Solvent-free Knoevenagel reaction catalysed by reusable pyrrolidinium base protic ionic liquids (PyrrILs): synthesis of long-chain alkylidenes†

R. C. M. Alves Sobrinho, a P. M. de Oliveira, a C. R. Montes D’Oca, a D. Russowsky b and M. G. Montes D’Oca∗a

In this work, an efficient and reusable pyrrolidinium ionic liquid (PyrrIL) catalysis system was developed and used in a Knoevenagel condensation reaction of long-chain aldehydes with several 1,3-dicarbonyl compounds. The Knoevenagel condensation promoted by the PyrrILs proceeded smoothly and cleanly in solvent-free conditions, yielding good quantities of the condensation products, long-chain alkylidenes. Moreover, this catalysis system was recyclable at least four times, and no significant loss of activity was observed. This protocol has notable advantages, such as ease of workup and convenient reuse of the ionic liquid, which could help reduce disposal costs and contribute to the development of new catalysts in chemical processes.

Introduction

The Knoevenagel condensation is a powerful, general, versatile and significant reaction for the formation of carbon–carbon bonds.1,2 The classic Knoevenagel transformation3 occurs between aldehydes and active methylene hydrogen compounds, with ammonia or another amines as catalysts in organic solvents. The reaction is considered to be a modification of the aldol condensation.4

The synthesis of benzyldienes or alkylidenes, important intermediate products, via the Knoevenagel reaction is largely related to structural variations in different nucleophiles, such as 1,3-ketoesters,5 diketones,2 ketothioesters,2 malonates, malonoritriles,6 keto amides, and cyclic esters, and with different aromatic7 or aliphatic aldehydes.8 Recently, long-chain alkylidene malonates (LoCAMs) have been identified with a novel class of KATs (protein acetyltransferase) modulators, and pentadecyldiene malonate, a simplified analogue of anacardic acid, exhibits a good modulation of the activity of histone acetyltransferases (Fig. 1).8

Another example comes from the total synthesis of the anticoagulant flocoumafen. The key synthetic step involves Knoevenagel condensation with ethyl cyanoacetate and p-methoxybenzaldehyde in the presence of acetic acid and pyrrolidine; this process generates an excellent yield of the desired product.9

In addition, different catalytic systems (such as amines5), Lewis acids, and solvents (such as benzene,5 toluene, dichloromethane10 and tetrahydrofuran) have been used, and Knoevenagel condensation in ionic liquids was recently demonstrated as a strongly solvent-dependent process.11

The use of a triethylamine–toluene system in place of pyridine was shown to provide ease of handling, separation, and recycling of the solvent and the catalyst. In that case, the synthesis of cinnamic acids was successfully performed using a pyridine-free Knoevenagel condensation, either in the presence of triethylamine as a solvent or in combination with toluene with catalytic amounts of piperidine.12

Knoevenagel condensation of β-ketothioesters with various aldehydes proceeds efficiently in the presence of molecular sieves (MS 5A), and molecular sieves in CH2Cl2 was the most effective. The reaction was examined using several β-ketothioesters and β-ketoesters with various aromatic and aliphatic aldehydes, and the Knoevenagel adducts were obtained in

![Fig. 1 KAT inhibitors and activator: anacardic acid and pentadecyldiene malonate, respectively.](image-url)
yields of 20% to 95%. In this work the reaction conditions were mild, and no self-condensation products of the aldehydes were observed. The amount of aldehydes can be reduced to 1.5 equiv. without affecting the yield, although a longer reaction time is necessary. The use of excessive amounts (4–6 equiv.) of aliphatic aldehydes in some cases is necessary to obtain a sufficient yield of the products in a reduced reaction time when the reaction is slow.

According to the literature, a large number of β- and β,β-substituted Morita–Baylis–Hillman (MBH) adducts can be synthesised using Knoevenagel condensation in piperidine and acetic acid or Lewis acid. For the synthesis of β-ketoesters, it was demonstrated that the stereoselectivity of the reaction is improved by alteration of various substituents on the ketone and ester group and various aldehydes. In addition, a Z-selective Knoevenagel condensation can be achieved by the use of tert-butyl acetoacetate with either aromatic or aliphatic aldehydes, although this results in low chemical yield.

In recent years, ionic liquids (ILs) have emerged as a greener alternative to commonly used organic solvents and catalysts. Their characteristics, combined with their low volatility, non-flammable nature, thermal stability, and capacity for reuse as catalysts, have made ILs an environmentally friendly option for organic synthesis.

Initially, Knoevenagel condensation was investigated using several classic 1,3-dicarbonyl compounds (β-ketoesters, 1,3-diketones, Meldrum’s acid, and malonates) with long aldehydes in a solvent-free media.

Under ultrasonic irradiation, hexamethylenetetramine (HMTA)–AcOH–H2O, a protic ionic liquid (PIL) solvent–catalyst, has been used in the Knoevenagel reaction of aromatic aldehydes with ethyl 2-cyanoacetate. However, in solvent-free conditions, the mixture solidifies as soon as the catalyst is added, making the reaction yield low.

Anouti et al. detailed the synthesis and characterisation of ILs using pyrrolidine as the cation source and different organic and inorganic anions in an easily reproducible experimental procedure. They found that pyrrolidinium-based protic ILs could be obtained in a relatively low cost and low toxicity and exhibit a large electrochemical window compared to other protic ILs. In addition, PyrrILs are superionic liquids with wide application for fuel cell devices, thermal transfer fluids, and acid-catalysed reaction media as an alternative to conventional inorganic acids.

As part of our ongoing efforts to synthesise new fatty derivatives, in this study, we describe the use of PyrILs 1–3 derived from formate, acetate, and trifluoroacetate (Fig. 2) as a catalyst to the synthesis of long-chain alkylidenes. The Knoevenagel reaction was investigated using several classic 1,3-dicarbonyl compounds (β-ketoesters, 1,3-diketones, Meldrum’s acid, and malonates) with long aldehydes in a solvent-free media.

Results and discussion

Initially, Knoevenagel condensation was investigated using the classic experimental protocol, and the catalysts pyrrolidine (Pyr) or piperidine (Pip) and acetic acid were added directly to a reactional flask containing both 1,3-dicarbonyl compound

![Fig. 2 Pyrrolidinium ionic liquids (PyrrILs) 1–3.](Image)

| Table 1 Synthesis of long-chain alkylidene 6g from Knoevenagel condensation |
|---|---|---|---|---|
| Ent. | Catalyst | Loading (mol%) | T (°C) | Time (h) | Yield (%) |
| 1 | Pyrr + CH3COOH | 10 | 0 | 3 | 60 |
| 2 | Pip + CH3COOH | 10 | 0 | 3 | 63 |
| 3 | [Pyrr][HCOO], 1 | 10 | 0 | 1.5 | 69 |
| 4 | [Pyrr][CH3COO], 1 | 10 | 0 | 1.5 | 80 |
| 5 | [Pyrr][CF3COO], 1 | 10 | 0 | 1.5 | 68 |
| 6 | [Pyrr][CH3COO], 2 | 5 | 0 | 1.5 | 65 |
| 7 | [Pyrr][CH3COO], 2 | 20 | 0 | 1.5 | 60 |
| 8 | [Pyrr][CH3COO], 2 | 10 | −20 | 1.5 | 56 |
| 9 | [Pyrr][CH3COO], 2 | 10 | 20 | 1.5 | 65 |
| 10 | [Pip][CH3COO] (solid catalyst) | 10 | 0 | 1.5 | 70 |

* Reaction performed with CH2Cl2 (2 mL), with addition of pyrrolidine or piperidine and acetic acid directly to the reactional flask.
Table 2  Synthesis of long-chain alkylidenes 6a–l under catalysis with pyrrolidinium acetate (2, [Pyrr][CH₃COO])

<table>
<thead>
<tr>
<th>Entry</th>
<th>Aldehydes (4a–g)</th>
<th>5a–c</th>
<th>Alkylidenes (6a–q)</th>
<th>Yield (%), (E : Z ratio)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4a</td>
<td>5a</td>
<td>6a</td>
<td>83 (1 : 2)</td>
</tr>
<tr>
<td>2</td>
<td>4b</td>
<td>5a</td>
<td>6b</td>
<td>77 (1 : 1.8)</td>
</tr>
<tr>
<td>3</td>
<td>4c</td>
<td>5a</td>
<td>6c</td>
<td>80 (1 : 1.5)</td>
</tr>
<tr>
<td>4</td>
<td>4d</td>
<td>5a</td>
<td>6d</td>
<td>89 (1 : 2.1)</td>
</tr>
<tr>
<td>5</td>
<td>4e</td>
<td>5a</td>
<td>6e</td>
<td>72 (1 : 2)</td>
</tr>
<tr>
<td>6</td>
<td>4f</td>
<td>5a</td>
<td>6f</td>
<td>90 (1 : 2.1)</td>
</tr>
<tr>
<td>7</td>
<td>4g</td>
<td>5a</td>
<td>6g</td>
<td>80 (1 : 2.5)</td>
</tr>
<tr>
<td>8</td>
<td>4h</td>
<td>5b</td>
<td>6h</td>
<td>70</td>
</tr>
<tr>
<td>9</td>
<td>4i</td>
<td>5c</td>
<td>6i</td>
<td>73</td>
</tr>
<tr>
<td>10</td>
<td>4j</td>
<td>5d</td>
<td>6j</td>
<td>70</td>
</tr>
<tr>
<td>11</td>
<td>4k</td>
<td>5e</td>
<td>6k</td>
<td>90</td>
</tr>
<tr>
<td>12</td>
<td>4l</td>
<td>5f</td>
<td>6l</td>
<td>95</td>
</tr>
</tbody>
</table>
The Knoevenagel reaction between long-chain dodecanaldehyde (4g) and methyl acetoacetate (5a) was tested with loading of 10 mol% of catalyst at 0°C and in the presence of anhydrous methylene chloride. The reactions were monitored by thin-layer chromatography (TLC), and the consumption of aldehyde was measured. However, pyrrolidine and piperidine in the presence of acetic acid each demonstrated low yields of the product 6g after 3 h. The results are shown in Table 1, entries 1 and 2, respectively.

Based on these results, we decided to investigate the Knoevenagel reaction employing PyrrILs 1–3 (Fig. 2).

The PyrrILs 1–3 were obtained using the same experimental protocol described by Anouti et al. The nuclear magnetic resonance spectroscopic data of PyrrILs were in agreement with the literature. Next, the behaviour and catalytic activity of the heterogeneous PyrrILs 1–3 were initially investigated in the Knoevenagel condensation between dodecanaldehyde (4g) and methyl acetoacetate (5a) using 10 mol% of catalyst at 0°C in a solvent-free condition.

The reaction using PyrrIL 1 was monitored by TLC and the total consumption of aldehyde 4g was observed after 1.5 h at 0°C. At this point, the reaction was considered complete, and a 69% yield of product 6g was recorded (Table 1, entry 3). Then PyrrILs 2 and 3 were tested with loading of 10 mol% under the same experimental conditions (Table 1, entries 4 and 5). Better catalytic behaviour was observed with pyrrolidinium acetate (2) (80%, Table 1, entry 4) than with the catalysts pyrrolidinium trifluoroacetate (3) and pyrrolidinium formate (1) (Table 1, entries 5 and 3, respectively).

The loading of catalyst 2 was then investigated, with the reactions performed with 5 mol% and 20 mol% (Table 1, entries 6 and 7, respectively). The use of 5 mol% provided a 65% yield of the product (Table 1, entry 6), while the use of 20 mol% resulted in a lower yield (Table 1, entry 7). Thus, 10 mol% was chosen for the Knoevenagel reactions catalysed by PyrrIL (Table 1, entry 4).

Next, we studied the influence of temperature on the reactions. In addition to performing the reactions at 0°C, the reactions were performed at −20°C and 20°C (Table 1, entries 8 and 9). Both temperatures resulted in lower yields than the reactions at 0°C (Table 1, entries 3–7).

In addition, the Knoevenagel reaction employing 10 mol% of piperidinium acetate ([Pip][CH₃COO]) was investigated. The catalyst [Pip][CH₃COO] was obtained from stoichiometric amount of piperidine and acetic acid using the same experimental protocol used for PyrrIL synthesis. The [Pip][CH₃COO] was isolated by crystallization in dry toluene. The reaction using

<table>
<thead>
<tr>
<th>Entry</th>
<th>Aldehydes (4a–g)</th>
<th>5a–c</th>
<th>Alkylidenes (6a–q)</th>
<th>Yield (%), [E : Z ratio]*</th>
</tr>
</thead>
<tbody>
<tr>
<td>13</td>
<td><img src="4d" alt="Image" /></td>
<td><img src="5e" alt="Image" /></td>
<td><img src="6m" alt="Image" /></td>
<td>92</td>
</tr>
<tr>
<td>14</td>
<td><img src="4f" alt="Image" /></td>
<td><img src="5e" alt="Image" /></td>
<td><img src="6n" alt="Image" /></td>
<td>85</td>
</tr>
<tr>
<td>15</td>
<td><img src="4g" alt="Image" /></td>
<td><img src="5e" alt="Image" /></td>
<td><img src="6o" alt="Image" /></td>
<td>85</td>
</tr>
<tr>
<td>16</td>
<td><img src="4h" alt="Image" /></td>
<td><img src="5e" alt="Image" /></td>
<td><img src="6p" alt="Image" /></td>
<td>80</td>
</tr>
<tr>
<td>17</td>
<td><img src="4i" alt="Image" /></td>
<td><img src="5e" alt="Image" /></td>
<td><img src="6q" alt="Image" /></td>
<td>83</td>
</tr>
</tbody>
</table>

* Ratio determined by gas chromatography/mass spectrometry.

Table 2 (Contd.)

and aldehyde. The Knoevenagel reaction between long-chain dodecanaldehyde (4g) and methyl acetoacetate (5a) was tested with loading of 10 mol% of catalyst at 0°C and in the presence of anhydrous methylene chloride. The reactions were monitored by thin-layer chromatography (TLC), and the consumption of aldehyde was measured. However, pyrrolidine and piperidine in the presence of acetic acid each demonstrated low yields of the product 6g after 3 h. The results are shown in Table 1, entries 1 and 2, respectively.

Based on these results, we decided to investigate the Knoevenagel reaction employing PyrrILs 1–3 (Fig. 2).

The PyrrILs 1–3 were obtained using the same experimental protocol described by Anouti et al. The nuclear magnetic resonance spectroscopic data of PyrrILs were in agreement with the literature. Next, the behaviour and catalytic activity of the heterogeneous PyrrILs 1–3 were initially investigated in the Knoevenagel condensation between dodecanaldehyde (4g) and methyl acetoacetate (5a) using 10 mol% of catalyst at 0°C in a solvent-free condition.

The reaction using PyrrIL 1 was monitored by TLC and the total consumption of aldehyde 4g was observed after 1.5 h at 0°C. At this point, the reaction was considered complete, and a 69% yield of product 6g was recorded (Table 1, entry 3). Then PyrrILs 2 and 3 were tested with loading of 10 mol% under the same experimental conditions (Table 1, entries 4 and 5). Better catalytic behaviour was observed with pyrrolidinium acetate (2) (80%, Table 1, entry 4) than with the catalysts pyrrolidinium trifluoroacetate (3) and pyrrolidinium formate (1) (Table 1, entries 5 and 3, respectively).

The loading of catalyst 2 was then investigated, with the reactions performed with 5 mol% and 20 mol% (Table 1, entries 6 and 7, respectively). The use of 5 mol% provided a 65% yield of the product (Table 1, entry 6), while the use of 20 mol% resulted in a lower yield (Table 1, entry 7). Thus, 10 mol% was chosen for the Knoevenagel reactions catalysed by PyrrIL (Table 1, entry 4).

Next, we studied the influence of temperature on the reactions. In addition to performing the reactions at 0°C, the reactions were performed at −20°C and 20°C (Table 1, entries 8 and 9). Both temperatures resulted in lower yields than the reactions at 0°C (Table 1, entries 3–7).

In addition, the Knoevenagel reaction employing 10 mol% of piperidinium acetate ([Pip][CH₃COO]) was investigated. The catalyst [Pip][CH₃COO] was obtained from stoichiometric amount of piperidine and acetic acid using the same experimental protocol used for PyrrIL synthesis. The [Pip][CH₃COO] was isolated by crystallization in dry toluene. The reaction using
this solid catalyst [Pip][CH₃COO] was monitored by TLC and resulted in a 70% yield of the product 6g (Table 1, entry 10).

From these results, it was concluded that the best conditions for the Knoevenagel reaction to synthesis of long-chain alkyldene 6g would employ PyrrIL 2, synthesised singly, at a load of 10 mol% at 0 °C (Table 1, entry 4).

Thus, the Knoevenagel reaction employing PyrrIL 2 was investigated using classic 1,3-dicarbonyl compounds (β-ketoesters, 1,3-diketones, Meldrum’s acid, and malonates) with long-chain aldehydes. This same experimental protocol was used for the synthesis of long-chain alkyldenes 6a–q from alkyl aldehydes 4a–g and 1,3-dicarbonyl compounds 5a–e (Table 2).

All tested examples resulted in good to reasonable alkyldene yields (70–95%), demonstrating the catalytic effectiveness of PyrrIL 2 in the several alkyldene syntheses. These results indicate that Knoevenagel condensation possesses catalytic versatility and efficiency, even in the presence of 1,3-dicarbonyl compounds with different pKₐ values, resulting in good yields of the products (Table 2, entries 7–17). As expected, good yields were observed in reactions performed with methyl acetooxocetate (Table 2, entries 1–7) and lower yields were observed with ethyl malonate (70%, Table 2, entry 10). Moreover, only the enol 6i from aldol product was observed in reaction performed with dimesidol (5e) (73%, Table 2, entry 9). The best results were obtained when Meldrum’s acid was used as the 1,3-dicarbonyl compound (80–95%, Table 2, entries 11–17).

Based on the literature, a tentative mechanistic pathway of the Knoevenagel reaction to synthesis of long-chain alkyldenes catalysed by PyrrIL 2 is proposed. We believe that the reaction may proceed through the formation of a partial oxonium ion formed from long-chain aldehyde and PyrrIL 2 (Scheme 1). The reaction of the oxonium ion, which is sufficiently electrophilic, with the enol form of 1,3-dicarbonyl compounds, together with the loss of H₂O, could lead to formation of the long-chain alkyldenes.

In addition, all PyrrILs tested (1–3) were insoluble in the reaction medium (Fig. 3); therefore, repeated reuse tests were performed. For this purpose, the reactions were scaled up, with the same optimised experimental conditions maintained. Repeated experiments were carried out with dodecanaldehyde (4g) and methyl acetooxocetate (5a) and 10 mol% of [Pyr] [CH₃COO] (2) at 0 °C. After each cycle, the PyrrIL 2 was decanted by centrifugation in the reactional flask, the supernatant was removed, and the process was repeated with the addition of new reagents in the reactional flask. The first use resulted in a slight decrease in yield. Catalytic activity was maintained well, and no decrease in the activity of PyrrIL was observed, even after the fourth reuse. The catalytic performance over four cycles is depicted in Fig. 4.

Our experiments show that the employment of PyrrILs as a catalytic system in the Knoevenagel reaction with aliphatic aldehydes and 1,3-dicarbonyl compounds resulted in good yield of alkyldenes. In addition, this technique can be performed easily, with readily available, inexpensive starting materials, and the products exhibit high stability and can be stored in air without any sign of degradation.

**Conclusions**

In this work, the synthesis of long-chain alkyldenes (fatty alkyldenes) was demonstrated under PyrrILs catalysis and
solvent-free conditions. The products showed good yields (70–90%) following Knoevenagel condensation, using classic 1,3-dicarbonyl compounds and long-chain aldehydes, in a few hours and using an eco-friendly approach. In addition, experiments with recycling the catalyst [Pyr]([CH3]COO) make this method an attractive alternative to existing methods for the synthetically useful Knoevenagel reaction, and catalytic activity is well maintained after four cycles of catalysis.

We are in the process of synthesising a series of lipophilic γ-amino-butyric acid derivatives via long-chain β-alkyl-γ-ni troesters using fatty alkylidenes 6a–q as a building block.

**Experimental**

**Apparatus and chemistry**

The reagents were purchased from Aldrich Chemical Co. and used without further purification. All organic solvents used for the synthesis were of analytical grade. Column chromatography was performed using a silica gel 60 A (ACROS Organics, 0.035–0.070 mesh). The reactions were monitored using thin-layer chromatography (TLC) performed with plates containing silica gel (Merck 60 GF254), and the spots were visualised using iodine. Yields refer to chromatographically and spectroscopically homogeneous materials. Infrared (IR) spectra were measured on a Shimadzu PRESTIGE-21 FT-IR spectrophotometer. The NMR spectra were recorded using a Brucker AVANCE III 400 spectrometer (1H at 400 MHz and 13C at 100 MHz) and a Varian VNMR 300 spectrometer (1H at 300 MHz and 13C at 75.5 MHz) in deuterchloroform (CDCl3) as the solvent. The chemical shift data are reported in units of δ (ppm) downfield from tetramethylsilane (TMS), which was used as an internal standard. The coupling constants (J) are reported in Hz and refer to apparent peak multiplicities. High resolution mass spectra (HRMS) were recorded on Waters XEVO G2 Q-TOF Mass Spectrometer.

**Synthesis**

General procedure for the synthesis of long-chain alkylidene 6a–q. To a round-bottom flask equipped with a magnetic stirring bar were added aldehyde 4a–i (5 mmol) and 1,3-dicarbonyl 5a–e (7.5 mmol), and the system was cooled to 0 °C. Immediately, the IL [Pyr][CH3]COO] PyrrIL 2 (10 mol%) was added, with stirring maintained at 0 °C for 1.5 h. The reaction was monitored by TLC with hexane: ethyl acetate (80: 20) ratio as eluent. After completion of the reaction, the raw product was purified by flash column chromatography on a silica gel, with hexane/ethyl acetate (95: 05) as eluent, to yield alkylidene 6a–q. The purified products were analysed by proton and carbon NMR, IR, and ESI-MS/MS.

((E/Z)-Methyl-2-acetyl-4-methylpent-2-enoate (6a). Yellow oil. Yield: 83%. IR (film, v_max cm⁻¹): 2229, 1740, 1409, 1390, 1200, 1170, 1156, 1123, 1021; 1H NMR (CDCl3, 400 MHz): δ 5.98 (s, 1H, J = 8.0 Hz, isomer E), 3.85 (s, 3H, isomer Z), 2.59 (m, 1H, isomer Z), 2.39 (s, 3H, isomer E), 1.31 (t, 3H, J = 7.5 Hz, isomer E), 1.23 (s, 3H, isomer E).

13C NMR (CDCl3, 100 MHz): δ 170.8, 148.2, 143.5, 143.1, 129.3, 126.3, 125.9, 120.7, 115.9, 112.1, 103.8, 56.9, 34.9, 29.6, 28.0, 21.8, 15.1.

(E/Z)-Methyl-2-acetyl-5-methylhex-2-enoate (6b). Yellow oil. Yield: 77%. IR (film, v_max cm⁻¹): 2229, 1740, 1409, 1390, 1200, 1170, 1156, 1123, 1021; 1H NMR (CDCl3, 400 MHz): δ 6.95 (t, 1H, J = 10 Hz, isomer E), 3.14 (s, 3H, isomer Z), 3.06 (s, 3H, isomer E), 2.5 (s, 3H, isomer E), 1.3 (t, 3H, J = 7.5 Hz, isomer E), 1.2 (s, 3H, isomer E). 13C NMR (CDCl3, 100 MHz): δ 170.8, 148.2, 143.5, 143.1, 129.3, 126.3, 125.9, 120.7, 115.9, 112.1, 103.8, 56.9, 34.9, 29.6, 28.0, 21.8, 15.1.

13C NMR (CDCl3, 100 MHz): δ 170.8, 148.2, 143.5, 143.1, 129.3, 126.3, 125.9, 120.7, 115.9, 112.1, 103.8, 56.9, 34.9, 29.6, 28.0, 21.8, 15.1.

2-(2-Methylpent-2-yn-1-yl)-5-methylhex-2-en-1-one (6c). Yellow oil. Yield: 95%. IR (film, v_max cm⁻¹): 2229, 1740, 1409, 1390, 1200, 1170, 1156, 1123, 1021; 1H NMR (CDCl3, 400 MHz): δ 6.96 (t, 1H, J = 10 Hz, isomer E), 3.15 (s, 3H, isomer Z), 3.07 (s, 3H, isomer E), 2.5 (s, 3H, isomer E), 1.3 (t, 3H, J = 7.5 Hz, isomer E), 1.2 (s, 3H, isomer E).

13C NMR (CDCl3, 100 MHz): δ 170.8, 148.2, 143.5, 143.1, 129.3, 126.3, 125.9, 120.7, 115.9, 112.1, 103.8, 56.9, 34.9, 29.6, 28.0, 21.8, 15.1.

13C NMR (CDCl3, 100 MHz): δ 170.8, 148.2, 143.5, 143.1, 129.3, 126.3, 125.9, 120.7, 115.9, 112.1, 103.8, 56.9, 34.9, 29.6, 28.0, 21.8, 15.1.

2-(2-Methylpent-2-yn-1-yl)-5-methylhex-2-en-1-one (6d). Yellow oil. Yield: 95%. IR (film, v_max cm⁻¹): 2229, 1740, 1409, 1390, 1200, 1170, 1156, 1123, 1021; 1H NMR (CDCl3, 400 MHz): δ 6.96 (t, 1H, J = 10 Hz, isomer E), 3.15 (s, 3H, isomer Z), 3.07 (s, 3H, isomer E), 2.5 (s, 3H, isomer E), 1.3 (t, 3H, J = 7.5 Hz, isomer E), 1.2 (s, 3H, isomer E).

13C NMR (CDCl3, 100 MHz): δ 170.8, 148.2, 143.5, 143.1, 129.3, 126.3, 125.9, 120.7, 115.9, 112.1, 103.8, 56.9, 34.9, 29.6, 28.0, 21.8, 15.1.

13C NMR (CDCl3, 100 MHz): δ 170.8, 148.2, 143.5, 143.1, 129.3, 126.3, 125.9, 120.7, 115.9, 112.1, 103.8, 56.9, 34.9, 29.6, 28.0, 21.8, 15.1.
1.53 J, 7.95 (t, 1H, J = 8.0 Hz, isomer E). Yield: 85%. IR (film, r_max cm⁻¹): 3398, 3009, 2920, 2847, 1802, 1748, 1738, 1641, 1568, 1462, 1381, 1309, 1203, 1009, 912, 807, 718. ¹H NMR (CDCl₃, 300 MHz): δ 7.96 (t, 1H, J = 7.2 Hz), 2.96 (m, 2H), 1.76 (s, 6H), 1.62 (m, 2H), 1.28 (m, 16H), 0.91 (t, 3H, J = 7.0 Hz). ¹C NMR (CDCl₃, 75 MHz): δ 169.7, 162.2, 160.5, 118.7, 105.4, 32.5, 31.8, 31.6, 30.2 (2C), 30.1 (2C), 29.2 (2C), 28.8, 28.3, 23.3, 14.7. HRMS calculated for C₁₉H₂ₐO₈ [M − H]⁻ 281.1758; found 281.1749.

5-Dodecylidene-2,2-dimethyl-1,3-dioxane-4,6-dione (6o). Yellow solid, mp 67–69 °C. Yield: 85%. IR (film, r_max cm⁻¹): 3398, 3009, 2920, 2847, 1802, 1748, 1738, 1641, 1568, 1462, 1381, 1309, 1203, 1009, 912, 807, 718. ¹H NMR (CDCl₃, 300 MHz): δ 7.96 (t, 1H, J = 7.2 Hz), 2.96 (m, 2H), 1.76 (s, 6H), 1.62 (m, 2H), 1.28 (m, 16H), 0.91 (t, 3H, J = 7.0 Hz). ¹C NMR (CDCl₃, 75 MHz): δ 169.7, 162.2, 160.5, 118.7, 105.4, 32.5, 31.8, 31.6, 30.2 (2C), 30.1 (2C), 29.2 (2C), 28.8, 28.3, 23.3, 14.7. HRMS calculated for C₁₉H₂ₐO₈ [M − H]⁻ 281.1758; found 281.1749.

5-Hexadecylidene-2,2-dimethyl-1,3-dioxane-4,6-dione (6p). Yellow solid, mp 81–83 °C. Yield: 80%. IR (film, r_max cm⁻¹): 3001, 2920, 2855, 1795, 1746, 1730, 1641, 1462, 1381, 1309, 1105, 1001, 799, 718. ¹H NMR (300 MHz, CDCl₃): δ 7.93 (t, 1H, J = 7.5 Hz), 2.95 (q, 2H, J = 6.0 Hz), 1.74 (s, 6H), 1.60 (m, 2H), 1.28 (m, 24H), 0.88 (t, 3H, J = 6.0 Hz). ¹C NMR (75 MHz, CDCl₃): δ 169.0, 161.9, 159.8, 118.0, 104.7, 31.9, 31.1, 29.6 (4C), 29.5 (2C), 29.3 (2C), 29.2, 28.1, 27.6 (2C), 14.0. HRMS calculated for C₂₀H₃₆O₃ [M − H]⁻ 325.2697; found 325.2690.

2,2-Dimethyl-5-octadecylidene-1,3-dioxane-4,6-dione (6q). Yellow solid, mp 78–79 °C. Yield 83%. IR (film, r_max cm⁻¹): 3001, 2920, 2847, 1786, 1738, 1624, 1471, 1390, 1293, 1195, 1009, 799, 718. ¹H NMR (300 MHz, CDCl₃): δ 7.95 (t, 1H, J = 7.5 Hz), 2.95 (q, 2H, J = 6.0 Hz), 1.76 (s, 6H), 1.61 (m, 2H), 1.27 (m, 28H), 0.90 (t, 3H, J = 6.0 Hz). ¹C NMR (75 MHz, CDCl₃): δ 168.5, 161.4, 159.3, 117.5, 104.3, 31.4, 30.7, 29.3 (2C), 29.1 (2C), 28.9 (2C), 28.8 (2C), 27.7, 27.2 (2C), 22.4, 13.6. HRMS calculated for C₂₄H₄₂O₄ [M − H]⁻ 365.2697; found 365.2690.

Acknowledgements

The authors are grateful for the financial support of Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), Fundação de Apoio à Pesquisa do Estado do Rio Grande do Sul (FAPERGS/PRONEM), and Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq). Fellowships from CAPES and CNPq (D. Russowsky and M. G. Montes D’Oca) are also acknowledged.

Notes and references


