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Highly efficient catalytic production of oximes from ketones using in situ generated H_2O_2

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Abstract.

The ammoximation of cyclohexanone using preformed hydrogen peroxide is currently applied commercially to produce cyclohexanone oxime, an important feedstock in Nylon-6 production. We demonstrate that by using supported AuPd alloyed nanoparticles in conjunction with a titanium silicate-1 catalyst, hydrogen peroxide can be generated in situ as needed, producing cyclohexanone oxime with >95% selectivity, comparable to the current industrial route. The ammoximation of several additional simple ketones is also demonstrated. Our approach avoids the need to transport and store highly concentrated, stabilized hydrogen peroxide, potentially achieving substantial environmental and economic savings. This approach could form the basis of an alternative route to numerous chemical transformations that are currently dependent on a combination of preformed H_2O_2 and TS-1, while allowing for considerable process intensification.

Cyclohexanone oxime is a key precursor in the production of caprolactam, a commodity chemical used in the production of the polyamide Nylon-6. With global production of Nylon-6 predicted to reach 8.9 million tons per annum by 2024 (*1*), there is a concurrent increase in demand for cyclohexanone oxime. The traditional route to cyclohexanone oxime production involves the reaction of cyclohexanone with hydroxylamine sulfate, producing ammonium sulfate, a low-value fertilizer with limited applications, as a major by-product (*2*). Alternative routes (fig. S1 and accompanying text) are hampered by the need to continually maintain a low reaction pH, by complex and energy-intensive extraction steps, or by low selectivity towards the desired product. A single-step ammoximation process, which overcomes these challenges, has been developed using titanium silicate-1 (TS-1) as the catalyst and cyclohexanone, ammonia and pre-formed H_2O_2 as reactants (*3*). In this process hydroxylamine is formed catalytically in situ by TS-1 (*4*), with this intermediate species subsequently reacting, non-catalytically, with cyclohexanone to produce the oxime (fig. S.1 and accompanying text) (*5*). The catalytic activity of TS-1 with H_2O_2, which has been crucial in the development of numerous selective oxidation processes (fig. S2), is often attributed to the ability of Ti^{IV} sites to readily co-ordinate multiple species which, in the case of cyclohexanone ammoximation, is crucial in the formation of hydroxylamine (*6*). Despite extensive advances in catalyst design leading to the development of a range of titanosilicates that are highly selective towards cyclohexanone ammoximation and offer greater catalytic stability (including Ti-MOR (*7*), Ti-Beta (*8*), TS-2 (*9*) Ti-MWW (*10*)), TS-1 is still widely considered the industrial standard for reactions involving H_2O_2 (*11*).

Although the industrial ammoximation process based on H_2O_2/TS-1, which accounts for approximately 6 million tons per annum of global oxime production (*12*), offers excellent catalytic selectivity, an excess of H_2O_2 is typically required, due to the low stability of the oxidant under the associated reaction conditions (elevated temperatures and high pH), leading to elevated process costs (*13*). In addition, the pre-formed H_2O_2 that is used requires transportation from a centralized point of production, where it is manufactured at concentrations greatly exceeding that needed in the ammoximation process; the requisite dilution wastes the energy previously used in distillation and concentration steps. Furthermore, the instability of H_2O_2 necessitates the addition of acid and halide stabilizing agents to prevent its degradation during transport and storage, which in turn can limit catalyst stability, decrease reactor lifetime through corrosion, and generate substantial costs associated with removal of these stabilizers from product streams (*14*). Likewise, all chemical transformations that use pre-formed H_2O_2 suffer from these drawbacks to a certain degree.

We have previously developed catalysts for the direct synthesis of H_2O_2 from the elements that offer high synthesis rates and >99% H_2 utilization (*15, 16*). However, to date the direct method has been unable to rival the current industrial route to H_2O_2 production, primarily because the dilute H_2 and O_2 streams necessary to avoid explosion risks limit the attainable product concentrations of H_2O_2. This disadvantage no longer pertains if the H_2O_2 is produced and then rapidly consumed in situ. Indeed, the application of in situ generated H_2O_2 has been a long-standing goal in the valorization of many chemical feedstocks, with investigations into a range of selective oxidation reactions reported, including propene epoxidation (*17*), alcohol oxidation (*18*) and the partial oxidation of methane (*19*). However, to date earlier works are yet to demonstrate a viable alternative to the current respective industrial processes and are typically hindered by low rates of conversion or poor selectivity towards desired products. Indeed, in many cases the in situ approach has often led to unforeseen complications, such as the generation of potentially hazardous by-products, often largely driven by competing hydrogenation reactions (*20*). Additionally, issues associated with catalyst deactivation and the requirement for unfavorable solvent systems or costly additives has hampered the adoption of an in situ generated H_2O_2 route to selective oxidation (*17*).

At first sight the application of such an in situ approach to cyclohexanone ammoximation is not only hampered by the potential drawbacks outlined in these earlier studies but also by the substantial conditions gap between the two key processes of the reaction sequence. Direct H_2O_2 formation is favored at low pH and sub-ambient temperatures, whereas both the high reaction temperature and basic conditions associated with the ammoximation process are detrimental to H_2O_2 stability. Herein we report that it is possible to bridge this conditions gap and pair the direct synthesis of H_2O_2 with cyclohexanone ammoximation to produce the oxime in yields comparable to those observed in the current commercial process that uses preformed H_2O_2 (Fig. 1 and accompanying text). This is achieved through the in situ generation of H_2O_2 over AuPd nanoparticles in conjunction with a commercial TS-1 catalyst.

The immobilization of chloride-based Au and Pd salts onto a range of support materials, via a wet co-impregnation procedure and subsequent calcination, has been extensively reported to produce alloyed nanoparticle catalysts that are highly active towards the direct synthesis of H_2O_2 (*21*). Using this industrially viable route to catalyst preparation, we initially prepared a series of AuPd catalysts, with a range of total metal loading, supported on TiO_2, which we exposed to an oxidative heat treatment (denoted AuPd/TiO_2(Chloride-O)). We observed a correlation between total metal loading and catalytic performance towards the direct synthesis of H_2O_2, under reaction conditions that are optimal for H_2O_2 production (*i.e.,* low pH and sub-ambient temperatures) (fig. S3).

We subsequently established the high efficacy of the in situ approach to cyclohexanone ammoximation using a physical mixture of the AuPd/TiO_2(Chloride-O) catalysts, of varied total metal loading, in conjunction with commercial TS-1 (fig. S4, table S1). With an optimal catalyst formulation of 0.33%Au-0.33%Pd/TiO_2(Chloride-O) (metal loading reported as wt.%), we observed an oxime yield and selectivity based on H_2 (*i.e.,* mol of H_2 consumed that lead to the formation of the oxime via H_2O_2) of 77% and 71%, respectively. We did not observe the formation of unwanted organic by-products, such as nitrocyclohexane or cyclohexenylcyclohexanone (analysis detection threshold for by-products equivalent to approximately 0.005M). Detailed characterization of the TS-1 material is presented in fig. S5, with further characterization via scanning transmission electron microscopy (STEM) presented in figs. S6A-D. Analysis of the 0.33%Au-0.33%Pd/TiO_2(Chloride-O) catalyst by high-angle annular dark-field scanning transmission electron microscopy (HAADF-STEM) imaging and X-ray energy dispersive spectroscopy (XEDS) mapping (fig. S7) revealed a bi-modal particle size distribution and distinct particle size/composition relationship: smaller particles (3-10 nm) were found to be Pd-rich alloys, whereas the larger (10-30 nm) particles were found to be Au-rich, often adopting a Au-rich core / Pd-rich shell morphology. Similar observations have previously been reported for AuPd catalysts prepared by this wet co-impregnation synthesis route (*22*).

Significant improvements in cyclohexanone oxime yield were obtained by using a gaseous reactant mixture consisting of H_2 and O_2, with an N_2 diluent, compared to that observed when using either component alone (fig. S8 and accompanying text). Indeed, the in situ approach also offers increased cyclohexanone oxime yields (77%) compared to that observed when using preformed H_2O_2 (41%), at concentrations of H_2O_2 comparable to those that could be present if all the H_2 in the in situ reaction was converted to H_2O_2. The relatively limited activity observed when using commercial H_2O_2 can be attributed to the complete addition of H_2O_2 at the start of the reaction; continual incremental addition of H_2O_2 over the course of the reaction is well known to influence the catalytic performance of the current industrial process (fig. S8 and accompanying text). Further investigation demonstrated that high catalytic performance (selectivity towards cyclohexanone oxime >95%) could be achieved regardless of the support (TiO_2, SiO_2, CeO_2, Al_2O_3, Nb_2O_5, ZrO_2) used to immobilize the AuPd nanoparticles (fig. S9).

Enhanced cyclohexanone oxime production was observed when both Au and Pd were immobilized onto the same support, with the activity of the 0.33%Au-0.33%Pd/TiO_2(Chloride-O) and TS-1 system (77% oxime yield) markedly outperforming analogues consisting of either mono-metallic catalysts or a physical mixture thereof (Fig. 2A, fig. S10). Indeed, the alloying of Au with Pd is known to be highly effective in both suppressing O-O bond dissociation (inhibiting H_2O production) and promoting the release of H_2O_2 from catalytic surfaces (*23, 24*). It is therefore plausible to consider that the role of Au is to facilitate the desorption of H_2O_2 (or peroxy species) from the precious metal surface, enabling subsequent diffusion to Ti^{IV} sites present within the TS-1 framework. TS-1 in turn catalyzes the formation of the hydroxylamine intermediate, with limited ammoximation activity observed in the absence of either the titanosilicate or AuPd supported catalyst (≤ 15% oxime selectivity) (fig. S11). Further analyses of the 0.33%Au-0.33%Pd/TiO_2(Chloride-O) and TS-1 dual catalyst system demonstrated that high H_2 selectivity can be achieved when the reaction is not limited by cyclohexanone availability, with a H_2 selectivity of 98% observed at a reaction time of 1 h and a cyclohexanone conversion of 30% (Fig. 2B).

We have also extended our studies to assess the ammoximation of a small range of other ketones (cyclopentanone, cycloheptanone, cyclooctanone and acetophenone), with many of the corresponding oximes finding application in the synthesis of pharmaceuticals (*25, 26*). Using the 0.33%Au-0.33%Pd/TiO_2(Chloride-O) and TS-1 catalysts (Fig. 2C), oxime selectivities >95% were observed for all substrates, demonstrating the versatility of the in situ approach to oxime formation. The variation in the rate of ketone conversion is considered to be primarily related to the differing intrinsic reactivity of the ketones with hydroxylamine, in addition to the limited ability of the larger ketones to access the interior of the titanosilicate pore structure (*27*).

Further optimization of the Au: Pd ratio revealed an optimal composition, with a physical mixture of the 0.55%Au-0.11%Pd/TiO_2(Chloride-O) and TS-1 catalysts exhibiting a cyclohexanone oxime yield of 96% and an apparent turnover frequency (TOF) (223 $mol_{oxime}mol_{metal}^{-1}h^{-1}$) far greater than the physical mixture of the 0.33%Au-0.33%Pd/TiO_2(Chloride-O) catalyst and TS-1 (143 $mol_{oxime}mol_{metal}^{-1}h^{-1}$), in a 3 h reaction (Fig. 2D, apparent TOFs shown in table S2). The improved catalytic performance may in part be due to a decrease in the number of contiguous Pd sites, which are known to be highly active towards O-O bond cleavage (*28*), and enhanced H_2O_2 utilization. Our determination of H_2 selectivity supports this hypothesis, with the combination of Au-rich catalysts in addition to TS-1 offering enhanced selectivity in comparison to the corresponding Au-lean analogues (table S2). In a similar manner, Au-rich compositions are observed to offer reduced rates of H_2O_2 degradation, under ideal direct synthesis conditions (fig. S12).

Although high yields of cyclohexanone oxime can be achieved using the co-catalyst system, for application on an industrial scale the use of a composite catalyst that can both synthesize H_2O_2 and catalyze the formation of hydroxylamine would be highly desirable. Hence, we investigated the efficacy of AuPd nanoparticles supported on a commercial TS-1 for the ammoximation of cyclohexanone, with the catalyst prepared by wet co-impregnation of $PdCl_2$ and $HAuCl_4$ onto TS-1 followed by calcination (denoted 0.33%Au-0.33%Pd/TS-1(Chloride-O)). The rate of H_2O_2 formation by this catalyst was comparable to that observed when using a range of oxide supports (fig. S13) (characterization of 0.33%Au-0.33%Pd/TS-1(Chloride-O) is presented in fig. S14), with the bifunctional catalyst offering >95% selectivity towards the oxime (fig. S15). However, the rate of cyclohexanone conversion (44%) was lower than that observed for the co-catalyst system, which comprised the 0.33%Au-0.33%Pd/TiO_2(Chloride-O) catalyst in conjunction with TS-1 (80%). This difference in catalytic performance is ascribed to the blocking of Ti^{IV} sites, as previously observed by Hölderich and co-workers (*29*) and the poor mixing of the Au and Pd metallic components upon immobilization onto the titanosilicate support, as evidenced by STEM-HAADF imaging and XEDS mapping (fig. S16).

We subsequently demonstrated that it is possible to further enhance catalytic performance through preparation of the titanosilicate supported catalyst via a sequential wet impregnation procedure, using $Pd(OAc)_2$ and $HAuCl_4$ precursors, followed by calcination (0.33%Au-0.33%Pd/TS-1(Acetate-O)) and a subsequent reductive heat treatment (2 h, 400 °C, 5%H_2/Ar) (0.33%Au-0.33%Pd/TS-1(Acetate-O+R) (characterization of the 0.33%Au-0.33%Pd/TS-1(Acetate-O+R) catalyst is reported in fig. S17). Catalytic performance towards cyclohexanone ammoximation was found to be markedly improved compared to the 0.33%Au-0.33%Pd/TS-1(Chloride-O) or 0.33%Au-0.33%Pd/TS-1(Chloride-O+R) analogues, with the yield of oxime achieved by the 0.33%Au-0.33%Pd/TS-1(Acetate-O+R) catalyst comparable to that observed when using the 0.33%Au-0.33%Pd/TiO_2(Chloride-O) and TS-1 physical mixture (Fig. 3A, with comparison of apparent TOFs shown in table S3). Indeed, our optimal results using in situ synthesized H_2O_2 rival those reported in the literature for a range of commonly used oxidants, including preformed H_2O_2 (table S.4), demonstrating the potential of this approach to supersede the current industrial route to cyclohexanone oxime.

With the nature of the catalyst surface, in particular the oxidation state of the active metals, crucial in obtaining high catalytic performance, we analyzed the titanosilicate supported AuPd catalysts via X-ray photoelectron spectroscopy (XPS) (fig. S18). Exposure of the 0.33%Au-0.33%Pd/TS-1(Acetate-O) catalyst to a reductive heat treatment (2h, 400 °C, 5%H_2/Ar) resulted in a complete shift in the Pd oxidation state to Pd^0, coinciding with an observed increase in catalytic performance towards both H_2O_2 synthesis (fig. S19) and cyclohexanone ammoximation (Fig. 3A). Detailed STEM analysis of the 0.33%Au-0.33%Pd/TS-1(Acetate-O+R) catalyst (Fig. 3B, additional analysis shown in fig S.20) identified significant metal decoration on both the TiO_2 minority and TS-1 majority phases. HAADF-STEM imaging and corresponding XEDS elemental mapping revealed that the metal nanoparticles present on the minority TiO_2 phase consist predominantly of larger (5-20 nm) AuPd alloys, in addition to some smaller (1-3 nm) Pd-only particles. By comparison analysis of the TS-1 majority phase shows the preferential immobilization of Pd onto the titanosilicate majority phase, with the absence of Au or AuPd alloys notable.

Time-on-line studies conducted using the 0.33%Au-0.33%Pd/TS-1(Acetate-O+R) catalyst showed high H_2 selectivity (94%) was possible when cyclohexanone availability is not limited, indicating that at extended reaction times H_2 is non-selectively consumed via H_2O_2 degradation or non-catalytic pathways (fig. S21), while regardless of reaction time, ammonia selectivity was found to be relatively high (*ca.* 75%).

Analysis of post-reaction solutions by inductively coupled plasma mass spectrometry (ICP-MS) (table S5) revealed the high stability of Au over a standard 3 h cyclohexanone ammoximation reaction. However, a significant loss of Pd (18.6%) was observed over this same time period. Further studies established the stability of the 0.33%Au-0.33%Pd/TS-1(Acetate-O+R) catalyst over multiple uses and found that there was some minimal additional leaching of Pd upon second use (table S5). Notably, no metal loss was observed following the third use and indeed the efficacy of the catalyst was retained over three consecutive ammoximation reactions (oxime yield ≥ 80%) (Fig. 3C).

Detailed STEM-HAADF analysis of the catalyst over three uses (Fig. 3D, figs. S22-24) identified that the observed Pd leaching was associated with the loss of the smaller non-alloyed Pd nanoparticles, which were found predominantly on the TS-1 majority phase in the as-prepared material. The composition and dispersion of the AuPd nanoalloys present on the minority TiO_2 component were retained after multiple uses. Hot filtration experiments, where the 0.33%Au-0.33%Pd/TS-1(Acetate-O+R) catalyst was replaced by bare TS-1, revealed there was no contribution of leached species towards the formation of cyclohexanone oxime (fig. S25 A-B and accompanying text). However, in the absence of the immobilized precious metals, i.e. when bare TS-1 alone was used, some additional conversion of the ketone was observed (7%), which in keeping with our previous observations (fig S.11) and can be attributed to the ability of TS-1 to promote the formation of unwanted by-products in the absence of H_2O_2 (*30*). Further studies, using reagent concentrations much greater than those used during the catalytic studies and comparable to those used under the industrial process, revealed the increased stability of the 0.33%Au-0.33%Pd/TS-1(Acetate-O+R) catalyst compared to a monometallic Pd analogue and indicated that a combination of NH_3 and H_2O_2 is responsible for promoting dissolution of active metals (table S6). In keeping with our STEM-HAADF analysis (Fig. 3D, figs. S22-24), the alloying of Au with Pd was found to significantly inhibit metal leaching, even under these harsh reaction conditions. These observations, when coupled with our earlier studies comparing the activity of supported AuPd catalysts with monometallic analogues (Fig. 2A) and the negligible activity of homogeneous Pd species (fig. S25 A-B and accompanying text) suggest that the AuPd alloy nanoparticles supported on the TiO_2 minority component of the TS-1 are key to achieving high catalytic performance, while the unalloyed Pd nanoparticles are largely spectator species.

A major challenge of the current industrial route to cyclohexanone oxime is associated with the deactivation of the TS-1 catalyst, through formation of TiO_2-SiO_2 domains, induced by the presence of relatively high concentrations of ammonia in reactant streams (*31*). In keeping with these observations our analysis by XPS (fig. S26, table S.7) indicated a minor shift in Ti speciation over sequential reuse in the ammoximation reaction, indicative of the formation of Ti^{IV} (TiO_2-like) surface species, although no loss in catalyst activity was observed. In recent years hollow titanium silicates (HTS-1) have been developed through the post-synthesis treatment of TS-1(*32*), with these materials found to offer far greater stability when used in the ammoximation reaction than the parent material (*33*). As such we consider that upon potential industrial application any deactivation of the TS-1 component can be readily overcome through the adoption of HTS-1 or alternative titanosilicate support.

We have previously demonstrated that supported AuPd nanoparticles offer high stability towards H_2O_2 production in a flow regime under conditions optimized for H_2O_2 selectivity (*34*). With these observations in mind and with the independence of the in situ route to the ammonia source established (table S.8), we next evaluated the stability of the 0.33%Au-0.33%Pd/TS-1(Acetate-O+R) catalyst towards the ammoximation of cyclohexanone via in situ H_2O_2 production, using a continuous flow reactor (fig S.27) and concentrations of cyclohexanone and ammonia comparable to those used in the industrial ammoximation process. In this case, the catalyst was exposed to an oxidative heat treatment (16 h, 110 °C, static air) prior to reduction (2 h, 200 °C, H_2), and exhibited comparable catalyst performance to analogous materials exposed to higher temperature heat treatments (Fig. 3A), under batch conditions (fig S.28). These continuous flow studies demonstrated that the high catalytic stability observed under batch conditions (Fig. 3C) can be readily translated to a flow system (Fig. 4.A), where liquid (cyclohexanone and ammonia (NH_3 aq.) and gaseous (H_2 and O_2) reagents are continuously introduced into the reactor. Indeed, using this continuous flow reactor, cyclohexanone oxime yield and H_2 selectivity were observed to be steady over several hours on-stream, at 48 and 70%, respectively, with no observable loss in catalytic stability detected over 40 h on-stream. Moreover, given the limited availability of ammonia (cyclohexanone: NH_3 (aq.) 1: 0.5), a near complete selective utilization of this reagent was observed (96% ammonia selectivity), which would avoid the substantial costs associated with reagent separation and recycling upon any potential industrial application of the in situ process. Further investigations revealed that the cyclohexanone oxime yield can be increased considerably through reaction condition optimization (87%) (fig S.29), although in keeping with our earlier studies (Fig. 2.B) H_2 selectivity was found to be inherently linked to cyclohexanone availability.

In an attempt to establish the industrial viability of the in situ route to cyclohexanone ammoximation and with a focus on the 0.33%Au-0.33%Pd/TS-1(Acetate-O+R) catalyst, we conducted extended lifetime studies, under industrially relevant reaction conditions and over 248 h on-stream (fig S.30, flow reactor schematic shown in fig S.31). While analysis of the post-reaction catalyst via x-ray diffraction (XRD) did not indicate any substantial loss in TS-1 crystallinity (figs S.32 i-ii), our XPS evaluation revealed a slight shift in Ti speciation (figs S.32 iii-iv), possibly indicative of the formation of TiO_2 domains within the titanosilicate component as previously observed during industrial application (*30*). Our analysis by STEM revealed no significant agglomeration of precious metal nanoparticles (figs S.32 v-viii) and the maintenance of the AuPd nanoalloys over the course of the reaction. This is in keeping with the high stability of the AuPd species previously observed under batch conditions (fig S.22-24) and further highlights the long-term stability of the catalyst, under prospective industrial conditions.

Finally, we conducted a detailed techno-economic evaluation, comparing the in situ approach and the current industrial process, which uses preformed H_2O_2, based on previous evaluations made by Zhu *et al.* (35) (fig S.33, based on flow data provided in Fig. 4.A, with further detail provided in table S.9). Assuming that the lifetime of the 0.33%Au-0.33%Pd/TS-1(Acetate-O+R) catalyst is comparable to that reported for TS-1 in the current industrial route and a comparable activity of the TS-1 component (*i.e.*, 0.3 kg of TS-1 catalyzes 1 ton cyclohexanone oxime production (*36*)), our calculations demonstrate the economic viability of the in situ approach and we estimate a saving of 13 % based on material costs alone, assuming a catalyst lifetime of 2.3 years. Indeed, even assuming a far more limited catalyst lifetime (0.75 years) our economic evaluation reveals that the materials cost of the in situ approach is comparable to the current industrial process. This evaluation does not account for the substantial savings associated with in situ H_2O_2 production, namely those associated with transport and storage of H_2O_2 and increased reactor longevity, as reactor corrosion is known to result from the presence of the stabilizing agents present in preformed H_2O_2 (*37*). Additionally, a significant environmental saving is associated with a less carbon-intensive manufacturing process of this key platform chemical. As such, the in situ route represents a positive step towards more sustainable selective chemical transformations and in particular has the potential to supersede the current industrial route to cyclohexanone oxime. More broadly we consider that this approach may find wider application in other industrial oxidation reactions that at present are currently dependent on the use of TS-1 with pre-formed H_2O_2.

Figure 1. Proposed key reaction pathways in the ammoximation of cyclohexanone-to-cyclohexanone oxime, via *in-situ* H_2O_2 synthesis.

Figure 2. Catalytic activity of supported 0.66%AuPd/TiO_2(Chloride-O) catalysts, used in conjunction with TS-1, towards the ammoximation of cyclohexanone via the in situ production of H_2O_2. (A) The synergistic effect of alloying Au and Pd. **(B)** Time-on-line activity of the 0.33%Au-0.33%Pd/TiO_2(Chloride-O) catalyst. **(C)** Catalytic activity of the 0.33%Au-0.33%Pd/TiO_2(Chloride-O) catalyst towards the ammoximation of a range of ketones. **(D)** The effect of Au:Pd ratio on catalytic activity of 0.66%AuPd/TiO_2(Chloride-O) towards cyclohexanone ammoximation. **Ammoximation reaction conditions:** Ketone (2 mmol), NH_4HCO_3 (4 mmol), 5% H_2/N_2 (420 psi), 25% O_2/N_2 (160 psi), catalyst (0.075 g), TS-1 (0.075 g), t-BuOH (5.9 g), H_2O (7.5 g), reaction time 3 h, reaction temperature 80 ^{O}C, stirring speed 800 rpm. ***Key***: Ketone conversion (*black bar*), selectivity towards oxime (*red bar*), oxime yield (*blue bar*), selectivity based on H_2 (*green bar*), selectivity based on NH_3 (*purple bar*), carbon balance (*black circles*). **Note for Fig 2C:** Au refers to 0.66%Au/TiO_2(Chloride-O), Pd to 0.66%Pd/TiO_2(Chloride-O), Au+Pd to a physical mixture of the two monometallic catalysts and AuPd to 0.33%Au-0.33%Pd/TiO_2(Chloride-O).

Figure 3. Performance and stability of composite AuPd catalysts supported on TS-1 towards the ammoximation of cyclohexanone via in situ production of H_2O_2. (A) Catalytic activity, as a function of Pd precursor and heat treatment regime. **(B)** Microstructural analysis of the unused 0.33%Au-0.33%Pd/TS-1(Acetate-O+R) sample, which had been calcined (flowing air, 400 °C, 3h) and then reduced (5%H_2/Ar, 400 °C, 2 h). **(i)** Low and **(ii)** higher magnification HAADF-STEM images of the titanosilicate majority component. **(iii)** XEDS map showing Pd metal attachment only and absence of Au on TS-1 **(iv)** XEDS overlay map showing Si (yellow), Pd (red) and low concentration Ti (blue). **(v)** HAADF-STEM images of the TiO_2 minority component showing much more significant metal attachment with **(vi)** corresponding XEDS elemental mapping (Si (yellow), Ti (blue), Pd (red) and Au (green)) showing that the larger metal particles on the TiO_2 particles are AuPd alloys. **(vii and viii)** HAADF-STEM and corresponding XEDS maps of the smaller Pd only particles. **(C)** Catalytic reusability of the 0.33%Au-0.33%Pd/TS-1(Acetate-O+R) catalyst in a batch regime. **(D)** Microstructural analysis of the 0.33%Au-0.33%Pd/TS-1(Acetate-O+R) catalyst after three consecutive ammoximation reactions. Low **(i)** and high **(ii)** magnification HAADF-STEM images of TiO_2 minority component and STEM-XEDS elemental mapping of Au (*green*) **(iii)** and Pd (*red*) **(iv)**, showing stability and retention of the AuPd alloy nanoparticles post reaction**. Ammoximation reaction conditions:** Cyclohexanone (2 mmol), NH_4HCO_3 (4 mmol), 5%H_2/N_2 (420 psi), 25%O_2/N_2 (160 psi), catalyst (0.075 g), t-BuOH (5.9 g), H_2O (7.5 g), reaction time 3 h, reaction temperature 80 °C, stirring speed 800 rpm. ***Key*****:** Cyclohexanone conversion (*black bar*), selectivity towards oxime (*red bar*), oxime yield (blue bar) carbon balance (*black circles*). **Note for Fig. 3C:** 0.33%Au-0.33%Pd/TiO_2 (Chloride-O) used in conjunction with TS-1 (0.075 g), all other conditions as stated.

Figure 4. Optimization of reaction parameters for the 0.33%Au-0.33%Pd/TS-1(Acetate-O+R) catalyst in a continuous regime. Ammoximation reaction conditions: Cyclohexanone (20 wt.%): NH_3 (26 wt.%) (1: 0.5), 3.6% H_2, 6.4% O_2, 90 % N_2 (580 psi, 20 mLmin^{-1}), catalyst (0.41 g), 0.33%Au-0.33%Pd/TS-1(Acetate-O+R): Al_2O_3 (4: 1) t-BuOH: H_2O (9: 1, 0.01 - 0.10 mLmin^{-1}), residence time 76 min at 0.01mLmin^{-1} liquid flow rate, reaction temperature 80 ^{O}C. ***Key:*** Cyclohexanone oxime yield (*blue squares*), H_2 conversion (*orange circles*), H_2 selectivity (*green triangles*) **Reaction conditions between 0 and 1.5 h:** as above with liquid flow of 0.1 mLmin^{-1}(*green background*). **Reaction conditions between 1.5 and 12.1 h:** as above with liquid flow of 0.02 mLmin^{-1} (*purple background*). **Reaction conditions between 12.1 and 24.4 h:** as above with liquid flow of 0.01 mLmin^{-1} (*orange background*). **Reaction conditions between 24.4 and 34.0 h:** as above with liquid flow of 0.01 mLmin^{-1} and total pressure of 290 psi (*blue background*). **Reaction conditions between 34.0 and 41.4 h**: as above with liquid flow of 0.01 mLmin^{-1} and total pressure of 145 psi (*yellow background*). **Note:** Given the ratio of cyclohexanone: NH_3 used in this study (1: 0.5) it is possible to conclude that under optimal reaction conditions (*orange background*) NH_3 selectivity approaches 100% (96%), given the near 50% (48%) oxime yield observed and the stoichiometry of the ammoximation reaction.

References.

1. HDIN Research, Global Nylon 6 Production Capacity reach to 8.86 million Tons in 2024 via Global Nylon 6 Production Capacity reach to 8.86 million Tons in 2024, via https://www.hdinresearch.com/news/56
2. R. Mokaya, M. Poliakoff, A cleaner way to nylon? *Nature,* **437**, 1243-1244 (2005). doi.org/10.1038/4371243a
3. P. Roffia, G. Leofanti, A. Cesana, M. Mantegazza, M. Padovan, G. Petrini, S. Toni, P. Gervasutti, Cyclohexanone Ammoximation: A Breakthrough In The 6-Caprolactam Production Process, *Stud. Surf. Sci. Catal.,* **55**, 43-52 (1990). doi.org/10.1016/S0167-2991(08)60132-9
4. P. Roffia, M. Padovan, G. Leofanti, M. A. Mantegazza, G. De Alberti, G. R. Tauszik, (Montedipe SpA) U.S. Patent US4794198A (1987).
5. A. Thangaraj, S. Sivasanker, P. Ratnasamy, Catalytic properties of crystalline titanium silicalites III. Ammoximation of cyclohexanone. *J. Catal,* **131**, 394-400 (1991). doi.org/10.1016/0021-9517(91)90274-8
6. A. Zecchina, S. Bordiga, C. Lamberti, G. Ricchiardi, D. Scarano, G. Petrini, G. Leofanti, M. Mantegazza, Structural characterization of Ti centres in Ti-silicalite and reaction mechanisms in cyclohexanone ammoximation. *Catal. Today,* **32**, 97-106 (1996). doi.org/10.1016/S0920-5861(96)00075-2
7. Y. Xu, Q. Yang, Z. Li, L. Gao, D. Zhang, S. Wang, X. Zhao, Y. Wang, Ammoximation of cyclohexanone to cyclohexanone oxime using ammonium chloride as nitrogen source. *Chem. Eng. Sci.,* **152**, 717-723 (2016). doi.org/10.1016/j.ces.2016.06.068
8. L. Xu, J. Ding, Y. Yang, P. Wu, Distinctions of hydroxylamine formation and decomposition in cyclohexanone ammoximation over microporous titanosilicates. *J. Catal.,* **309**, 1-10 (2014). doi.org/10.1016/j.jcat.2013.08.021
9. J. S. Reddy, S. Sivasanker, P. Ratnasamy, Ammoximation of cyclohexanone over a titanium silicate molecular sieve, TS-2. *J. Mol. Catal.,* **69**, 383-392 (1991). doi.org/10.1016/0304-5102(91)80117-L
10. S. Zhao, W. Xie, J. Yang, Y. Liu, Y. Zhang, B. Xu, J. Jiang, M. He, P. Wu, An investigation into cyclohexanone ammoximation over Ti-MWW in a continuous slurry reactor. *Appl. Catal., A,* **394**, 1-8 (2011). doi.org/10.1016/j.apcata.2010.10.037
11. Sumitomo, EniChem to Build a Plant Featuring New Caprolactam Process via https://www.icis.com/explore/resources/news/2000/10/16/124121/sumitomo-enichem-to-build-a-plant-featuring-new-caprolactam-process/
12. B. Zong, B. Sun, S. Cheng, X. Mu, K. Yang, J. Zhao, X. Zhang, W. Wu, Green prodcution Technology of the Monmer of Nylon-6: Caprolactam. *Engineering*, **3**, 379-384 (2017). doi.org/10.1016/J.ENG.2017.03.003

13. A. C. K. Yip, X. Hu, Formulation of Reaction Kinetics for Cyclohexanone Ammoximation Catalyzed by a Clay-Based Titanium Silicalite-1 Composite in a Semibatch Process. *Ind. Eng. Chem. Res.,* **50**, 13703-13710 (2011). doi.org/10.1021/ie201467u

14. R. J. Lewis, G. J. Hutchings, Recent Advances in the Direct Synthesis of H_2O_2. *ChemCatChem,* **11**, 298-308 (2019). doi.org/10.1002/cctc.201801435

15. J. K. Edwards, B. Solsona, E. N. Ntainjua, A. F. Carley, A. A. Herzing, C. J. Kiely, G. J. Hutchings, Switching off hydrogen peroxide hydrogenation in the direct synthesis process. Science, 323, 1037-1041 (2009). doi.org/10.1126/science.1168980

16. S. J. Freakley, Q. He, J. H. Harrhy, L. Lu, D. A. Crole, D. J. Morgan, E. N. Ntainjua, J. K. Edwards, A. F. Carley, A. Borisevich, C. J. Kiely, G. J. Hutchings, Palladium-tin catalysts for the direct synthesis of H_2O_2 with high selectivity. *Science*, **351**, 965-968 (2016). doi.org/10.1126/scienceaad5705

17. Q. Chen, E. J. Beckman, One-pot green synthesis of propylene oxide using in situ generated hydrogen peroxide in carbon dioxide. *Green Chem.* **10**, 934-938 (2008). doi.org/10.1039/B803847C

18. C. M. Crombie, R. J. Lewis, R. L. Taylor, D. J. Morgan, T. E. Davies, A. Folli, D. M. Murphy, J. K. Edwards, J. Qi, H. Jinag, C. J. Kiely, M. S. Skjøth-Rasmussen, G. J. Hutchings, Enhanced Selective Oxidation of Benzyl Alcohol via In Situ H_2O_2 Production over Supported Pd-Based Catalysts. *ACS Catal. 5*, 2701-2714 (2021). doi.org/10.1021/acscatal.0c04586

19. Z. Jin, L. Wang, E. Zuidema, K. Mondal, M. Zhnag, J. Zhang, C. Wang, X. Meng, H. Yang, C. Mesters, F. Xiao*,* Hydrophobic zeolite modification for in situ peroxide formation in methane oxidation to methanol. *Science* **367**, 193-197 (2020). 10.1126/science.aaw1108

20. G. Wang, W. Du, X. Duan, Y. Cao, Z. Zhang, J. Xu, W. Chen, G. Qian, W. Yuan, X. Zhao, D. Chen *et al.*, Mechanism-guided elaboration of ternary Au–Ti–Si sites to boost propylene oxide formation. *Chem Catalysis,* **1**, 885-895 (2021). doi.org/10.1016/j.checat.2021.06.006

21. R. J. Lewis, K. Ueura, Y. Fukuta, S. J. Freakley, L. Kang, R. Wang, Q. He, J. K. Edwards, D. J. Morgan, Y. Yamamoto, G. J. Hutchings, The Direct Synthesis of H_2O_2 Using TS-1 Supported Catalysts. *ChemCatChem,* **11***,* 1673-1680 (2019). doi.org/10.1002/cctc.201900100

22. G. J. Hutchings, C. J. Kiely, Strategies for the synthesis of supported gold palladium nanoparticles with controlled morphology and composition. *Acc. Chem. Res.,* **46**, 1759-1772 (2013). doi.org/10.1021/ar300356m

23. J. Li, T. Ishihara, K. Yoshizawa, Theoretical Revisit of the Direct Synthesis of H_2O_2 on Pd and Au@Pd Surfaces: A Comprehensive Mechanistic Study. *J. Phys. Chem. C,* **115**, 25359-25367 (2011). doi.org/10.1021/jp208118e

24. T. Richards, J. H. Harrhy, R. J. Lewis, A. G. Howe, G. M. Suldecki, A. Folli, D. J. Morgan, T. E. Davies, E. J. Loveridge, D. A. Crole, J. K. Edwards, P. Gaskin, C. J. Kiely, Q. He, D. M. Murphy, J. Maillard, S. J. Freakley, G. J. Hutchings, A residue-free approach to water disinfection using catalytic in situ generation of reactive oxygen species. *Nat. Catal.* **4**, 575-585 (2021) doi.org/10.1038/s41929-021-00642-w.

25. A. B. Fernandez, I Lezcano-Gonzales, M. Boronat, T. Blasco, A. Corma, Study of the Beckmann rearrangement of acetophenone oxime over porus solids by means of solid state NMR spectrscopy. *Phys.Chem.Chem.Phys*., **11,** 5134-5141 (2009) doi.org/10.1039/B816276J

26. L. Li, M. Chen, F. Jiang, Design, syntheis and evaluation of 2-piperidone derivatives for the inhibition of β-anyloid aggregation and inflammation mediated neurotoxicity. *Bioorg. Med. Chem*. **24**, 1853-1865 (2016) doi.org/10.1016/j.bmc.2016.03.010

27. P. Wu, T. Komatsu, T. Yashima, Ammoximation of Ketones over Titanium Mordenite. *J. Catal.,* **168**, 400-411 (1997). doi.org/10.1006/jcat.1997.1679

28. T. Ricciardulli, S. Gorthy, J. S. Adams, C. Thompson, A. M. Karim, M. Neurock, D. W. Flaherty, Effect of Pd Coordination and Isolation on the Catalytic Reduction of O_2 to H_2O_2 over PdAu Bimetallic Nanoparticles. *J. Am. Chem. Soc.,* **143**, 5445-5464 (2021). doi.org/10.1021/jacs.1c00539

29. W. Laufer, R. Meiers, W. Hölderich, Propylene epoxidation with hydrogen peroxide over palladium containing titanium silicalite. *J. Mol. Catal. A: Chem.,* **141**, 215-221 (1999). doi.org/10.1016/S1381-1169(98)00265-9

30. A. Cesana, M. A. Mantegazza, M. Pastori, A study of the organic by-products in the cyclohexanone ammoximation. J. Mol. Catal. A: Chem., **117**, 367-373 (1997). doi.org/10.1016/S1381-1169(96)00296-8

31. G. Petrini, A. Cesana, G. De Alberti, F. Genoni, G. Leofanti, M. Padovan, G. Paparatto, P. Roffia, Deactivation Phenomena on Ti-Silicate, *Stud. Surf. Sci. Catal.,* **68**, 761-766 (1991). doi.org/10.1016/S0167-2991(08)62710-X

32. Y. Wang, M. Lin, A. Tuel, Hollow TS-1 crystals formed via a dissolution-recrystallization process, *Microporous Mesoporous Mater.,* **102**, 80-85 (2007). doi.org/10.1016/j.micromeso.2006.12.019

33. C. Xia, X. Peng, Y. Zhang, B. Wang, M. Lin, B. Zhu, Y. Luo, X. Shu in “Processes Based on Hierarchical Titanium Silicates at SINOPEC” in Green Chemical Processing and Synthesis, I. Karame, H. Srour Eds. (Intech Open, 2017), chap 6.

34. S. J. Freakley, M. Piccinini, J. K. Edwards, E. N. Ntainjua, J. A. Moulijin, G. J. Hutchings, Effect of Reaction Conditions on the Direct Synthesis of Hydrogen Peroxide with a AuPd/TiO_2 Catalyst in a Flow Reactor. *ACS Catal.,* **3**, 487-501 (2013). doi.org/10.1021/cs400004y
35. Z. Zhu, G. Li, J. Yang, Y. Dai. Improving the energy efficiency and production performance of the cyclohexanone ammoximation process via thermodynmics, kinetics and economic analysis, *Energy Convers. Manag.* **192**, 100-113 (2019). doi.org/10.1016/j.enconman.2019.04.037
36. Romano and Ricci, Liquid Phase Oxidation via Heterogeneous Catalysis: Organic Synthesis and Industrial Applications, Chapter 10 Industrial Applications, page 470.
37. G. Gao, Y. Tian, X. Gong, Z. Pan, K. Yong, B. Zong. Advances in the production technology of hydrogen peroxide, *Chin J. Catal.*, **41**, 1039-1047 (2020). doi.org/10.1016/S1872-2067(20)63562-8
38. The data supporting the findings of this study are available within the article and its Supplementary Materials or from the authors upon reasonable request, with the underlying data found at the Cardiff University Data Repository via http://doi.org/10.17035/d.2022.0163568304
39. A. Santos, R. J. Lewis, G. Malta, A. G. R. Howe, D. J. Morgan, E. Hampton, P. Gaskin, G. J. Hutchings, Direct Synthesis of Hydrogen Peroxide over Au–Pd Supported Nanoparticles under Ambient Conditions. *Ind. Eng. Chem. Res.* **58**, 12623-12631 (2019). doi.org/10.1021/acs.iecr.9b02211
40. C. Wu, Y. Wang, Z. Mi, L, Xue, W. Wu, E. Min, S. Han, F. He, S. Fu, Effects of organic solvents on the structure stability of TS-1 for the ammoximation of cyclohexanone. *React. Kinet. Catal. Lett.* **77**, 73-81 (2002). doi.org/10.1023/A:1020391803295
41. J. H. Scofield, Hartree-Slater subshell photoionization cross-sections at 1254 and 1487 eV. J. Electron Spectrosc. Relat. Phenom. **8**, 129-137 (1976). doi.org/10.1016/0368-2048(76)80015-1
42. G. Dahlhoff, J. P. M. Niederer, W. F. Hoelderich, ϵ-Caprolactam: new by-product free synthesis routes. *Catal. Rev.* **43**, 381-441 (2001). doi.org/10.1081/CR-120001808
43. J. M. Thomas, R. Raja, Design of a “green” one-step catalytic production of ε-caprolactam (precursor of nylon-6). *Proc. Natl. Acad. Sci. U.S.A* **102**, 13732-13736 (2005). doi.org/10.1073/pnas.0506907102
44. H Liao, Y. Xiao, H. Zhang, P. Liu, K. You, C. Wei, H. Luo, Hydrogenation of nitrocyclohexane to cyclohexanone oxime over Pd/CNT catalyst under mild conditions. *Catal. Commun.,* 19, 80-84 (2012). doi.org/10.1016/j.catcom.2011.12.027

45. P. Liu, H. Zhang, S. Liu, Z. Yao, F. Hao, H. Liao, K. You, H. Luo, Palladium Supported Catalysts for Nitrocyclohexane Hydrogenation to Cyclohexanone Oxime with High Selectivity. *ChemCatChem,* **5**, 2932-2938 (2013). doi.org/10.1002/cctc.201300377
46. Du Pont, Improvements in the production of oximes, **1961**, G.B. Patent 857902
47. I. Yoshikazu, Method of Producing Nitroso Compounds or Oximes, **1963**, US3090739A
48. M. Taramasso, G. Perego, B. Notari, (Montedipe SpA) U.S. Patent, US4410501A (1983).
49. G. Wu, Y. Wang, L. Wang, W. Feng, H. Shi, Y. Lin, T. Zhang, X. Jin, S. Wang, X. Wu, P. Yao, Epoxidation of propylene with H_2O_2 catalyzed by supported TS-1 catalyst in a fixed-bed reactor: Experiments and kinetics. *Chem. Eng. J.,* **215-216**, 306-314 (2013). doi.org/10.1016/j.cej.2012.11.055
50. Z. Song, D. Ren, T Wang, F. Jin, Q. Jiang, Z. Huo, Highly selective hydrothermal production of cyclohexanol from biomass-derived cyclohexanone over Cu powder. Catal Today., **274**, 94-98 (2016). doi.org/10.1016/j.cattod.2015.11.016
51. J. K. Edwards, S. F. Parker, J. Pritchard, M. Piccinini, S. J. Freakley, Q. He, A. F. Carley, C. J. Kiely, G. J. Hutchings, Effect of acid pre-treatment on AuPd/SiO_2 catalysts for the direct synthesis of hydrogen peroxide. Cat. Sci. Technol., **3**, 812-818 (2013). doi.org/10.1039/C2CY20767B
52. A. C. K. Yip, X. Hu, Catalytic Activity of Clay-Based Titanium Silicalite-1 Composite in Cyclohexanone Ammoximation. *Ind. Eng. Chem. Res.,* 48, 8441-8450 (2009). doi.org/10.1021/ie900731s
53. Y. Xue, Y. Wen, H. Wei, M. Liu, X. Huang, X. Ye, X. Wang, B. Li, Hollow TS-1 mesocrystals: hydrothermal construction and high catalytic performances in cyclohexanone ammoximation. *RSC Adv.,* **5**, 51563-51569 (2015). doi.org/10.1039/C5RA05999B
54. Y. Qi, C. Ye, Z. Zhuang, F. Xin, Preparation and evaluation of titanium silicalite-1 utilizing pretreated titanium dioxide as a titanium source. *Microporous Mesoporous Mater.* **142**, 661-665 (2011). doi.org/10.1016/j.micromeso.2011.01.012
55. D. Huang, X. Zhang, T. Liu, C. Huang, B. Chen, C. Luo, E. Ruckenstein, Z. Chao, Synthesis of High-Performanced Titanium Silicalite-1 Zeolite at Very Low Usage of Tetrapropyl Ammonium Hydroxide. *Ind. Eng. Chem. Res.,* 52, 3762-3772 (2013). doi.org/10.1021/ie302130x
56. T. Liu, L. Wang, H. Wan, G. Guan, A magnetically recyclable TS-1 for ammoximation of cyclohexanone. *Catal. Commun.,* 49, 20-24 (2014). doi.org/10.1016/j.catcom.2014.02.004

57. C. Shen, Y. J. Wang, C. Dong, G. S. Luo, In situ growth of TS-1 on porous glass beads for ammoximation of cyclohexanone. *Chem. Eng. J.,* **235**, 75-82 (2014). doi.org/10.1016/j.cej.2013.09.028

58. Y. Hu, C. Dong, T. Wang, G. Luo, Cyclohexanone ammoximation over TS-1 catalyst without organic solvent in a microreaction system. *Chem. Eng. Sci.,* **187**, 60-66 (2018). doi.org/10.1016/j.ces.2018.04.044

59. R. Chen, H. Mao, X. Zhang, W. Xing, Y. Fan, A Dual-Membrane Airlift Reactor for Cyclohexanone Ammoximation over Titanium Silicalite-1. *Ind. Eng. Chem. Res.,* **53**, 6372-6379 (2014). doi.org/10.1021/ie500573d

60. J. Lin, F. Xin, L. Yang, Z. Zhuang, Synthesis, characterization of hierarchical TS-1 and its catalytic performance for cyclohexanone ammoximation. *Catal. Commun.,* **45**, 104-108 (2014). doi.org/10.1016/j.catcom.2013.11.005

61. H. Xu, W. Tian, L. Xu, X. Jin, T. Xue, L. Chen, M. He, P. Wu, Crossed intergrowth triggered TS-2 microsphere: Formation mechanism, modification and catalytic performance. *Chin. J. Catal.,* **41**, 1109-1117 (2020). doi.org/10.1016/S1872-2067(20)63546-X

62. Y. Wang, S. Wang, T. Zhang, J. Ye, X. Wang, D. Wang, Effect of Extra-Framework Titanium in TS-1 on the Ammoximation of Cyclohexanone. *Trans. Tianjin Univ.,* **23**, 230-236 (2017). doi.org/10.1007/s12209-017-0042-5

63. Y. Wang, J. Ye, S. Wang, Y. Lin, S. Wang, W. Liu, Synthesis of mesoporous titanium silicalite-1 with high stability in cyclohexanone ammoximation. *Trans. Tianjin Univ.,* **22**, 254-260 (2016). doi.org/10.1007/s12209-016-2774-z

64. G. Liu, J. Wu, H. Luo, Ammoximation of Cyclohexanone to Cyclohexanone Oxime Catalyzed by Titanium Silicalite-1 Zeolite in Three-phase System. *Chin. J. Chem. Eng.,* **20**, 889-894 (2012). doi.org/10.1016/S1004-9541(12)60414-5

65. H. Mao, R. Chen, W. Xing, W. Jin, Organic Solvent-Free Process for Cyclohexanone Ammoximation by a Ceramic Membrane Distributor. *Chem. Eng. Technol.,* **39**, 883-890 (2016). doi.org/10.1002/ceat.201500641

66. F. Song, Y. Liu, L. Wang, H. Zhang, M. He, P. Wu, Highly selective synthesis of methyl ethyl ketone oxime through ammoximation over Ti-MWW. *Appl. Catal., A.,* 327, 22-31 (2007). doi.org/10.1016/j.apcata.2007.04.025

67. S. Zhang, H. Wei, X. Gao, M. Huang, X. Wang, Y. Wen, A cleaner ammoximation of cyclohexanone over Ti-MWW in dimethyl carbonate. *Catal. Commun.,* 139, 105968 (2020). doi.org/10.1016/j.catcom.2020.105968

68. H. Xu, Y. Zhang, H. Wu, Y. Liu, X. Li, J. Jiang, M. He, P. Wu, Postsynthesis of mesoporous MOR-type titanosilicate and its unique catalytic properties in liquid-phase oxidations. *J. Catal.,* 281, 263-272 (2011). doi.org/10.1016/j.jcat.2011.05.009

69. F. Song, Y. Liu, H. Wu, M. He, P. Wu, T. Tatsumi, A novel titanosilicate with MWW structure: Highly effective liquid-phase ammoximation of cyclohexanone. *J. Catal.,* **237**, 359-367 (2006). doi.org/10.1016/j.jcat.2005.11.018
70. X. Xue, F. Song, B. Ma, Y. Yu, C. Li, Y. Dong, Selective ammoximation of ketones and aldehydes catalyzed by a trivanadium-substituted polyoxometalate with H_2O_2 and ammonia. *Catal. Commun.,* **33**, 61-65 (2013). doi.org/10.1016/j.catcom.2012.12.021
71. L. Li, B. Liu, Z. Wu, X. Yuan, H. Luo, Preparation of Keggin-type mono-lacunary phosphotungstic-ammonium salt and its catalytic performance in ammoximation of cyclohexanone. *Chem. Eng. J.,* **280**, 670-676 (2015). doi.org/10.1016/j.cej.2015.06.048
72. R. Raja, G. Sankar, J. M. Thomas, Bifunctional Molecular Sieve Catalysts for the Benign Ammoximation of Cyclohexanone: One-Step, Solvent-Free Production of Oxime and ε-Caprolactam with a Mixture of Air and Ammonia. *J. Am. Chem. Soc.* **123**, 8153-8154 (2001). doi.org/10.1021/ja011001+
73. G. Moretti, A. M. Salvi, M. R. Guascito, F. Langerame, An XPS study of microporous and mesoporous titanosilicates. *Surf. Interface Anal.,* **36**, 1402-1412 (2004). doi.org/10.1002/sia.1931
74. S. Fen, L. Yueming, W. Haihong, H. Mingyuan, W. Peng, T. Takashi, Highly Effective synthesis of Cyclohexanone Oxime over a Novel Titanosilicate Ti-MWW, *Chem Lett.,* **35**, 1436-1437 (2005). doi.org/10.1246/cl.2005.1436
75. G. Schinitkey. Weekly farm Economics: Fertilizer Prices Higher for 2019 Crops, *Farmdoc Daily*, **8**, 178 (2018) via https://farmdocdaily.illinois.edu/2018/09/fertilizer-prices-higher-for-2019-crop.html
76. R. Ciriminna, L. Albanese, F. Meneguzzo, M. Pagliaro. Hydrogen Peroxide: A Key Chemical for Today's Sustainable Development. *Chem Sus Chem., **9**,* 3374-3381 (2016). doi.org/10.1002/cssc.201600895
77. Kayfeci, Ke and Kutlucan, Solar Hydrogen Production Processes, Systems and Technologies, Chapter 3 Hydrogen Production, page 81.
78. Palladium prices – Interactive Historical Chart via https://www.macrotrends.net/2542/palladium-prices-historical-chart-data (2020 average closing price)
79. Gold prices – 100 Year Historical Chart via https://www.macrotrends.net/1333/historical-gold-prices-100-year-chart (2020 average closing price)
80. S. Phillips, The Use of Metal Scavengers for Recovery of Palladium Catalyst from Solution, Platinum Metals Rev., 54, 69 (2010). doi.org/10.1595/147106709x481093.

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Author Contributions:

R.J.L, K.U, Y.F, S.J.F and G.J.H contributed to the design of the study; R.J.L and K.U conducted experiments and data analysis. R.J.L, K.U, Y.F, J.S, J.K.E, S.J.F, C.J.K, Y.Y and G.J.H provided technical advice and result interpretation. R.J.L, X.L, T.E.D, D.J.M, L.C, J.Q, and C.J.K conducted catalyst characterization and corresponding data processing. R.J.L, C.J.K and G.J.H wrote the manuscript; R.J.L and C.J.K wrote the supplementary material, all authors commented on and amended both documents. All authors discussed and contributed to the work.

Competing Interests:

The authors declare no competing interests.

Data Availability:

The data supporting the findings of this study are available within the article and its Supplementary Materials or from the authors upon reasonable request, with the underlying data found at the Cardiff University Data Repository via http://doi.org/10.17035/d.2022.0163568304 (*38*)

Supplementary Materials.

Materials and Methods

Figs S1 to S33

Supplementary Text

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