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Simple salts of abundant metals (Fe, Bi, and Ti) supported on Montmorillonite as efficient and recyclable catalysts for regioselective intramolecular and intermolecular hydroalkoxylation reactions of double bonds and tandem processes

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The transfer of catalytic hydroalkoxylation reactions of olefins from homogeneous to heterogeneous 10 conditions has been studied using two types of solid catalysts, namely Montmorillonite (MMT) doped with metal cations and metal nanoparticles supported on oxides. In the case of intramolecular reactions, 38-99% yields of cyclic ethers have been obtained using Fe-MMT and Bi-MMT both in CH₃NO₂ and dimethylcarbonate (DMC) compared with other supported metals salts or metal nanoparticles. In the case of more challenging intermolecular reactions, conversions up to 72% and yields up to 54% were obtained 15 with metal-doped MMT as well, such as Fe-, Bi-, and Ti-MMT. In this paper, we detail the substrate scope and limitations for both classes of reactions and tandem processes, their transposition in flow and some mechanistic insights concerning the active species, in processes identified as truly heterogeneously catalysed. As a general trend, it was observed that trisubstituted double bonds allowed the best results both in intra- and intermolecular reactions. The transfer of homogeneous catalysts onto heterogeneous in 20 the case of Fe-MMT and Bi-MMT was successful and even allowed enhanced catalytic activities in the case of Bi-MMT.

Introduction

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Metal-based catalysts, and in particular transition metal-based catalysts, have been successfully used for decades in a myriad of ²⁵ organic transformations.¹⁻⁴ Most of the developpements of metal catalysis in fine chemicals transformations have been designed in organic solvents which allow, in the same phase, pre-catalysts, catalysts, intermediates, substrates and products solubilisation (homogeneous catalysis). Despite many assets, homogeneous

- ³⁰ metal-based catalysis rarelly go beyond the laboratory scale. The main reasons are related to cost (metal and ligands), tedious recycling operations, scale up issues, and in the case of ther synthesis of active pharmaceutical principles, the presence of residual metal in the final product.⁵ So, for industrial applications,
- ³⁵ cost-effective solid catalysts are prefered, allowing an easy recycling, and/or amenability to continuous processes.⁶ However, solid catalysts have been so far mostly designed for commodity chemicals' synthesis, and do not offer the same degree of selectivity and efficiency when dealing with sophisticated ⁴⁰ reactions.
 - As a result, a significant part of current research in catalytic methodologies is thus directed towards the transfer of the reactions from homogenous to heterogeneous conditions.⁷ The most straightforward strategy probably consists in attaching

- ⁴⁵ homogeneous catalysts to inert supports, the latter being either organic (polymers, dendrimers, polysaccharides, ...) or inorganic (mesoporous silica, metal oxides, aluminosilicates, ...).⁸⁻¹⁰
- In the context of sustainable chemistry, a stronger stress is placed to design new catalysts being based on abondant metals and ⁵⁰ easily recyclable, most of the metals conventionally used in catalysis being under a threat of depletion within 50 years.¹¹ Metals such as iron, copper, and bismuth have thus attracted the attention of chemists, these metals being abundant and having
- also acceptable (eco)toxicity profiles.¹²⁻¹⁶ ⁵⁵ For all these reasons, we have chosen to study simple and salts of sustainable metals supported on clays such as MMT, a layered inorganic material with exchangeable cations in the interlamellar space. MMT is a cheap, natural and abundant inorganic material with both Lewis and Bronsted acidic site very attractive as a ⁶⁰ support for catalysts.¹⁷ To test these catalysts, we have selected the hydroalkoxylation of olefins: a very useful reaction widely studied in homogeneous catalysis, and rarely in heterogeneous catalysis.¹⁸⁻³⁶ Zeolites have been the most studied heterogeneous catalysts for this reaction and generally required elevated ⁶⁵ temperatures (85-150 °C) to proceed, sometimes with selectivity issues.^{34,37,38} Lanthanide triflates could be used and recycled efficiently in intramolecular reaction at 120 °C upon their sequestration in ionic liquids.³⁶ Gold nanoclusters were also

reported as efficient catalysts in intramolecular reactions, although limited to monosubstituted olefins.³⁰

In a preliminary communication, we reported our results in the intramolecular version of the reaction catalysed by Fe(III) and ⁵ Bi(III) salts supported on MMT.³⁹ In the present paper, our intention is to provide full experimental studies, the scope and limitations of the intramolecular reaction, as well as new data for the intermolecular version, introducing Ti-MMT as catalyst, and a mechanistic rationale.

10 Results and discussion

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Catalysts preparation and characterisation

Metal doped Montmorillonites (M-MMT)

M-MMT materials were perpared by impregnating solutions of chlorides salts in MeOH with lyophilized MMT. Namely, BiCl₃, 15 FeCl₃, CuCl₂, and TiCl₄ were added to a suspension of Na-MMT in MeOH in a 1 mmol/g of metal salt/MMT ratio. Exchange reached the thermodynamic equilibrium within few hours as monitored by conductimetry using a Na⁺-selective electrode. After filtration and trituration in degased MeOH, M-MMT were 20 dried extensively under reduced pressure for 24 h. ICP-MS titration of metal content in the modified clays showed between 1.8 and 4.9% w/w metal content (Cu-MMT 2.04%, Fe-MMT 2.67%, Bi-MMT 4.87%, Ti-MMT 1.81%). As witnessed by XPS analysis, the oxidation state of inserted metal ions remained 25 identical except in the case of Fe where a Fe^{3+}/Fe^{2+} 53/47 ratio was shown to be the thermodynamic resulting mixture of the process. SMAXS analysis clearly showed metal insertion in the interlayer spacing, although in the case of Bi-MMT remaining BiOCl formed upon hydrolysis of BiCl₃ was simultaneously 30 observed.

Silica supported Metal Nanoparticles (M NP@SiO₂)

For the fabrication of silica supported metal/metal oxide nanoparticles (Table 1, entries 1-5), we used supercritical CO₂ (scCO₂) as the main solvent in a batch mode setup. A detailed ³⁵ description of the setup and experimental conditions can be found elsewhere.⁴⁰ In summary, in a stainless steel batch reactor, the silica support is mixed with a metal hexafluoroacetylacetonate precursor (5% w/w of metal loading) in the absence of H₂ (as reducing agent) but using EtOH, as co-solvent and reducing ⁴⁰ agent, together with a surfactant (hexadecylamine) typically used

in wet chemistry for metal reduction. After reaction, a fast depressurization in parallel with CO₂ purging yielded dry clean powder in the form of metal/metal oxide nanoparticles deposited on the silica support (catalyst physicochemical properties and ⁴⁵ TEM images are presented in ESI).

Intramolecular hydroalkoxylation

Intramolecular hydroalkoxylation of olefins is the most direct and atom-economical route to cyclic ethers. It is typically achieved following two disctincts modes of activation and mechanisms

- ⁵⁰ (Scheme 1). In the former, the double bond is activated by a Bronsted or a Lewis acid facilitating the nucleophilic attack of the pendant hydroxyl group: carbenium intermediates are involved.^{41,42} In the latter, transition metals are first coordinated to the double bond which then undergo the attack of the pendant ⁵⁵ hydroxyl group resulting in the formation of an organometallic
- intermediate featuring a carbon-metal bond eventually cleaved by

protonolysis.¹⁹ These differences in terms of intermediates influence the regioselectivity and the ring-closure overall efficiency. Substrates with trisubstituted double donds, leading to 60 tertiary carbenium ions, are efficiently cyclised under Bronsted acid-type activation while substrates with a terminal monosubstituted double bond are more efficiently cyclised by transition metal-catalysts. Hybrid mechanisms based on Lewis acid-assisted Bronsted acid catalysis have been invoked in 65 reactions with metal triflates where activation of the hydroxyl group by the Lewis acid provides an acidified proton further transferred to the double bond.²²



Scheme 1. Generic reaction pathways for H⁺- and metal-catalysed intramolecular hydroalkoxylation

We initially screened a series of supported catalysts, either MMTsupported metal salts and metal oxides-supported transition metal nanoparticles to possibly observed the abovementionned types of activation on substrates **1a** and **1b**. (Table 1).

85 Table 1. Initial screening of catalysts and conditions for the intramolecular hydroalkoxylation of olefins.^a

Catalvet

 $R_1 OH/$

			Ť II	Outu			Ī
			$R_2 \xrightarrow{I}_{R_2}$	Solvent	t, T°C	R_2	
R ₁ =Me, R ₂ =H: R ₁ =H, R ₂ =Ph:			1a 1b			2a 21	a D
Entry	R_1	R_2	Catalyst	Solvent ^b	T°C	Conversion	Yield
1	Me	Η	Pt NPs/SiO ₂	А	40 °C	0%	-
2	Me	Н	Pt-Cu NPs/SiO2	А	40 °C	0%	-
3	Me	Η	Cu NPs/SiO ₂	А	40 °C	0%	-
4	Me	Η	Cu _x O NPs/SiO ₂	А	40 °C	0%	-
5	Me	Н	SnO ₂ NPs/SiO ₂	А	40 °C	0%	-
6	Н	Ph	Au NPs/TiO ₂ °	А	60 °C	0%	-
7	Н	Ph	Au NPs/TiO2 c	Α	60 °C	0%	-
8	Н	Ph	Ni-LDH	В	$40 \ ^{\circ}\mathrm{C}$	0%	-
9	Н	Ph	Mg-LDH	В	40 °C	0%	-
10	Н	Ph	Fe-MMT	CH ₃ NO ₂	40 °C	35%	35%
11	Н	Ph	Bi-MMT	DMC	80 °C	100%	76%
12	Н	Ph	Bi-MMT	CH ₃ NO ₂	80 °C	100%	77%
13	Н	Ph	Bi-MMT	CH ₃ CN	80 °C	100%	76%
14	Н	Ph	Fe-MMT	DMC	80 °C	100%	86%
15	Н	Ph	Cu-MMT	DMC	80 °C	39%	36%
16	Н	Ph	Cu-MMT	CH ₃ NO ₂	80 °C	100%	81%
17	Н	Ph	Fe-MMT	CH ₃ NO ₂	80 °C	100%	83%
18	Н	Ph	None	DMC	80 °C	0%	-

^a Reaction conditions: substrate (0.25 mmol), anhydrous and degassed
 ⁹⁰ solvent (1 mL) and catalyst (1-5 mol% metal/substrate ratio). ^b A: Either CH₃NO₂ or DCE. B: Either toluene, CH₃OH, heptane, CH₃CN, dioxane, acetone, AcOEt, THF, H₂O/THF (9:1), DMF, CH₃NO₂, or DCE. ^c Commercially available from Strem.

R1__O_/

The metal choice was guided in both cases by the frequency of appearance of those in homogenous catalysis for hydroalkoxylation reactions of multiple bonds: Pt, Cu, Au and Sn for NPs, Fe, Bi, and Cu for supported metal salts.

- ⁵ Unfortunately, in our reaction conditions, metal/metal oxides NPs of Pt, Pt-Cu, Cu, Cu_xO, Au and SnO₂ supported on SiO₂ or TiO₂ (entries 1-7), as well as Ni-LDH and Mg-LDH (entries 8,9), were unreactive. MMT doped with metal cations such Fe(III) (Fe-MMT) exhibited a promising 35% yield in cyclised product **2b** at
- ¹⁰ 40 °C (entry 10). This result was further confirmed at 80 °C with Bi-MMT, Fe-MMT, and Cu-MMT allowing conversion rates to reach 100% and 76-86% isolated yields of **2b** (entries 11-17). Control reactions were performed with pristine MMT, and in the absence of catalyst in CH₃NO₂ at 80 °C. In these conditions, no ¹⁵ conversion of the starting material **1b** was observed.
- Recyclability of the catalysts was tested with Fe-MMT in DMC and CH_3NO_2 in the reaction conditions of entry 14 (Table 1). In DMC, the yield of **2b** could be maintained 5 times without significant loss, while in CH_3NO_2 , it rapidly decreased down to ²⁰ zero at 4th cycle.



Figure 1. Recycling studies of Fe-MMT in DMC and CH₃NO₂.

This significant difference of results only depending on the solvent used suggested that the metal could be washed out of MMT in polar CH₃NO₂ (μ =3.46 D), while in DMC (μ =0.91 D) leaching was avoided. As a result, we selected DMC for the transposition of the reaction in continuous flow systems. Satisfyingly, using a 25 cm long stainless steel column with 10

- ³⁰ mm of internal diameter charged with Fe-MMT, 15.3 grams of cyclised product **2a** could be obtained in 1 h at a flow rate of 1 mL.min⁻¹ of a **1a** 2M solution in DMC. The key parameter of the system turned out to be the temperature, all reactions conducted above 75 °C leading to complete conversions with this system.
- ³⁵ We further evaluated the scope of the reaction in terms of substrates. With this type of catalysts, a mechanism involving carbenium ions was likely to occur. In such case, we expected that the reaction would be influenced by the class of alcohol, for the reason of steric hindrance and the competition with acid-
- 40 catalysed dehydration reaction, and the class of the double bond,

densely substituted ones presenting increased steric hindrance but leading ot more stable carbenium ions.

- A series of unsaturated alcohols was thus prepared following several synthetic routes (see ESI for details). Secondary ⁴⁵ homoallylic alcohols were obtained by Grignard reaction of prenylmagnesium bromide with the corresponding aldehydes. Methallyl ethers derived from glycerol were obtained in two steps from solketal (glycerol acetonide) to yield **1f** (R₄=H). Upon
- protection of the primary alcohol, **1g** and **1h** were obtained ⁵⁰ bearing an acetyl or a TBDMS group, respectively. Primary bishomoallylic alcohols **1i-k** were formed by a Wittig reaction of γbutyrolactol with the corresponding phosphonium salts.⁴³ Allylation of phenol was performed with the desired allylbromide (allyl, prenyl, geranyl) in the presence of NaH.⁴⁴
- ⁵⁵ Our optimised conditions based on Fe-MMT in DMC at 80 °C were thus tested firstly on secondary alcohols bearing a trisubstituted double bond (Table 2).

Intramolecular hydroalkoxylation of trisubstituted double bonds by secondary alcohols

- ⁶⁰ With substrate **1a**, the reaction was almost quantitative in 7 hours in cyclised product **2a**, for which the yield was determined by ¹H-NMR by the method of external calibration to avoid evaporation during work-up (entry 1). Substrates **1c** and **1d** were cleanly cyclised to their corresponding products both in 89% yield
- 65 (entries 2,3). When a tolyl substituent was introduced (substrate 1e), a competition with the dehydration reaction was observed. The cyclised product 2e was obtained in 38%, together with 12% of styrene derivative; we assumed that the mass loss was due to the polymerisation of the latter at 80 °C in this acidic medium
- ⁷⁰ (entry 4). A limitation of this reaction was thus identified when stabilised carbenium ion could be formed upon the loss of HO⁻ as exemplified by **1e** possibly leading to a benzylic cation.

Table 2. Cyclisation of alcohols 1a, 1c-e.^a

5		R ₃ OH	Fe-MM	T (5 mol% C, 80 °C	\mathbf{R}_3	
	Entry	R ₃	Substrate	Time (h)	Conversion	Isolated yield
	1	Me	1a	7	100%	98% ^b
	2	$n-C_5H_{11}$	1c	7	100%	89%
	3	Ph-CH ₂ -CH ₂	1d	7	100%	89%
	4	p-CH ₃ C ₆ H ₄	1e	7	100%	38% ^c

^a Reaction conditions: substrate (0.25 mmol), anhydrous and degassed DMC (1 mL) and Fe-MMT (5 mol% metal/substrate ratio).
 ^b Due to the so high volatility of product 2a, the reaction was performed in DMC-d6 and the yield determined by ¹H-NMR using benzene as internal standard.
 ^c Along with 12% of dehydration product.

Intramolecular hydroalkoxylation of 1,1-disubstituted double 85 bonds by secondary alcohols derived from glycerol

We next turned our attention to secondary alcohols bearing a disubstituted terminal double bond derived from glycerol. These unsaturated alcohols were obtained from solketal by methallylation/deprotection (1f, R₄=H) and with an additional ⁹⁰ protection of the primary alcohol by an acetyl or a TBDMS group (1g and 1h, respectively). These substrates where tested under our optimised reaction conditions based on Fe-MMT in DMC at

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7^b

Me, Me

(E,Z)-1k

80 °C (Table 3).

Table 3. Cyclisation of alcohols 1f-h.^a



^a Reaction conditions: substrate (0.25	mmol), anhydrous and degassed
DMC (1 mL) and Fe-MMT (5 mol%	metal/substrate ratio). ^b Together
with 31% of the corresponding dioxane	.

With these substrates featuring an oxygen atom on the tether on ¹⁰ the allylic position, the reaction yielded 1,3-dioxolanes. This reaction could either proceed by isomerisation/cyclisation, involving the formation of an enol ether intermediate, in a process already described with α-methallyloxy carboxylic acids in the presence of Cu(OTf)₂ as the catalyst,⁴⁵ or by formation of a ¹⁵ transient oxonium ion (Scheme 2). With unprotected substrate **1f**, a 5:3 mixture of the corresponding 1,3-dioxolane and 1,3-dioxane was obtained upon the nucleophilic attack of either one or the other alcohol function. With the primary alcohol function blocked by an acetyl group (substrate **1g**), only the 1,3-dioxolane was ²⁰ formed in 59% isolated yield. With TBDMS-protected substrate **1h** however, the silyl protecting group was partially removed in our reaction conditions and a mixture of protected and nonprotected 1,3-dioxolanes and 1,3-dioxanes was obtained.



³⁵ Scheme 2. Possible mechanisms accounting for the formation of 1,3-dioxolanes **2f-g**.

Intramolecular hydroalkoxylation of 1,2-disubstituted double bonds by primary alcohols

The catalytic system was then tested on substrates **1i-j** featuring a ⁴⁰ combination of primary alcohol function and a 1,2-disubstituted double bond (Table 4).



⁴⁵ ^a Reaction conditions: substrate (0.25 mmol), anhydrous and degassed solvent (1 mL) and Fe-MMT (5 mol% metal/substrate ratio). ^b T °C=80 °C. ^c T °C=40 °C. ^d 2i/2i²=95:5.

24

72%

Mixture

DMC

Substrate **1i** was commercially available as the (Z)-stereoisomer. Substrate **1j** was prepared by Wittig olefination of γ -butyrolactol. However, since the reaction with benzyltriphenylphosphonium bromide delivered a mixture of (*E*)- and (*Z*)-**1j**, the stereoisomer (*E*)-**1j** was obtained independently in two steps. Treatment of 1phenylprop-2-en-1-ol with triethylorthoacetate furnished ethyl so (*E*)-**5**-phenylpent-4-enoate which was then reduced to (*E*)-**1j** unsing LiAlH₄ (see ESI for details).

When (Z)-1i was put to react with Fe-MMT at 80 °C in DMC, the expected cyclisation was observed leading to 2pentyltetrahydrofuran 2i (28% GC-MS yield) but the main 60 product was the methylcarbonate formed upon reaction with DMC. Only trace amount of 2-butyltetrahydropyran 2i' was formed (entry 1). With (E,Z)-1j under the same reaction conditions, the (Z)-isomer reacted faster and the formation of the methycarbonate was again observed (36% GC-MS yield) while 65 the cyclic ether 2j was formed in 46% yield (entry 2). By replacing DMC by CH₃NO₂, at 40 °C the reaction of 1i was very slow and only 4% conversion was observed after 48 hours (entry 3). However, at 100 °C the reaction proceeded with 89% conversion in 72 hours and delivered 2i in 62% vield and 95% ⁷⁰ regioselectivy compared with **2i'** (entry 4). With (Z)- and (E)-1j, the reaction was completed in shorter reaction times and quantitatively provided the cyclic ether 2j (entries 5,6). Substrate 1k was partially converted (72%) to a mixture of elimination products and isomers, as suggested by GC-MS analysis (entry 7). 75 The double bond substitution was thus shown to impact significantly the reaction efficiency. The stabilisation of positively charged intermediates formed by activation of the double bond requires substitution by electron-donating groups. In the case of 1j, the presence of the phenyl group allowed to 80 reached both high conversions and yields.

Intramolecular hydroalkoxylation of trisubstituted double bonds by phenols

We further tested the efficiency of the catalytic system on phenolic substrates **11-n** featuring mono- and trisusbituted double

bonds (Table 5).



					2111-11		
Entry	R6. R7	Substrate	М	Solvent	Time	Conversion	Isolated
					(h)		yield of 21-n
1	H, H	11	Fe	DMC	48	0%	_b
2°	Н, Н	11	Bi	DMC	48	0%	_b
3 ^d	Н, Н	11	Bi	DMC	48	64%	50%
4 ^c	Me, Me	1m	Bi	DCE	24	100%	99%
5°	Me, Me	1 m	Bi	CH ₃ NO ₂	24	100%	57%
6 ^c	Me, Me	1 m	Bi	DMC	24	91%	90%
7	Me, Me	1 m	Fe	DMC	24	100%	99%
8	Me, prenyl	1n	Fe	DMC	5	100%	40% ^e
9°	Me, prenyl	1n	Bi	DMC	24	100%	$32\%^{\rm f}$
10	Me, prenyl	1n	Fe	CH ₃ NO ₂	5	100%	21% ^g
11°	Me, prenyl	1n	Bi	CH ₃ NO ₂	24	100%	_h

^a Reaction conditions: substrate (0.25 mmol), anhydrous and degassed solvent (1 mL) and Fe-MMT (5 mol% metal/substrate ratio).
^b Quantitative recovery of the starting material. ^c Bi-MMT prepared from BiCl₃ was used as catalyst. ^d Bi-MMT prepared from Bi(OTf)₃ was used as catalyst. ^e Together with 39% of tricyclic product **3n** formed upon tandem reaction. ^f Together with 42% of product **3n**. ^g Together with 79% of product **3n**. ^h Product **3n** formed in 96% was the sole product.

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With substrate **11** featuring a monosubstituted double bond, no conversion was observed under our optimised conditions either using Fe-MMT or Bi-MMT (entries 1,2). Interestingly, by using a Bi-MMT prepared by impregnation of Bi(OTf)₃ instead of BiCl₃, ²⁰ a conversion of 64% was observed in DMC for an isolated yield of cyclised product **21** of 50% (entry 3). Substrate **1m**, with the phenol ring *ortho*-substituted with a prenyl side chain, cyclised readily either with Fe-MMT or Bi-MMT in DMC or CH₃NO₂

- (entries 4-7), the best result being obtained in our standard 25 conditions with 100% conversion and a quantitative yield of **2m** (entry 7). Finally, substrate **1n**, an *ortho*-geranylated phenol, reacted faster than **11** and **1m** reaching total conversion in 5 hours in our optimised conditions but to yield a mixture of the expected
- chromane **2n** and a tricyclic compound **3n** resulting from a ³⁰ tandem reaction involving both double bonds (entries 8-10). While with Fe-MMT, only a mixture was obtained after several attempts, with Bi-MMT (ex-BiCl₃) in CH₃NO₂, tricyclic product **3n** was formed in 96% yield as the sole product (entry 11 and Scheme 3). We hypothetised that the tandem process might start
- ³⁵ by the activation of the remote double bond by the catalyst followed by the attack of the internal double bond and interception of the carbenium ion formed by the phenolic hydroxyl group. It is worth mentioning that olefins that should be formed upon proton elimination from these intermediates were
- ⁴⁰ not observed,⁴⁶ suggesting a fast ring closure to **2n**.



55 Scheme 3. Tandem reaction of **1n** with Bi-MMT as catalyst and possible mechanism.

The superiority of Bi-MMT over Fe-MMT in this specific process could be a consequence of the difference of ionic radii 60 between Fe³⁺ and Bi³⁺, the larger Bi³⁺ being most likely to interact with the remote position of the substrate (Bi: 0.96-1.17 Å; Fe: 0.49-0.78 Å). To test our hypothesis, we engaged dienol substrate 10, featuring similarly to 1n an internal trisubstituted double bond, but with a terminal primary hydroxyl group and a 65 tetrasubstituted double bond. In our optimised conditions with Fe-MMT, only the intramolecular hydroalkoxylation was observed and delivered the corresponding cyclic ether 20 in 56% yield (89% conversion) in DMC and 71% yield in CH₃NO₂. With Bi-MMT in CH₃NO₂, a mixture of cyclic products was obtained 70 without selectivity (Scheme 4). It is worth noting that in Bronsted acid-promoted reaction. 10 is the precursor of an industrially relevant odorant molecule, ambroxide, formed upon a tandem cyclisation process.47



Scheme 4. Cyclisation of **10** to **20**.

Intermolecular hydroalkoxylation

⁸⁵ Having in hand an efficient catalytic system for the intramolecular hydroalkoxylation of olefins, we next focused on the more challenging intermolecular version of the reaction. For this reaction, one has to address several hurdles compared with the intramolecular version, such as the difficulty to run a
⁹⁰ bimolecular reaction with two substrates of low affinity, typically a polar protic alcohol and an apolar hydrophobic olefin, and the energetic penalties due to an entropically disfavoured process. Consequently, most of the catalytic systems described in the literature report modest conversion rates and yields and reactions
⁹⁵ performed at elevated temperatures. For example, in

homogeneous catalysis, a combination of Pd(II) complexes and Cu(II) salts was used for the hydroalkoxylation of styrene derivatives¹⁸ and vinylphenols.²⁰ Metal triflates such as Zr(II), La(III)⁴⁸ and Hg(II)⁴⁹ have been used for styrene and α -olefins ⁵ hydroalkoxylation, respectively. Styrenes and α -olefins could also be converted into ethers by additon of simple alcohols with Au(III) chloride as catalyst in the presence of Cu(II) salts.⁵⁰ In heterogeneous catalysis, zeolite beta could be used to catalyse the ethoxylation of α -olefins in continuous flow,³⁸ while in batch ¹⁰ reaction limonene and α -pinene could be functionalised with various C1-C5 alcools.²¹

In this context, we tested several MMT doped with metal cations and metal nanoparticles supported on inorganic matrix as possible catalysts for the reaction. Initial attempts on a typical α -olefin (1-

15 decene) in various alcoholic solvents (MeOH, EtOH, n-PrOH, n-BuOH) or in organic solvents in the presence of alcohols with the catalysts of Table 1 were unsuccessful, the starting material being recovered unchanged. Positive control experiments of the catalysts activity were performed on the cyclisation of 1b to 2b 20 for MMT doped with metals and dipolar cycloaddition reaction following a recently published procedure for Cu nanoparticles.⁵¹ The olefin class could significantly account for the absence of reactivity in our conditions and we thus moved towards trisubstituted double bonds such as in 1p and 1q-r obtained by 25 alkylation of citronellol and Wittig olefination, respectively (Scheme 5) and oct-1-en-3-one 1s presenting an activated terminal double bond. Substrate 1p has been already studied for intermolecular hydroalkoxylation catalysed by Sn(OTf)₄ by some of us and could be useful to compare with a homogeneous 30 system.²³



Scheme 5. Preparation of 1p, 1q and 1r.

For these substrates, we focused on the use of MMT doped with metal cations or nanoparticles, and proceeded to an initial ⁵⁰ screening (Table 6).

The results showed olefins conversions below 72% and yields of hydroalkoxylation product up to 54%. Substrate **1s** led to degradation products (entry 12). Interestingly, comparing entries 1-3 with 9-11, the presence of the methoxy substituent (R_{10}) of **1p**

⁵⁵ instead of a methyl group allow for better results in terms of both conversion and yield. This trend could be seen as an effect on the overall polarity of the electrophile, as well as an improvement of its coordination ability. In order to favour the contact between the polar protic nucleophiles with hydrophobic electrophiles, several attempts to use ionic liquids or surfactants were performed with M-MMT as catalysts but did not allow to improve conversions and yields (data not shown).

Table 6. Hydroalkoxylation of olefins 1p-r.^a

		R ₉			Rg)
5			R ₁₀	M-MMT(x mol%) R ₁₁ OH solvent, T°C		R ₁₀
0		1p-r			2(p-r)	, (a-d)
	>	<= Η ₂ , Ο			R ₁₁ =	-
	F	₹ ₈ =Н, Ме				a
	F	R ₉ =H, Me			Et: C)
	F	R ₁₀ =Me, E	t, OMe		<i>n</i> -Pr	". C
5					<i>п-</i> Вเ	u: d
	Entry	Substrate	M (x)	Solvent, R ₁₁ OH	Conversion ^b	Product, yield ^b
	1	1p	Fe (5)	MeOH ^c , reflux	63%	2pa , 54%
	2	1p	Bi (5)	MeOH ^c , reflux	72%	2pa , 45%
	3	1p	Fe (5)	EtOH ^e , reflux	40%	2pb , 16%
	4	1p	Bi (5)	EtOH ^c , reflux	24%	2pb , 13%
	5	1p	Fe (5)	<i>n</i> -PrOH ^c , reflux	37%	2pc , 26% ^d
	6	1p	Bi (5)	<i>n</i> -PrOH ^c , reflux	30%	2pc , 17% ^d
	7	1p	Fe (5)	<i>n</i> -BuOH ^c , reflux	29%	2pd , 19% ^a
	8	1p	Bi (5)	<i>n</i> -BuOH ^c , reflux	79%	2pd , 8% ^a
	9	1q	Fe (5)	MeOH ^c , reflux	27%	2qa , 9%
	10	1q	Bi (5)	MeOH [°] , reflux	17%	2qa, 14%
	11	1q	11(5) C:: ND-	MeOH ⁻ , reflux	35%	2qa , 22%
	12	1s	(0.25)	MeOH ^c , reflux	100%	Degradation

^a Reaction conditions: substrate (0.25 mmol), anhydrous and degassed solvent (1 mL) and M-MMT stirred at the specified temperature for 48 h. ^b Determined by ¹H-NMR or GC-TCD by external calibration. ^c Used as the solvent. ^d Determined by GC-MS.

Finally we tested equimolar amounts of our recyclable Ti-MMT for the hydroalkoxylation of **1q-r** (Table 7).

Table 7. Hydroalkoxylation of olefins 1q-r with equimolar Ti-MMT.^a



LII	uу	Substrate	KIIOII	Conversion	Tiouuci, yielu
1	l	1q	Et	36%	2qb , 36%
2	2	1r	<i>n</i> -Pr	45%	2rc, 45%
3	3	1r	n-Bu	42%	2rd, 42%
4	1	1r	solketal	23%	2re, 23%

^a Reaction conditions: substrate (0.25 mmol), anhydrous and degassed ⁹⁰ solvent (1 mL) and Ti-MMT stirred at the specified temperature for 48 h. ^b Determined by GC-TCD by external calibration.

By increasing the molar fraction of Ti-MMT, improved yields could thus be obtained for hydrophobic olefins 1q-r at 70 °C ⁹⁵ even with higher alcohols such as *n*-propanol and *n*-butanol or

35

solketal which are typically leading to low yields.

Mechanistic studies

A reasonnable question when using supported catalysts is 5 whether or not the process is truly heterogeneously catalysed. I our case, metal cations are simply anchored to the MMT support by electrostatic binding and could be displaced in the reaction medium. For example, the result presented in Figure 1 with CH₃NO₂ as the solvent suggest a loss of a fraction of supported 10 metal at each cycle, solubilised in such a polar solvant, resulting in an overall decrease of the solid catalyst efficiency. In DMC however, a solvent in which the activity was maintained, we hypothetised that most of metal cations remained bound to MMT. We further performed a hot filtration test to determine whether or 15 not solubilised metal species could be active in solution. The test consisted of a monitoring of the reaction progress (product formation) until the conversion reached ca. 50% conversion. The whole reaction mixture was then filtered over a fritted glass heated at 80 °C and the filtrate was put to react again at the same 20 temperature under monitoring. The results are presented in Figure

2 for reactions of **1b** with Fe-MMT and Bi-MMT in DMC.



Figure 2. Hot filtration tests on reaction of **1b** with Fe-MMT and ²⁵ Bi-MMT in DMC at 80 °C.

It is clear that upon removal of the solid catalyst, no additional product formation was observed, which endorsed a truly heterogeneous process. For the sake of comparison, we tested the ³⁰ activity of FeCl₃ and BiCl₃ in homogeneous conditions on the same reaction, these halide salts being the precursors of Fe-MMT and Bi-MMT, respectively (Scheme 6).



45 Scheme 6. Comparison between heterogeneous and homogeneous version of the reaction

With FeCl₃ (5 mol%) after 7 hours, the expected cyclised product **2b** was formed in 76% yield, along with 5% of

- talysts is
talysed. Ipresence of active bismuth species within the solid catalyst.support55 Supported catalysts Fe-MMT and Bi-MMT were thus superior to
their homogeneous equivalents in terms of activity and
selectivity.reactionselectivity.re 1 with
supportedControl reactions with solid catalytic materials such as pristine
Na-MMT, MMT K10, Amberlyst and Nafion were performed on
 - ⁶⁰ various substrates (Table 8). With Na-MMT, no conversion of starting material **1a**, **1e**, **1f** was observed (entries 2-4). With a physical mixture of Na-MMT and BiCl₃ (5 mol%) as catalyst, conversion was not complete and a complex mixture of products was obtained (entry 5), as well as with MMT K10 (entry 6). With ⁶⁵ acidic resins Ambelyst-15 and Nafion SAC-13, a good reaction profile was observed in terms of conversion and yields, but the formation of the undesired hydroarylation product **2b**^{*} was observed with 17-18% selectivity (entries 7,8). The reaction could thus be observed under Bronsted catalysis, but the most ⁷⁰ efficient conditions and catalyst remained those described above

50 tetrahydronaphtalene derivative formed upon Lewis acidcatalysed Friedel-Crafts type addition of the phenyl ring to the double bond. With BiCl₃, substrate **1b** was recovered unchanged

while with Bi-MMT, 2b was formed in 76% yield, indicating the

with Fe-MMT. These data suggested a truly metal-catalysed rather than a proton-catalysed process.

Table 8. Comparison of Fe-MMT with solid catalysts.

Entry	Catalyst	Substrate	Time (hr)	Conversion ^c	Products, selectivity ^c
1 ^a	Fe-MMT	1b	7	100%	2b/2b' 100/0
2 ^b	Na-MMT	1a	24	0%	-
3 ^b	Na-MMT	1e	12	0%	_ ^d
4 ^b	Na-MMT	1f	4.5	0%	-
5 ^b	Na-MMT + 5 mol% BiCl ₃	1 a	7	Mix	ture
6 ^b	MMT K10	1a	7	100%	Mixture
7 ^a	Amberlyst 15	1b	24	100%	2b/2b' 83/17
8^{a}	Nafion SAC-13	1b	24	100%	2b/2b' 82/18

^a Reaction conditions: substrate (0.25 mmol), anhydrous and degassed 75 CH₃NO₂ (1 mL) at 60 °C. Fe-MMT: 25 mg; Amberlyst: 20 mg; Nafion: 20 mg. ^b Reaction conditions: substrate (0.5 mmol), anhydrous and degassed DMC (2 mL) at 80 °C. Na-MMT, MMT K10: 50 mg. ^c Determined by GC-TCD by external calibration. ^d Less than 5% yield of dehydrated product was observed by GC-MS.

The question of the characterisation of the coordination sphere of the cations is difficult to address on these solid catalysts. It is reasonable to imagine mixed species with one or two chlorine atoms replaced by silicates from the interlamellar surface of 85 MMT (Scheme 7).



Scheme 7. Hypothetical metal species within MMT doped with metal cations.

In such hypothesis where the binding to a pseudo-surface brings a large degree of steric hindrance, the metal-oxygen bond lenghts should be longer than expected and cations should therefore exhibit an enhanced Lewis acid character, as it is the case with ⁵ metal salts with bulky anions of low nucleophilicity, e.g. triflates or triflimidates.^{52,53}

Conclusions

Efficient. cost-effective, and sustainable catalysts for hydroalkoxylation reactions of olefins could be obtained upon 10 impregnation of Fe(III), Bi(III), and Ti(IV) salts on Montmorillonite. For intramolecular reactions, a large number of substrates with various substitution patterns could be efficiently cyclised. For intermolecular reactions, the results were modests in terms of both conversions and yields but remained in the range of 15 what is typically observed under homogeneous and heterogeneous catalysis. These catalytic systems were shown to proceed under truly heterogeneous catalysis and could be transferred in continuous flow conditions, the first step towards industrial transfer.

20 Experimental

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¹H NMR and ¹³C NMR spectra were recorded on BRUCKER AC 200 (200 MHz). ¹H NMR spectra are reported as follows: chemical shift in ppm (δ) relative to the chemical shift of CDCl₃ at 7.26 ppm, integration, multiplicities (s = singlet, d = doublet, t ²⁵ = triplet, q = quartet, m = multiplet and br = broadened), and coupling constants (Hz). ¹³C NMR spectra reported in ppm (δ) relative to CDCl₃ at 77.16 ppm. Column chromatography was carried out on silica gel (spherical, neutral, 63-200 um, Geduran Si 60, Merck KGaA). GC-TCD analysis were carried out using a ³⁰ Shimadzu QP2010plus gas chromatograph, under the following operation conditions: vector gas, He; injector temperature, 250 °C; detector temperature, 210 °C at 60 mA; split ratio, 1/20; total

- flow, 22,5 mL/min; Phenomenex Zebron ZB5MS column, polydimethylsiloxane (10 m, inside diameter 0.10 mm, film ³⁵ thickness 0.10 μm); temperature program, 80-200 °C at 10 °C/min and 200 °C for 8 min. GC/MS analysis were performed by using a Shimadzu QP2010 gas chromatograph (conditions:
- carrier gas, He; injector and detector temperatures, 250 °C; injected volume, 0.5 μL; split ratio, 1/100; (pressure, 180 kPa);
 40 SLB-5ms capillary column (thickness: 0.25 mm, length: 30 m, inside diameter 0.25 mm) temperature gas and 0.250 °C;
- inside diameter: 0.25 mm); temperature program, 60-250 °C at 2 °C/min, and 250 °C, coupled to a mass selective detector. Mass spectra were obtained by electron ionisation at 70 eV, m/z 35-400, source temperature 250 °C; only the most abundant ions are given. Use program were approximately approximately (UBMS) were
- ⁴⁵ given. High resolution mass spectrometry (HRMS) was performed at ERINI platform (Grasse, FRANCE) using a Waters APGC coupled with a Waters Xevo G2 QTOF spectrometer. Screening reactions were performed in a Carousel 12 Plus parallel synthesizer purchased from Radleys.

General procedure for cyclisation of unsaturated alcohols

In a Schlenk tube, substrate (1 mmol), Fe-MMT (5 mol% of metal, 100 mg of material) and DMC (2 ml) are introduced and the tube closed with a PTFE cap. The mixture is stirred at the ⁵⁵ desired temperature and the reaction monitored by TLC or GC-

TCD. After completion, the mixture is filtered through a cotton wool pad. The filter is rinsed with diethyl ether and the solution concentrated at reduced pressure affording the crude cyclic ether which is then purified by flash chromatography over silica gel ⁶⁰ (petroleum ether/Et₂O).

- 2,2,6-Trimethyltetrahydro-2H-pyran **2a**.^{22,42} ¹H NMR (DMC- d_6 , 200 MHz): δ 3.78-3.54 (m, 1H), 1.75 1.53 (m, 2H), 1.52-1.25 (m, 4H), 1.17 (s, 3H), 1.13(s, 3H), 1.04 (d, J = 6.1 Hz, 3H). ¹³C NMR (DMC- d_6 , 50 MHz): δ 71.64, 66.65, 36.43, 33.99, 31.84,
- ⁶⁵ 22.53, 21.67, 20.59. MS (EI; 70 eV) 128(0) [M]⁺, 113(47), 95(7), 70(10), 59(100), 56(36), 43(80).
 2,2-Dimethyl-5,5-diphenyltetrahydro-2H-pyran **2b**.¹⁹ ¹H NMR (CDCl₃, 200 MHz): δ 7.37-7.10 (m, 10H), 4.06 (s, 2H), 2.50-2.33
- (CDCl₃, 200 MHz): 0.7.577.10 (III, 1011), 4.00 (S, 2H), 2.30-2.35 (m, 2H), 1.40 (dd, J = 7.3, 5.0 Hz, 1H), 1.23 (s, 6H). ¹³C NMR 70 (CDCl₃, 50 MHz): 146.54, 128.21, 128.02, 126.05, 71.32, 69.06,
- 45.96, 32.65, 30.91, 26.46. MS (EI; 70 eV) 266(5) [M]⁺, 236(15), 180(100), 165(36), 152 (4); 129(2), 115(13), 103(4), 91(14), 73(8), 65(3), 43(10), 41(5).
- 2,2-Dimethyl-6-pentyltetrahydro-2H-pyran **2c**. ¹H NMR (CDCl₃, ⁷⁵ 200 MHz): δ 3.50-3.41 (m, 1H), 1.67-0.94 (m, 14H), 1.19 (s, 3H), 1.17 (s, 3H), 0.87 (t, *J* = 6.8 Hz, 3H). ¹³C NMR (CDCl₃, 50 MHz): δ 71.57, 70.46, 37.10, 36.45, 32.10, 31.66, 25.39, 22.79, 22.13, 20.28, 14.22. MS (EI; 70 eV) 184(0) [M]⁺, 169(16), 151 (4), 126(3), 113(63), 99 (15), 95(61), 83(15), 69(38), 59(100),
- ⁸⁰ 56(72), 43(57). HRMS calculated for C₁₂H₂₃O (M-H)⁺: 183.1749; found: 183.1743. 1ΔI= 3.3 ppm.
 2,2-Dimethyl-6-(2-phenylethyl)-tetrahydro-2H-pyran 2d. ¹H NMR (CDCl₃, 200 MHz): δ 7.43-7.01 (m, 5H), 3.66-3.30 (m, 1H).
- 1H), 2.89-2.46 (m, 2H), 1.90-0.99 (m, 8H), 1.23 (s, 3H), 1.17 (s, ⁸⁵ 3H). ¹³C NMR (CDCl₃, 50 MHz): δ 142.64, 128.62, 128.23, 125.60, 77.80, 77.16, 76.53, 71.62, 69.19, 38.49, 36.39, 32.05, 31.76, 22.07, 20.18. MS (EI; 70 eV) 218(12) [M]⁺⁺, 185(6), 157 (7), 140(25), 129(14), 113(34), 104(36), 91(100), 69(22), 56(14), 43(29). HRMS calculated for C₁₅H₂₃O (M+H)⁺: 219.1749; found: ⁹⁰ 203.1751. $|\Delta| = 0.9$ ppm.
- 2,2-Dimethyl-6-(*p*-tolyl)tetrahydro-2H-pyran **2e**. ¹H NMR (CDCl₃, 200 MHz): δ 7.25 (d, J = 8 Hz, 2H), 7.12 (d, J = 8 Hz, 2H), 4.55 (dd, J = 11.5, 1.9 Hz, 1H), 2.31 (s, 3H), 1.82-1.41 (m, 6H), 1.30 (s, 3H), 1.29 (s, 3H). ¹³C NMR (CDCl₃, 50 MHz): δ
- ⁹⁵ 141.33, 136.76, 129.04, 126.15, 72.90, 72.42, 36.19, 34.21, 32.13, 22.07, 21.24, 20.61. MS (EI; 70 eV) 204(14) [M]⁺, 189(5), 146 (25), 131(15), 121(100), 105 (5), 91(19), 84(4), 77(6), 69(6), 56(31), 43(11). HRMS calculated for $C_{14}H_{19}O$ (M-H)⁺: 203.1436; found: 203.1436. $|\Delta|=0.0$ ppm.
- ¹⁰⁰ *cis/trans*-(2-Isopropyl-1,3-dioxolan-4-yl)methanol **2f** and *cis,trans*-2-isopropyl-1,3-dioxan-5-ol **2f**⁵⁴ [*cis/trans*-**2f**] ¹H NMR (CDCl₃, 200 MHz): δ 4.75 (d, J = 4.7 Hz, 1H), 4.66 (d, J = 4.6 Hz, 1H), 4.32-4.02 (m, 3H), 4.00-3.16 (m, 7H), 2.04 (*br* s, 2H), 1.94-1.70 (m, 2H), 0.97 (d, J = 5.6 Hz, 6H),
- ¹⁰⁵ 0.94 (d, J = 6.6 Hz, 6H). ¹³C NMR (CDCl₃, 50 MHz): δ 108.79, 108.65, 76.52, 76.29, 66.80, 66.55, 63.52, 62.76, 32.30, 31.85, 16.99, 16.95, 16.89, 16.80. MS (EI; 70 eV) 146(0) [M]⁺, 145(1), 115(3), 103(82), 97(7), 86(2), 71(5), 69(2), 57(100), 55(31), 43(24), 41(15). (I stereoisomer). MS (EI; 70 eV) 146(0) [M]⁺, ¹¹⁰ 145(2), 115(4), 103(80), 97(10), 86(1), 71(6), 69(3), 57(100),
- 55(31), 43(26), 41(16). (II stereoisomer). [*cis/trans-***2f**^{*}] ¹H NMR (CDCl₃, 200 MHz): δ 4.27 (d, J = 5 Hz, 1H), 4.20 (d, J = 5 Hz, 1H), 4.13 (t, J = 4.6 Hz, 2H), 4.01 (d, J = 11.2 Hz, 1H), 3.93-3.76

⁵⁰

- (m, 3H), 3.86 (d, J = 11.2 Hz, 1H), 3.54-3.45 (m, 1H), 3.36 (d, J = 10.9 Hz, 1H), 3.31 (d, J = 10.2 Hz, 1H), 2.02 (br s, 2H), 1.91-1.66 (m, 2H), 0.94 (d, J = 6.8 Hz, 6H), 0.92 (d, J = 6.8 Hz, 6H). ¹³C NMR (CDCl₃, 50 MHz): δ 106.35, 105.69, 71.88, 71.70,
- ⁵ 64.28, 61.61, 32.82, 32.35, 17.31, 16.94. MS (EI; 70 eV) 146(0)
 [M]⁺, 145(1), 116(1), 103(100), 73(53), 57(63), 55(31), 43(42), 41(15). (I stereoisomer). MS (EI; 70 eV) 146(0) [M]⁺, 145(1), 116(2), 103(100), 73(54), 57(64), 55(33), 43(46), 41(17). (II stereoisomer).
- ¹⁰ *cis/trans*-(2-Isopropyl-1,3-dioxolan-4-yl)-methyl acetate **2g**. ¹H NMR (CDCl₃, 200 MHz): δ 4.73 (d, J = 4.6 Hz, 1H), 4.66 (d, J = 4.4 Hz, 1H), 4.37-4.18 (m, 2H), 4.17-3.98 (m, 3H), 3.91 (dd, J= 8.3, 6.9 Hz, 1H), 3.74 (dd, J= 8.3, 4.9 Hz, 1H), 3.58 (dd, J= 8.4, 6.7 Hz, 1H), 2.08 (s, 3H), 2.06 (s, 3H), 1.94-1.67 (m, 2H), 0.97-
- ¹⁵ 0.88 (m, 12H). ¹³C NMR (CDCl₃, 50 MHz): 170.89, 170.84, 109.02, 108.51, 73.70, 73.53, 67.27, 67.19, 64.72, 64.30, 32.06, 31.77, 20.89, 20.86, 16.93, 16.87, 16.59, 16.55. MS (EI; 70 eV) 188(0) [M]⁺, 187(0), 145(43), 115(1), 97(4), 86(1), 71(3), 61(4), 57(18), 43(100), 41(7). (I stereoisomer). MS (EI; 70 eV) 188(0) [M]⁺, 187(1), 145(42), 115(2), 07(45), 8((1)), 71(4), (0(2))
- ²⁰ $[M]^{+}$, 187(1), 145(46), 115(2), 97(45), 86(1), 71(4), 69(2), 57(19), 43(100), 41(7). (II stereoisomer). HRMS calculated for $C_9H_{15}O_4$ (M-H)⁺: 187.0970; found: 187.0967. $|\Delta|$ = 1.6 ppm.

2-Hexyltetrahydrofuran **2i** and 2-pentyltetrahydro-2H-pyran **2i**'.^{42,55} [THF-ether/**2i**] ¹H NMR (CDCl₃, 200 MHz): δ 3.97-3.59

- ²⁵ (m, 3H), 2.08-1.69 (m, 3H), 1.69-1.03 (m, 11H), 0.86 (t, J = 6.8 Hz, 3H). ¹³C NMR (CDCl₃, 50 MHz): δ 79.59, 67.70, 35.89, 31.97, 31.51, 29.55, 26.50, 25.84, 22.73, 14.19. MS (EI; 70 eV) 156(1) [M]⁺, 138 (1), 96 (1), 81(1), 71(100), 55(6), 43(31), 41(31). [THP-ether/**2i**'] ¹H NMR (CDCl₃, 200 MHz): δ 4.01-3.88
- ³⁰ (m, 1H), 3.40 (td J= 10.9, 3.6 Hz, 1H), 3.29-3.08 (m, 1H), 2.17-1.04 (m, 14H), 0.87 (t, J = 6.5 Hz, 3H). ¹³C NMR (CDCl₃, 50 MHz): δ 78.08, 68.63, 36.78, 32.12, 32.09, 26.40, 25.36, 23.76, 22.77, 14.19. MS (EI; 70 eV) 156(1) [M]⁺, 138 (1), 95 (1), 85(100), 67(16), 57(15), 43(21), 41(24).
- ³⁵ 2-Phenyltetrahydro-2H-pyran **2j**.⁴¹ ¹H NMR (CDCl₃, 200 MHz): δ 7.39-7.15 (m, 5H), 4.36-4.24 (m, 1H), 4.12 (dd, J = 11.4, 3.5 Hz, 1H), 3.76-3.46 (m, 1H), 2.01-1.46 (m, 6H). ¹³C NMR (CDCl₃, 50 MHz): 143.45, 128.38, 127.38, 125.95, 80.26, 69.11, 34.14, 26.02, 24.14. MS (EI; 70 eV) 162(54) [M]⁺, 161 (46), 145.12 MS (EI; 70 eV) 162(54) [M]⁺, 161 (46), 145.12 MS (EI; 70 eV) 162(54) [M]⁺, 161 (46), 145.12 MS (EI; 70 eV) 162(54) [M]⁺, 161 (46), 145.12 MS (EI; 70 eV) 162(54) [M]⁺, 161 (46), 145.12 MS (EI; 70 eV) 162(54) [M]⁺, 161 (46), 145.12 MS (EI; 70 eV) 162(54) [M]⁺, 161 (46), 145.12 MS (EI; 70 eV) 162(54) [M]⁺, 161 (46), 145.12 MS (EI; 70 eV) 162(54) [M]⁺, 161 (46), 145.12 MS (EI; 70 eV) 162(54) [M]⁺, 161 (46), 145.12 MS (EI; 70 eV) 162(54) [M]⁺, 161 (46), 145.12 MS (EI; 70 eV) 162(54) [M]⁺, 161 (46), 145.12 MS (EI; 70 eV) 162(54) [M]⁺, 161 (46), 145.12 MS (EI; 70 eV) 165.12 MS (EI; 70 eV) 1
- ⁴⁰ 144(2), 133(4), 129(4), 115 (6), 105 (100), 91(29), 77(45), 65(8), 55(26), 51(19), 41(31). 2-Methyl-2,3-dihydrobenzofuran **21**.⁵⁶ ¹H NMR (CDCl₃, 200 MHz): δ 7.23-7.05 (m, 2H), 6.85 (dd, *J* = 7.4, 0.9 Hz, 1H), 6.77
- 6.2 Hz, 3H). ¹³C NMR (CDCl₃, 50 MHz): δ 159.63, 128.07, 127.15, 125.08, 120.28, 109.44, 76.52, 37.25, 21.88. MS (EI; 70 eV) 134(100) [M]⁺, 133(42), 119(66), 115(27), 113(34), 119(11), 107(100), 91(22), 77(25), 65(6), 51(13), 41(11).
- ⁵⁰ 2,2-Dimethylchromane **2m**.^{57,58} ¹H NMR (CDCl₃, 200 MHz): δ 7.15-7.05 (m, 2H), 6.90-6.70 (m, 2H), 2.80 (t, J = 6.7 Hz, 2H), 1.83 (t, J = 6.7 Hz, 2H), 1.36 (s, 6H). ¹³C NMR (CDCl₃, 50 MHz): δ 153.48, 128.93, 126.73, 120.39, 119.08, 116.72, 73.56, 32.29, 26.37 (2), 21.94. MS (EI; 70 eV) 162(11) [M]⁺, 147(17), ⁵⁵ 133(17), 119(40), 107(100), 91(5), 77(8), 51(8), 41(9).
- 2-Methyl-2-(4-methylpent-3-enyl)chromane **2n** and *cis/trans*-1,1,4a-trimethyl-2,3,4,4a,9,9a-hexahydro-1H-xanthene **3n**.⁵⁹ [**2n**] ¹H NMR (CDCl₃, 200 MHz): δ 7.06 (d, J = 7.3 Hz, 2H), 6.88-

6.70 (m, 2H), 5.17-5.06 (m, 1H), 2.82-2.52 (m, 2H), 2.08-1.39 60 (m, 6H), 1.72 (s, 3H), 1.64 (s, 3H), 1.34 (s, 3H). ¹³C NMR (CDCl₃, 50 MHz): δ 154.09, 129.50, 127.33, 124.38, 121.22, 119.64 117.41, 76.02, 39.66, 31.06, 25.80, 24.37, 22.40, 22.24, 17.71. MS (EI; 70 eV) 230(52) [M]⁺, 215(2), 187(20), 174(17), 161(27), 147(48), 133(20), 123(59), 107(94), 91(40), 81(40), (0)75) 55(10, 41(100)) 5.5 (10, 100) 5.5 (10,

- ⁶⁵ 69(74), 55(16), 41(100). [*cis*-**3n**] ¹H NMR (CDCl₃, 200 MHz): δ 7.05 (d, *J* = 7.1 Hz, 2H), 6.88-6.69 (m, 2H), 3.05 (dd, *J* = 17.7, 7.9 Hz, 1H), 2.76 (d, *J* = 17.7 Hz, 1H), 2.08-1.20 (m, 7H), 1.21 (s, 3H), 0.97 (s, 3H), 0.65 (s, 3H). ¹³C NMR (CDCl₃, 50 MHz): δ 154.64, 129.04, 126.81, 122.18, 119.94, 117.23, 75.36, 44.58, 70 41.80, 39.71, 34.12, 32.41, 27.16, 23.74, 21.54, 18.23. MS (EI; 70 eV) 230(31) [M]⁺, 214(4), 187(2), 173(1), 159(11), 145(17), 123(100), 107(39), 91(10), 81(30), 77(10), 67(12), 55(10), 43(9), 41(18). [*trans*-**3n**] ¹H NMR (CDCl₃, 200 MHz): δ 7.09 (d, *J* = 7.1
- Hz, 2H), 6.81-6.72 (m, 2H), 2.73 (dd, J = 16.2, 6.7 Hz, 1H), 2.57 (d, J = 16.4 Hz, 1H), 2.17-1.16 (m, 7H), 1.23 (s, 3H), 1.04 (s, 3H), 0.94 (s, 3H). ¹³C NMR (CDCl₃, 50 MHz): δ 154.38, 129.75, 127.23, 122.72, 119.74, 117.15, 76.29, 48.19, 41.63, 40.13, 33.49, 32.22, 23.37, 20.80, 19.96, 19.91. MS (EI; 70 eV) 230(54) [M]⁺, 215(14), 187(10), 173(3), 159(26), 145(37), 123(100), 80 107(92), 91(21), 81(31), 77(17), 67(13), 55(18), 43(14), 41(32).
- ⁸⁰ 10 (92), 91(21), 81(31), 7/(17), 87(13), 55(18), 45(14), 41(32).
 ²⁻Methyl-2-(2-(2,6,6-trimethylcyclohex-1-en-1-yl)ethyl)tetrahydrofuran 20.⁶⁰ ¹H NMR (CDCl₃, 200 MHz): δ 3.97-3.68 (m, 1H), 2.17-1.33 (m, 14H), 1.59 (s, 1H), 1.21 (s, 1H), 0.98 (s, 1H). ¹³C NMR (CDCl₃, 50 MHz): δ 137.12, 126.90, 82.88, 67.20, 41.13, 85 40.05, 36.83, 35.22, 32.92, 28.78, 26.24, 25.48, 23.63, 19.84, 19.69. MS (EI; 70 eV) 236(2) [M]⁺, 221(2), 203(2), 177(4), 161(2), 149(2), 136(18), 123(15), 121(25), 107(15), 95(17), 93(17), 85(100), 81(14), 69(9), 67(10), 55(14), 43(52), 41(24).
- 1,7-Dimethoxy-3,7-dimethyloctane **2pa**.²³ ¹H NMR (CDCl₃, 200 MHz): δ 3.39 (t, *J*=6.7 Hz, 2H), 3.32 (s, 3H), 3.16 (s, 3H), 1.79-1.20 (m, 9H), 1.12 (s, 6H), 0.88 (d, *J*=6.4 Hz, 3H). ¹³C NMR (CDCl₃, 50 MHz): δ 74.6, 71.2, 58.6, 49.1, 40.1, 37.7, 36.7, 30.2, 21.2, 19.6. MS (EI; 70 eV) 202(0) [M]⁺, 187(4), 138(11),
- 123(29), 109(14), 95(50), 81(95), 73(100), 55(94). ⁹⁵ 7-Ethoxy-1-methoxy-3,7-dimethyloctane **2pb**.²³ ¹H NMR (CDCl₃, 200 MHz): δ 3.50-3.25 (m, 7H); 1.70-1.00 (m, 18H); 0.82 (d, *J*=6.4 Hz, 3H). MS (EI; 70 eV) 216(0) [M]⁺, 87(100), 59(59), 55(9), 45(13), 43(13), 41(9).
- 1-Methoxy-7-propyloxy-3,7-dimethyloctane $2pc.^{23}$ ¹H NMR (CDCl₃, 200 MHz): δ 3.39 (t, *J*=6.7 Hz, 2H), 3.31 (s, 3H), 3.23 (t, *J*=6.7 Hz, 3H), 1.80-1.10 (m, 11H), 1.06 (s, 6H), 0.90-0.75 (m, 6H). MS (EI; 70 eV) 230(0) [M]⁺, 215(1), 101(74), 83(9), 69(7), 59(100), 55(11), 45(16), 43(21), 41(14).
- 7-Butoxy-1-methoxy-3,7-dimethyloctane **1pd**.²³ ¹H NMR ¹⁰⁵ (CDCl₃, 200 MHz): δ 3.40-3.10 (m, 7H); 1.70-1.00 (m, 22H); 0.82 (d, *J*=6.4 Hz, 3H). MS (EI; 70 eV) 244(0) [M]⁺, 229 (1), 115(55), 83(7), 69(7), 59(100), 55(10), 45(15), 43(10), 41(16).
- 2-Methoxy-2-methyldecane **2qa**. ¹H NMR (CDCl₃, 200 MHz): δ 3.17 (s, 3H), 1.52-1.37 (m, 2H), 1.37-1.20 (m, 12H), 1.12 (s, 6H),
- ¹¹⁰ 0.88 (d, J=6.4 Hz, 3H). ¹³C NMR (CDCl₃, 50 MHz): δ 74.79, 49.20, 39.97, 32.06, 30.41, 29.79, 29.47, 25.12 (2), 24.03, 22.82, 14.26. MS (EI; 70 eV) 186(0) [M]⁺, 171(3), 73(100), 69(4), 55(8), 43(10).

2-Ethoxy-2-methyldecane **2qb**. ¹H NMR (CDCl₃, 200 MHz): δ ¹¹⁵ 3.29 (q, *J*=7.0 Hz, 2H), 1.45-1.30 (m, 2H), 1.30-1.15 (m, 12H),

1.08 (t, J=7.0 Hz, 3H), 1.07 (s, 6H), 0.81 (d, J=6.4 Hz, 3H). ¹³C

NMR (CDCl₃, 50 MHz): δ 74.59, 56.38, 40.29, 32.06, 30.40, 29.79, 29.47, 25.85 (2), 24.06, 22.82, 16.36, 14.25. MS (EI; 70 eV) 200(0) [M]⁺, 185(3), 87(100), 59(57), 43(16).

- 2-Propyloxy-2-methylnonane **2rc**. ¹H NMR (CDCl₃, 200 MHz): δ 5 3.25 (t, *J*=6.8 Hz, 2H), 1.66-1.38 (m, 4H), 1.38-1.19 (m, 10H), 1.13 (s, 6H), 0.90 (t, *J*=7.3 Hz, 3H), 0.88 (d, *J*=6.4 Hz, 3H). ¹³C NMR (CDCl₃, 50 MHz): δ 74.39, 62.93, 40.44, 32.04, 30.38, 29.51, 25.78 (2), 24.05, 23.99, 22.83, 14.26, 10.94. MS (EI; 70 eV) 200(0) [M]⁺, 171(4), 87(100), 69(13), 59(64), 43(19).
- ¹⁰ 2-Butyloxy-2-methylnonane 2rd. ¹H NMR (CDCl₃, 200 MHz): δ
 3.28 (t, *J*=6.4 Hz, 2H), 1.61-1.34 (m, 6H), 1.34-1.18 (m, 10H),
 1.12 (s, 6H), 1.01-0.81 (m, 6H). ¹³C NMR (CDCl₃, 50 MHz): δ
 74.37, 60.91, 40.43, 32.96, 32.04, 30.38, 29.50, 25.76 (2), 24.04,
 22.83, 19.65, 14.25, 14.13. MS (EI; 70 eV) 214(0) [M]⁺, 199(1),
 ¹⁵ 173(22), 115(95), 101(68), 85(28), 71(31), 57(84), 43(100).
- 2,2-Dimethyl-4-(2-methylnonan-2-yloxy)methyl)-1,3-dioxolane
 2re. ¹H NMR (CDCl₃, 200 MHz): δ 4.18-4.11 (m, 1H), 4.10-4.01 (m, 1H), 3.80-3.69 (m, 1H), 3.50-3.38 (m, 1H), 3.32-3.19 (m, 1H), 1.52-1.38 (m, 5H), 1.36 (s, 3H), 1.30-1.18 (m, 10H), 1.13 (s, 20 6H), 0.88 (t, J=6.4 Hz, 3H). ¹³C NMR (CDCl₃, 50 MHz): δ 109.25, 75.36, 75.14, 67.68, 62.98, 40.35, 32.03, 30.32, 29.49, 26.95, 25.62, 25.56 (2), 24.01, 22.82, 14.25. MS (EI; 70 eV) 272(0) [M]⁺, 257(8), 173(19), 115(84), 101(65), 85(25), 71(28),

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57(77), 43(100).

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Notes and references

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Simple salts of abundant metals (Fe, Bi, Ti) supported and on Montmorillonite as efficient and recyclable catalysts for regioselective intramolecular and intermolecular hydroalkoxylation reactions of double bonds and tandem processes

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