J Am Oil Chem Soc
DOI 10.1007/s11746-016-2879-5

ORIGINAL PAPER

Synthesis of Fatty Acetoacetates Under Microwave Irradiation Catalysed by Sulfamic Acid in a Solvent-Free System

Andressa C. H. Weber[1] · Thaís C. Batista[1] · Bruno Gonçalves[1] · Carolina R. L. Hack[1] · Larissa M. Porciuncula[1] · Tamara G. M. Treptow[1] · Caroline Da R. Montes D'Oca[2] · Dennis Russowsky[2] · Marcelo G. Montes D'Oca[1]

Received: 1 December 2015 / Revised: 28 July 2016 / Accepted: 28 July 2016

Abstract The 1,3-dicarbonyl compounds are important building blocks to obtain products with various biological activities and technological applications. In this work, we used a simple transesterification method to develop fatty acetoacetates in a solvent-free medium using a green catalyst, sulfamic acid (NH_2SO_3H), under microwave irradiation. The experimental results demonstrate good yields in a short reaction time (13 min), which makes this method an efficient approach to synthesize fatty acetoacetates from a wide range of saturated, unsaturated, and polyunsaturated long chain fatty alcohols, and ricinoleic derivatives. Experiments of recycling of the catalyst were performed and no decrease in catalytic activity of sulfamic acid was observed.

Keywords Castor oil · Renewable resources · Transesterification reaction · 1,3-dicarbonyl compounds · Microwave-assisted

Introduction

The 1,3-dicarbonyl compounds, such as acetoacetates or β-ketoesters, are important building blocks in the synthesis of polymers, drugs and biologically active compounds [1–3]. They have also been studied as biofuel additives [4].

Using acetoacetates as the building blocks in multicomponent reactions (MCR) [5] yields several different structures based on the dihydropyridinone (DHPM) or dihydropyridine (DHP) skeleton, which creates an extensive library of compounds with various biological activities [6–10]. MCR have been recognized for their high convergence, atomic economy and operational simplicity and are emphasized as important tools to synthesize high-molecular-complexity compounds in accordance with green chemistry principles [2, 11].

The transesterification reaction to synthesize acetoacetates is a notably useful tool in organic synthesis, and various methods have been reported to affect the transesterification of methyl or *tert*-butyl acetoacetates. The uncatalyzed transesterification of acetoacetates requires the use of either an excess of ketoester or a longer reaction time and a high boiling alcohols or solvents limiting their usage [12].

According to the literature, the transesterification process to synthesize β-ketoesters under solvent-free conditions without catalysis results in high yields when excess alcohol is used at a high temperature [13]. In addition, the rate of transesterification of acetoacetates is significantly affected by steric factors; thus, tertiary alcohols are less active. Primary, secondary, and tertiary alcohols have been tested in the presence of molecular sieves, which results in good acetoacetate yields [12]. The catalysts in the transesterification reaction vary and include new silica-based hybrid materials, triethylamine, boric acid, and triphenylphosphine [14–17].

However, the development of a new method that enables transesterification in milder conditions should heighten the synthetic potential of the reaction. Considering the importance of acetoacetates, cleaner methodologies have been studied for their synthesis; solvent-free conditions [18] and replacement of catalysts [13] render the protocol to obtain

Electronic supplementary material The online version of this article (doi:10.1007/s11746-016-2879-5) contains supplementary material, which is available to authorized users.

✉ Marcelo G. Montes D'Oca
dqmdoca@furg.br

[1] Laboratório Kolbe de Síntese Orgânica, Escola de Química e Alimentos, Universidade Federal do Rio Grande, Av. Italia, Km 08, Rio Grande, RS, Brazil

[2] Laboratório de Sínteses Orgânicas, Instituto de Química, Universidade Federal do Rio Grande do Sul, Av. Bento Gonçalves 9500, Porto Alegre, RS 91501-970, Brazil

Published online: 09 August 2016

1,3-dicarbonyl compounds an environmentally friendly process [19, 20]. The employment of enzymatic catalysis have been reported, because this approach allows high yields under mild conditions, thereby fulfilling the general principles of green chemistry [21, 22]. The use of heterogeneous catalytic systems, such as sulfamic acid (NH_2SO_3H), is wanted in green chemistry [23]. This relatively stable, white crystalline solid is odorless, non-volatile, non-hygroscopic, non-corrosive, and low-cost, and it is a highly efficient catalyst in organic synthesis [15, 24, 25]. Sulfamic acid and alcohol as an organic reaction promoter system have been proven to have remarkable efficiency because of a synergistic effect of sulfamic acid in zwitterionic form ($NH_3^+SO_3^-$), as demonstrated in the synthesis of quinoxalines [26], benzimidazole derivatives [27] and 2,3-dihydroquinazolinones [28]. According to the literature, an efficient approach to 1,4-dihydropyridines with new substituted pyrazole involves the synthesis via a three-component reaction of pyrazolyl aldehyde, β-ketoester, and ammonium acetate under sulfamic acid catalysis [29].

Ultrasound and microwave (MW) radiation systems have been increasingly used in organic reactions, and they are considered clean and easy to operate [30]. Furthermore, they can obtain products in short reaction times and produce higher energy usage than the traditional heating techniques [31–34]. Another advantage is that microwaves can promote infeasible transformations to traditional heating after energy is directly applied to the reactants, and global warming can be minimized using simultaneous colds [35].

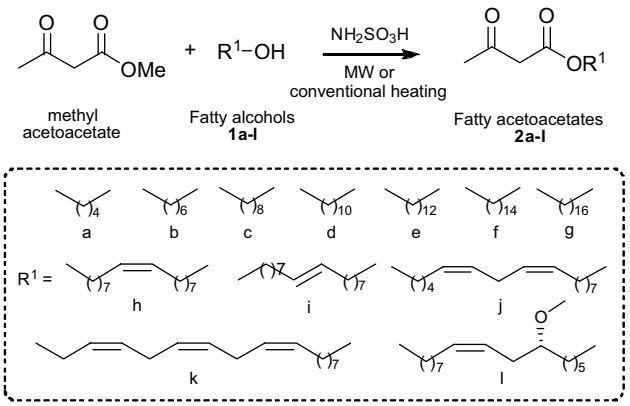
Recently, we demonstrated for the first time the synthesis of new fatty β-ketoesters from fatty acid families in good yields [36]. A series of fatty β-ketoesters were obtained from several fatty acids and Meldrum's acid using *N*,*N*-dicyclohexylcarbodiimide (DCC) and dimethylaminopyridine (DMAP).

In a continuation of our studies to synthesize compounds from renewable resources [37–40], we describe here the synthesis of fatty acetoacetates **2a-l** derivatives from renewable saturated, unsaturated, polyunsaturated and ricinoleic fatty acids using the transesterification reaction under sulfamic acid (NH_2SO_3H) catalysis and solvent-free conditions using long chain alcohols (Scheme 1).

Experimental Procedures

Apparatus and Chemistry

The fatty acids and sulfamic acid (98 wt%) were supplied by Aldrich Chemical Co. Ricinoleic acid (*cis*-C18:1,12-OH) was obtained from castor oil or via castor oil biodiesel hydrolysis. The other reagents were purchased from Aldrich Chemical Co. and used without further purification.



Scheme 1 Synthesis of fatty acetoacetates **2a-l** under MW or conventional heating catalyzed by NH_2SO_3H

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) with plates containing silica gel (Merck 60GF245), and the spots were visualized using iodine. The yields refer to chromatographically and spectroscopically homogeneous materials. The melting points were obtained using a Fisatom 430D apparatus and were uncorrected. The infrared (IR) spectra were measured using a Schimadzu PRESTIGIE-21 FT-IR spectrophotometer. The NMR spectra were recorded using a Varian VNMRS 300 spectrometer (^{1}H at 300 MHz and ^{13}C at 75.5 MHz) in $CDCl_3$ as 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 (^3J) are reported in Hz and refer to apparent peak multiplicities.

*General Procedure to Synthesize Fatty Acetoacetates **2a-l** in Conventional Heating*

A mixture of fatty alcohol (1 mmol), methyl acetoacetate (4 mmol) and NH_2SO_3H (0.3 mol%) in a solvent-free condition was stirred for 6 h at 80 °C. Then, 3 × 10 mL of ethyl acetate was added, and the residual catalyst was filtrated. The organic layer was washed (3 × 10 mL), and dried with Mg_2SO_4. The solvent was removed by rotary evaporation, and the obtained residue was purified using flash column chromatography on a silica gel 35–70 μm thick and the eluent hexane/ethyl acetate (97:3) to afford fatty acetoacetates **2a-l**.

*General Procedure to Synthesize Fatty Acetoacetates **2a-l** Under MW Irradiation*

A mixture of fatty alcohol (1 mmol), methyl acetoacetate (4 mmol) and NH_2SO_3H (0.3 mol%) in a solvent-free

condition was stirred for 30 s. Then, in a max power mode at 300 W and 120 °C, the reaction occurred for 13 min in an appropriate 10-mL tube in a Discovery CEL Discovery & Explorer SP microwave. Subsequently, 3 × 10 mL of ethyl acetate was added, and the residual catalyst was filtered. The organic layer was washed (3 × 10 mL) and dried with Mg_2SO_4. The solvent was removed by rotary evaporation, and the obtained residue was purified using flash column chromatography on a silica gel 35–70 μm thick with the eluent hexane/ethyl acetate (97:3) to afford fatty acetoacetates **2a-l**.

All procedures applying these methods were performed in triplicate

Hexyl 3-oxobutanoate (2a)

MW 186.25 g mol^{-1}; Colorless oil; Yield 81 %; FT-IR (KBr, $\nu = cm^{-1}$): 1467, 1714, 1743, 2856, 2927, 2954; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 4.13 (t, 2H, $J = 6.0$ Hz), 3.44 (s, 2 H), 2.26 (s, 3 H), 1.64 (m, 2 H), 1.28 (m, 6H), 0.87 (t, 3H, $J = 6.0$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) 200.5, 167.2, 65.5, 50.1, 31.3, 30.1, 28.4, 25.4, 22.4, 13.9.

Octyl 3-oxobutanoate (2b)

MW 214.30 g mol^{-1}; Colorless oil; Yield 80 %; FT-IR (KBr, $\nu = cm^{-1}$): 1454, 1712, 1745, 2858, 2931, 2958; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 4.04 (m, 2H), 3.44 (s, 2H), 2.25 (s, 3 H), 1.57 (m, 2 H), 1.27–1.39 (m, 10H), 0.87 (t, 3H, $J = 7.5$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 200.4, 167.1, 67.6, 50.0, 38.5, 30.1, 30.0, 28.7, 23.5, 22.8, 13.9, 10.8.

Decyl 3-oxobutanoate (2c)

MW 242.35 g mol^{-1}; Colorless oil; Yield 75 %; FT-IR (KBr, $\nu = cm^{-1}$): 1463, 1745, 2852, 2924; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 4.11 (t, 2H, $J = 6.0$ Hz), 3.43 (s, 2H), 2.25 (s, 3 H), 1.62 (m, 2 H), 1.25 (m, 12H), 0.86 (t, 3H, $J = 6.0$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 200.5, 167.1, 65.5, 50.0, 31.8, 29.9, 29.4, 29.3, 29.2, 29.1, 28.4, 25.7, 22.6, 13.9.

Dodecyl 3-oxobutanoate (2d)

MW 270.41 g mol^{-1}; Colorless oil; Yield 73 %; FT-IR (KBr, $\nu = cm^{-1}$): 1465, 1716, 1743, 2852, 2922; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 4.15 (t, 2H, $J = 6.0$ Hz), 3.46 (s, 2H), 2.28 (s, 3 H), 1.65 (m, 2 H), 1.27 (m, 16H), 0.89 (t, 3H, $J = 6.0$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 200.6, 167.2, 65.6, 50.1, 31.9, 30.1, 29.6 (2C), 29.5, 29.4, 29.3, 29.2, 28.4, 25.8, 22.6, 14.1.

Tetradecyl 3-oxobutanoate (2e)

MW 298.46 g mol^{-1}; White solid; m.p. 28–30 °C; Yield 75 %; FT-IR (KBr, $\nu = cm^{-1}$): 1471, 1710, 1734, 2848, 2916; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 4.15 (t, 2H, $J = 6.0$ Hz), 3.46 (s, 2H), 2.28 (s, 3 H), 1.65 (m, 2 H), 1.27 (m, 20H), 0.89 (t, 3H, $J = 6.0$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 200.6, 167.2, 65.6, 50.1, 31.9, 30.1, 29.6 (3C), 29.4, 29.3 (2C), 29.2 (2C), 28.4, 25.7, 22.6, 14.1.

Hexadecyl 3-oxobutanoate (2f)

MW 326.51 g mol^{-1}; White solid; m.p. 40–41 °C; Yield 85 %; FT-IR (KBr, $\nu = cm^{-1}$): 1473, 1710, 1734, 2848, 2912, 2953; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 4.13 (t, 2H, $J = 7.5$ Hz), 3.45 (s, 2 H), 2.27 (s, 3 H), 1.64 (m, 2 H), 1.26 (m, 26 H, 0.88 (t, 3H, $J = 6.0$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 200.6, 167.1, 65.5, 50.1, 31.9, 30.1, 29.6 (4C), 29.5 (2C), 29.4 (2C), 29.3, 29.1, 28.4, 25.8, 22.6, 14.1.

Octadecyl 3-oxobutanoate (2g)

MW 354.57 g mol^{-1}; White solid; m.p. 45–46 °C; Yield 86 %; FT-IR (KBr, $\nu = cm^{-1}$): 1465, 1705, 1741, 2848, 2916, 2953; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 4.15 (t, 2H, $J = 6.0$ Hz, 3.46 (s, 2 H), 2.28 (s, 3 H), 1.65 (m, 2 H), 1.27 (m, 28 H), 0.89 (t, 3H, $J = 6.0$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 200.1, 166.7, 65.1, 49.6, 31.4, 29.6, 29.2 (3C), 29.1 (3C), 29.0 (2C), 28.9 (2C), 28.7 (2C), 27.9, 25.3, 22.2, 13.6.

(9*Z*)-Octadec-9-en-1-yl 3-oxobutanoate (2h)

MW 352.55 g mol^{-1}; Yellow oil; Yield 80 %; FT-IR (KBr, $\nu = cm^{-1}$): 1465, 1647, 1714, 1743, 2852, 2924; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 5.37 (m, 2 H), 4.15 (t, 2H, $J = 7.5$ Hz), 3.47 (s, 2 H), 2.29 (s, 3H), 2.03 (m, 4 H), 1.66 (m, 2 H), 1.29–1.32 (m, 22 H), 0.90 (t, 3H, $J = 6.0$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 200.4, 167.1, 129.8, 129.6, 65.4, 49.9, 32.5, 31.8, 29.6 (2C), 29.5, 29.4 (2C), 29.2 (2C), 29.1, 28.4, 27.1 (2C), 25.7, 22.6, 13.9.

(9*E*)-Octadec-9-en-1-yl 3-oxobutanoate (2i)

MW 352.55 g mol^{-1}; White solid; m.p. 30–32 °C; Yield 75 %; FT-IR (KBr, $\nu = cm^{-1}$): 1458, 1656, 1726, 1743, 2852, 2924; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 5.39 (m, 2 H), 4.14 (t, 2H, $J = 6.0$ Hz), 3.45 (s, 2H), 2.28 (s, 3 H), 1.97 (m, 4H), 1.65 (m, 2H), 1.27 (m, 22 H), 0.89 (t, 3H, $J = 6.0$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 200.5, 167.1, 130.3, 130.1, 65.5, 50.0, 32.5 (2C), 31.8, 30.0, 29.6 (2C), 29.5, 29.4; 29.3, 29.2, 29.1, 28.9, 28.4, 25.7, 22.6, 14.0.

(9*Z*,12*Z*)-Octadeca-9,12-dien-1-yl 3-oxobutanoate (2j)

MW 350.54 g mol^{-1}; Yellow oil; Yield 79 %; FT-IR (KBr, ν = cm^{-1}): 1465, 1662, 1728, 1743, 2854, 2926, 3008; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 5.36 (m, 4H), 4.14 (t, 2H, J = 7.5 Hz), 3.45 (s, 2 H), 2.77 (t, 2H, J = 6.0 Hz), 2.27 (s, 3 H), 2.03 (q, 4H, J = 6.0 Hz), 1.64 (m, 2 H), 1.30 (m, 16 H), 0.89 (t, 3H, J = 6.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 200.6, 167.1, 130.1, 129.9, 127.9, 127.8, 65.5, 50.1, 31.4, 30.1, 29.5, 29.3, 29.2, 29.1 (2C), 28.4, 27.1, 25.7, 25.5, 22.6, 22.5, 14.0.

(9*Z*,12*Z*,15*Z*)-Octadeca-9,12,15-trien-1-yl 3-oxobutanoate (2k)

MW 348.52 g mol^{-1}; Yellow oil; Yield 76 %; FT-IR (KBr, ν = cm^{-1}): 1435, 1656, 1732, 1759, 2870, 2922, 2954, 2999, 3062; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 5.34 (m, 6H), 4.14 (t, 2H, J = 7.5 Hz), 3.45 (s, 2 H), 2.77 (t, 4H, J = 6.0 Hz), 2.27 (s, 3 H), 2.05 (m, 4H), 1.64 (m, 2 H), 1.30 (m, 10 H), 0.89 (t, 3H, J = 6.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 200.1, 166.7, 129.7, 128.6 (3C), 127.5 (2C), 65.0, 49.6, 31.0, 29.1, 28.9, 28.7, 27.9, 26.7 (3C), 25.3, 25.1, 22.1, 13.6.

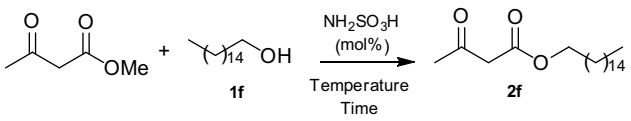
(12*R*,9*Z*)-12-Methoxyoctadec-9-en-1-yl 3-oxobutanoate (2l)

MW 382.58 g mol^{-1}; Yellow oil; Yield 75 %; FT-IR (KBr, ν = cm^{-1}): 1238, 1458, 1645, 1726, 1743, 2852, 2926, 3005; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 5.42 (m, 2H), 4.14 (t, 2H, J = 6.0 Hz), 3.45 (s, 2 H), 3.34 (s, 3H), 3.17 (m, 1H), 2.27 (s, 3 H), 2.25 (m, 2H), 2.04 (m, 2H), 1.64 (m, 2 H), 1.45 (m, 2H), 1.28 (m, 18H), 0.88 (t, 3H, J = 6.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 200.5, 167.2, 131.7, 125.4, 80.9, 65.5, 56.5, 50.1, 33.5, 31.8, 31.0, 30.1, 29.5, 29.4, 29.3, 29.2, 29.1, 28.4, 27.4, 25.7, 25.3, 22.6, 14.0; $[\alpha]_D^{20}$ = +13.02 (*c* 0.41, CH_2Cl_2).

Results and Discussion

The synthesis of fatty acetoacetate was investigated with conventional heating and microwave irradiation in a solvent-free medium with fatty alcohols and sulfamic acid catalysis, which has been studied in our group as an effective catalyst for several organic transformations.

The fatty alcohols precursors **1a-k** were synthesized from the reduction of methyl esters [41] according to the literature [42, 43]. Then, initial tests to optimize the experimental conditions were performed using palmitic alcohol (**1f**, Scheme 2) as the template under different experimental conditions such as the reaction time, temperatures, catalysis loading, and stoichiometry amounts.



Scheme 2 Synthesis of fatty acetoacetate **2f** under conventional heating catalyzed by NH_2SO_3H

The reactions were monitored using thin layer chromatography (TLC), and the results are shown in Table 1. Initially, we evaluated the synthesis of **2f** using conventional heating (80 °C) in a solvent-free medium with 10 mol% of sulfamic acid for 3 h with constant stirring (Table 1, entry 1) according to the described experimental protocol in the literature using ionic liquid [20]. However, in our hands, this protocol has provided notably low yield using palmitic alcohol (**1f**) a long chain alcohol.

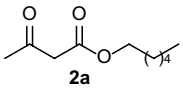
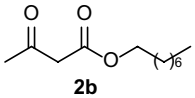
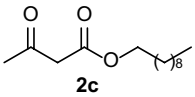
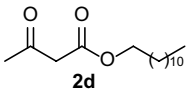
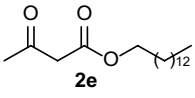
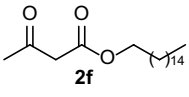
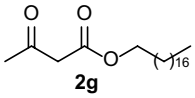
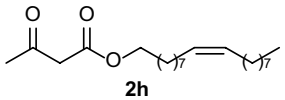
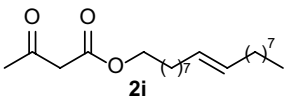
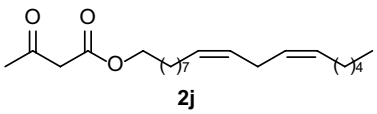
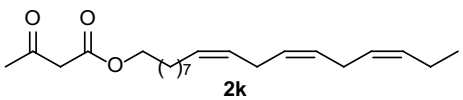
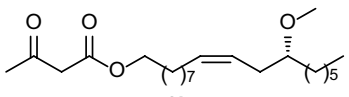
From these results, the effect of 1,3-dicarbonilic excess in a longer reaction time was studied (Table 1, entries 2–7). In addition, the reaction was investigated in the presence of different solvents (Table 1, entries 5 and 6), but all tested conditions led to lower yields and the starting materials were recovered and no ketalization product of β-carbonyl [20] of the methyl acetoacetate with fatty alcohol was detected. However, the use of 4 equivalents of 1,3-dycarbonilic in a solvent-free medium had better yields (Table 1, entry 7). Afterward, the catalyst loading was also tested. The reactions were performed in the presence of 20 mol% and 30 mol% of sulfamic acid (Table 1, entries 8–11). According to Table 1, it was possible to observe better

Table 1 Experimental *screening* to synthesis of fatty acetoacetate **2f** catalyzed by NH_2SO_3H under conventional heating

Entry	Fatty alcohol (**1f**, equiv)	Methyl acetoacetate (equiv)	NH_2SO_3H (mol%), solvent	T (h)	Fatty acetoacetate (**2f**, %)[a]
1	1.2	1.0	10, Solvent-free	3	35
2	1.0	2.0	10, Solvent-free	6	40
3	1.0	3.0	10, Solvent-free	6	60
4	1.0	4.0	10, Solvent-free	3	65
5	1.0	4.0	10, Hexane	3	58
6	1.0	4.0	10, CH_2Cl_2	3	61
7	1.0	4.0	10, Solvent-free	6	75
8	1.0	4.0	20, Solvent-free	3	60
9	1.0	4.0	20, Solvent-free	6	69
10	1.0	4.0	30, Solvent-free	6	83
11	1.0	4.0	30, Solvent-free	9	78

[a] Isolated yield after column chromatography on a silica gel

Table 2 Synthesis of fatty-1,3-dicarbonyl **2a-l** in a solvent-free medium catalyzed by 30 mol% NH_2SO_3H under conventional heating (80 °C, 6 h) and MW irradiation (120 °C, 13 min, 300 W)

Entry	Alcohol	Fatty acetoacetate	Conventional heating	MW irradiation	Melting point
1	**1a**	 **2a**	79%	81%	oil[12]
2	**1b**	 **2b**	77%	80%	oil[19]
3	**1c**	 **2c**	68%	75%	oil
4	**1d**	 **2d**	69%	73%	oil[12, 46]
5	**1e**	 **2e**	69%	75%	28-30 °C
6	**1f**	 **2f**	83%	85%	40-41 °C[6]
7	**1g**	 **2g**	85%	86%	45-46 °C[6]
8	**1h**	 **2h**	78%	80%	oil[6]
9	**1i**	 **2i**	73%	75%	30-32 °C
10	**1j**	 **2j**	75%	79%	oil
11	**1k**	 **2k**	72%	76%	oil
12	**1l**	 **2l**	70%	75%	oil

results employing 30 mol% of catalyst, at a temperature of 80 °C and a reaction time of 6 h under conventional heating conditions (Table 1, entry 10). In addition, we evaluated the synthesis of **2f** using conventional heating at 100 and 120 °C in a solvent-free medium with 30 % sulfamic acid. However, within the experimental conditions, an increase in the temperature not significantly increases the yield of **2f**.

These findings using conventional heating were used as initial protocol for the investigation of reaction behavior under microwave irradiation conditions to synthesis of fatty acetoacetates. Were evaluated the effect of the temperature (80–150 °C), time (5 min–2 h) and power (100–300 W) of the microwave irradiation system in the transesterification reaction, in a solvent-free medium with 30 mol% sulfamic acid catalyst. The reaction course was monitored by TLC and the best results were observed with 30 s of pre-stirring, at 120 °C of temperature, reaction time of 13 min and 300 W power. This protocol resulted in 80 % yield of **2f** from palmitic alcohol (**1f**).

The reaction scope was investigated, performing the synthesis of fatty acetoacetates **2a–k** based on the natural availability of fatty acids derived from renewable resources, i.e., saturated, unsaturated and polyunsaturated fatty chains. The synthesis of **2a–k** was performed under the experimental conditions optimized to conventional heating (30 mol% NH_2SO_3H, 6 h, 80 °C) and microwave irradiation (30 mol% NH_2SO_3H, 13 min, 120 °C, 300 W). The results are shown in Table 2.

Because slightly higher results were observed under microwave irradiation, the consumption of starting materials in short reaction times makes this method an efficient approach to synthesize fatty compounds. In addition, the fatty acetoacetates **2l** and **2m** derived from ricinoleic acid (12-hydroxy-9-*cis*-octadecenoic acid), which is the major constituent (80–90 %) of castor oil (*Ricinus communis*) [44] and an uncommon fatty acid that contains a double bond and a hydroxyl group, were synthesized. According to previous work, the 12-hydroxy-methyl ricinoleate was obtained in 90 % yield from castor oil via the transesterification reaction (Scheme 3) [45].

The 12-hydroxy-methyl ricinoleate was protected with CH_3I to obtain the corresponding alcohol **1l** (Scheme 3). Then, the transesterification reaction from **1l** and methyl acetoacetate under sulfamic acid catalysis led to the formation of **2l** in good yields (Table 2, entry 12) under conventional heating and MW irradiation.

The transesterification reaction was also realized in the presence of the fatty diol [(12*R*,9*Z*)-octadecene-1,12-diol], which is a derivative of ricinoleic acid. The diol was obtained from the castor oil transesterification reaction

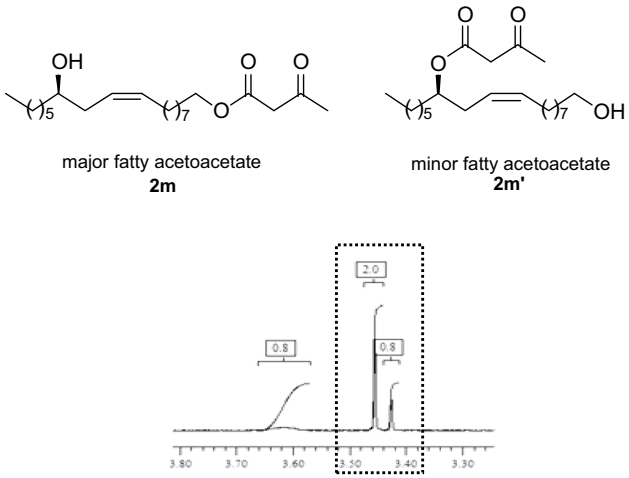
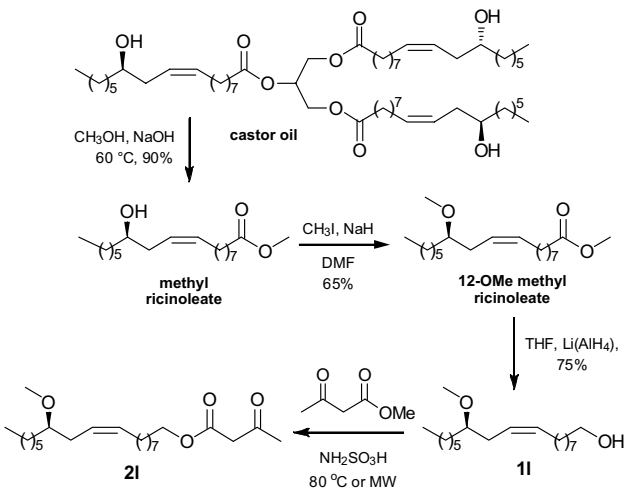


Fig. 1 Fatty acetoacetates **2m** and **2m′** and the selected region of NMR ^1H (300 MHz, $CDCl_3$)



Scheme 3 Synthesis of fatty acetoacetate **2l** derived from ricinoleic acid under conventional heating and MW irradiation in NH_2SO_3H

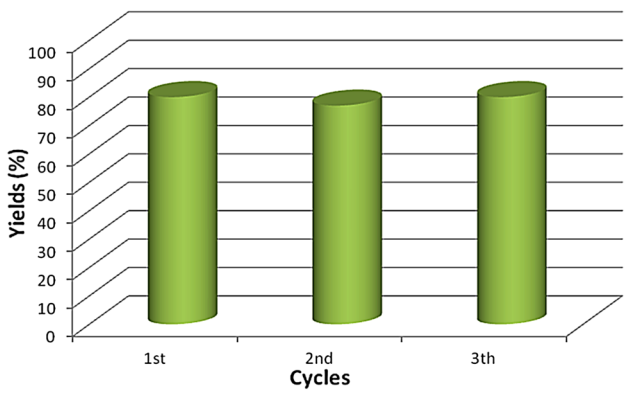


Fig. 2 Experiments of recycling of catalyst sulfamic acid in the transesterification reaction under MW irradiation

with subsequent reduction of methyl ricinoleate. However, as expected, the transesterification reaction from diol and methyl acetoacetate under conventional heating and MW irradiation, which was catalyzed by sulfamic acid, led to the formation of isomers **2m** and **2m′** (2:1 mixture) as observed in the selected region of the ^{1}H-NMR spectrum (Fig. 1).

Experiments of recycling of catalyst sulfamic acid were performed. The reaction was carried out in the presence of 30 mol% of sulfamic acid under microwave irradiation (13 min, 120 °C, 300 W) using 1 g of palmitic alcohol (**1f**) in a solvent-free medium. After completion of the reaction, hexane was added and the filtered was separate of the sulfamic acid. The recycled catalyst was used in further runs. The 1st reuse resulted in a slightly diminishing of the yield. However, no decrease in catalytic activity of sulfamic acid was observed even after 2nd and 3rd reuses (Fig. 2).

Conclusion

In conclusion, in this work, the synthesis of fatty acetoacetates from renewable resources was demonstrated under sulfamic acid catalysis and solvent-free conditions using MW irradiation. The products were isolated in good yields (73–86 %) from transesterification process with long chain alcohols in a few minutes using an eco-friendly approach, which makes this method attractive over the existing methods for synthetically useful transesterification. In addition, the catalytic activity of sulfamic acid is well maintained after three cycles of catalysis.

Acknowledgments The authors are thankful for financial support from 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 (A. C. H. Weber) and CNPq (D. Russowsky and M. G. Montes D'Oca) are also acknowledged.

Compliance with ethical standards

Conflict of interest The authors declare no conflict of interests.

References

1. Koizumi T, Sakamoto J, Gondo Y, Endo T (2002) Pd(0)-Catalyzed polyaddition of bifunctional vinyloxiranes with 1,3-dicarbonyl compounds: the synthesis of polymers containing hydroxyl and carbonyl groups. J Polym Sci Part A Polym Chem 40:2487–2494
2. Hulme C, Gore V (2003) Multi-component reactions: emerging chemistry in drug discovery 'from xylocaine to crixivan'. Curr Med Chem 10:51–80
3. Touré BB, Hall DG (2009) Natural product synthesis using multicomponent reaction strategies. Chem Rev 109:4439–4486
4. Cao L, Wang J, Liu K, Han S (2014) Ethyl acetoacetate: a potential bio-based diluent for improving the cold flow properties of biodiesel from waste cooking oil. Appl Energy 114:18–21
5. Zhu J, Bienaymé H (2005) Multicomponent reactions. Wiley-VCH Publishing, Weinheim
6. Treptow TGM, Figueiró F, Jandrey EHF, Battastini AMO, Salbego CG, Hoppe JB, Taborda PS, Rosa SB, Piovesan LA, D'Oca CRM, Russowsky D, D'Oca MGM (2015) Novel hybrid DHPM-fatty acids: synthesis and activity against glioma cell growth in vitro. Eur J Med Chem 95:552–562
7. Liu L, Sarkisian R, Deng Y, Wang H (2013) Sc(OTf)3-Catalyzed Three component cyclization of arylamines β, γ-unsaturated α-ketoesters, and 1,3-dicarbonyl compounds for the synthesis of highly substituted 1,4-dihydropyridines and tetrahydropyridines. J Org Chem 78:5751–5755
8. Russowsky D, Canto RFS, Sanches SAA, D'Oca MGM, Fátima A, Pilli RA, Konhn LK, Antônio MA, Carvalho JE (2006) Synthesis and differential antiproliferative activity of Biginelli compounds against cancer cell lines: monastrol, oxo-monastrol and oxygenated analogues. Bioorg Chem 34:173–182
9. Crespo A, El Maatougui A, Biagini P, Azuaje J, Coelho A, Brea J, Loza MI, Cadavid MI, Garcia-Mera X, Gutierrez-de-Teran H, Sotelo E (2013) Discovery of 3,4-dihydropyrimidin-2(1H)-ones as a novel class of potent and selective A_{2B} adenosine receptor antagonists. ACS Med Chem Lett 4:1031–1036
10. Bonne D, Coquerel Y, Constantieux T, Rodriguez J (2010) 1,3-Dicarbonyl compounds in stereoselective domino and multicomponent reactions. Tetrahedron Asymm 21:1085–1109
11. Cioc RC, Ruijterand E, Orru RVA (2014) Multicomponent reactions: advanced tools for sustainable organic synthesis. Green Chem 16:2958–2975
12. Koval KLI, Dzyuba VI, Ilnitska OL, Pekhnyo VI (2008) Efficient transesterification of ethyl acetoacetate with higher alcohols without catalysts. Tetrahedron Lett 49:1645–1648
13. Heravi MM, Baghernejad B, Oskooie HA (2009) Application of sulfamic acid in organic synthesis—a short review. Curr Org Chem 13:1002–1014
14. Sathicq G, Musante L, Romanelli G, Pasquale G, Autino J, Thomas H, Vazquez P (2008) Transesterification of β-ketoesters catalyzed by hybrid materials based on silica sol-gel. Catal Today 133:455–460
15. Mhasni O, Rezgui F (2011) The first Et_3N-mediated transesterifications of β-keto esters using Baylis & Hillman alcohols. Tetrahedron 67:6322–6326
16. Kondaiah GCM, Reddy LA, Babu KS, Gurav VM, Huge KG, Bandichhor R, Reddy PP, Bhattacharya A, Anand RV (2008) Boric acid: and efficient and environmentally benign catalyst for transesterification of ethyl acetoacetate. Tetrahedron Lett 49:106–109
17. Yadav JS, Reddy BVS, Krishna AD, Reddy CS, Narsaiah AV (2007) Triphenylphosphine: an efficient catalyst for transesterification of β-ketoesters. J Mol Catal A Chem 261:93–97
18. Loupy ACR (2004) Solvent-free microwave organic synthesis as an efficient procedure for green chemistry. Chim 7:103–112
19. Rao GBD, Acharya BN, Kaushik MP (2013) An efficient synthesis of β-ketoesters via transesterification and its application in Biginelli reaction under solvent-free, catalyst-free conditions. Tetrahedron Lett 54:6644–6647
20. Wang B, Yang LM, Shuan SJ (2003) Ionic liquid-regulated sulfamic acid: chemoselective catalyst for the transesterification of β-ketoesters. Tetrahedron Lett 44:5037–5039
21. Wisniewska C, Koszelewski D, Zysk M, Klossowski S, Zadlo A, Brodzka A, Ostaszewski R (2015) Enzymatic synergism in the synthesis of β-keto esters. Eur J Org Chem 24:5432–5437
22. Cordova A, Janda KD (2001) A highly chemo and stereoselective synthesis of β-keto esters via a polymer-supported lipase catalyzed transesterfication. J Org Chem 66:1906–1909

23. Jin TS, Sun G, Li YW, Li TS (2002) An efficient and convenient procedure for the preparation of 1,1-diacetates form aldehydes catalyzed by H_2NSO_3H. Green Chem 4:255–256
24. Rostami A, Ahmad-Jangi F (2011) Sulfamic acid: an efficient, cost-effective and green catalyst for crossed-aldol condensation of ketones with aromatic aldehydes under solvent-free. Chin Chem Lett 22:1029–1032
25. Wang B (2005) Sulfamic Acid: a very useful catalyst. Synlett 8:1342–1343
26. Darabi HR, Mohandessi S, Aghapoor K, Mohsenzadeh F (2007) A recyclable and highly effective sulfamic acid/MeOH catalytic system for the synthesis of quinoxalines at room temperature. Catal Commun 8:389–392
27. Zhang ZH, Li TS, Li J (2007) A highly effective sulfamic acid/methanol catalytic system for the synthesis of benzimidazole derivatives at room temperature. J Mon Chem 138:89–94
28. Rostami A, Tavakoli A (2011) Sulfamic acid as a reusable and green catalyst for efficient and simple synthesis of 2-substituted-2,3-dihydroquinazolin-4(1H)-ones in water or methanol. Chin Chem Lett 22:1317–1320
29. Li JP, Qiu JK, Li HJ, Zhang GS (2011) An efficient, three-component one-pot preparation of 1,4-dihydropyridines containing novel substituted pyrazole under sulfamic acid catalysis. Chin J Chem 29:511–514
30. Kappe CO, Stadler A (2005) Microwaves in organic and medicinal chemistry. Wiley-VCH Publishing, Weinheim
31. Madhav JV, Kumar VN, Rajitha B (2008) Sulfamic acid-catalyzed one-pot synthesis of 3-(4,6-dimethyl-oxazolo[4,5-c]quinolin-2-yl)-chromen-2-ones using the conventional method and microwave irradiation. Synth Commun 38:1799–1807
32. Kappe CO (2004) Controlled microwave heating in modern organic synthesis. Angew Chem Int Ed 43:6250–6284
33. Polshettiwar V, Varma RS (2008) Microwave-assisted organic synthesis and transformations using benign reaction media. Acc Chem Res 41:629–639
34. Lindstrom P, Tierney J, Wathey B, Westman J (2002) Microwave assisted organic synthesis—a review. Tetrahedron 57:9225–9283
35. Ranu BC, Saha A, Jana R (2007) Microwave-assisted simple and efficient ligand free copper nanoparticle catalyzed aryl-sulfur bond formation. Adv Synth Catal 349:2690–2696
36. Brinkerhoff RC, Fontecha-Tarazona HD, de Oliveira PM, Flores DC, D'Oca CRM, Russowsky D, D'Oca MGM (2014) Synthesis of β-ketoesters from renewable resources and Meldrum's acid. RSC Adv 4:49556–49559
37. Rodrigues MO, Cantos JB, D'Oca CRM, Soares KL, Coelho TS, Piovesan LA, Russowsky D, da Silva PA, D'Oca MGM (2013) Synthesis and antimycobacterial activity of isoniazid derivatives from renewable fatty acids. Bioorg Med Chem 21:6910–6914
38. D'Oca CRM, Coelho T, Marinho TG, Hack CRL, Duarte RC, da Silva PA, D'Oca MGM (2010) Synthesis and antituberculosis activity of new fatty acid amides. Bioorg Med Chem Lett 20:5255–5257
39. Duarte RC, Ongaratto R, Piovesan LA, de Lima VR, Soldi V, Merlo AA, D'Oca MGM (2012) New *N*-acylamino acids and derivatives from renewable fatty acids: gelation of hydrocarbons and thermal properties. Tetrahedron Lett 53:2454–2460
40. dos Santos DS, Piovesan LA, D'Oca CRM, Hack CRL, Treptow TGM, Rodrigues MO, Vendramini-Costa DB, Ruiz ALTG, de Carvalho JE, D'Oca MGM (2015) Antiproliferative activity of synthetic fatty acid amides from renewable resources. Bioorg Med Chem 23:340–347
41. D'Oca MGM, Soares RM, Moura RR, Granjão VF (2012) Sulfamic acid: an efficient acid catalyst for esterification of FFA. Fuel 97:884–886
42. Brown HC, Krishnamurthy S (1979) Forty years of hydride reductions. Tetrahedron 35:567–607
43. Wang X, Li X, Xue J, Zhao Y, Zhang Y (2009) A novel and efficient procedure for the preparation of allylic alcohols from α-β-unsaturated carboxylic esters using $LiAlH_4$/BnCl. Tetrahedron Lett 50:413–415
44. Lakshminarayana G, Paulose MM, Kumari NB (1984) Characteristics and composition of newer varieties of Indian castor seed and oil. J Am Oil Chem Soc 61:1871–1872
45. Lopes CR, D'Oca CRM, Duarte RC, Kurz MHS, Primel EG, Clementin RM, Villarreyes JAM, D'Oca MGM (2010) Síntese de novas amidas graxas a partir da aminólise de ésteres metílicos. Quim Nova 33:1335–1341
46. Mhasni O, Erray I, Rezgui F (2014) General and efficient transesterification of β-keto esters with various alcohols using Et_3N as a change by Brønsted base additive. Synt Comm 44:3320–3327