Green Chemistry

Accepted Manuscript

This article can be cited before page numbers have been issued, to do this please use: R. Arias-Ugarte and T. W. Hudnall, *Green Chem.*, 2017, DOI: 10.1039/C6GC03629E.

ROYAL SOCIETY OF CHEMISTRY

rsc.li/green-chem

View Article Online
DOI: 10.1039/C6GC03629E

Green Chemistry

ARTICLE

Antimony(V) Catalyzed Acetalisation of Aldehydes: An Efficient, Solvent-Free, and Recyclable Process

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

www.rsc.org/

Renzo Arias Ugarte and Todd W. Hudnall*

A highly selective, solvent-free process for the acetalisation of aldehydes was achieved by the use of a readily accessible and antimony(V) catalyst which we previously prepared in our lab as a tetraarylstibonium triflate salt ([**1**][OTf]). High yields of the acetals were achieved in the presence of stoichimetric amounts of either triethoxymethane or triethoxysilane. It was found that triethoxymethane reactions required longer time to reach completion when compared to triethoxysilane reactions which were completed upon mixing of the reagents. The products can be easily separated from the catalyst by distillation which enabled further use of [**1**][OTf] in additional calytic reactions (up to 6 cycles). Moreover, the stibonium [**1**]$^{+}$ also catalyzed the deprotection of the acetals into their corresponding aldehydes using only water as a solvent.

Introduction

Acetalisation serves as the principal methodology for the protection of carbonyl groups[1] that enables access to novel compounds and materials with important synthetic applications.[2] Acetals are also used as flavouring agents and as aroma enhancers in cosmetic and food products.[3] More recently, acetals have been utilized as diesel additives to increase fuel efficiency and as anti-freezing additives for biodiesel fuels.[4,5] Traditionally, the acetalisation of carbonyl moieties has been performed using alcohols in organic solvents, and often necessitate the inclusion of orthoesters such as trimethoxymethane (TMM) or triethoxymethane (TEM) as water scavengers.[6] Additionally, these reactions are often catalysed by strong mineral and hydrohalic acids such like H_2SO_4, H_3PO_4,[7] or HCl.[8] However, there have been few reports of environmentally friendly methods for the acetalisation reaction disclosed recently to overcome these disadvantages.[9] Some examples rely on the use of transition metal Lewis acids such as: $[Cu][BF_4]_2$,[10] $Fe(OTs)_3$,[11] $Fe(BF_4)_2.6H_2O$),[12] and $RuCl_3$;[13] or metal organic frameworks (MOFs) containing thiourea derivatives,[14] acidic functional groups,[15] and copper hydroxysulfates.[16] Similarly, zeolites;[17] or simple functionalised silica derivatives such as HBF_4-SiO_2,[18] $HClO_4$-SiO_2,[19] and bis(perfluorooctane)sulfonylimide supported on fluorous silica.[20] Ionic liquids derived from imidazolium salts,[21] PEG_{1000}(DA)-polyethylenglycol ionic liquid systems.[22] Other systems that employ Brönsted acids using N-chlorosuccinimide and urea or $[nBu_4N][Br_3]$ have also been explored.[23,24]

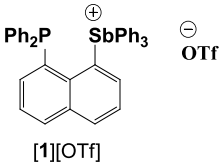
These methods have been effectively used in homo- and heterogeneous systems with high efficiency; however, the use of excess reagents (alcohols or orthoesters), result in environmentally deleterious processes due to excessive organic waste. Motivated by this challenge, researchers have optimized reaction conditions by reducing the alcohol:orthoester ratio. Indeed several reactions can be performed in the presence of pure alcohol or orthoester;[14-17,19,21-23,25,26] however, a large excess of these reagents and higher catalyst loadings are required. Additionally, exhaustive reaction work up, or harsh reaction conditions such as high temperature and pressures are necessary.

In line with these discoveries the use of Lewis acid catalysts has also been reported.[27-32] Specifically, Lewis acid catalysts that are stable to water and air, are easy to handle and recycle, and which are atom economic are highly desirable for environmental reasons.[33] To date, most Lewis acid catalysts employed are corrosive transition metal, or main group halides such as WCl_6,[27] $InCl_3$,[28] GaI_3.[29] More recently, the triflate salts $Bi(OTf)_3.4H_2O$,[30] $Yb(Otf)_3$,[31] and $In(OTf)_3/MnO_2$[32] have shown enhanced activity with low catalyst loadings, but suffer from a larger excess of alcohol and orthoester requirement. In contrast, $Al(OTf)_3$[34] displays exceptional activity and atom economy (low alcohol/orthoester requirement) for the acetalisation of carbonyl compounds; however, it is unknown if deprotection of acetals is possible with this catalyst. Indeed, catalysts which function to both protect and deprotect carbonyl moieties are fundamentally more valuable.[18-20, 28, 31] For this reason, we believe new catalysts systems that are highly active, atom economic, and stable toward air and moisture must be developed to make a large environmental impact in this arena.

Herein we report that the tetraarylstibonium salt, 1-diphenylphosphinonaphthyl-8-triphenylstibonium triflate

Department of Chemistry and Biochemistry, Texas State University, San Marcos, TX, 78666, United States. E-mail: hudnall@txstate.edu.
†Electronic Supplementary Information (ESI) available: spectral, computational, and crystallographic data are available. See DOI: 10.1039/x0xx00000x

([**1**][OTf], Figure 1), which was developed by our group,[35] serves as an air and water stable Lewis acid catalyst for the acetalisation of aliphatic and aromatic aldehydes. This catalyst is highly active at low loadings (0.1 mol%) and effectively protects the aldehydes in the presence of stoichiometric triethoxymethane (TEM) or triethyoxysilane (TES). These reactions are carried out in the absence of organic solvents, obviating the need for tedious aqueous workup, and reducing the creation of waste by-products. Moreover, the stibonium catalyst can be recycled with negligible loss of efficacy (over 6 cycles). Interestingly, reactions conducted using TES were markedly faster than those with TEM which may be associated with the increased oxophilicity of silicon versus carbon.



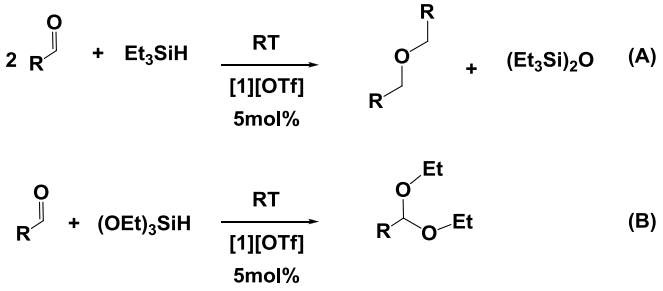
[**1**][OTf]

Figure 1. 1-diphenylphosphinonaphthyl-8-triphenylstibonium triflate ([**1**][OTf]) prepared by our lab.

In addition to catalysing the acetalisation of aldehydes, we also show that [**1**][OTf] is a potent catalyst for the deprotection of the carbonyl group. From an environmental point of view, [**1**][OTf] reverses the acetalisation reaction in water, eliminating the need for organic solvents and reducing waste streams.

Results and Discussion

We recently reported the synthesis and Lewis acidic properties of the stibonium salt [**1**][OTf], and evaluated it's potential utility in the catalytic transformation of aldehydes into α-β unsaturated aldehydes, 1,3,5-trioxanes, and symmetric ethers.[35] We demonstrated that aldehydes are catalytically transformed into symmetric ethers by a reductive coupling mechanism in the presence of triethylsilane as a reducing agent, Scheme 1A. During these studies, we were excited to discover that the use of the more sterically encumbered silane, triethoxysilane (TES), afforded diethoxy acetals under identical

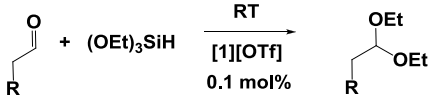


Scheme 1. Two orthogonal reactions with aldehydes that are catalyzed by [**1**]$^+$: A) etherification using triethylsilane, and B) acetalisation using triethoxysilane.

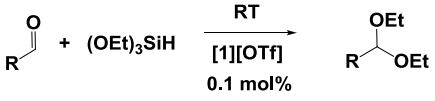
experimental conditions ($CDCl_3$ or dichloromethane as a solvent, 5 mol% of [1][OTf]), Scheme 1B.

We then optimized the reaction, and found that the catalyst loading could be reduced 0.1mol % of [1][OTf], and acetalisation proceeded in the absence of any organic solvent with 100% conversion, and 100% selectivity. Moreover, these reactions are extremely rapid, and 100% conversion is achieved essentially on mixing as detected by ^{1}H and ^{13}C NMR (Table 1 entries 1-7, 9-12, and 15-17). The substrate scope included several aliphatic and aromatic aldehydes, all with high conversion.

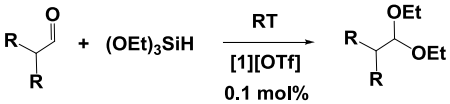
Table 1. Substrate scope for the acetalisation of aldehydes using TES and [**1**][OTf][a]



Entry	aldehyde (R)	Time (h)	acetal	Selectivity (%)	Yield[b](c)%
1	$-CH_2CH_3$	0.16	(A_1)	95*	96(100)
2	$-(CH_2)_7CH_3$	0.16	(A_2)	95*	76(100)
3	Ph	0.16	(A_3)	100	99(100)
4	$-CH_2Ph$	0.16	(A_4)	100	98(100)



Entry	aldehyde (R)	Time (h)	acetal	Selectivity (%)	Yield[b](c)%
5	cyclohexyl	0.16	(A_5)	100	76(100)
6	Ph	0.16	(A_6)	100	31(100)
7	C_6F_5	0.16	(A_7)	100	71(100)
8	$2\text{-}BrC_6H_4$	1	(A_8)	100	97(100)
9	$3\text{-}BrC_6H_4$	0.16	(A_9)	100	97(100)
10	$3\text{-}FC_6H_4$	0.16	(A_{10})	100	96(100)
11	$4\text{-}CF_3C_6H_4$	0.16	(A_{11})	100	98(100)
12	$4\text{-}NO_2C_6H_4$	0.16	(A_{12})[c]	100	94(100)
13	$4\text{-}OMeC_6H_4$	1	(A_{13})	100	66(100)
14	$4\text{-}MeC_6H_4$	1.5	(A_{14})	100	76(100)



Entry	aldehyde (R)	Time (h)	acetal	Selectivity (%)	Yield[b](c)%
15	Me	0.16	(A_{15})	100	78(100)
16	Et	0.16	(A_{16})	100	75(100)
17	Ph	0.16	(A_{17})	100	93(100)

(a) Reactions conditions: 0.1 mol% [**1**][OTf], room temperature. (b) Isolated yields, (c) yields by ^{1}H NMR are shown in parenthesis, and (d) Excess TES was used 2mmol instead of 1 mmol. (*) traces 1,3,5-trioxane was observed.

For aromatic aldehydes substituted at the *ortho*- or *para*-position with electron-donating groups we observed longer

reaction times (Table 1, entries 8, 13, and 14) analogous to other reports.[10, 24, 31] For example, the synthesis of 4-(CH_3)-C_6H_4-CH($OEt)_2$ (**A_{14}**) took 90 minutes with a TES:aldehyde ratio of 1:1. Despite this longer reaction time, we still observed nearly 50 % conversion to the acetal upon mixing (see Figure 2). We hypothesize that the introduction of electron donating substitutents in conjugation with the acyl carbon of the aldehyde effectively reduces the electrophilicity of the carbonyl group, hampering nucleophilic attack of an ethoxide that is furnished by the silane (*vide infra*).[10, 24, 31] Despite these longer reaction times, the catalytic activity of [**1**][OTf] in these acetalisations is superb when compared to other systems reported owing to: lower catalyst loading, stoichiometric amount of silane, absence of organic solvent, easy purification, and catalyst recovery/recyclability. Indeed, the majority of the acetals are volatile compounds with low boiling points and can be separated from the catalyst by simple distillation. Additionally, our method reduces organic waste production as highly pure alcohols are not needed as a reagent in these reactions as opposed to systems that utilize alcohols to increase reaction efficiency while lowering reaction times.[20, 30, 34]

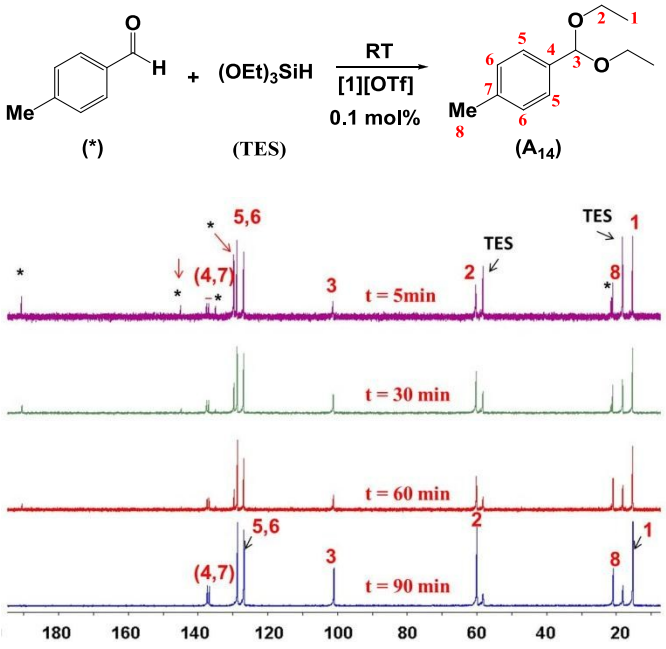


Figure 2: Stacked ^{13}C NMR spectra from time = 5 min. (top) to 90 min. (bottom), showing the conversion of 4-methylbenzaldehyde (denoted with *) into 4-methylbenzaldehydediethylacetal (**A_{14}**) catalysed by [**1**]$^+$ in the presence of TES .

Even though electron-donating groups resulted in longer reaction times, in a 1:1 ratio (triethoxysilane:aldehyde) the reaction always reached 100% conversion. However, we found that by increasing the TES:aldehyde ratio, we could speed up the reaction time (Table 2). For example, when 4-methylbenzaldehyde was treated with 2 molar equivalents of TES in the presence of 0.2 mol% of [**1**][OTf], acetal **A_{14}** was obtained quantitatively in 15 minutes (Table 2, entry 1).

We hypothesize that the addition of excess TES improved the reaction times by serving as a solvent for the reaction, and providing a more homogeneous environment. Interestingly, when 0.5 molar equivalents of TES were used (Table 2, entry 3) the observed reaction time was also decreased (5 minutes), however, only 37% of the aldehyde was converted to acetal **A_{14}**. Although this reaction was quite rapid, the residual aldehyde increased the difficulty in purifying the desired acetal from the reaction mixture.

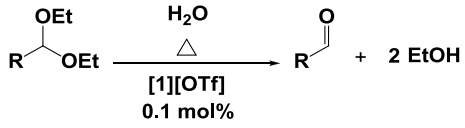
Table 2: Effect of TES:aldehyde ratio for the formation of **A_{14}**

Entry	[1][OTf] mol %	TES mmol	aldehyde mmol	Time (min)	% conversion[(a)]
1	0.2	2	1	15	100
2	0.2	1	1	90	100
3	0.2	0.5	1	5	37

Reaction conditions: 0.2 mol % [**1**][OTf], 4-CH_3-C_6H_4-CHO, TES, RT. (a) By ^1H NMR.

During the course of these reactions, we have observed the formation of a new silicon-containing species at -67ppm by ^{29}Si NMR spectroscopy. While we hypothesize that this compound is the silicon analogue of ethylformate (*vide infra*), we have been unable to isolate this compound to confirm its identity despite our best efforts. Indeed, this species appears to be unstable even in solution as we have observed the conversion of this compound into another silicon-containing molecule with a ^{29}Si chemical shift of -76 ppm over the course of these reactions. Fortunately, these silicon-containing compounds to not appear to impede the production of the desired acetals, and are easily separated from the product. For acetals with low boiling points, the products were removed by simple distillation, for non-volatile acetals, these silicon by-products were removed using silica gel column chromatography (eluent: DCM).

One of the major disadvantages for preparing acetals from alcohols and aldehydes is the presence of water generated in the reaction, which as has been shown to inhibit the reaction by Sedran and co-workers.[17] In our case, the use of the silicon orthoester precludes the generation of water in our acetalisation reactions. Typically, water can enhance the hydrolysis of acetals back to their corresponding aldehyde or ketone in the presence of a Lewis acid catalyst.[18-20, 28,31] For this reason, we questioned if [1][OTf] could catalyse the deprotection of the diethylacetals prepared in this study. Gratifyingly, we found that the acetals are efficiently hydrolysed to their corresponding aldehydes with the release two equivalents of ethanol in the presence of 0.1 mol% of [**1**][OTf] (Scheme 2).



Scheme 2. Stibonium-catalysed deprotection of acetals using water as a solvent.

To illustrate this reaction, Figure 3 depicts ^{13}C NMR spectra of the reaction of acetal **A_8**, derived from 2-bromobenzaldehyde, with water and 0.1 mol % [**1**][OTf] in

$CDCl_3$. After 30 minutes at 70°C, we observed the conversion of **A_8** into the corresponding aldehyde and ethanol in a 1:2 ratio (confirmed by ^{1}H NMR spectroscopy, Figure 4). As a control experiment, when the same reaction was carried out in the absence of the catalyst, we did not observe the formation of the aldehyde or ethanol.

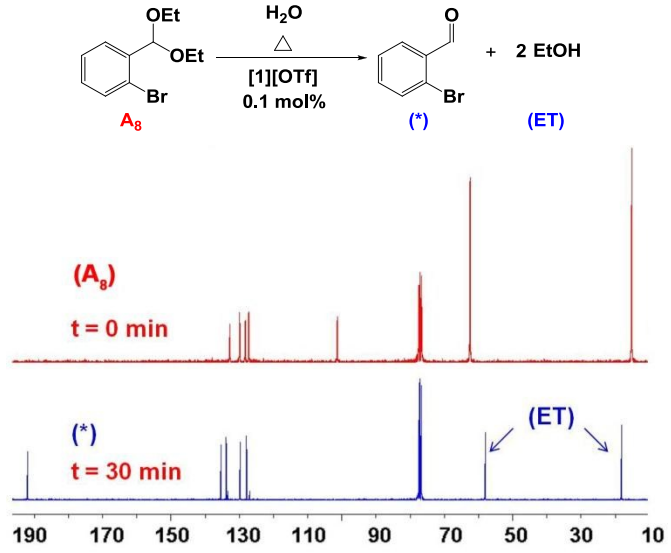


Figure 3: Stacked ^{13}C NMR spectra at time = 0 min (top) and 30 min. (bottom) that show the deprotection of 2-bromobenzaldehyde diethylacetal (**A_8**) to afford 2-bromobenzaldehyde (denoted by *) and ethanol in the presence of 0.1 mol% [**1**]$^+$ and water, at 70°C.

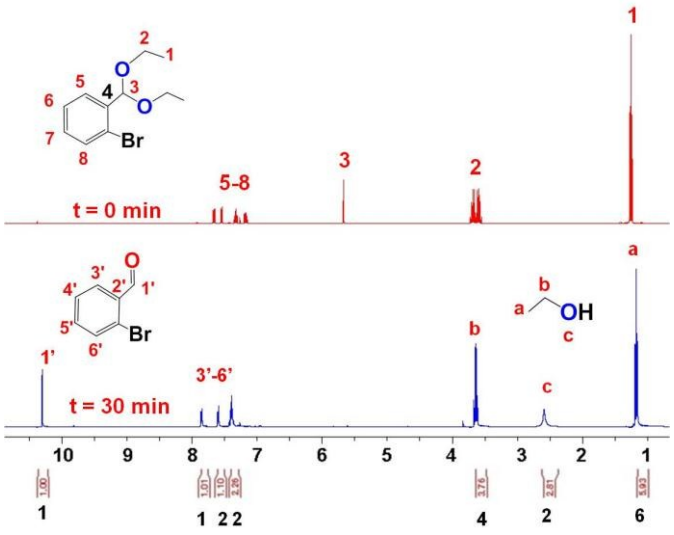


Figure 4: Stacked ^{1}H NMR spectra at time = 0 min (top) and 30 min. (bottom) that show the deprotection of 2-bromobenzaldehyde diethylacetal (**A_8**) to afford 2-bromobenzaldehyde and 2 equivalents of ethanol (integrations provided) in the presence of 0.1 mol% [**1**]$^+$ and water, at 70°C.

These experiments demonstrate that stibonium cation [**1**]$^+$ serves as a catalyst for a new, efficient and environmentally more attractive methodology for the acetalisation of aldehydes. These reactions are also much faster than standard approaches, and provide clean, selective conversion to the desired acetals. In all cases no aldehyde-derived intermediates were observed in these reactions, and only one silicon-containing intermediate was observed at 67 ppm (^{29}Si NMR). While we suspect that this compound may be the silicon analogue of ethylformate of the formula (H(Si=O)OEt), we were unable to isolate this compound as it rapidly decomposes to another species with a ^{29}Si resonance at -76 ppm. Additionally, this new compound also degrades into a variety of silicon-containing polymeric materials. Fortunately, these polymeric species are highly insoluble in the reaction mixture and are non-volatile, which facilitated the isolation of the desired acetals.

Mechanistic Considerations

In order to determine the key species in the solution and to elucidate the mechanism for acetalisation, triethoxymethane (TEM) was used as a triethoxysilane surrogate. Gratifyingly, under identical reaction conditions to those described with the silane, we were able to observe and isolate ethyl formate (H(C=O)OEt), which was generated as a byproduct of the reaction of 4-methylbenzaldehyde with TEM (Figure 5, Entry 14, Table 3). In addition to providing mechanistic insight into these reactions, this result demonstrated that TEM serves as an atom-economical and inexpensive reagent that is suitable for the protection of aldehydes.

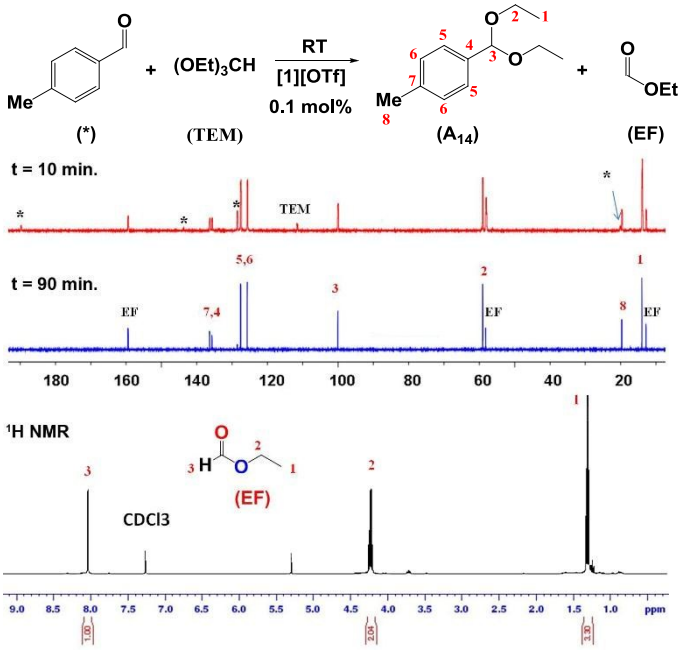
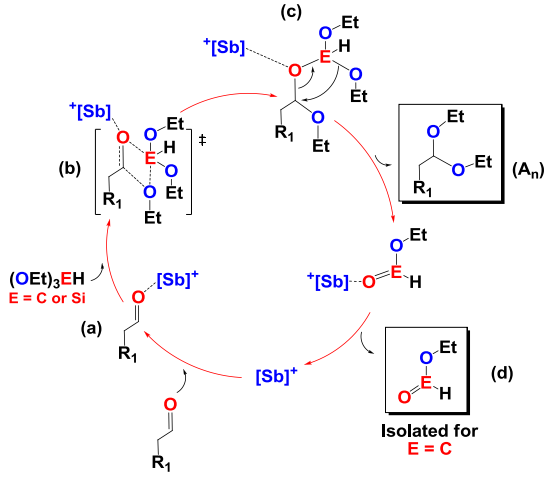


Figure 5. Stacked NMR spectra (^{13}C at time = 10 min (top), time = 90 minutes (middle), and ^{1}H NMR of ethylformate produced in the reaction (bottom)) that show the conversion of 4-methylbenzaldehyde into 4-methylbenzaldehydediethylacetal (**A_{14}**) when treated with TEM in the presence of 0.1 mol% of [**1**]$^+$.

As we have previously reported, we believe that the electron deficient stibonium centre in cation 1$^+$ serves as a potent Lewis acid that can activate aldehydes toward nucleophilic attack as shown in **Scheme 3(a)**. This [Sb$^+$]··· aldehyde interaction was calculated to be thermodynamically favoured by 6.2 kcal.[35] Upon activation, we believe that the

orthoester TES or TEM then engages the aldehyde to afford a cyclobutane transition state as shown in **Scheme 3(b)** where the silicon or carbon of the orthoester is coordinated to the oxygen atom of the aldehyde, while simultaneously delivering one ethoxide to the acyl carbon. We hypothesize this transition state as the more electropositive silicon atom in TES would more readily coordinate the oxygen atom of the aldehyde when compared to TEM, thus resulting in more facile reactions when the silane is employed. The rapid delivery of a second equivalent of ethoxide concomitant with cleavage of the former C=O bond as shown in **Scheme 3(c)** releasing the desired acetal (**A**) along with a stibonium-coordinated formate species which liberates the free formate **3(d)**. Although we have not been able to isolate the purported silyl derivative of ethylformate, we believe that these species are not stable and undergo rapid polymerization giving insoluble materials.



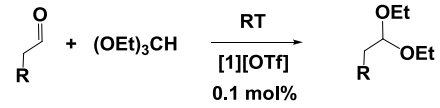
Scheme 3. Proposed catalytic cycle for the acetalisation of aldehydes with the elimination of ethyl-formate esters using stibonium cation [**1**]$^+$ and TES or TEM.

The ability of one equivalent of the orthoester to deliver both alkoxy groups to the aldehyde with the elimination of only ethylformate is significant in terms of efficiency and waste reduction. Despite longer reaction times when compared to the reactions involving triethoxysilane as the ethoxide source (see Table 3), we were able to efficiently obtain the desired acetals by simple distillation under solvent-free conditions with the one exception being 4-nitrobenzaldehyde which was not soluble in TEM and required 0.5 mL of chloroform to be added. Additionally, we have been able to isolate the novel compound, 1-(diethoxymethyl)-2,3,4,5,6-pentafluorobenzene (see **Entry 7 Table 3**) using this green methodology.

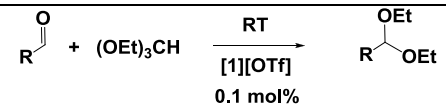
Catalyst Efficiency

As we have demonstrated previously, the stibonium cation [**1**]$^+$ behaves as a potent Lewis acid catalyst and requires very low loading (0.1 mol %). Due to the stability of [**1**]$^+$ toward water and oxygen, we were able to recycle our stibonium salt and able to recycle the catalyst for up to six cycles using 2-ethylbutanal as a model substrate (Figure S55 in the ESI for full discussion). However, we notice a sharp decrease in activity on cycle six, and noticed an increase in the reaction. Indeed, on mixing only 50% conversion was observed, however, the reaction was still completed in two hours. Similar to previous observations, aliphatic aldehydes were shown to react faster than aromatics.

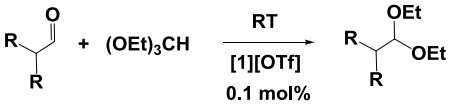
Table 3: Aldehydes to acetal in the presence of triethoxymethane (TEM)[a]



Entry	aldehyde (R)	Time (h)	acetal	Yield[b],[c]%
1	-CH_2CH_3	2	(A_1)	[d](100)82
2	-$(CH_2)_7CH_3$	2	(A_2)	[d](100)76
3	Ph	2	(A_3)	(100)95
4	-CH_2Ph	12	(A_4)	(100)94



Entry	aldehyde (R)	Time (h)	acetal	Yield[b],[c]%
5	cyclohexyl	12	(A_5)	(100)70
6	Ph	24	(A_6)	(100)60
7	C_6F_5	12	(A_7)	(100)70
8	2-BrC_6H_4	12	(A_8)	(100)96
9	3-BrC_6H_4	12	(A_9)	(100)98
10	3-FC_6H_4	12	(A_{10})	(100)70
11	4-$CF_3C_6H_4$	12	(A_{11})	(100)98
12	4-$NO_2C_6H_4$ [e]	12	(A_{12})	(100)98
13	4-$OMeC_6H_4$	24	(A_{13})	(100)75
14	4-MeC_6H_4	12	(A_{14})	(100)73



Entry	aldehyde (R)	Time (h)	acetal	Yield[d][b]%
15	Me	0.16	(A_{15})	(100)78
16	Et	01.6	(A_{16})	(100)75
17	Ph	0.16	(A_{17})	(100)93

(a) Reaction conditions: [**1**][OTf] 0.1 mol%, room temperature, (b) yield based on ^{1}H NMR (shown in parenthesis), (c) Isolated yields after purification, (d) 95% selectivity observed with 5% of 1,3,5 trioxane formed, and (e) 0.5 mL of $CDCl_3$ was used to dissolve the aldehyde and the reaction was heated to 70 °C.

Experimental

General Considerations

Unless otherwise noted, these procedures were all carried out using typical Schlenk techniques under an atmosphere of

View Article Online
DOI: 10.1039/C6GC03629E

nitrogen or in a nitrogen-filled glove box. Solvents were dried and degassed by an Innovative Technology solvent purification system and stored over a 3 Å molecular sieves in a nitrogen-filled glove box. Dichloromethane and hexanes were dried under nitrogen over CaH and Na/K, respectively and distilled prior to use. Aldehydes with 95 to 98% purity have been purchased either from Sigma Aldrich or Alfa Aesar and were used as received. [**1**][OTf] as synthetized according to previous report.[35] Melting points were recorded on a Mel-Temp apparatus in sealed capillary tubes and are uncorrected. All reagents were used as received. NMR spectra were recorded on Bruker Avance 400 MHz/52mm spectrometer. Chemical shifts (δ) are given in ppm and are referenced to the residual solvent $CDCl_3$ (which was used to characterize all compounds after isolation): ^{1}H: 7.26 ppm; ^{13}C:, 77.0 ppm. All column chromatography was performed using small columns (5 x 60 mm) with silica gel (Aldrich), 700-230 mesh, 60 Å, and pore volume of 0.75 cm3/g as the stationary phase. Elemental analyses were performed at Midwest Microlabs, LLC (Indianapolis, IN).

Methodology using triethoxysilane

In a NMR tube 0.1 mol % of the [**1**][OTF] was added followed by 1 mmol the triethoxysilane (TES), which was added drop wise directly to the catalyst to ensure complete dissolution. After that, 1 mmol of the corresponding aldehyde was added drop wise to this mixture which was then monitored by ^{13}C NMR spectroscopy as a neat liquid. After a period of time ranging from 5 to 90 min we confirmed that all the aldehyde had been consumed, and then the solution was transferred to a 10ml round bottom flask followed by distillation of the product under reduced pressure (300 mTorr). Low boiling point products were obtained as pure compounds via distillation, however higher boiling point materials purified, first by distillation to remove volatiles (traces of unreactive triethoxysilane or aldehyde), and then the residue in the flask was immediately passed through a small plug of silica gel using dichloromethane as the eluent to remove silicon-containing byproducts. The solution was then concentrated under vacuum to get colourless oils in very good yields. The isolated products were then characterized by NMR spectroscopy in $CDCl_3$.

Methodology using triethoxymethane

Analogous to the previous methodology, 0.1 mol % of [**1**][OTf] was added to an NMR tube followed by 1 mmol of triethoxymethane and then 1 mmol of the corresponding aldehyde. The mixture was left to stand for 12 hours to reach completion (monitored by ^{13}C NMR spectroscopy as a neat liquid). After that time the solution was transferred to a 10 ml round bottom flask and distilled under reduced pressure to remove the final product and ethyl formate from the catalyst. Ethyl formate was then evaporated under a flow of nitrogen for 5 minutes. For higher boiling point acetals, all volatile components (including ethyl formate) were removed by distillation to give the product as a pure compound. The isolated products were then characterized by NMR spectroscopy in $CDCl_3$.

Recycling of catalyst study

In an NMR tube 0.1mol % of [**1**][OTf] was added initially, and then 1 mol triethoxysilane (TES) was added dropwise directly to the stibonium salt to ensure complete dissolution. Next, 100 mg (1 mmol) of 2-ethylbutanal was added dropwise over this mixture which was then agitated and monitored by ^{13}C NMR spectroscopy. After 1h we confirmed that all the aldehyde was consumed, and the reaction was purified according to the main text in the manuscript. The resulting compound was then characterized by ^{13}C NMR in $CDCl_3$, and was labeled Run 1 (Figure S55, ESI). The residue containing the catalyst after distillation of the acetal was then recycled by adding more reagents (TES and aldehyde). We found that the acetalisation could be performed 5 times without a noticeable drop in activity of the catalyst (Figure S55, ESI).

Spectral Data of Compounds

Butyraldehyde diethylacetal (A_1): ^{1}H NMR (400 MHz) ($CDCl_3$): δ 0.87-0.91(t, 3H, Me, J = 7.2MHZ); 1.15-1.18(t, 6H, Me, J = 7.2MHZ); 1.32-1.38,1.53-1.58(m, 4H, CH_2); 3.41-3.49, 3.56-3.64(m, 4H, CH_2O); 4.44-4.47(t, 1H, CHO, J = 5.6 MHZ); ^{13}C NMR (100.61 MHZ) ($CDCl_3$): δ 13.75(Me_2); 15.15(Me); 17.91, 35.58(CH_2); 60.64(CH_2-O); 102.63(CH).

Decanal diethylacetal (A_2): ^{1}H NMR (400 MHz) ($CDCl_3$): δ. 0.84-0.87(t, 3H, Me, J = 6.8 MHZ); 1.16-1.19(t, 6H, Me-CH2O, J = 7.2 MHZ); 1.24-1.40(s, 16H, CH_2); 3.44-3.50, 3.57-3.63(m, 4H, CH2-O); 4.43-4.46(t, 1H, CH, J = 6.0 MHZ). ^{13}C NMR (100.61 MHZ) ($CDCl_3$): δ 14.03(Me-CH2); 15.30(Me-CH_2O); 22.63, 24.73, 29.27, 29.46, 29.50, 29.55, 31.86, 33.58(CH2); 60.75(CH2-O); 102.96(CH).

4-methylbenzaldehyde diethylacetal (A_3): ^{1}H NMR (400 MHz) ($CDCl_3$): δ.1.15-1.19(t, 6H, Me. J = 6.80 MHZ); 2.92-2.93(d, 2H, CH_2-Ph, J = 5.6 MHZ); 3.41-3.49, 3.62-3.71(m, 4H, CH_2-O); 4.61-4.64(t, 1H, CH-O, J = 5.6 MHZ); 7.20-7.28(m, 5H, CH-Ph). ^{13}C NMR (100.61 MHZ) ($CDCl_3$): δ. 15.21(Me); 40.86(CH2-Ph); 61.83(CH2-O); 103.84(CH); 126.22, 128.16, 129.54(CH-Ph); 137.33(C-Ph).

3-phenylpropionaldehyde diethylacetal (A_4): ^{1}H NMR (400 MHz) ($CDCl_3$): δ.1.23-1.27(t, 6H, Me, J = 7.2 MHZ); 1.96-2.01(m, 2H, CH_2-(CHO)); 2.71-2.75(m, 2H, CH2-(Ph)); 3.52-3.71(m, 4H, CH2-O); 4.51-4.54(t, 1H, CH-O); 7.21-7.31(m, 5H, CH-Ph). ^{13}C NMR (100.61 MHZ) ($CDCl_3$): δ. 15.34(Me); 30.98, 35.07(CH2); 60.99(CH2-O); 102.18(CH-O); 125.77, 128.32, 128.37(CH-Ph); 141.76(C-Ph).

Isobutyraldehyde diethylacetal (A_5): ^{1}H NMR (400 MHz) ($CDCl_3$): δ 0.84-0.86(d, 6H, Me, J = 6.8 MHZ); 1.12-1.16(t, 6H, Me-CH2O, J = 7.2 MHZ); 1.78-1.83(m, 1H, CH-Me); 3.41-3.45, 3.54-3.61(m, 4H, CH2); 4.01-4.03(d, 1H, CH-O). ^{13}C NMR (100.61 MHZ) ($CDCl_3$): δ 15.17(Me-CH2O); 17.59(Me-CH); 31.30(CH-Me); 61.71(CH2); 107.66(CH-O).

Butyraldehyde 2-ethyl diethylacetal (A_6): ^{1}H NMR (400 MHz) ($CDCl_3$): δ 0.85-0.88(t, 6H, Me-CH, J =7.2 MHZ); 1.17-1.20(t, 6H, Me-CH_2O, J = 7.2 MHZ); 1.28-1.36, 1.46-1.51(m, 5H,

CH,CH_2); 3.45-3.49, 3.62-3.66(m, 4H, CH_2O); 4.28-4.30(d, 1H, CHO, J = 6.0 MHZ). ^{13}C NMR (100.61 MHZ) ($CDCl_3$): δ 11.00(Me-(CH_2CH)); 15.29(Me-(CH_2O)); 20.77(CH_2-CH); 43.56(CH-CH_2); 61.98(CH_2-O); 105.26(CH-O).

2,2-dipheylacetaldehyde diethylacetal (A_7): ^{1}H NMR (400 MHz) ($CDCl_3$): δ.1.13-1.16(t, 6H, Me, J = 7.2 MHZ); 3.50-3.54, 3.70-3.74(m, 4H, CH2); 4.32-4.34(d, 1H, CH-Ph, J = 7.6 MHZ); 5.15-5.17(d, 1H, CH-O, J = 7.6 MHZ); 7.23-7.44(m, 10H, CH-Ph). ^{13}C NMR (100.61 MHZ) ($CDCl_3$): δ. 14.97(Me-CH2O); 55.29(CH-Ph); 62.33(CH2); 104.72(CH-O); 126.13, 128.03, 128.83, 129.03(CH-Ph); 141.29(C-Ph).

Cyclohexanecarboxaldehyde diethylacetal (A_8): ^{1}H NMR (400 MHz) ($CDCl_3$): δ.0.91-1.5, 1.51-1.80(m, 11H, CH_2 and CH); 1.17-1.20(t, 6H, Me, J = 7.2 MHZ); 3.43-3.50, 3.59-3.67(m, 4H, CH_2-O); 4.09-4.11(d, 1H, CH-O, J = 7.2 MHZ). ^{13}C NMR (100.61 MHZ) ($CDCl_3$): δ. 15.28(Me); 25.80, 26.43, 28.19(CH_2); 40.79(CH-Cyclohex); 61.59(CH_2-O); 106.77(CH-O).

Benzaldehyde diethylacetal (A_9): ^{1}H NMR (400 MHz) ($CDCl_3$): δ 1.23-1.27(t, 6H, Me, J = 7.2MHZ); 3.53-3.65(m, 4H, CH_2O); 5.52(s, 1H, CHO); 7.31-7.38, 7.48-7.50(m, 5H, Ph). ^{13}C NMR (100.61 MHZ) ($CDCl_3$): δ 15.12(Me); 60.91(CH_2); 101.48(CHO); 126.57, 128.07, 128.18(CH-Ph); 139.05(C-Ph).

2,3,4,5,6-pentafluorobenzaldehyde diethylacetal (A_{10}): ^{1}H NMR (400 MHz) ($CDCl_3$): δ.1.22-1.26(t, 6H, Me, J = 7.2 MHZ); 3.55-3.59, 3.74-3.78(m, 4H, CH_2); 5.70(s, 1H, CH). ^{13}C NMR (100.61 MHZ) ($CDCl_3$): δ 14.90(Me); 63.70(CH_2); 96.52(CH); 113.22, 136.26, 138.77, 143.53, 146.06(C-F). ^{19}F NMR(376.4983 MHz) : δ. -162.09, -154.28, -142.62. Elemental analysis calculated (%) for $C_{11}H_{11}F_5O_2$: C. 48.90, H 4.10. Found: C. 48.66, H. 4.09.

2-bromobenzaldehydediethylacetal (A_{11}): ^{1}H NMR (400 MHz) ($CDCl_3$): δ 1.23-1.27(t, 6H, Me, J = 7.2 MHZ); 3.54-3.71(m, 4H, CH_2); 5.27(s, 1H, CHO); 7.14-7.16, 7.30-7.34, 7.52(m, 4H,). ^{13}C NMR (100.61 MHZ) ($CDCl_3$): δ

3-bromobenzaldehyde diethylacetal (A_{12}): ^{1}H NMR (400 MHz) ($CDCl_3$): δ.1.24-1.27(t, 6H, Me, J = 6.8 MHZ); 3.55-3.67(m, 4H, CH2); 5.48(s, 1H, CH); 7.22-7.26, 7.40-7.45, 7.65-7.66(m, 4H, CH-Ph). ^{13}C NMR (100.61 MHZ) ($CDCl_3$): δ. 15.09(Me); 61.03(CH_2); 100.47(CH); 122.35(C-Br); 125.28, 129.72, 129.79, 131.28(CH-Ph); 141.42(C-CHO).

3-fluorobenzaldehyde diethylacetal (A_{13}): ^{1}H NMR (400 MHz) ($CDCl_3$): δ. 1.22-1.26(t, 6H, Me, J = 7.2 MHZ); 3.52-3.64(m, 4H, CH2); 5.50(s, 1H, CH); 6.97-7.02, 7.19-7.35(m, 4H, CHPh). ^{13}C NMR (100.61 MHZ) ($CDCl_3$): δ. 15.09(Me); 61.01(CH2); 100.58(CH); 113.57-113.79, 114.95-115.16, 122.27, 129.67(CH-Ph); 141.82(C-CHO); 164.04(C-F). ^{19}F NMR(376.4983 MHz) : δ. -113.36

4-trifluorobenzaldehyde diethylacetal (A_{14}): ^{1}H NMR (400 MHz) ($CDCl_3$): δ.1.22-1.26(t, 6H, Me, J = 7.2 MHZ); 3.52-3.63(m, 4H, CH2); 5.54(s, 1H, CH-O); 7.60-7.62(m, 4H, CH-Ph). ^{13}C NMR (100.61 MHZ) ($CDCl_3$): δ.15.11(Me); 61.15(CH_2); 100.65(CH-O); 125.09(C-F); 125.14, 127.08(CH-Ph); 129.50(C-CF_3), 143.13(C-CHO). ^{19}F NMR(376.4983 MHz) : δ. -62.58

4-nitrobenzaldehyde diethylacetal (A_{15}): ^{1}H NMR (400 MHz) ($CDCl_3$): δ.1.22-1.26(t, 6H, Me, J = 7.2 MHZ); 3.54-3.61(m, 4H, CH_2); 5.57(s, 1H, CH); 7.65-7.67(d, 2H, CH-Ph, J = 8.8 MHZ); 8.19-8.21(d, 2H, CH-Ph, 8.8). ^{13}C NMR (100.61 MHZ) ($CDCl_3$): δ 15.02(Me); 61.22(CH_2); 100.06(CH); 123.27, 127.62(CH-Ph); 146.08(C-CHO); 147.80(C-NO_2).

4-methoxybenzaldehydediethylacetal (A_{16}): ^{1}H NMR (400 MHz) ($CDCl_3$): δ 1.20-1.24(t, 6H, H_1, J = 7.2 MHZ); 3.49-3.53;3.58-3.62(m, 4H, H_2); 3.78(s, 3H, H8); 5.45(s, 1H, H_3); 6.86-6.88(d, 2H, H_5, J = 8.8MHZ); 7.37-7.40(d, 2H, H_6, J = 8.4 MHZ). ^{13}C NMR (100.61 MHZ) ($CDCl_3$): δ 15.07(Me); 55.07(MeO); 60.73(CH_2O); 101.29(CH); 113.36, 127.72(CH-Ph); 131.35(C-CH); 159.45(C-OMe).

4-methylbenzaldehyde diethylacetal (A_{17}): ^{1}H NMR (400 MHz) ($CDCl_3$): δ.1.25-1.29(t, 6H, Me-(CH_2O), J = 7.2 MHZ); 2.38(s, 3H, Me); 3.54-3.67(m, 4H, CH2); 5.52(s, 1H, CH-O); 7.19-7.21(d, 2H, CH-Ph, J = 7.6 MHZ); 7.39-7.41(d, 2H, CH-Ph, J = 7.6 MHZ). ^{13}C NMR (100.61 MHZ) ($CDCl_3$): δ. 15.13(Me-CH_2O); 21.09(Me-Ph); 60.84(CH_2); 101.52(CH-O); 126.49, 128.75(CH-Ph); 136.15(C-CHO); 137.85(C-Me).

Conclusions

We have developed a new, efficient and environmentally-benign process for the acetalisation of a variety of aldehydes that is catalysed by the potent Lewis acidic stibonium cation [**1**][OTf]. The speed of the reactions were found to increase from aromatic to aliphatic derivatives, and longer reaction times were observed when for electron-withdrawing groups were incorporated into the aldehyde. The use of triethoxysilane as an ethoxide source resulted in rapid reaction times when compared to triethoxymethane. The easy to handle nature, stability, and lower loading (0.1mol %) of [**1**][OTf] provides an elegant, rapid, and green method for protecting aldehydes. Additionally, the requirement of only a stoichiometric quantity of alkoxide source (i.e.: 1:1 ratio aldehyde triethoxy derivative) as opposed to excess alcohol, acid, or other alkoxide source offers synthetic chemists with a superior method for protecting aldehydes. Further studies and calculations are underway in an effort to fully elucidate the mechanism involved in these transformations, however our previous studies suggest the key success of these reactions is rooted in the potent Lewis acidity of the stibonium centre.[35]

Acknowledgements

The authors would like to acknowledge the Donors of the American Chemical Society – Petroleum Research Fund for grant 54584-UR3 (TWH), The National Science Foundation for grants CHE-0821254 and CHE-0946998 (MRI), and the Welch Foundation for a Department Research Grant (AI-0045).

Notes and references

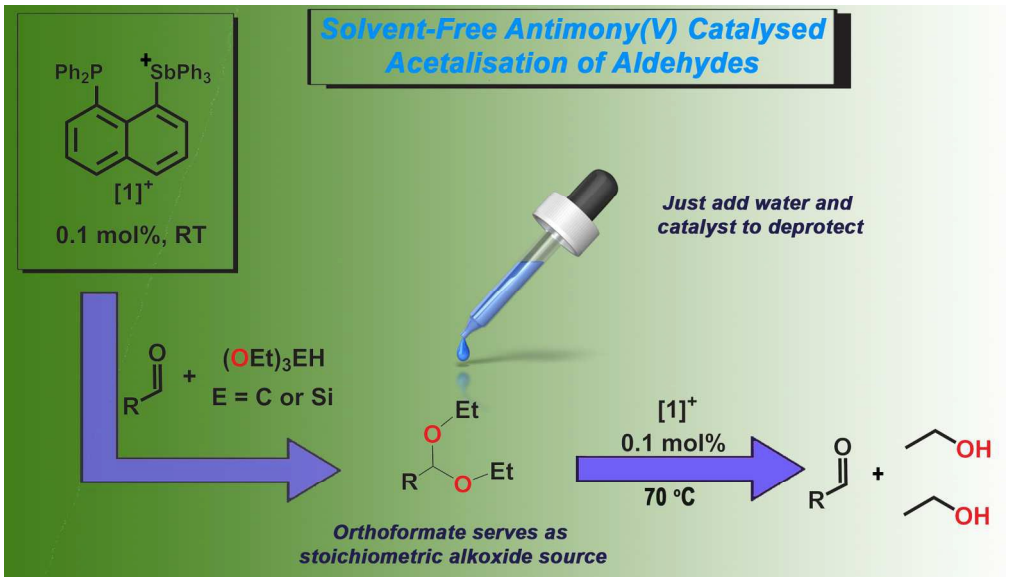
‡ Footnotes relating to the main text should appear here. These might include comments relevant to but not central to the matter under discussion, limited experimental and spectral data, and crystallographic data.

1. a) J. R. Hanson, *Black-Well Science, Inc, Malden, MA, 1st edn.*, 1999; b) T. W. Greene and P. G. M. Wuts, *John Willey and Sons,*

New York, 3rd edn, 1999; c) P. J. Kocienski, *Georg Thieme. Stuttgart, 1st edn.* , 1994.
2. a) P. A. Bartlett, W. S. Johnson and J. D. Elliott, *J. Am. Chem. Soc.*, 1983, **105**, 2088-2089; b) A. Mori and H. Yamamoto, *J. Org. Chem.*, 1985, **50**, 5444-5446; c) A. Ladépêche, E. Tam, J.-E. Ancel and L. Ghosez, *Synthesis*, 2004, 1375-1380; d) X. Xu, C. Wang, Z. Zhou, Z. Zeng, X. Ma, G. Zhao and C. Tang, *Heteroat. Chem.*, 2008, **19**, 238-244; e) T. Xu, Z. Yu and L. Wang, *Org. Lett.*, 2009, **11**, 2113-2116; f) Z.-B. Zhu, Y. Wei and M. Shi, *Chem. – Eur. J.*, 2009, **15**, 7543-7548; g) Y. Geng, H. M. Faidallah, H. A. Albar, I. A. Mhkalid and R. R. Schmidt, *Eur. J. Org. Chem.*, 2013, 7035-7040; h) I. Suzuki, M. Yasuda and A. Baba, *Chem. Commun.*, 2013, **49**, 11620-11622; i) C. A. Swamy P, R. N. Priyanka and P. Thilagar, *Dalton Trans.*, 2014, **43**, 4067-4075; j) Q. Yang, T. Xu and Z. Yu, *Org. Lett.*, 2014, **16**, 6310-6313; k) M. Kuroda and K. Kobayashi, *Helv. Chim. Acta*, 2015, **98**, 279-286.
3. H. Maarse, *Volatile Compounds I Foods and Beverages*, Marcel Dekker, Inc., New York, 1991.
4. a) L. N. Dodge, D., *Southwest Research Institute, San Antonio, TX, National Renewable Energy Laboratory*, 1994. ; b) K. D. O. Vertin, J. M.; Naegeli, D. W.; Childress, K. H.; Hagen, G. P.; McCarthy, C. I.; Cheng, a S.; Dibble, R. W. , *SAE, International Spring Fuel&Lubricants Meeting&Exposition*, 1999, 1-13.
5. P. H. R. Silva, V. L. C. Gonçalves and C. J. A. Mota, *Bioresour. Technol.*, 2010, **101**, 6225-6229.
6. F. A. J. Meskens, *Synthesis*, 1981, 501-522.
7. a) M. E.-C. Kaufhold, Moustafa, *Patent*, 1995, DE 4404515 A4404511 19950817, Germany.; b) S. Sugai, T. Kodama, S. Akaboshi and S. Ikegami, *Chem. Pharm. Bull.*, 1984, **32**, 99-105.
8. T. H. Fife and L. K. Jao, *J. Org. Chem.*, 1965, **30**, 1492-1495.
9. G. M. Sartori, R., *Chem. Rev*, 2010, **113**, PR1-PR54.
10. R. Kumar and A. K. Chakraborti, *Tet. Lett.*, 2005, **46**, 8319-8323.
11. H. Mansilla and M. M. Afonso, *Synth. Commun.*, 2008, **38**, 2607-2618.
12. A. Dutta Chowdhury and G. Kumar Lahiri, *Chem. Commun.*, 2012, **48**, 3448-3450.
13. J.-Y. Qi, J.-X. Ji, C.-H. Yueng, H.-L. Kwong and A. S. C. Chan, *Tet. Lett.*, 2004, **45**, 7719-7721.
14. Y. Luan, N. Zheng, Y. Qi, J. Tang and G. Wang, *Catal. Sci. Technol.*, 2014, **4**, 925-929.
15. Y. Luan, N. Zheng, Y. Qi, J. Yu and G. Wang, *Eur. J. Inorg. Chem.*, 2014, **2014**, 4268-4272.
16. H. Gao, Y. Luan, K. Chaikittikul, W. Dong, J. Li, X. Zhang, D. Jia, M. Yang and G. Wang, *ACS Appl. Mater. Interfaces*, 2015, **7**, 4667-4674.
17. M. a. R. Capeletti, L. Balzano, G. de la Puente, M. Laborde and U. Sedran, *App. Catal. A Gen.*, 2000, **198**, L1-L4.
18. D. Kumar, R. Kumar and A. K. Chakraborti, *Synthesis*, 2008, **2008**, 1249-1256.
19. R. Kumar, D. Kumar and A. K. Chakraborti, *Synthesis*, 2007, **2007**, 299-303.
20. M. Hong and G. Xiao, *J. Fluor. Chem.*, 2012, **140**, 121-126.
21. L. Myles, R. G. Gore, N. Gathergood and S. J. Connon, *Green Chem.*, 2013, **15**, 2740-2746.
22. Y. Wang, H. Zhi and J. Luo, *J. Mol. Catal. A Chem.*, 2013, **379**, 46-52.
23. Y. Mei, P. A. Bentley and J. Du, *Tet. Lett.*, 2009, **50**, 4199-4200.
24. R. Gopinath, S. J. Haque and B. K. Patel, *J. Org. Chem.*, 2002, **67**, 5842-5845.
25. W. Gong, B. Wang, Y. Gu, L. Yan, L. Yang and J. Suo, *Synth. Commun.*, 2004, **34**, 4243-4247.
26. N. Hamada, K. Kazahaya, H. Shimizu and T. Sato, *Synlett*, 2004, **2004**, 1074-1076.
27. H. Firouzabadi, N. Iranpoor and B. Karimi, *Synth. Commun.*, 1999, **29**, 2255-2263.
28. B. C. Ranu, R. Jana and S. Samanta, *Adv. Synth. Catal.*, 2004, **346**, 446-450.
29. J.-C. Ding, R. Xu, M.-C. Liu, X.-A. Chen and H.-Y. Wu, *J. Indian Chem. Soc.*, 2008, **85**, 566-568.
30. N. M. Leonard, M. C. Oswald, D. A. Freiberg, B. A. Nattier, R. C. Smith and R. S. Mohan, *J. Org. Chem.*, 2002, **67**, 5202-5207.
31. G.-Q. Li, W.-G. Shan, W.-K. Su and Z.-J. Yao, *Chinese J. Chem.*, 2007, **25**, 90-94.
32. B. M. Smith and A. E. Graham, *Tet. Lett.*, 2007, **48**, 4891-4894.
33. A. Corma and H. García, *Chem. Rev.*, 2003, **103**, 4307-4366.
34. D. B. G. Williams and M. C. Lawton, *Green Chem.*, 2008, **10**, 914-917.
35. R. Arias Ugarte, D. Devarajan, R. M. Mushinski and T. W. Hudnall, *Dalton Trans*, 2016, **45**, 11150-11161.

View Article Online
DOI: 10.1039/C6GC03629E

View Article Online
DOI: 10.1039/C6GC03629E



177x101mm (300 x 300 DPI)