

NJC

Accepted Manuscript



This is an *Accepted Manuscript*, which has been through the Royal Society of Chemistry peer review process and has been accepted for publication.

Accepted Manuscripts are published online shortly after acceptance, before technical editing, formatting and proof reading. Using this free service, authors can make their results available to the community, in citable form, before we publish the edited article. We will replace this *Accepted Manuscript* with the edited and formatted *Advance Article* as soon as it is available.

You can find more information about *Accepted Manuscripts* in the [Information for Authors](#).

Please note that technical editing may introduce minor changes to the text and/or graphics, which may alter content. The journal's standard [Terms & Conditions](#) and the [Ethical guidelines](#) still apply. In no event shall the Royal Society of Chemistry be held responsible for any errors or omissions in this *Accepted Manuscript* or any consequences arising from the use of any information it contains.

Catalytic intramolecular carbonyl-ene reaction with ketones: evidence for a retro-ene process†

Received 00th May 2015,
Accepted 00th 2015

P. Tremel^a, C. Iacobucci^a, L. Massi^a, S. Olivero^a, J.-F. Gal^a and E. Duñach*^a

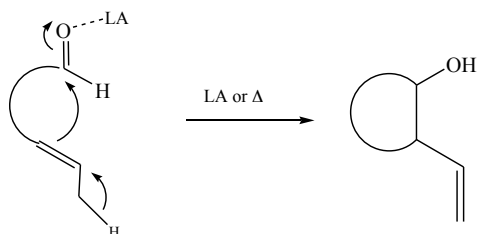
DOI: 10.1039/x0xx00000x

www.rsc.org/

The ene-process with unsaturated ketones was catalyzed by Lewis acids such as bismuth or indium triflates. Unlike aldehydes, the reverse ene-process occurs with ketones, resulting in incomplete conversions, as shown by control experiments and analysis by ESI-MS.

Introduction

Since the description by K. Alder of the « ene » reaction in 1943, this rearrangement has been shown to be a useful methodology in organic synthesis.¹ The carbonyl-ene reaction has been widely reported, either under thermal conditions² or under Lewis acid catalysis.³ It mainly concerns inter- or intramolecular reactions of unsaturated aldehydes which afford homoallylic alcohols (Scheme 1).



Scheme 1. Intramolecular carbonyl-ene reaction. (LA = Lewis Acid)

Catalysis by a variety of Lewis acids has been reported, for example with AlMe₂Cl,⁴ ZnCl₂,⁵ SnCl₂,⁶ or BF₃.OEt₂,⁷ mostly used in stoichiometric amounts. Catalytic and/or asymmetric processes using chiral ligands have also been reported,⁸ in particular with titanium(IV),⁹ chromium(III)¹⁰ or copper(I)¹¹ derivatives and with ytterbium(III)¹² or bismuth(III) triflates.¹³ Examples concerning the carbonyl-ene reaction involving ketones are scarce; they generally need electron-withdrawing groups on the carbonyl moiety to enhance its electrophilicity, as for reactions involving trifluoromethyl ketones¹⁴ or α -ketoesters,¹⁵ generally using stoichiometric amounts of Lewis

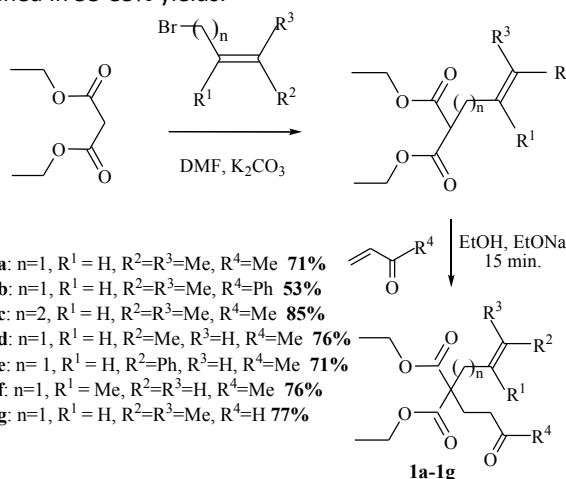
acids. Non-activated ketones have only been reported in specific cases with excess AlCl₃¹⁶ or AlMe₂Cl.¹⁷

We present here our studies on the catalytic ene reaction with non activated ketones, together with some kinetic experiments and their analysis by mass spectrometry.

Results and Discussion

Reactivity of model ketone compounds

Interested in the catalytic activity of strong Lewis acids derived from triflic and triflimidic acids,¹⁸ we prepared a series of unsaturated ketones **1a-1f** and aldehyde **1g**, via a first diethyl malonate alkylation with several allylic bromides, followed by a Michael addition on diversely substituted α,β -enone derivatives (Scheme 2). The unsaturated ketones were obtained in 53-85% yields.

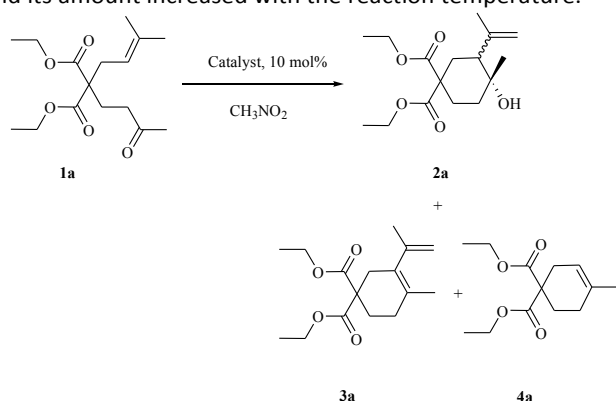


Scheme 2. Preparation of unsaturated ketones **1a-1f** and unsaturated aldehyde **1g**.

^a Institut de Chimie de Nice, UMR 7272, Université Nice Sophia Antipolis, CNRS, Parc Valrose, 06108 Nice Cedex 2 France.

† Electronic Supplementary Information (ESI) available: ¹H and ¹³C NMR, MS and ESI-MS data. See DOI: 10.1039/x0xx00000x

Ketone **1a**, bearing a trisubstituted double bond, was chosen as a model compound for examining the catalytic activity of several metal triflates and triflimides in nitromethane solutions at different temperatures. Whereas Bi(OTf)₃ and In(OTf)₃ were commercially available, Fe(OTf)₂, In(NTf₂)₃ and In(NTf₂)₃ were prepared according to electrochemical or sonochemical procedures.¹⁹ The expected product from the ene reaction of **1a** was the cyclic alcohol **2a** (*cis/trans* diastereoisomers), as illustrated in Scheme 3. The reaction led also to the diene **3a**, issued from the alcohol dehydration, together with the non-expected compound **4a**. The formation of **4a** could be explained by an intramolecular-type hydroalkoxylation from **2a**,²⁰ evolving towards loss of acetone. The loss of acetone in a similar case has already been reported by the stoichiometric use of BF₃·Et₂O.²¹ This cyclohexene derivative **4a** was formed in low yields at room temperature and its amount increased with the reaction temperature.



Scheme 3. Reactivity of substrate **1a** in the ene reaction.

Interestingly, products **2-4** arise all from a first ene-reaction with the starting unsaturated ketone. As illustrated in Table 1, at 25 °C, the best conversions were attained with Bi(OTf)₃ and In(OTf)₃ catalysts (entries 1, 2); use of In(III) triflate resulted in better conversion than the corresponding triflimide (entries 2, 3). The Fe(II) salts were poorly active (entries 4, 5). Bi(OTf)₃ showed also a good catalytic activity at 0 °C (entry 6), and all the tested catalysts converted **1a** at refluxing nitromethane (101 °C, entries 8-10).

Table 1 Catalyst screening for the carbonyl-ene reaction with ketone **1a** in nitromethane.^a

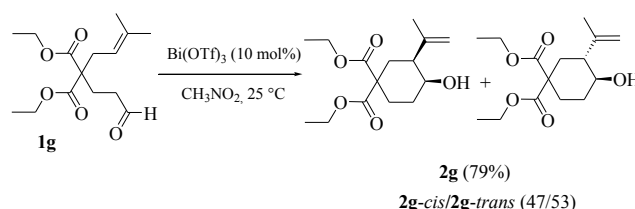
Entry	Catalyst (Temp., Time)	Conv. of 1a (%)	Yield of ene products 2+3+4	Selectivities		
				2a (<i>cis:trans</i>)	3a	4a
1	Bi(OTf) ₃ (25 °C, 5 h)	85	32	41 (59:41)	50	9
2	In(OTf) ₃ (25 °C, 5 h)	63	43	60 (92:8)	33	7
3	In(NTf ₂) ₃ (25 °C, 5 h)	40	31	65 (80:20)	25	10
4	Fe(NTf ₂) ₂ (25 °C, 5 h)	18	18	83 (58:42)	11	6
5	Fe(OTf) ₂	33	29	97	3	-

		(25 °C, 5 h)			(62:38)	
6	Bi(OTf) ₃ (0 °C, 5 h)	82	49	60 (69:31)	33	7
7	In(OTf) ₃ (0 °C, 4 h)	58	58	86 (74:26)	9	5
8	In(NTf ₂) ₃ (101 °C, 14 h)	85	58	7 (75:25)	62	31
9	Fe(NTf ₂) ₂ (101 °C, 2 h)	86	60	Traces	60	39
10	Fe(NTf ₂) ₂ (101 °C, 5 h)	100	34	-	26	74

^a General conditions: **1a** (1 mmol) in distilled nitromethane (5 mL) with the catalyst (0.1 mmol, 10 mol%), stirring at the reported temperature. Yields are calculated by GC analysis using dodecane as internal standard.

The results of Table 1 indicate that the ene reaction with non-activated ketones was possible with catalytic amounts of selected strong Lewis acids. The formation of the ene-products (**2a** + **3a** + **4a**) occurred in up to 49% yield with Bi(OTf)₃ at 0 °C (entry 6). With In(OTf)₃, the ene-products reached 58% yield at 0 °C (entry 7) and 60% with Fe(NTf₂)₂ (entry 9), though in this case with formation of the elimination compounds **3a** and **4a**, only. Concerning the formation of alcohol **2a**, Bi(III) and In(III) triflates showed the best yields. A diastereoselectivity **2a-cis/2a-trans** of 92:8 was reached with In(OTf)₃ at 25 °C (entry 2).

In contrast with these results, when comparing with those of the corresponding ene reaction of the analogous aldehyde **1g**, the reaction catalyzed by Bi(OTf)₃ at 25 °C led cleanly to **2g-cis/2g-trans** in 79% yield with a 47/53 isomer ratio (Scheme 4). No elimination processes were observed in this case.



Scheme 4. Ene reactivity of aldehyde substrate **1g**.

Evidence for a retro-ene reaction

The follow-up of the reaction of **1a** by GC analysis indicated the initial formation of alcohols **2a** and their further conversion into **3a** and/or **4a**. The amount of diene **3a** slowly diminished with time, due to its slow polymerization. The increase of the reaction temperature led generally to higher elimination ratios. We also observed that at low temperature, the ene reaction seemed to reach equilibrium. In particular, with **1a** and indium triflate (10 mol %) in dry nitromethane under nitrogen atmosphere at -5 °C and at 0 °C, the concentration of the different compounds remained stable after 2 hours reaction, with 42% of **1a**, the two isomeric alcohols **2a-cis** and **2a-trans** in 50% yield and a 74:26 ratio

respectively, and only a very small amount of compounds **3a** and **4a** (see entry 7 of Table 1).

This observation led us to hypothesize a possible reversibility of the ene reaction for such ketone substrates,²² reversibility that may also explain the moderate yields and the incomplete conversions achieved.

Thus, after isolation of **2a-cis** and **2a-trans**, we separately tested the reactivity of the two alcohols in order to prove the occurrence of a retro-ene reaction.

The two isomeric alcohols **2a-cis** and **2a-trans** were treated individually with 10% of $\text{In}(\text{OTf})_3$ in dry nitromethane, under nitrogen atmosphere at -5°C . Their reaction kinetics were followed by GC/MS using dodecane as internal reference (Figure 1). These experiments indicated that both alcohols **2a-cis** and **2a-trans** underwent a retro-ene reaction to the starting **1a**. Interestingly, the different kinetic profiles of the two diastereomeric alcohols indicated that only the **2a-trans** isomer underwent direct elimination reactions to **3a** and **4a**. In contrast, **2a-cis** led only to isomerization via the retro-ene reaction; after reformation of **1a**, the resulting **2a-trans** was responsible for the appearance of the further elimination products and formation of **2a-cis**.

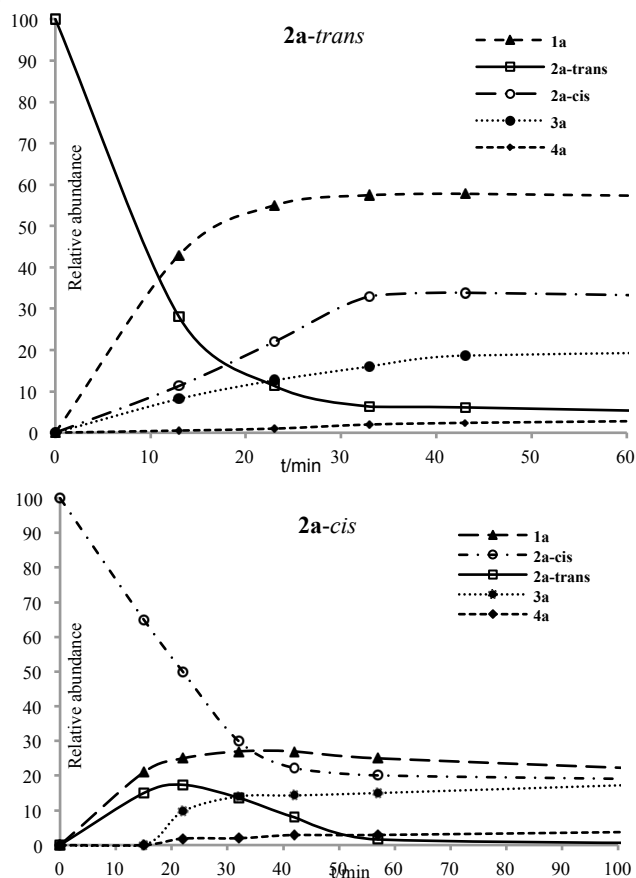
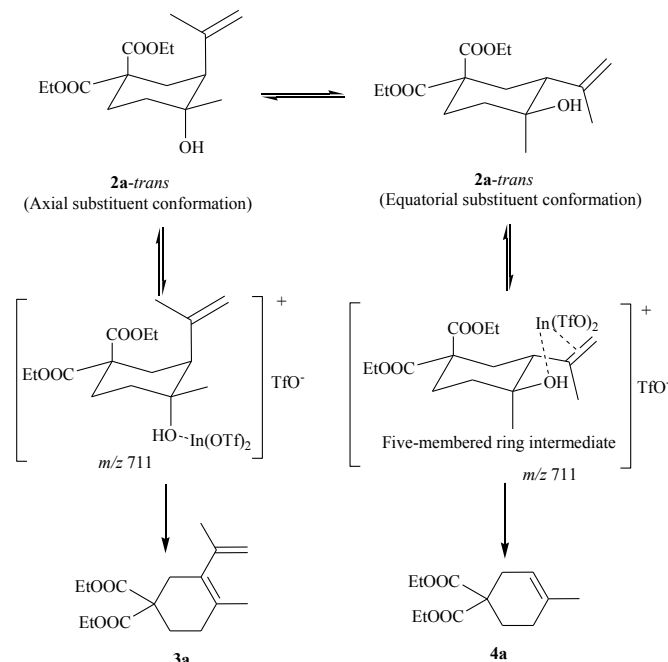


Figure 1. Evolution of the retro-ene reactions of **2a-trans** and **2a-cis** in the presence of $\text{In}(\text{OTf})_3$ (10 mol %) in dry nitromethane, under nitrogen atmosphere, at -5°C , as measured by GC analysis using dodecane as internal standard.

This evidence is in agreement with the lower yield obtained for the isomer **2a-trans** as compared to that of **2a-cis** in the reaction of **1a** and suggests that the diastereoselectivity

observed in the presence of $\text{In}(\text{OTf})_3$, derives from stereoselective eliminations reactions rather than from the initial ene reaction.

Looking more precisely at the unexpected loss of acetone, **2a-trans** is the only isomer with the hydroxyl group and the double bond close enough to form an indium five-membered ring intermediate, leading to elimination (Scheme 5). The ESI-MS follow-up of the reaction mixture (see next section) shows an indium cationic species at m/z 711, that could correspond to these transient species.



Scheme 5. Evolution of **2a-trans** to dehydration product **3a** and/or to acetone elimination **4a**, catalysed by $\text{In}(\text{OTf})_3$.

From the kinetic study, evidence was obtained for the first time of a retro-ene reaction in the case of an unsaturated ketone. Moreover, it was shown that both alcohol-ene diastereoisomers, **2a-cis** and **2a-trans** behaved differently in the presence of the Lewis acid.

ESI-MS investigation

To get some more insight on the ene-reaction with ketone **1a**, we investigated the reaction mechanism by mass spectrometry.

During the last few years, mass spectrometry (MS) has gained widespread acceptance as a technique for mechanistic studies of organic reaction and catalysis.²³⁻²⁵ In this context, electrospray ionization (ESI), owing to its "soft" character, occupies a prominent position at the interface between the ions and ionizable species existing in solution and those observed in the gas phase.

The reaction mixture compositions may be followed over time by the so-called source capability of "fishing" ionic or ionizable intermediates from the solution. In favorable cases, crucial species with short life-times at very low concentrations can be effectively transferred from the reaction mixture to the gas

phase where they become stable enough to be characterized. In particular, this would be of interest in characterizing organometallic intermediates with their entire coordination sphere.²⁶ Recently, several MS studies yielded detailed information about elementary reaction steps of important reactions²⁷ such as the Heck^{28,29} or the Stille coupling,³⁰ the Baylis-Hillman,³¹⁻³⁴ or the Biginelli reactions³⁵⁻³⁷ or some gold-catalyzed reactions.^{38,39}

Electrospray mass spectrometry may be also used to investigate the Lewis acid/base interactions involving adducts of metal triflate (or triflimide) salts with organic functionalities.⁴⁰

An ESI-MS screening of the catalytic systems employed in Table 1 was realized, in order to optimize electrospray ionization process in nitromethane solutions. The use of nitromethane as ESI-solvent has already been reported in the context of characterization of metal triflates by ESI-MS.⁴¹ This preliminary study led us to choose $\text{In}(\text{OTf})_3$ among the tested Lewis acids, as the best candidate for the ene-reaction investigation. In fact, nitromethane solutions of indium triflate resulted in excellent quality electrospray spectra and this catalyst led to an adapted reaction rate for detecting possible reaction intermediates.

We performed off-line ESI-MS screening of the reaction mixture by infusing periodically a nitromethane solution of **1a** in the presence of 10% of $\text{In}(\text{OTf})_3$. The ESI-MS spectra collected over time showed the gradual formation of the expected products **2a**, **3a** and **4a** as protonated species, respectively at m/z 299, 281 and 241 and revealed the presence of adducts containing indium and organic substrates (Figure 2). These intercepted organo-indium adducts suggested that the cycloisomerization proceeds through a metal-based catalysis involving the activation of the carbonyl moiety.

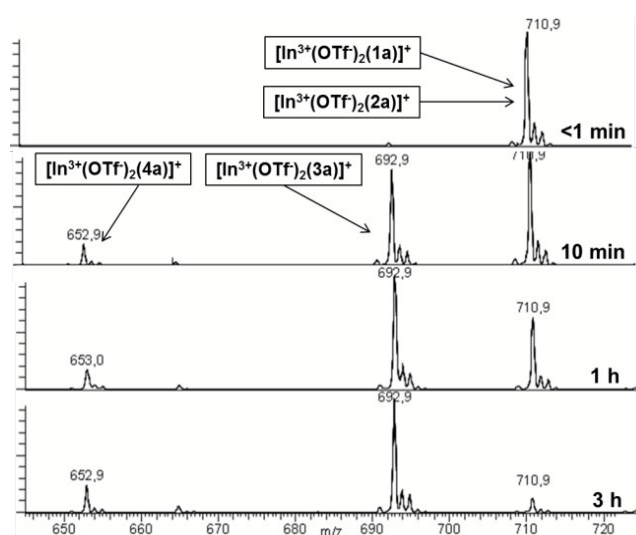


Figure 2. Evolution of ESI-MS spectra: ESI-MS over time monitoring of **1a** in the presence of $\text{In}(\text{OTf})_3$.

Since compounds **1a** and **2a** have the same mass, it should be noted that the ion at m/z 299 can be the protonated form of

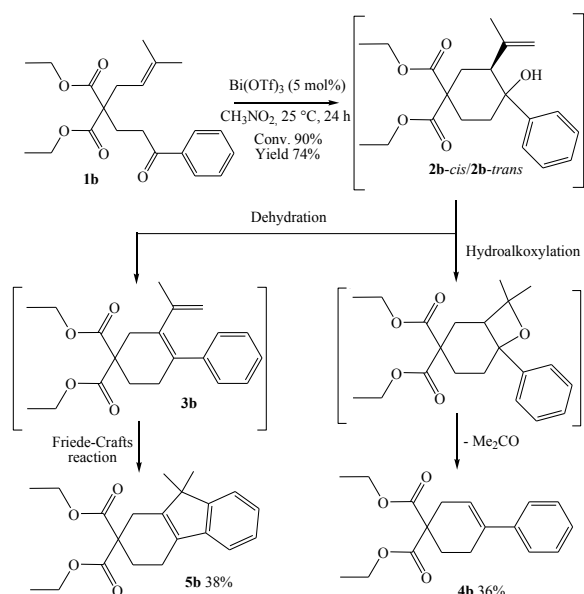
1a or of **2a**. Similarly, the ion at m/z 711 could correspond to both $[\text{In}(\text{OTf})_2(\mathbf{1a})]^+$ and $[\text{In}(\text{OTf})_2(\mathbf{2a})]^+$. These two isobaric species are particularly interesting because they could be the two organometallic intermediates responsible firstly for the ene-reaction and secondly for the elimination reactions. A set of experiments were planned to assign the peaks at m/z 299 and at m/z 711 found in full scan MS spectra. ESI-MS/MS spectra of these ions were collected at several collision energies during the reaction monitoring experiments.

In addition to MS/MS spectra recorded over time, two other experiments were carried out in order to shorten the dead time of the ESI-MS reaction monitoring. The first one consisted in mixing nitromethane solutions of **1a** and $\text{In}(\text{OTf})_3$ in a T-shape microreactor directly coupled to the ESI source of the mass spectrometer. This configuration reduces the dead time down to a few seconds. In the second set-up, the $\text{In}(\text{OTf})_3$ solution was injected through the sheath liquid source inlet, while **1a** was injected using the regular inlet. This setting produced two coaxial flows that mixed only at the stage of the Taylor cone, less than one second before ionization (see SI data). Therefore, this sheath liquid interface appears to be particularly relevant to the study of reaction mechanisms.

All these spectra were compared with those recorded from nitromethane solutions containing only the purified product **2a**. In all cases, the MS/MS spectra were essentially indistinguishable, suggesting that, even in the gas phase, **2a** underwent a fast retro-ene reaction and it further followed the same fragmentation pattern as for **1a**.

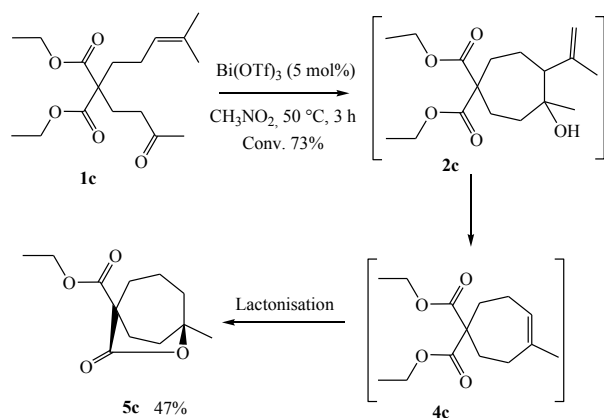
Extension to other substrates

The ene-reaction was extended to other unsaturated ketones under $\text{Bi}(\text{OTf})_3$ catalysis. Thus, the phenyl ketone **1b** was reacted according to Scheme 6, to afford compounds **4b** and **5b** in 74% overall yield. Both products arose from a first ene reaction of **1b**. Compound **4b** is formed from the ene-intermediate **2b** (not isolated) after acetone elimination. The formation of **5b** could be explained by a first dehydration of **2b** to **3b**, followed by a Friedel-Crafts cyclization in the presence of the Lewis acid (Scheme 6).⁴²



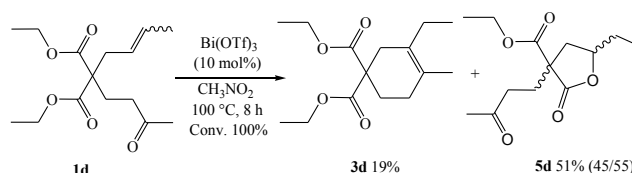
Scheme 6. Ene reaction products obtained from **1b**.

Compound **1c**, bearing a methyl ketone group and a trisubstituted double bond (but on a longer unsaturated side-chain), reacted to afford the bicyclic compound **5c** in 47% yield with a 73% conversion (Scheme 7). The formation of **5c** could be explained through a first ene reaction to afford the seven-membered ring alcohol **2c**, followed by acetone elimination to **4c** and further lactonization. The Lewis acid-catalyzed lactonization of unsaturated esters has already been reported.⁴²



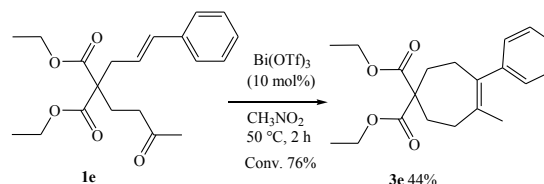
Scheme 7. Formation of lactone **5c**.

We then turned our interest to ketones with a 1,2-disubstituted double bond, such as **1d** or **1e** (Schemes 8, 9). In these cases, the elimination of acetone was not to be expected. The ene reaction with **1d** afforded the water elimination product **3d** in 19% yield. The main product was the lactone **5d**, issued from the reaction of one of the ester groups of **1d** with the double bond (Scheme 8).



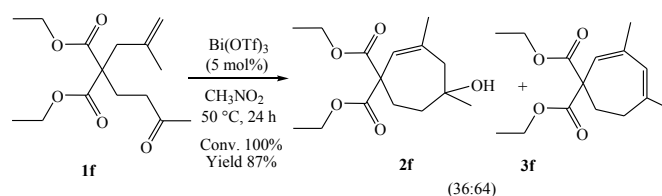
Scheme 8. Reactivity of **1d** with $\text{Bi}(\text{OTf})_3$ catalysis.

In the presence of $\text{Bi}(\text{OTf})_3$ (10 mol%), ketone **1e** led to the seven-membered ring **3e** as the main compound in 44% yield, with 76% conversion (Scheme 9).



Scheme 9. Formation of a seven-membered **3e** ring from the ene reaction of unsaturated ketone **1e**.

The substituted ketone **1f** afforded the expected ene products **2f** and **3f** in 87% overall yield, in a 36:64 ratio (Scheme 10).



Scheme 10. Ene reaction of ketone **1f**.

Experimental Section

Typical carbonyl-ene reaction procedure

To a nitromethane solution (5 mL, anhydrous and degassed) of the catalyst (0.05 to 0.1 mmol) was added the substrate **1** (1 mmol) at the desired temperature under a N_2 atmosphere. The consumption of the starting material was monitored by GC-FID analysis. The reaction mixture was quenched with 5 mL of water and extracted by 3 x 5 mL of diethyl ether. After concentration of organic phases, the residue was purified by silica gel chromatography to afford the ene compounds.

Electronic Supplementary Information available: Spectral data for the obtained compounds and ESI-MS conditions and experiments.

Conclusions

In conclusion, the ene-process with unsaturated ketones can be catalyzed by Lewis acids, in particular by $\text{In}(\text{OTf})_3$ and $\text{Bi}(\text{OTf})_3$; nevertheless, it suffers from the low stability of the tertiary alcohol products formed. Dehydration is one of the main side-reactions observed. The reverse ene-process can

also occur, resulting in incomplete conversions, as shown by control experiments. The results with ketones bearing terminal dimethyl substituted double bonds indicate that the ene reaction can be followed by acetone elimination.

The carbonyl-ene reaction with unsaturated ketones was examined by following the formation of products and by ESI-MS analysis of the reacting solutions in the early stage of the reaction. Some insight on organometallic intermediates and on reaction mechanism was gained by this approach.

Acknowledgements

We thank the French ANR project ALEA (2013-009-01) for financial support. The authors are grateful to Galderma R&D, Sophia-Antipolis, for the gift of mass spectrometers to our institute.

Notes and references

- M. L. Clarke and M. B. France, *Tetrahedron*, 2008, **64**, 9003.
- M. I. Johnston, J. A. Kwass, R. B. Beal and B. B. Snider, *J. Org. Chem.* 1987, **52**, 5419. K. Mikami, H. Matsueda and T. Nakai, *Synlett*, 1993, 23. H. Helmboldt and M. Hiersemann, *J. Org. Chem.*, 2009, **74**, 1698.
- B. B. Snider, *Acc. Chem. Res.*, 1980, **13**, 426.
- M. I. Johnston, J. A. Kwass, R. B. Beal and B. B. Snider, *J. Org. Chem.*, 1987, **52**, 5419. J. Robertson, G. O'Connor, C. L. Ringrose and D. S. Middleton, *Tetrahedron*, 2000, **56**, 8321. F. Alonso, M. Rodriguez-Fernandez, D. Sanchez, M. Yus, *Eur. J. Org. Chem.*, **2011**, 6459.
- V. K. Aggarwal, G. P. Vennall, P. N. Davey and C. Newman, *Tetrahedron Lett.*, 1998, **39**, 1997.
- N. H. Andersen, S. W. Hadley, J. D. Kelly and E. R. Bacon, *J. Org. Chem.*, 1985, **50**, 4144. L. A. Paquette and Y. K. Han, *J. Am. Chem. Soc.* 1981, **103**, 1835.
- . Alcaide, P. Almendros, C. Pardo, C. Rodriguez-Ranera and A. Rodriguez-Vicente, *J. Org. Chem.*, 2003, **68**, 3106. A. Srikrishna and V. H. Pardeshi, *Tetrahedron*, 2010, **66**, 8160.
- K. Mikami and M. Shimizu, *Chem. Rev.*, 1992, **92**, 1021.
- K. Mikami, M. Terada and T. Nakai, *J. Am. Chem. Soc.*, 1989, **111**, 1940 and *J. Am. Chem. Soc.*, 1990, **112**, 3949. K. Mikami, M. Terada, E. Sawa and T. Nakai, *Tetrahedron Lett.*, 1991, **32**, 6571.
- M. L. Grachan, M. T. Tudge and E. N. Jacobsen, *Angew. Chem. Int. Ed.*, 2008, **47**, 1469.
- D. A. Evans, C. S. Burgey, N. A. Patras, T. Vojkovsky and S. W. Tregay, *J. Am. Chem. Soc.*, 1998, **120**, 5824. D. A. Evans, S. W. Tregay, C. S. Burgey, N. A. Patras and T. Vojkovsky, *J. Am. Chem. Soc.*, 2000, **122**, 7936.
- P. C. Page, G. Gambera, C. M. Hayman and M. Edgar, *Synlett*, 2006, 3411.
- E. D. Anderson, J. J. Erenat, M. P. Nguyen, A. C. Palma and R. S. Mohan, *Tetrahedron Lett.*, 2005, **46**, 7747.
- M. Sridhar, C. Narsaiah, B. C. Ramanaiah, V. M. Ankathi, R. B. Pawar and S. N. Asthana, *Tetrahedron Lett.*, 2009, **50**, 1777. C. Aubert and J. P. Begue, *Tetrahedron Lett.*, 1988, **29**, 1011. A. Abouabdellah, C. Aubert, J. P. Begue, D. Bonnetdelpon and J. Guilhem, *J. Chem. Soc. Perkin Trans 1*, 1991, 1397.
- Y.-J. Zhao, B. Li, L.-J. Serena, Z.-L. Shen and T.-P. Loh, *J. Am. Chem. Soc.*, 2010, **132**, 10242. D. Yang, M. Yang and N.-Y. Zhu, *Org. Lett.*, 2003, **5**, 3749.
- L. E. Overman and D. Lesuisse, *Tetrahedron Lett.*, 1985, **26**, 4167.
- C. M. Cheung, D. Craig and R. S. Todd, *Synlett*, 2001, 1611.
- S. Antoniotti, V. Dalla and E. Duñach, *Angew. Chem. Int. Ed.* 2010, **49**, 7860.
- I. Favier and E. Duñach, *Tetrahedron Lett.*, 2003, **44**, 2031. E. Duñach, I. Favier, D. Hébrault and J. R. Desmurs, *Appl. Pat.*, Fr 2818994, **2002**. N. Legrave, A. Couhert, S. Olivero, J. R. Desmurs and E. Duñach, *Eur. J. Org. Chem.*, 2012, 901. E. Duñach, S. Antoniotti, S. Olivero and J. R. Desmurs, PCT Int. Appl. (2012), WO 2012010752.
- L. Coulombel, M. Rajzmann, J.-M. Pons, S. Olivero and E. Duñach, *Chem. - Eur. J.*, 2006, **12**, 6356. X. Chaminade, L. Coulombel, S. Olivero and E. Duñach, *Eur. J. Org. Chem.*, 2006, **16**, 3554.
- A. Soicke, N. Slavov, J.-M. Neudörfl and H.-G. Schmalz, *Synlett*, 2011, **17**, 2487.
- J. L. Ripoll, Y. Landais, *Synthesis*, **1993**, 659.
- L. S. Santos (Ed.), *Reactive Intermediates: MS Investigations in Solution*, Wiley-VCH, Weinheim, Germany, 2010.
- F. Coelho and M. N. Eberlin, *Angew. Chem. Int. Ed.*, 2011, **23**, 5261.
- D. Schröder, *Acc. Chem. Res.*, 2012, **45**, 1521.
- K. L. Vikse, Z. Ahmadi and J. S. McIndoe, *Coord. Chem. Rev.* 2014, **279**, 96.
- F. M. Nachtigall, M. N. Eberlin, *Organic Reaction Studies by ESI-MS*, in *Reactive Intermediates: MS Investigations in Solution* (Ed. L. S. Santos), Wiley-VCH, Weinheim, Germany, 2010, Chapter 3.
- S. A. Adão, A. H. L. Machado, C. R. D. Correia and M. N. Eberlin, *Angew. Chem. Int. Ed.*, 2004, **43**, 2514.
- T. de A. Fernandes, B. G. Vaz, M. N. Eberlin, A. J. M. Da Silva and P. R. R. Costa, *J. Org. Chem.*, 2010, **75**, 7085.
- S. L. Silva, G. B. Rosso, R. A. Pilli and M. N. Eberlin, *J. Org. Chem.*, 2007, **72**, 5809.
- S. L. Silva, C. H. Pavam, W. P. Almeida, F. Coelho and M. N. Eberlin, *Angew. Chem. Int. Ed.*, 2004, **43**, 4330.
- S. L. Silva, B. A. DaSilveira Neto, C. S. Consorti, C. H. Pavam, W. P. Almeida, F. Coelho, J. Dupont and M. N. Eberlin, *J. Phys. Org. Chem.*, 2006, **19**, 731.
- G. W. Amarante, H. M. S. Milagre, B. G. Vaz, B. R. Vilachã Ferreira, M. N. Eberlin and F. Coelho, *J. Org. Chem.*, 2009, **74**, 3031.
- R. Thais, V. G. Santos, M. N. Godoi, B. G. Vaz, M. N. Eberlin and F. Coelho, *Chem. Commun.*, 2011, **47**, 6593.
- R. O. M. A. De Souza, E. T. Da Penha, H. Milagre, S. J. Garden, P. M. Esteves, M. N. Eberlin and O. A. C. Antunes, *Chem. Eur. J.*, 2009, **15**, 9799.
- L. M. Ramos, C. G. Bruna, C. C. Nobrega, J. R. Corrêa, R. G. Silva, H. C. B. De Oliveira, A. F. Gomes, F. C. Gozzo and B. A. D. Neto, *Chem. Eur. J.*, 2013, **19**, 4156.
- L. M. Ramos, A. Y. Ponce de Leon y Tobio, M. R. Dos Santos, H. C. B. De Oliveira, A. F. Gomes, F. C. Gozzo, A. L. De Oliveira and B. A. D. Neto, *J. Org. Chem.*, 2012, **77**, 10184.
- J. Roithová, Š. Janková, L. Jašíková, J. Váňa, S. Hybelbauerová, *Angew. Chem. Int. Ed.*, 2012, **51**, 8378.
- A. Simonneau, F. Jaroschik, D. Lesage, M. Karanik, R. Guillot, M. Malacria, J.-C. Tabet, J.-P. Goddard, L. Fensterbank, V. Gandon and Y. Gimbert, *Chem. Sci.*, 2011, **12**, 2417.
- I. Monfardini, L. Massi, E. Duñach, S. Olivero, J. F. Gal, *Chem. Commun.* **2010**, 46, 8472-8474. J. F. Gal, C. Iacobucci, I. Monfardini, L. Massi, E. Duñach and S. Olivero, *J. Am. Soc. Mass Spectrom.*, 2012, **23**, 2059.
- I. Monfardini, L. Massi, P. Tremel, A. Hauville, S. Olivero, E. Duñach and J.-F. Gal, *Rapid Commun. Mass Spectrom.*, 2010, **24**, 2611.
- B. Cacciottolo, S. Poulain-Martini and E. Duñach, *Eur. J. Org. Chem.*, 2011, 3710.
- F. Grau, A. Heumann and E. Duñach, *Angew. Chem. Int. Ed.* 2006, **45**, 7285.