



Metal triflates: On the question of Lewis versus Brønsted acidity in retinyl carbocation formation

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ABSTRACT

$\text{Al}(\text{OTf})_3$ generates blue carbocations from retinyl acetate. The mechanism appears to be exclusively water-derived induced Brønsted acidity causing loss of acetic acid, not Lewis-mediated acetate abstraction. Dry DCM (1 ppm water) avoided water interference. The hindered base 2,6-di-*tert*-butylpyridine, used to distinguish between Lewis- and Brønsted acidity, was also probed. The results implicate a possible mechanism for similar transformations involving carbocations.

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1. Introduction

Lewis acids are used to facilitate manifold organic transformations. We have recently shown the efficacy of $\text{Al}(\text{OTf})_3$ for the ring-opening of epoxides with alcohols [1] and amines [2], for atom-efficient acetal formation [3] and for the Pd-catalysed methoxycarbonylation reaction [4]. We compared the activity of triflic acid, argued [5] to be an hydrolysis product of metal triflates in the presence of water and sometimes also argued to be the active catalyst, against that of $\text{Al}(\text{OTf})_3$ and found significant differences between the two in terms of reactivity and reaction outcomes [1–4]. Similarly significant differences have been noted several times by others when using triflic acid for comparison purposes against metal triflate catalysts [6], pointing away from triflic acid as the active catalyst. In one case [6c], triflic acid fails to provide any product at all under the given conditions. Nonetheless, Lewis acids are known to induce Brønsted acidity by co-ordination of a protonic species to the metal centre, thereby polarising the X–H bond (X=heteroatom) and rendering it substantially more Brønsted acidic than the parent compound [7,8]. Indeed, many systems have been specifically designed with this induced Brønsted acidity in mind as the active catalyst [9].

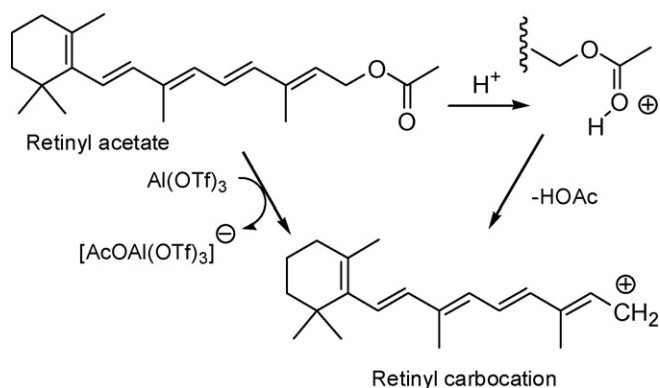
We have recently raised similar points [4], namely those that induced Brønsted acidity arising due to Al-bound MeOH may be one of the causative agents that improves the overall catalyst

efficiency in the $\text{Al}(\text{OTf})_3$ -mediated Pd-catalysed methoxycarbonylation reaction of styrene or 1-pentene. Others have also offered evidence for the implication of Brønsted acidity as the active catalyst entity in the presence of $\text{L}_2\text{Pt}(\text{OTf})_2$ species [8a] and of Lewis acids [8b].

Retinol and its acetate derivative (Scheme 1) have been used several times in order to demonstrate the presence of Brønsted acidity by the generation of retinyl carbocations, which display a characteristic blue colour in solution (Fig. 1) [10]. The present work discusses our efforts to unravel the possible formation of retinyl carbocations (Scheme 1) by direct acetate abstraction from retinyl acetate by $\text{Al}(\text{OTf})_3$. The results and conclusions may be relevant to a fundamental understanding of other studies, particularly as it relates to the intimate mechanism of substrate activation in the presence of metal triflate Lewis acids. For example, benzyl alcohols have recently been used as substrates for the benzylation of aromatic substrates (Friedel–Crafts chemistry) and of diketones amongst others, in the presence of several rare earth triflates [11,12]. The authors propose a mechanism for the observed benzylation reactions that relies on carbocation formation. They indicate that the carbocation intermediate is generated but not how it is generated.

Retinyl acetate (Scheme 1), when treated with a sufficiently strong Brønsted acid in various organic media such as alkanes or alcohols at low temperature [10], produces carbocations of sufficiently long lifetime to be detected visually or by UV–vis spectrophotometry. Such carbocations have high extinction coefficients ($\log \epsilon = 4.5\text{--}5$) and absorption maxima at about 600 nm (the exact λ_{max} value is influenced to some extent by its surrounding medium) [10], rendering sensitive their detection by UV–vis spec-

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Scheme 1. Retinyl carbocation formation.

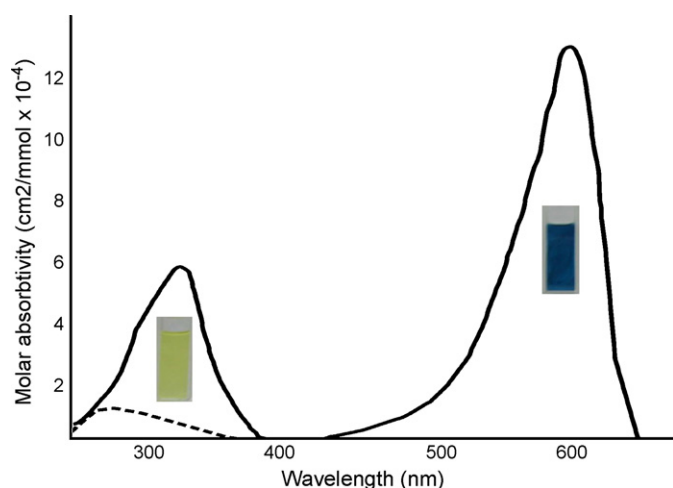


Fig. 1. UV-vis absorption spectra of DCM solutions of retinyl acetate (yellow/green) and retinyl carbocations (blue).

trophotometry. In fact, the molar absorptivity of the retinyl cation was measured in a mixture of methanol/concentrated sulfuric acid at -46°C [10]. Retinyl derivatives have also been used to detect Brønsted acidity on zeolites [13].

We herein probe the generation of retinyl carbocations making use of $\text{Al}(\text{OTf})_3$, one of the metal triflates that has been shown to be an excellent catalyst for several organic transformations [1–4]. Two possible routes/mechanisms towards the generation of such retinyl carbocations are envisaged. The first is by direct acetate abstraction while the second invokes induced Brønsted acidity as a consequence of Al-bound water. This work aims to shed some light, even if by inference in the more general case, on the generation of carbocations in the presence of Lewis acids.

2. Experimental

2.1. General

All manipulations were carried out in an MBraun glovebox under nitrogen. A Mettler Toledo Karl Fischer DL32 Coulometric diaphragm-based apparatus was used for determining water measurements. This instrument was housed within the glovebox to ensure the greatest accuracy and precision of the water measurements. Accuracy and precision of the instrument were measured using a certified Hydranal® 100 ppm water standard. A Carey 100 Conc UV-vis spectrophotometer was used with quartz cuvettes. All UV-vis measurements were performed while the instrument was being flushed with dry nitrogen at ambient temperature. A Mettler

Toledo DSC822e differential scanning calorimetry apparatus was used to track the $\text{Al}(\text{OTf})_3$ drying process. Dry solvents were prepared inside the glovebox by passage of the solvent over a column of activated alumina (activated at 250°C , 24 h).

2.2. Sample preparation

0.01 M and 0.001 M solutions of retinyl acetate were prepared in dichloromethane inside the glovebox. Equivolumes of stock solutions of triflic acid or $\text{Al}(\text{OTf})_3$ at 0.01 M or 0.001 M in dichloromethane were added to the retinyl acetate solution in a quartz cuvette. The capped cuvettes were rapidly transferred to the nitrogen-flushed UV-vis spectrophotometer.

3. Results and discussion

We found $\text{Al}(\text{OTf})_3$ to generate carbocations from retinyl acetate only weakly in diethyl ether at -50°C , primarily by virtue of limited solubility of the Lewis acid in this solvent at the low temperature and consequently investigated other solvents in which $\text{Al}(\text{OTf})_3$ may be more soluble.

Dichloromethane (DCM) was found to be more suitable to the solubilisation of $\text{Al}(\text{OTf})_3$ and, importantly, should not generate protons by O–H bond polarisation or ‘enolisation’ the way that the more polar methanol or nitromethane, sometimes used as co-solvents for metal triflates to enhance their solubility, might [7]. Nitrobenzene also provided adequate solubility but was not pursued in depth. Surprisingly, DCM sustained long-lived triflic acid-generated carbocations even at ambient temperature, providing UV-vis absorption profiles similar to those produced elsewhere [10]. The solution displays a light yellow colour prior to carbocation formation, an intense blue colour while carbocations are present and a dull green colour once the carbocations have decomposed. DCM has been used in many instances as a solvent to generate stabilised cations [14].

Pleasingly, $\text{Al}(\text{OTf})_3$ also allowed carbocations to be generated in DCM from retinyl acetate (albeit quite weakly so as compared to the presence of triflic acid). Such samples provided similar absorption spectra to those generated from the triflic acid (Fig. 2). Whatever the source of the activity of the system, *i.e.* the Lewis acid acting as acetate abstractor or induced Brønsted acidity causing loss of acetic acid from the retinyl acetate, the activity is significantly lower than that when triflic acid is used at identical or even ten times lower concentrations for this procedure. Barrett has previously found that $[\text{Yb}(\text{H}_2\text{O})_9](\text{OTf})_3$ failed to generate carbocations from solutions of retinol but that a mixture of the Yb triflate and a resorcinarene caused the formation of the highly coloured carbocation [15]. These

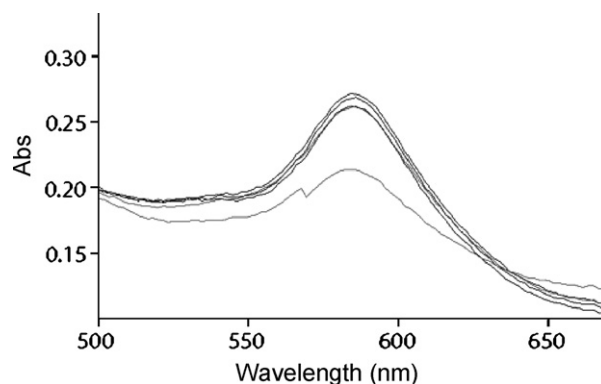
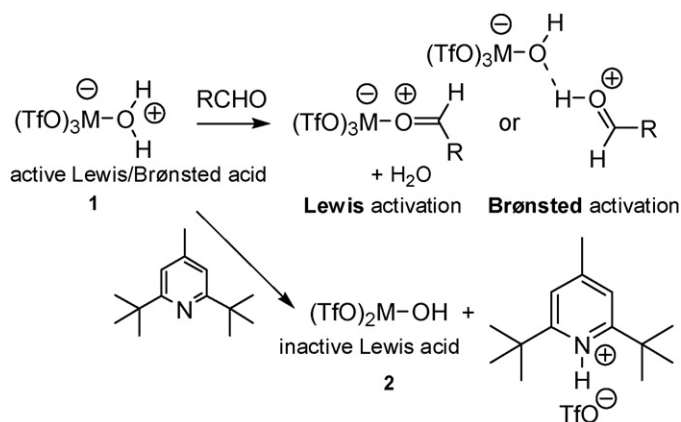


Fig. 2. UV-vis scans of ‘wet’ $\text{Al}(\text{OTf})_3$ and retinyl acetate in dry DCM showing weak carbocation formation.



Scheme 2. Metal triflate mode of action and deactivation mechanism.

results suggest the formation of a strong Brønsted acid under those conditions.

2,6-Di-*tert*-butylpyridine and its 4-methyl analogue have been used to discriminate between Lewis and Brønsted acidity [16]. This application is based on work that demonstrates steric hindrance on N-bound protons in such di-*tert*-butyl systems manifesting in unusual $\text{p}K_{\text{a}}$ values for such bases in 2,6-dialkylpyridine series [17]. The 2,6-di-*tert*-butylpyridine is about 1.4 $\text{p}K_{\text{a}}$ units weaker a base than expected and about 0.8 $\text{p}K_{\text{a}}$ units weaker a base than pyridine. This base has been found to react with HCl but not with BF_3 [18], a feature that has been put to use in subsequent work to distinguish not only between Brønsted and Lewis acids but also between accessible and hindered acid sites in zeolites [19]. The notion of steric hindrance even to the proton shown by this base is supported by earlier work demonstrating relatively low rates of protonation thereof [20]. In the context of metal triflates, quenching of catalytic ability by this base has been interpreted to implicate triflic acid as the catalytically active species [5]. However, the possibility of Lewis acid deactivation (and thus also catalyst deactivation) according to the process shown in Scheme 2 cannot be ignored. The Scheme shows two possible ways in which a Lewis base may be activated (using an aldehyde purely as an example), since the $(\text{TfO})_3\text{M}-\text{OH}_2$ species (**1**) possesses simultaneously both Lewis acidity and Brønsted acidity. Conversion of the metal triflate into a metal hydroxide species **2** by the pyridine base would diminish/quench both Lewis and Brønsted acidity, providing a plausible explanation to the loss of catalyst ability of the metal triflate (especially since even ‘dry’ organic solvents contain significant amounts of residual water [21]: without having to invoke the presence of triflic acid as a necessary concomitant to metal hydrolysis).

In our case, a three-fold excess [5b] of 2,6-di-*tert*-butyl-4-methylpyridine with respect to the Lewis acid, when added to the $\text{Al}(\text{OTf})_3$ -DCM solution, completely quenched the activity of the Lewis acid, which consequently failed to generate carbocations in the presence of the base; a similar feature was observed when adding the base to the triflic acid-DCM solution as would be expected. This observation hints that the carbocations are generated by induced Brønsted acidity in the presence of $\text{Al}(\text{OTf})_3$. Such induced Brønsted acidity presumably arises from water in the DCM solvent, which was shown by Karl Fischer titration to be present at 24 ppm ($n=6$, $\sigma=1.2$ ppm). Since base-promoted conversion of the active Lewis acid into an hydroxide complex such as **2** of significantly lower activity cannot be excluded as the mechanism of quenching of the observed activity (Scheme 2), it was proposed to dry the solvent with the aim of altogether removing the possibility of producing Al-bound water species (Scheme 2) that could act as

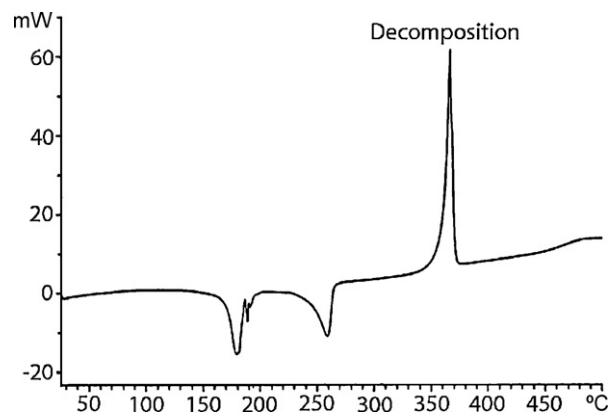


Fig. 3. Differential scanning calorimetry scan of ‘wet’ commercial grade $\text{Al}(\text{OTf})_3$ showing two endotherms and decomposition exotherm.

sources of Brønsted acidity. In this way, the presence or absence of activity towards carbocation formation could be more strongly linked to Lewis or Brønsted acidity.

Given the alternative activation/deactivation possibilities presented in Scheme 2, it occurred to us that a more direct method of demonstrating Lewis versus Brønsted ability was required. In order to eliminate the possibility of induced Brønsted acidity, the DCM was dried to 1 ppm water (Karl Fischer titration, $n=6$, $\sigma=0.3$ ppm) by passage thereof over activated neutral alumina in a glovebox. The carbocation formation experiment was repeated. UV-vis spectrophotometry showed weak carbocation formation, despite having used dried solvent. This activity was also effectively quenched in the presence of the pyridine base. That the activity of the system was much lower than in wet DCM already indicated more strongly that water-derived Brønsted acidity was causative of carbocation formation. To produce the driest system possible, the $\text{Al}(\text{OTf})_3$ was heated under vacuum to dryness (120°C , 0.01 mm Hg), as shown by differential scanning calorimetry (DSC): commercial grade $\text{Al}(\text{OTf})_3$ produced a DSC scan with two endotherms arising due to the presence of water (at ca. 180°C and 260°C , Fig. 3), while the dried Al compound showed a flat line DSC scan that ended in a decomposition exotherm at about 365°C . The endotherms could be recreated by brief periods of exposure of the dried sample to the atmosphere. The higher temperature endotherm was the first to return, while longer periods of exposure also allowed the lower temperature endotherm to be seen again. The retinyl acetate solution in dry DCM, prepared in a glovebox to ensure the integrity of the dried samples, was treated with the dried $\text{Al}(\text{OTf})_3$ and no carbocation formation at all was noted.

When considering the literature references cited that provide comparative studies involving triflic acid, together with the results obtained with the 2,6-di-*tert*-butylpyridine as a base which discriminates between Lewis and Brønsted acids, and the results of the experiments in dry solvents, the observations very strongly suggest that retinyl carbocation formation in the presence of $\text{Al}(\text{OTf})_3$ is exclusively precipitated by induced Brønsted acidity as the causative agent. It further strongly indicates that Al-bound water is what gives rise to such induced Brønsted acidity. Indeed, the B-water complex $\text{H}_2\text{O}\cdot\text{B}(\text{C}_6\text{F}_5)_3$ has been crystallographically characterised and has been used to protonate, and hence to oxidise, several metallocenes [22]. This acid source provides $[(\text{C}_6\text{F}_5)_3\text{B}(\text{OH})\cdot\text{H}_2\text{O}\cdot\text{B}(\text{C}_6\text{F}_5)_3]^-$ as the counterion to the metallocene cation $[\text{M}(\text{III})(\eta\text{-C}_5\text{H}_5)_2]^+$. In these instances, the B-bound water also acts as a strong Brønsted acid, similar to that which we propose here as the active species in the retinyl carbocation formation in the presence of $\text{Al}(\text{OTf})_3$ in wet solvents.

4. Conclusions

The work discussed in this paper points away from direct acetate abstraction from retinyl acetate by the Al entity as the mechanism of retinyl carbocation formation. Rather, it indicates that induced Brønsted acidity through Al-bound water is causative. This is despite the relatively high hydrolysis constant of Al(III) [23], which would lead to the supposition that Al(OTf)₃ readily hydrolyses to HOTf – but the experimental evidence [[1–4,6], present study] points against this mechanism of action. It distinctively shows that, in the present instance, Al(OTf)₃ is not only water tolerant but is water-dependent for its activity. It is possible that other reactions performed making use of metal triflates also proceed *via* this mechanism of induced water-derived Brønsted acidity (Lewis-assisted Brønsted acidity [9,15]) acting as the active catalyst. The results highlight the possibility that a variety of metal triflate-promoted organic transformations that proceed *via* cationic intermediates may be catalysed (or co-catalysed) by water-derived Lewis-assisted Brønsted acidity rather than directly or exclusively by Lewis acidity. Such (co)catalysis and activation of water is well-known in biochemistry and is one of the activation mechanisms in Zn-containing hydrolytic enzymes [24] and their synthetic biomimetics [25]. Finally, the discussion here and elsewhere [8] highlights the need to carefully consider the role of hindered pyridine bases in assessing the nature of the active catalyst and its mode of action.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.molcata.2009.10.023.

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