{III}(L)\text{-}(3\text{-}Cl\text{-}acac)Cl]ClO_4$ [d]	Batch. L/G	$KHSO_5$	$MeCN/H_2O$	6.9	RT	0.5	CH_3COOH (85), EtOH (15)	13.72	6.8	[75]
4	H_2CrO_4	Batch. L/G	H_2O_2	MeCN	30	60	1	CH_3CHO (52), EtOOH (23), EtOH (19)	5253.71	620	[70]
5	$NaVO_3 + H_2SO_4$	Batch. L/G	H_2O_2	MeCN	30	50	4	EtOH (51), CH_3CHO (32), CH_3COOH (17)	385.47	47.5	[71]
6	$[PMo_{11}VO_{40}](Bu_4N)_4$	Batch. L/G	H_2O_2	MeCN	30	60	10	CH_3CHO (44), EtOOH (34), EtOH (22)	0.50	1.4	[67]
7	$[L_2Mn_2O_3](PF_6)_2$ [d]	Batch. L/G	H_2O_2	MeCN	20	25	2	EtOOH (39), CH_3CHO (33), EtOH (28)	227.74	180	[68]
8	$Fe(ClO_4)_3$	Batch. L/G	H_2O_2	MeCN	27	25	3	EtOOH (88), CH_3CHO (9), EtOH (3)	64.00	22.7	[72]
9	$Fe(OAC)_2(OH)$ + PCA [e]	Batch. L/G	H_2O_2	MeCN	27	25	2	EtOH (68), CH_3CHO (29), EtOOH (3)	31.43	6.0	[72]
10	$FeCl_3$	Batch. L/G	H_2O_2	H_2O	30	90	1	CH_3CHO (66), EtOH (18), CO_2 (16)	189.27	30.7	[74]
11	$PdCl_2$	Batch. L/G	H_2O_2	H_2O	30	90	1	CH_3CHO (56), CO_2 (31), EtOH (13)	170.87	30.3	[74]
12	$OsCl_3$	Batch. L/G	H_2O_2	H_2O	30	90	1	CH_3CHO (56), CO_2 (26) EtOH (18)	161.17	47.8	[74]
13	H_2PtCl_6	Batch. L/G	H_2O_2	H_2O	30	90	1	CH_3CHO (67), EtOH (33)	13.18	5.4	[74]
14	$HAuCl_4$	Batch. L/G	H_2O_2	H_2O	30	90	1	CH_3CHO (62), CO_2 (22) EtOH (15)	94.32	32.1	[74]
15	-	Batch. L/G	$Tl(TFA)_3$	HTFA	34.4	180	3	EtTFA (67), $EG(TFA)_2$ (33)	0.46 [f]	-	[76]
16	-	Batch L/G	$Pb(TFA)_4$	HTFA	34.4	180	3	EtTFA (70), $EG(TFA)_2$ (30)	0.46 [f]	-	[76]
17	-	Batch. L/G	$C_6F_5I^{III}(TFA)_2$	TFAA/HTFA	34.5	150	3	EtTFA (91), 1,2-$Et(TFA)_2$ (8%)	0.51 [f]	-	[77]
18	*Methylococcus capsulatus* (sMMO)	Batch. L/G	O_2/NADH	H_2O	-	45	0.2	EtOH (100)	4.10	-	[79]
19	Cytochrome P450 BM3	Batch. L/G	O_2/NADPH	H_2O	5	20	2	EtOH (100)	-	40.0	[84]
20	Cytochrome P450 BM3 mutant	Batch. L/G	O_2/NADPH	H_2O	1.38	25	0.5	EtOH (100)	-	24.0	[82]
21	Cytochrome $P450_{cam}$ mutant	Batch. L/G	O_2/NADH	H_2O	-	30	-	EtOH (100)	-	4700	[83]
22	Cytochrome 450 PMO A6	Batch. L/G	PhIO	H_2O	1.38	25	0.17	EtOH (100)	-	15.0	[85]
23	Cytochrome 450 PMO A6	Batch. L/G	MCPBA	H_2O	1.38	25	0.17	EtOH (100)	-	2.0	[85]
24	Cytochrome 450 PMO A6	Batch. L/G	H_2O_2	H_2O	1.38	25	0.17	EtOH (100)	-	1.4	[85]
25	$FePO_4$	Flow, G/S	O_2/H_2	-	0.34	400	-	CH_3CHO (24), HCHO (18), EtOH (12) [g]	4.20	1.3	[86]
26	$[Cu^{I}Cu^{I}Cu^{I}(7\text{-N-Etppz})]^{1+}$ [h]	Batch. L/G	H_2O_2	MeCN	1.79	RT	1	EtOH (100)	19.06	11.0	[89]
27	$Fe_{0.1}Mg_{1.9}$(dobdc)	Batch. G/S	N_2O	-	7.5	75	24	EtOH (96), CH_3CHO (4)	-	0.07	[90]
28	$[Fe_2(HPTB)(\mu\text{-}OH)(NO_3)_2]$ $(NO_3)_2 \cdot CH_3OH \cdot 2H_2O$ + PCA [e]	Batch. L/G	H_2O_2	MeCN	30	25	6	EtOOH (82), CH_3CHO (17), CH_3COOH (1)	3.28	3.5	[88]
29	5% Pd/C	Batch. L/G/S	H_2O_2 [i]	DCl/D_2O	34.5	70	24	CH_3COOH (85), HCOOH (10), EtOH (6)	0.65	1.4	[91]
30	5% Pd/C	Batch. L/G/S	H_2O_2 [i]	DCl/D_2O	34.5	85	24	CH_3COOH (78), HCOOH (22)	3.40	7.2	[91]
31	5% Pt/C	Batch. L/G/S	H_2O_2 [i]	DCl/D_2O	34.5	95	24	CH_3OOH (100)	0.14	0.5	[91]
32	TS-1	Batch. L/G/S	H_2O_2	H_2O	30	60	12	CH_3CHO (94), EtOH (6)	0.25	-	[92]
33	$(FePc)_2N/SiO_2$	Batch. L/G/S	H_2O_2	H_2O	32	60	20	CH_3COOH (69), HCOOH (31)	0.054	2.7	[95]
33	$(FePc^tBu)_2N/SiO_2$	Batch. L/G/S	H_2O_2	H_2O	32	60	20	CH_3COOH (71), HCOOH (29)	0.047	2.3	[95]
34	TS-1	Batch. L/G/S	H_2O_2	PPh_3/H_2O	30	120	2	CH_3COOH (84), CO_2 (9), HCOOH (4)	9.53	-	[69]
35	H-β	Batch. L/G/S	H_2O_2	PPh_3/H_2O	30	120	2	CH_3COOH (65), HCOOH (20), CO_2 (11)	14.09	-	[69]
36	5% W/H-ZSM-5	Batch. L/G/S	H_2O_2	PPh_3/H_2O	30	120	2	CH_3COOH (44), HCOOH (38), CO_2 (16)	13.41	-	[69]
37	H_4PVMoO_{40}	Batch. L/G/S	H_2O_2	PPh_3/H_2O	30	120	2	CH_3COOH (61), HCOOH (19), CO_2 (12)	15.37	-	[69]
38	H-ZSM-5	Batch. L/G/S	H_2O_2	PPh_3/H_2O	30	120	2	CH_3COOH (48), HCOOH (36), CO_2 (12)	17.24	-	[69]
39	H-ZSM-5	Batch. L/G/S	H_2O_2	H_2O	20	50	0.5	CH_3COOH (37), EtOH (26) HCOOH (17)	3.00	1211.4	[7]
40	0.4% Fe/ZSM-5	Batch. L/G/S	H_2O_2	H_2O	20	50	0.5	CH_3COOH (49), EtOH (19) HCOOH (14)	16.50	233.2	[7]
41	1.1% Fe/ZSM-5 [j]	Batch. L/G/S	H_2O_2	H_2O	20	50	0.5	CH_3COOH (55), EtOH (23) HCOOH (16)	49.50	251.3	[7]
42	1.25% Fe 1.25% Cu/ZSM-5	Batch. L/G/S	H_2O_2	H_2O	20	50	0.5	C_2H_4 (34), CH_3COOH (31), EtOH (26)	24.00	32.6	[7]
43	2.5% Fe/SiO_2	Batch. L/G/S	H_2O_2	H_2O	20	50	0.5	CH_3CH_3OOH (34), CH_3CHO (33), CH_3COOH (13)	4.50	12.9	[7]
44	0.5% Fe-Silicalite-1	Batch. L/G/S	H_2O_2	H_2O	20	50	0.5	EtOH (40), CH_3COOH (30), HCOOH (14)	6.00	66.5	[7]
45	1.1% Fe/ZSM-5 [k]	Batch. L/G/S	H_2O_2	H_2O	20	50	0.5	EtOH (33), CH_3COOH (44), HCOOH (13)	56.00	284.3	[97]
46	0.4% Fe/ZSM-5	Flow. L/G/S	H_2O_2	H_2O	2	50	0.06 [l]	CH_3COOH (73), HCOOH (19), CH_3CHO (3)	0.26	3.6	[96]

[a] defined as $mol_{ethane\ converted} \cdot kg_{cat}{}^{-1} \cdot h^{-1}$; [b] defined as $mol_{ethane\ converted} \cdot mol_{active\ site}{}^{-1} \cdot h^{-1}$; [c] Tp = hydrotris (1-pyrazolyl1)-borate; [d] L = 1,4,7-trimethyl-1,4,7-triazacylononane; [e] HPTB = *N*,*N*,*N*′,*N*′-tetrakis(2-benzimidazolylmethyl)-2-hydroxo-1,3-diaminopropane), PCA = pyrazine-2-carboxylic acid; [f] $mol_{ethane\ converted} \cdot mol_{oxidant}{}^{-1} \cdot h^{-1}$; [g] Major products C_2H_4, CO_2 and CO. Partially oxygenated product selectivities shown; [h] (7-*N*-Etppz) = 3,3′-(1,4-diazepane-1,4-diyl)bis[1-(4-ethyl piperazine-1-yl)propan-2-ol]; [i] H_2O_2 generated *in situ*. From H_2 and O_2; [j] Catalyst calcined in static air, 3 h, 550 °C, 20 °C· min^{-1}; [k] Catalyst reduced in 5% H_2/Ar, 3 h, 550 °C, 20 °C· min^{-1}; [l] Calculated catalyst bed residence time.

4. Conclusions and Outlook

It is apparent that partial ethane oxidation is of continued interest to the research community, in spite of its scientific complexity. However despite this, only one direct oxidation process has been commercialised; the SABIC process discussed in Section 3.1. Indeed, methanol carbonylation continues to dominate the current market for acetic acid production. Other alternatives include direct formation of acetic acid from ethene, as in the Showa Denko process, or a two- step ethene- acetaldehyde- acetic acid process. However these first require steam cracking of ethane to ethene in order to activate the alkane substrate. Whilst studies have shown such routes to approach economic equivalence with methanol carbonylation at comparable levels of scale, direct oxidation of ethane is still preferable as it circumvents the need for intermediate isolation steps.

The data in Table 1 indicates the wide range of catalyst systems that have been employed for ethane direct oxidation to oxygenates. None of these have demonstrated performance required for industrial commercialisation, and significant scope remains for the development of improved catalysts. Whilst studies within the past decade have advanced the field significantly, with high rates of ethane activation observed even at low temperatures of <100 °C, process viability is limited due to a dependence on activated oxidants. Here biological systems serve as a benchmark; affording total selectivity to ethanol using dioxygen as the oxidant, under ambient conditions. However these require stoichiometric equivalents of reducing cofactors such as NADPH. In the absence of cofactor some enzymes catalyse ethane hydroxylation, however these require activated oxidants such as H_2O_2 and show low reaction rates relative to synthetic analogues.

The prevailing trend in recent years favours low reaction temperatures and H_2O_2 as oxidant. Unfortunately no study has reported stoichiometric utilisation of H_2O_2. This is a key economic concern when working with H_2O_2, which is expensive relative to dioxygen, and raises doubts as to the environmental benefit of direct processes over current indirect processes. One possible solution requires that the H_2O_2 be generated *in situ* through reduction of dioxygen with H_2, as in the work of Lin *et al.* [91] However, the expense of H_2 would again demand a high efficiency of H_2O_2 formation and use. Whilst an array of catalyst systems have shown appreciable rates of ethane conversion in the aqueous phase using H_2O_2, extraction of dilute concentrations of the target oxygenated products from the aqueous phase would prove problematic and energy intensive upon scale-up. The challenges posed by separations might be avoided by operation in the gas phase, however this would most likely require elevated temperatures, at which further oxidation of the desirable C_2 oxygenated products to CO_x becomes more favourable. This leads to potential limitations on product yields. It is clear that, at least in the longer term, a key focus should be the design of an efficient catalyst that selectively partially oxidises ethane with dioxygen at sufficiently mild reaction conditions, so as not to sacrifice C_2 product selectivity. It should be noted that selective partial oxidation of ethane is a similar challenge as the direct catalytic oxidation of methane to methanol, and many in the catalyst community are now focussed on these major challenges.

Conflicts of Interest: The authors declare no conflict of interest.

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