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

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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.

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## 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.<sup>1</sup> The carbonyl–ene reaction has been widely reported, either under thermal conditions<sup>2</sup> or under Lewis acid catalysis.<sup>3</sup> It mainly concerns inter- or intramolecular reactions of unsaturated aldehydes which afford homoallylic alcohols (Scheme 1).

Catalysis by a variety of Lewis acids has been reported, for example with AlMe<sub>2</sub>Cl,<sup>4</sup> ZnCl<sub>2</sub>,<sup>5</sup> SnCl<sub>2</sub><sup>6</sup> or BF<sub>3</sub>.OEt<sub>2</sub>,<sup>7</sup> mostly used in stoichiometric amounts. Catalytic and/or asymmetric processes using chiral ligands have also been reported,<sup>8</sup> in particular with titanium(rv),<sup>9</sup> chromium(m)<sup>10</sup> or copper(n)<sup>11</sup> derivatives and with ytterbium(m)<sup>12</sup> or bismuth(m) triflates.<sup>13</sup> 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 ketones<sup>14</sup> or  $\alpha$ -ketoesters,<sup>15</sup> generally using stoichiometric



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

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amounts of Lewis acids. Non-activated ketones have only been reported in specific cases with excess  $AlCl_3^{16}$  or  $AlMe_2Cl_3^{17}$ 

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,<sup>18</sup> 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  $\alpha$ , $\beta$ -enone derivatives (Scheme 2). The unsaturated ketones were obtained in 53–85% yields.



Scheme 2 Preparation of unsaturated ketones  ${\bf 1a-1f}$  and unsaturated aldehyde  ${\bf 1g}.$ 

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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)<sub>3</sub> and In(OTf)<sub>3</sub> were commercially available,  $Fe(OTf)_2$ ,  $In(NTf_2)_3$  and  $In(NTf_2)_3$  were prepared according to electrochemical or sonochemical procedures.<sup>19</sup> 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 intramoleculartype hydroalkoxylation from 2a,<sup>20</sup> evolving towards loss of acetone. The loss of acetone in a similar case has already been reported by the stoichiometric use of BF<sub>3</sub>·Et<sub>2</sub>O.<sup>21</sup> This cyclohexene derivative 4a was formed in low yields at room temperature and its amount increased with the reaction temperature.

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)<sub>3</sub> and In(OTf)<sub>3</sub> catalysts (entries 1 and 2); use of In(m) triflate resulted in better conversion than the corresponding triflimide (entries 2 and 3). The Fe(n) salts were poorly active (entries 4 and 5). Bi(OTf)<sub>3</sub> 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).

The results of Table 1 indicate that the ene reaction with non-activated ketones was possible with catalytic amounts of



Scheme 4 Ene reactivity of aldehyde substrate 1g

selected strong Lewis acids. The formation of the ene-products (2a + 3a + 4a) occurred in up to 49% yield with Bi(OTf)<sub>3</sub> at 0 °C (entry 6). With In(OTf)<sub>3</sub>, the ene-products reached 58% yield at 0 °C (entry 7) and 60% with Fe(NTf<sub>2</sub>)<sub>2</sub> (entry 9), though in this case with formation of the elimination compounds **3a** and **4a**, only. Concerning the formation of alcohol **2a**, Bi(m) and In(m) triflates showed the best yields. A diastereoselectivity **2a**-*cis*/**2a**-*trans* of 92 : 8 was reached with In(OTf)<sub>3</sub> 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.

#### 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,<sup>22</sup> reversibility that may also explain the moderate yields and the incomplete conversions achieved.

Table 1       Catalyst screening for the carbonyl-ene reaction with ketone 1a in nitromethane <sup>a</sup>						
Entry	Catalyst (Temp., time)	Conv. of <b>1a</b> (%)	Yield of ene products <b>2</b> + <b>3</b> + <b>4</b>	Selectivities		
				2a (cis:trans)	3a	4a
1	$Bi(OTf)_3$ (25 °C, 5 h)	85	32	41 (59:41)	50	9
2	In(OTf) <sub>3</sub> (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	$Fe(OTf)_{2}$ (25 °C, 5 h)	33	29	97 (62:38)	3	_
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 <sub>2</sub> ) <sub>3</sub> (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 <sub>2</sub> ) <sub>2</sub> (101 °C, 5 h)	100	34	—	26	74

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

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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  $In(OTf)_3$  in dry nitromethane, under nitrogen atmosphere at -5 °C. Their reaction kinetics were followed by GC/MS using dodecane as internal reference (Fig. 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*.

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 In(OTf)<sub>3</sub>, 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 a indium five-membered



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



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

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.

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.<sup>23–25</sup> 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.<sup>26</sup> Recently, several MS studies yielded detailed information about elementary reaction steps of important reactions<sup>27</sup> such as the Heck<sup>28,29</sup> or the Stille coupling,<sup>30</sup> the Baylis–Hillman,<sup>31–34</sup> or the Biginelli reactions<sup>35–37</sup> or some gold-catalyzed reactions.<sup>38,39</sup> 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.<sup>40</sup>

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.<sup>41</sup> This preliminary study led us to choose  $In(OTf)_3$  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  $In(OTf)_3$ . 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 (Fig. 2). These intercepted organo-indium adducts suggested that the cycloisomerization proceeds through a metal-based catalysis involving the activation of the carbonyl moiety.

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  $[In(OTf)_2(1a)]^+$  and  $[In(OTf)_2(2a)]^+$ . 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  $In(OTf)_3$  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  $In(OTf)_3$  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 ESI† 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  $Bi(OTf)_3$  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).<sup>42</sup>

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.<sup>43</sup>



Fig. 2 Evolution of ESI-MS spectra: ESI-MS over time monitoring of **1a** in the presence of In(OTf)<sub>3</sub>.



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



We then turned out our interest to ketones with a 1,2disubstituted double bond, such as 1d or 1e (Schemes 8 and 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).

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

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



Scheme 8 Reactivity of 1d with Bi(OTf)<sub>3</sub> catalysis.



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



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 guenched with 5 mL of water and extracted by  $3 \times 5$  mL of diethyl ether. After concentration of organic phases, the residue was purified by silica gel chromatography to afford the ene compounds.

## Conclusions

In conclusion, the ene-process with unsaturated ketones can be catalyzed by Lewis acids, in particular by In(OTf)<sub>3</sub> and Bi(OTf)<sub>3</sub>; nevertheless, it suffers from the low stability of the tertiary alcohol products formed. Dehydration is one of the main sidereactions 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.

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## Notes and references

- 1 M. L. Clarke and M. B. France, Tetrahedron, 2008, 64, 9003.
- 2 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.
- 3 B. B. Snider, Acc. Chem. Res., 1980, 13, 426.
- 4 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. Ringrosse and D. S. Middleton, Tetrahedron, 2000, 56, 8321; F. Alonso, M. Rodriguez-Fernandez, D. Sanchez and M. Yus, Eur. J. Org. Chem., 2011, 6459.
- 5 V. K. Aggarwal, G. P. Vennall, P. N. Davey and C. Newman, Tetrahedron Lett., 1998, 39, 1997.
- 6 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.
- 7 B. Alcaide, P. Almendros, C. Pardo, C. Rodriguez-Ranera and A. Rodriguez-Vicente, J. Org. Chem., 2003, 68, 3106;

NJC

- 8 K. Mikami and M. Shimizu, Chem. Rev., 1992, 92, 1021.
- 9 K. Mikami, M. Terada and T. Nakai, J. Am. Chem. Soc., 1989, 111, 1940; K. Mikami, M. Terada and T. Nakai, J. Am. Chem. Soc., 1990, 112, 3949; K. Mikami, M. Terada, E. Sawa and T. Nakai, Tetrahedron Lett., 1991, 32, 6571.
- 10 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.
- 12 P. C. Page, G. Gambera, C. M. Hayman and M. Edgar, Synlett, 2006, 3411.
- 13 E. D. Anderson, J. J. Ernat, 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.
- 15 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.
- 16 L. E. Overman and D. Lesuisse, Tetrahedron Lett., 1985, 26, 4167.
- 17 C. M. Cheung, D. Craig and R. S. Todd, Synlett, 2001, 1611.
- 18 S. Antoniotti, V. Dalla and E. Dunach, Angew. Chem., Int. Ed., 2010, 49, 7860.
- 19 I. Favier and E. Duñach, *Tetrahedron Lett.*, 2003, 44, 2031;
  E. Duñach, I. Favier, D. Hébrault and J. R. Desmurs, *Appl. Pat.*, Fr2818994, 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.*, WO2012010752, 2012.
- 20 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, 3554.
- 21 A. Soicke, N. Slavov, J.-M. Neudörfl and H.-G. Schmalz, *Synlett*, 2011, 2487.
- 22 J. L. Ripoll and Y. Landais, Synthesis, 1993, 659.
- 23 Reactive Intermediates: MS Investigations in Solution, ed. L. S. Santos, Wiley-VCH, Weinheim, Germany, 2010.
- 24 F. Coelho and M. N. Eberlin, Angew. Chem., Int. Ed., 2011, 23, 5261.
- 25 D. Schröder, Acc. Chem. Res., 2012, 45, 1521.

- 26 K. L. Vikse, Z. Ahmadi and J. S. McIndoe, *Coord. Chem. Rev.*, 2014, **279**, 96.
- 27 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, ch. 3.
- 28 S. A. Adão, A. H. L. Machado, C. R. D. Correia and M. N. Eberlin, Angew. Chem., Int. Ed., 2004, 43, 2514.
- 29 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.
- 30 S. L. Silva, G. B. Rosso, R. A. Pilli and M. N. Eberlin, J. Org. Chem., 2007, 72, 5809.
- 31 S. L. Silva, C. H. Pavam, W. P. Almeida, F. Coelho and M. N. Eberlin, *Angew. Chem., Int. Ed.*, 2004, **43**, 4330.
- 32 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.
- 33 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.
- 34 R. Thais, V. G. Santos, M. N. Godoi, B. G. Vaz, M. N. Eberlin and F. Coelho, *Chem. Commun.*, 2011, 47, 6593.
- 35 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.
- 36 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.
- 37 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.
- 38 J. Roithová, Š. Janková, L. Jašíková, J. Váňa and S. Hybelbauerová, Angew. Chem., Int. Ed., 2012, 51, 8378.
- 39 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, 2(12), 2417.
- 40 I. Monfardini, L. Massi, E. Duñach, S. Olivero and 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.
- 41 I. Monfardini, L. Massi, P. Tremel, A. Hauville, S. Olivero,
  E. Duñach and J.-F. Gal, *Rapid Commun. Mass Spectrom.*, 2010, 24, 2611.
- 42 B. Cacciuttolo, S. Poulain-Martini and E. Duñach, *Eur. J. Org. Chem.*, 2011, 3710.
- 43 F. Grau, A. Heumann and E. Duñach, *Angew. Chem., Int. Ed.*, 2006, **45**, 7285.