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An improved solvent-free system for the microwave-assisted decarboxylation of malonate derivatives based on the use of imidazole

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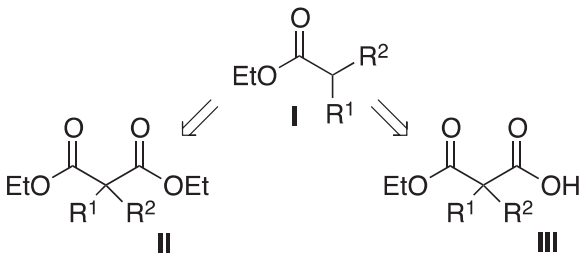
ABSTRACT

A comparative study of the thermal and microwave-assisted decarboxylation of a series of mono- and disubstituted monohydrolyzed malonate derivatives has been carried out. It has been found out that in both circumstances the use of imidazole has a profound effect on the success of the reaction. In general terms the assistance of microwave irradiation accelerates the decarboxylation process significantly and, at the same time, permits the use of minored temperatures with respect to the thermal via. It has been also found that both the thermal and the microwave-assisted transformation can be developed under solvent-free conditions.

1. Introduction

1,3-Dicarbonyl compounds are probably one of the organic functionalities with the highest diverse reactivity, which is due to the occurrence of up to five contiguous reaction sites with an alternative electrophilic and nucleophilic nature. The existence of a growing plethora of different chemical transformations based on such building block is today at chemist's disposal. Multicomponent reactions,[1] the Knoevenagel reaction[2] and the malonic ester synthesis,[3] which are of essential significance in synthetic work, are clear examples of it.

In particular, the malonic synthesis—the successive combination of C-2 functionalization of malonate esters, followed by hydrolysis of one or both ester groups and final decarboxylation reactions—represents a powerful tool to obtain highly functionalized esters or related carboxylic acids. Each of these steps is under constant revision with the aim of developing more efficient procedures in terms of stereocontrol, use of friendly reaction conditions and for the obtaining of better yields. In this context (see Scheme 1), the most employed alternatives for the preparation of esters **I** lie on the thermal deethoxycarbonylation of **II** in the presence of a metal halide or NaCN at very high temperatures in a DMSO-H_2O solvent system (Krapcho reaction),[4] or in the presence of a chiral base,[5] or, alternatively, by heating monoacid **III** under a variety of particular conditions. Although feasible, the decarboxylation of diacids (malonic acid derivatives) is somehow discouraging for several reasons: they are more reluctant—when compared to esters—to react,[6a] the bis-decarboxylation is an occasionally accompanying process[7] and the manipulation of free carboxylic acids in further transformations is more complicated.[8] To circumvent some of these disadvantages, the assistance of microwave irradiation has been implemented to facilitate the decarboxylation of malonic acids.[6b]



Scheme 1. Decarboxylation of malonate derivatives.

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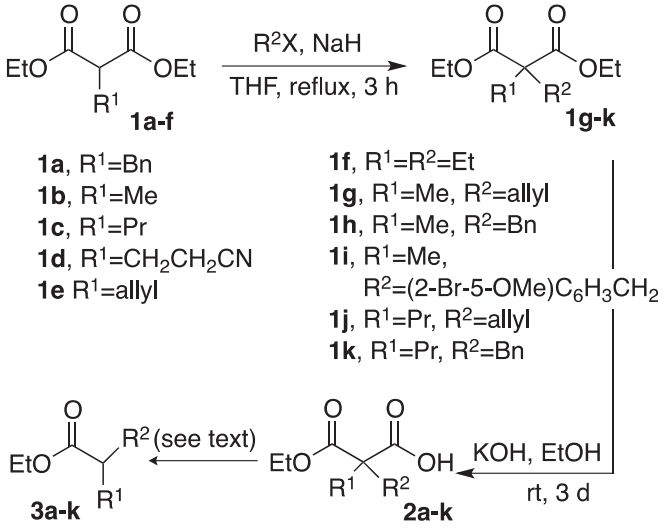
Attracted by the ongoing developments in microwave-accelerated organic syntheses,[9] we initiated a study directed to establish a simple solvent-free protocol to promote the decarboxylation step from mono- and disubstituted malonate monoacid derivatives of type **III** under such conditions and, hence, to avoid the extremely hard conditions (up to 200 °C for a prolonged time, from hours to days) that conventional heating processes normally requires.

2. Results and discussion

Listed in Scheme 2 is shown the series of malonate derivatives **1** required for our study. They were either available from commercial sources (**1a**–**f**) or had to be prepared (**1g**–**k**). In particular, treatment of enolates derived from malonates **1c**,**d** with the desired allyl or benzyl halides in refluxing THF rendered malonates **1g**–**k** in moderate to excellent yields. This selection includes substrates with nitrile, halide or alkoxy containing substituents, as well as additional aromatic or olefinic groups, that will let us evaluate the scope of the projected synthesis. For the next step we found that treatment of malonates **1a**–**k** under basic alcoholic conditions (KOH, EtOH, rt) was suitable to obtain the monohydrolyzed derivatives **2a**–**k** efficiently. They were all isolated in high yields, in the absence of malonic acids, by simple extraction at adjusted pH, and, indeed, no further purifications were required to face the next step.

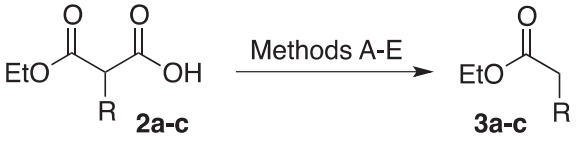


Scheme 2. Series of commercially available and synthetically prepared malonates **1a**–**k**: **1g** (91% from **1b**), **1h** (45% from **1b**), **1i** (47% from **1b**), **1j** (91% from **1c**), **1k** (80% from **1c**). Series of monoacid malonate derivatives **2a**–**k**: **2a** (89%), **2b** (81%), **2c** (85%), **2d** (92%), **2e** (76%), **2f** (85%), **2g** (74%), **2h** (79%), **2i** (77%), **2j** (45%), **2k** (70%).

It is known that the polar carboxylic salts formed with imidazole favors the promotion ability for efficient microwave energy absorption over other ammonium salts.[10] To corroborate this statement for our particular challenge, monoacids **2a**–**c** were selected to optimize the decarboxylation step carrying parallel control experiments both in the presence and in the absence of imidazole, and with microwave assistance and under simple thermal conditions (see Table 1). In addition, since the development of a quick procedure would be more attractive, we did not investigate reaction times longer than ten minutes.

From the first experiments it could be concluded that the actual need of imidazole, as announced, seemed to be mandatory. In fact, no conversion was detected in the absence of it (Method A) even in combination of microwave assistance (Method C). For an efficient transformation, both the presence of imidazole and the microwave radiation are required (Method D). It was also observed that comparable yields could be obtained with very short reaction times (1 min) if the temperature was raised to 150 °C (Method E).

Table 1
Optimization screening of Methods A–D for the decarboxylation of monoacids **2a**–**c**

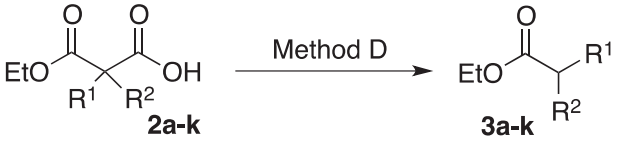


Methods					
2/3	A	B	C	D[a]	E
	3 (%)	3 (%)	3 (%)	3 (%)	3 (%)
a	0	15	0	85 (69 °C)	91
b	0	32	0	92 (115 °C)	87
c	0	20	0	89 (125 °C)	83

Method A: 125 °C, 10 min, solvent free.
Method B: 125 °C, 4 min, solvent free, imidazole (1 equiv).
Method C: 125 °C, 10 min, solvent free, μw.
Method D: 125 °C, 4 min, solvent free, imidazole (1 equiv), μw.
Method E: 150 °C, 1 min, solvent free, imidazole (1 equiv), μw.
[a] Method D was always established at a maximum-programmed temperature of 125 °C. The actual experimental temperature is given for each case in brackets.

With such results in hand, and having established the convenience of the microwave assistance, over the thermal via, for our purposes, Method D was applied to the rest of monoacids **2d**–**k** (Table 2) to demonstrate the generality of the procedure.[11] In fact, in all cases under study esters **3a**–**k** were obtained in good to excellent yields (72–100%) in a very short reaction time under relatively low temperatures. To show the convenience of the established protocol, Table 2 includes previously reported (if available) synthetic information on the requirements to obtain esters **3** directly from malonates **1** under Krapcho's conditions. In this case, substrates must be submitted to much higher temperatures (up to 210 °C) for several hours to render the desire product in a comparable yield. It is also noticeable that, contrary to our positive results (entries 7–11), Krapcho's conditions are not effective with disubstituted substrates, even at very high temperatures and microwave assistance.[12]

Table 2
Decarboxylation of monoacids **2a**–**k**



Entry	2/3	3, method D[a] % yield (actual T)	Krapcho's condt.[b] % yield/time/°C
1	**a**	85 (69 °C)	89/30 min/210[13]
2	**b**	92 (115 °C)	—
3	**c**	89 (125 °C)	59/14 h/180[14]
4	**d**	99 (125 °C)	—
5	**e**	97 (124 °C)	82/8 h/180[15]
6	**f**	98 (62 °C)	90/12 h/180[16]
7	**g**	100 (92 °C)	72/24 h/180[17]
8	**h**	100 (75 °C)	—
9	**i**	72 (124 °C)	—
10	**j**	88 (117 °C)	—
11	**k**	82 (96 °C)	—

[a] Method C was always established at a maximum-programmed temperature of 125 °C. The actual experimental temperature is given for each case.
[b] Literature data (if available) for the deethoxycarbonylation of the corresponding diethyl malonate **1** in the presence of a salt in a mixture of DMSO/H_2O as solvent media.

3. Conclusion

In summary, we have shown that the microwave irradiation in the presence of imidazole has a profound effect on the ease of decarboxylation of malonate-derived monoacids. The described procedure features various fundamental aspects: (1) high yields for a number of different models, (2) very high temperatures, that would be harmful for more elaborated molecules, are avoided, (3) the procedure is effective both for mono- and for disubstituted substrates, (4) reactions are completed in less than 4 min, and (5) the possibility to carry out the reaction in the absence of any solvent, which facilitates further manipulations.

4. Experimental section

4.1. General information

All reagents were purchased and used as received. Melting points were measured using open glass capillaries and are uncorrected. Infrared spectra were recorded as KBr plates or as thin films and peaks are reported in cm^{-1}. Only representative absorptions are given. NMR spectra were recorded on a Bruker AV300 (300 MHz for ^1H and 75.4 MHz for ^{13}C) instrument at 20 °C using $CDCl_3$ as solvent. Chemical shifts (δ) were measured in ppm relative to chloroform (δ=7.26 for ^1H or 77.0 for ^{13}C) as internal standard. Coupling constants, *J*, are reported in hertz. DEPT experiments were used to assist with the assignation of the signals. HRMS spectra were measured by using a Waters GCT Mass Spectrometer under ESI^+ conditions; data for $M+H^+$ is reported. Microwave irradiation experiments were performed with a CEM Discover instrument. Temperature was set up at a maximum of 125 °C, but tables show the actual monitored temperature.

4.2. General procedure for the synthesis of malonates 1g–k. Synthesis of malonate 1g

Malonate **1b** (5 mL, 29.4 mmol) was slowly added to a suspension of NaH (1.76 g, 73.5 mmol) in 25 mL of THF at 0 °C. Then, allyl iodide (2.7 mL, 29.4 mmol) was added and the mixture was stirred at reflux for 3 h. When cooled, the mixture was diluted with 15 mL of diethyl ether and washed with brine (3×10 mL). Layers were decanted and the organic phase was dried over Na_2SO_4, filtered, and solvent was removed under vacuum to afford malonate **1g** as a yellowish oil (91%). Malonate **1g** was obtained as a chromatographically pure compound and no further purification was required for its use. Its spectroscopic behavior was in total agreement with reported data.

*4.2.1. Diethyl 2-allyl-2-methylmalonate (**1g**).*[18] Yellowish oil, 91% yield. ^1H NMR (300 MHz, $CDCl_3$) δ 5.73–5.63 (m,1H), 5.13–5.07 (m, 2H), 4.15 (q, *J*=7.2 Hz, 4H), 2.57 (d, *J*=7.4 Hz, 2H), 1.35 (s, 3H), 1.21 (t, *J*=7.2 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.8, 132.6, 119.0, 61.1, 53.4, 40.0, 16.6, 14.0; IR (cm^{-1}): 1730, 1246, 1207.

*4.2.2. Diethyl 2-benzyl-2-methylmalonate (**1h**).*[19] Yellowish oil, 45% yield, purified by column chromatography (CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$) δ 7.20–7.05 (m, 5H), 4.18 (q, *J*=6.0 Hz, 4H), 3.33 (s, 2H), 1.32 (s, 3H), 1.24 (t, *J*=6.0 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.9, 136.2, 130.2, 128.2, 126.9, 61.2, 58.8, 41.1, 16.7, 14.0; IR (cm^{-1}): 1735, 1275, 1103.

*4.2.3. Diethyl 2-(2-bromo-5-methoxybenzyl)-2-methylmalonate (**1i**).* Yellowish oil, 47% yield, purified by column chromatography (CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$) δ 7.35 (d, *J*=9.0 Hz, 1H), 6.69 (d, *J*=3.0 Hz, 1H), 6.60 (dd, *J*=9.0, 3.0, Hz, 1H), 4.19 (q, *J*=7.1 Hz, 4H), 3.68 (s, 3H), 3.42 (s, 2H), 1.34 (s, 3H), 1.21 (t, *J*=7.1 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.7, 158.6, 137.2, 133.4, 116.8, 116.6, 114.2, 61.4, 55.2, 55.1, 39.4, 19.2, 14.0; IR (cm^{-1}): 1727, 1462, 1239; HRMS calculated for $C_{16}H_{21}BrO_5 \cdot H^+$: 373.0651, found: 373.0641.

*4.2.4. Diethyl 2-allyl-2-propylmalonate (**1j**).*[20] Yellowish oil, 91% yield, purified by column chromatography (CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$) δ 5.73–5.52 (m, 1H), 5.10–5.04 (m, 2H), 4.12 (q, *J*=7.1 Hz, 4H), 2.59 (d, *J*=7.4 Hz, 2H), 1.90–1.70 (m, 2H), 1.24–1.10 (m, 8H), 0.86 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.2, 132.6, 118.6, 61.0, 57.4, 36.9, 34.3, 17.2, 14.3, 14.1; IR (cm^{-1}): 1730, 1218, 1196.

*4.2.5. Diethyl 2-benzyl-2-propylmalonate (**1k**).* Yellowish oil, 80% yield, purified by column chromatography (CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$) δ 7.35–7.00 (m, 5H), 4.18 (q, *J*=7.2 Hz, 4H), 3.25 (s, 2H), 1.78 (m, 2H), 1.50–1.10 (m, 8H), 0.93 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.2, 136.4, 129.9, 128.2, 126.8, 61.0, 58.8, 38.1, 34.0, 17.5, 14.1; IR (cm^{-1}): 1727, 1210, 1178; HRMS calculated for $C_{17}H_{24}O_4 \cdot H^+$: 293.1753, found: 293.1756.

4.3. General procedure for the monohydrolysis of malonates 1a–k. Synthesis of monoacid 2a

Malonate **1a** (7.5 g, 30.0 mmol) was added to a solution of KOH (1.68 g, 30.0 mmol) in 45 mL of EtOH at room temperature and the solution was stirred for 72 h. For the work-up the solvent was evaporated and the resulting residue was dissolved in $NaHCO_3$ 5% (20 mL) and washed with ethyl acetate (15 mL). The aqueous layer was acidified and extracted with ethyl acetate (3×15 mL). The combined organic layers were dried over Na_2SO_4, filtered, and solvent evaporated to give monoacid **2a** as a colorless oil (89%). Monoacid **2a** was obtained as a chromatographically pure compound and no further purification was required. Its spectroscopic behavior was consisted with reported data.

*4.3.1. 2-(Ethoxycarbonyl)-3-phenylpropionic acid (**2a**).*[21] Colorless oil, 89% yield. ^1H NMR (300 MHz, $CDCl_3$) δ 10.84 (br s, 1H), 7.32–7.28 (m, 5H), 4.18 (q, *J*=7.1 Hz, 2H), 3.72 (t, *J*=7.7 Hz, 1H), 3.25 (d, *J*=7.7 Hz, 2H), 1.21 (t, *J*=7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.4, 168.8, 137.5, 128.9, 128.7, 126.9, 61.9, 53.7, 34.6, 13.9; IR (cm^{-1}): 1716.

*4.3.2. 2-(Ethoxycarbonyl)propionic acid (**2b**).*[22] Colorless oil, 81% yield. ^1H NMR (300 MHz, $CDCl_3$) δ 10.80 (br s, 1H), 4.13 (q, *J*=7.1 Hz, 2H), 3.47 (q, *J*=7.3 Hz, 1H), 1.42 (d, *J*=7.3 Hz, 3H), 1.27 (t, *J*=7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.1, 170.1, 61.7, 46.0, 13.7, 13.4; IR (cm^{-1}): 3100, 1716.

*4.3.3. 2-(Ethoxycarbonyl)pentanoic acid (**2c**).*[21] Colorless oil, 85% yield. ^1H NMR (300 MHz, $CDCl_3$) δ 9.50 (br s, 1H), 4.23 (q, *J*=7.1 Hz, 2H), 3.40 (t, *J*=7.3 Hz, 1H), 1.95–1.88 (m, 2H), 1.37–1.31 (m, 2H), 1.23 (t, *J*=7.1 Hz, 3H), 0.95 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.0 (C-2), 169.5 (C-4), 61.6 (C-5), 51.5 (C-3), 30.8 (C-7), 20.5 (C-8), 14.0 (C-6), 13.6 (C-9); IR (cm^{-1}): 1713.

*4.3.4. 4-Cyano-2-(ethoxycarbonyl)pentanoic acid (**2d**).* Colorless oil, 92% yield. ^1H NMR (300 MHz, $CDCl_3$) δ 10.69 (br s, 1H), 4.18 (q, *J*=7.1 Hz, 2H), 3.50 (t, *J*=7.1 Hz, 1H), 2.48 (t, *J*=7.3 Hz, 2H), 2.18–2.16 (m, 2H), 1.23 (t, *J*=7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.6, 168.0, 118.5, 62.3, 49.9, 24.2, 14.9, 13.9; IR (cm^{-1}): 3050, 2247, 1727; HRMS calculated for $C_8H_{11}NO_4 \cdot H^+$: 186.0766, found: 186.0749.

*4.3.5. 2-(Ethoxycarbonyl)-4-pentenoic acid (**2e**).*[23] Colorless oil, 76% yield. ^1H NMR (300 MHz, $CDCl_3$) δ 10.84 (br s, 1H), 5.80–5.76 (m, 1H), 5.25–5.10 (m, 2H), 4.21 (q, *J*=7.2 Hz, 2H), 3.45 (t, *J*=7.5 Hz, 1H),

2.68–2.62 (m, 2H), 1.26 (t, J=7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.7, 168.7, 133.6, 117.9, 61.8, 51.4, 32.8, 14.0; IR (cm^{-1}): 1716.

*4.3.6. 2-(Ethoxycarbonyl)-2-ethylbutanoic acid (**2f**).* Colorless oil, 85% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.01 (br s, 1H), 4.16 (q, J=7.1 Hz, 2H), 1.88 (m, 4H), 1.21 (t, J=7.1 Hz, 3H), 0.77 (t, J=6.2 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.0, 172.5, 61.5, 58.6, 25.8, 13.9, 8.5; IR (cm^{-1}): 3050, 1705; HRMS calculated for $C_9H_{16}O_4 \cdot H^+$: 189.1127, found: 189.1110.

*4.3.7. 2-(Ethoxycarbonyl)-2-methyl-4-pentenoic acid (**2g**).* Colorless oil, 74% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.60 (br s, 1H), 5.80–5.62 (m, 1H), 5.15–5.09 (m, 2H), 4.20 (q, J=7.2 Hz, 2H), 2.69–2.55 (m, 2H), 1.42 (s, 3H), 1.26 (t, J=7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.9, 171.6, 132.2, 119.5, 61.7, 53.5, 40.0, 19.8, 14.0; IR (cm^{-1}): 3100, 1710; HRMS calculated for $C_9H_{14}O_4 \cdot H^+$: 187.0970, found: 187.0954.

*4.3.8. 2-Benzyl-2-(ethoxycarbonyl)propionic acid (**2h**).*[24] Yellowish oil, 79% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.14 (br s, 1H), 7.24–7.18 (m, 5H), 4.24 (q, J=7.1 Hz, 2H), 3.33 (d, J=13.6 Hz, 1H), 3.24 (d, J=13.6 Hz, 1H), 1.43 (s, 3H), 1.29 (t, J=7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.1, 171.8, 135.8, 130.2, 128.4, 127.1, 61.9, 55.0, 41.2, 19.7, 14.0; IR (cm^{-1}): 3085, 1710.

*4.3.9. 2-(2-Bromo-5-methoxybenzyl)-2-(ethoxycarbonyl)-propionic acid (**2i**).* White solid, 77% yield, mp 64–65 °C (hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.20 (br s, 1H), 7.42 (d, J=8.9 Hz, 1H), 6.78 (d, J=3.0 Hz, 1H), 6.66 (dd, J=8.9, 3.0 Hz, 1H), 4.25 (q, J=7.1 Hz, 2H), 3.75 (s, 3H), 3.53 (d, J=3.0 Hz, 1H), 3.49 (d, J=3.0 Hz, 1H), 1.45 (s, 3H), 1.28 (t, J=7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.0, 171.5, 158.7, 136.8, 133.6, 116.7, 116.6, 114.7, 62.0, 55.2, 39.5, 19.2, 13.9; IR (cm^{-1}): 1713; HRMS calculated for $C_{14}H_{18}BrO_5 \cdot H^+$: 345.0338, found: 345.0343.

*4.3.10. 2-(Ethoxycarbonyl)-2-propyl-4-pentenoic acid (**2j**).* Yellowish oil, 45% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.67 (br s, 1H), 5.68–5.53 (m, 1H), 5.13–5.09 (m, 2H), 4.21 (q, J=7.1 Hz, 2H), 2.72–2.57 (m, 2H), 1.84–1.75 (m, 2H), 1.23 (m, 5H), 0.9 (t, J=7.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.1, 172.5, 132.1, 119.1, 61.8, 57.7, 38.2, 35.8, 17.6, 14.2, 14.1; IR (cm^{-1}): 3100, 1710; HRMS calculated for $C_{11}H_{18}O_4 \cdot H^+$: 215.1283, found: 215.1272.

*4.3.11. 2-Benzyl-2-(ethoxycarbonyl)pentanoic acid (**2k**).* Colorless oil, 70% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.97 (br s, 1H), 7.30–7.00 (m, 5H), 4.24 (q, J=7.1 Hz, 2H), 3.37 (d, J=13.8 Hz, 1H), 3.16 (d, J=13.8 Hz, 1H), 2.02–1.93 (m, 2H), 1.40–1.29 (m, 5H), 0.94 (t, J=7.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.9, 174.4, 135.8, 129.5, 128.5, 127.3, 62.3, 59.3, 41.3, 37.5, 18.3, 14.0, 13.9; IR (cm^{-1}): 3100, 1709; HRMS calculated for $C_{15}H_{20}O_4 \cdot H^+$: 265.1440, found: 265.1429.

4.4. General procedure for the microwave assisted decarboxylation of 2a–k. Synthesis of ester 3a

A cap closed-vessel that has been charged with monoacid **2a** (52 mg, 0.23 mmol) and imidazole (28 mg, 0.23 mmol) was irradiated for the programmed time and temperature (see Table 2). For the work-up, the residue was diluted with CH_2Cl_2 and washed with water (to remove imidazole), the organic layer was dried over Na_2SO_4, and the solvent evaporated under vacuum to render chromatographically pure ester **3a** as a colorless oil (82% yield).[25]

*4.4.1. Ethyl 3-phenylpropionate (**3a**).* Colorless oil, 82% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42–7.30 (m, 5H), 4.13 (q, J=7.1 Hz, 2H), 2.96 (t, J=7.8 Hz, 2H), 2.62 (t, J=7.8 Hz, 2H), 1.24 (t, J=7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.0, 140.6, 128.4, 128.0, 126.2, 60.4, 36.0, 31.0, 14.2; IR (cm^{-1}): 1731.

*4.4.2. Ethyl propionate (**3b**).* Yellowish oil, 91% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.16 (q, J=7.1 Hz, 2H), 2.32 (q, J=7.6 Hz, 2H), 1.24 (t, J=7.1 Hz, 3H), 1.14 (t, J=7.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.8, 60.3, 27.6, 14.2, 9.1.

*4.4.3. Ethyl pentanoate (**3c**).* Yellowish oil, 86% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.15 (q, J=7.1 Hz, 2H), 2.29 (t, J=7.4 Hz, 2H), 1.62–1.56 (m, 2H), 1.33–1.28 (m, 2H), 1.24 (t, J=7.1 Hz, 2H), 0.91 (t, J=7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.1, 60.2, 34.1, 27.0, 22.2, 13.9, 13.3.

*4.4.4. Ethyl 4-cyanobutanoate (**3d**).*[26] Yellowish oil, 99% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.15 (q, J=7.1 Hz, 2H), 2.54–2.31 (m, 4H), 2.03–1.95 (m, 2H), 1.27 (t, J=7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.8, 118.6, 60.8, 32.4, 20.8, 16.6, 14.2.

*4.4.5. Ethyl 4-pentenoate (**3e**).* Yellowish oil, 97% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.85–5.63 (m, 1H), 5.11–4.99 (m, 2H), 4.13 (q, J=7.1 Hz, 2H), 2.38 (m, 4H), 1.25 (t, J=7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.8, 137.6, 115.3, 60.2, 33.9, 30.5, 15.8.

*4.4.6. Ethyl 2-ethylbutanoate (**3f**).*[27] Yellowish oil, 98% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.14 (q, J=7.1 Hz, 2H), 2.18 (m, 1H), 1.54 (m, 4H), 1.25 (t, J=7.1 Hz, 3H), 0.88 (t, J=7.4 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.4, 59.9, 49.0, 25.1, 14.3, 11.8.

*4.4.7. Ethyl 2-methyl-4-pentenoate (**3g**).* Yellowish oil, 100% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.82–5.61 (m, 1H), 5.08–5.00 (m, 2H), 4.12 (q, J=7.1 Hz, 2H), 2.59–2.28 (m, 2H), 2.23–2.17 (m, 1H), 1.24 (t, J=7.1 Hz, 3H), 1.14 (d, J=6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.2, 135.5, 116.8, 60.2, 39.2, 37.8, 16.5, 14.2; IR (cm^{-1}): 1730.

*4.4.8. Ethyl 2-methyl-3-phenylpropionate (**3h**).*[28] Yellowish oil, 100% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30–7.10 (m, 5H), 4.11 (q, J=7.1 Hz, 2H), 3.08–2.96 (m, 1H), 2.82–2.60 (m, 2H), 1.25–1.18 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.1, 139.4, 129.0, 128.3, 126.3, 60.2, 41.5, 39.8, 16.8, 14.2; IR (cm^{-1}): 1730.

*4.4.9. Ethyl 3-(2-bromo-5-methoxyphenyl)-2-methylpropionate (**3i**).* Yellowish oil, 72% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35 (d, J=8.7 Hz, 1H), 6.72 (d, J=3.1 Hz, 1H), 6.59 (dd, J=8.7, 3.1 Hz, 1H), 4.05 (q, J=7.0 Hz, 2H), 3.70 (s, 3H), 3.12–3.00 (m, 1H), 2.80–2.69 (m, 1H), 1.15 (t, J=7.0 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.7, 158.7, 139.8, 133.3, 115.1, 116.8, 113.7, 60.3, 55.3, 40.0, 39.7, 17.0, 14.1; IR (cm^{-1}): 1730; HRMS calculated for $C_{13}H_{17}BrO_3 \cdot H^+$: 301.0441, found: 301.0439.

*4.4.10. Ethyl 2-propyl-4-pentenoate (**3j**).* Yellowish oil, 88% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.83–5.60 (m, 1H), 5.11–5.05 (m, 2H), 4.13 (q, J=7.1 Hz, 2H), 2.50–2.15 (m, 3H), 1.68–1.25 (m, 4H), 1.24 (t, J=7.1 Hz, 3H), 0.90 (t, J=7.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.1, 135.6, 116.5, 61.1, 53.4, 36.5, 34.0, 20.5, 14.3, 14.0.

*4.4.11. Ethyl 2-benzylpentanoate (**3k**).*[29] Yellowish oil, 82% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33–7.18 (m, 5H), 4.06 (q, J=7.1 Hz, 2H), 2.97–2.86 (m, 1H), 2.70–2.60 (m, 2H), 1.62–1.18 (m, 4H), 1.15 (t, J=7.0 Hz, 3H), 0.90 (t, J=7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.7, 139.5, 128.9, 128.3, 126.2, 60.1, 47.5, 38.6, 34.3, 20.5, 14.1, 13.9; IR (cm^{-1}): 1731.

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Supplementary data

Supplementary data (NMR copies of compounds **1**–**3**) related to this article can be found at http://dx.doi.org/10.1016/j.tet.2015.09.012.

References and notes

1. Peshkov, V. A.; Peshkov, A. A.; Pereshivko, O. P.; Van Hecke, K.; Zamigaylo, L. L.; Van der Eycken, E. V.; Gorobets, N. Y. *ACS Comb. Sci.* **2014**, *16*, 535–542 and references therein.
2. List, B. *Angew. Chem., Int. Ed.* **2010**, *49*, 1730–1734.
3. (a) Carruthers, W. *Some Modern Methods of Organic Synthesis*, 3rd ed.; Cambridge University Press: Cambridge, UK, 1986; p 1; (b) Carey, F. A.; Sundberg, R. J. *Advanced Organic Chemistry (Part B)*, 5th ed.; Plenum Press: New York, NY, 2007; pp 22–24; and references cited therein.
4. (a) Krapcho, A. P. *Arkivoc* **2007**, *ii*, 1–53; (b) A recent modification of these conditions that includes the use of microwave irradiation avoids the use of DMSO leading to a more facile work up Mason, J. D.; Murphree, S. S. *Synlett* **2013**, 1391–1394.
5. The first example of an enantioselective decarboxylation reaction of this type was reported by Marckwald in 1904: (a) Marckwald, W. *Ber. Dtsch. Chem. Ges.* **1904**, *37*, 349–354; (b) Marckwald, W. *Ber. Dtsch. Chem. Ges.* **1904**, *37*, 1368–1370; (c) For a recent advance, see Amere, M.; Lasne, M.-C.; Rouden, J. *Org. Lett.* **2007**, *9*, 2621–2624 and references therein. This alternative can be conducted at room temperature, but in a prolonged (up to seven days) reaction time.
6. (a) Toussaint, O.; Capdevielle, P.; Maumy, M. *Synthesis* **1986**, 1029–1031; (b) Zara, C. L.; Jin, T.; Giguere, R. *Synth. Commun.* **2000**, *30*, 2099–2104.
7. Valla, A.; Le Guillou, R.; Cartier, D.; Labia, R. *Tetrahedron Lett.* **2003**, *44*, 4737–4740.
8. (a) For that reason, a mild decarboxylative procedure that leaves the remaining carboxylic group in an activated stage for ulterior transformations is of great interest Lafrance, D.; Bowles, P.; Leeman, K.; Rafka, R. *Org. Lett.* **2011**, *13*, 2322–2325 See also: Lebedyeva, I. O.; Biswas, S.; Goncalves, K.; Sileno, S. M.; Jackson, A. R.; Patel, K.; Steel, P. J.; Katritzky, A. R. *Chem.—Eur. J.* **2014**, *20*, 11695–11698; (b) Stereocontrolled enzyme-assisted decarboxylations are also possible from diacids. See, for example Okrasa, K.; Levy, C.; Wilding, M.; Goodall, M.; Baudendistel, N.; Hauer, B.; Leys, D.; Micklefield, J. *Angew. Chem., Int. Ed.* **2009**, *48*, 7691–7694 and references therein.
9. (a) Kappe, C. O. *Angew. Chem., Int. Ed.* **2004**, *43*, 6250–6284; (b) De la Hoz, A.; Díaz-Ortíz, A.; Moreno, A. *Chem. Soc. Rev.* **2005**, *34*, 164–178; (c) Varma, R. S. *Green Chem.* **2009**, *1*, 43–55; (d) Lidström, P.; Tierney, J.; Wathey, B.; Westman, J. *Tetrahedron* **2001**, *57*, 9225–9283; (e) Perreux, L.; Loupy, A. *Tetrahedron* **2001**, *57*, 9199–9223.
10. (a) Baldwin, B. W.; Hirose, T.; Wang, Z.-H. *Chem. Commun.* **1996**, 2669–2670; (b) Loupy, A.; Pigeon, P.; Ramdani, M. *Tetrahedron* **1996**, *52*, 6705–6712.
11. A milder reaction temperature (125 °C, 4 min, method D) was preferred over more stressed conditions (150 °C, 1 min, method E).
12. Curran, D. P.; Zhang, Q. *Adv. Synth. Catal.* **2003**, *345*, 329–332.
13. Mason, J. D.; Murphree, S. S. *Synlett* **2013**, 1391–1394.
14. Hunter, D. H.; Patel, V.; Perry, R. *Can. J. Chem.* **1980**, *58*, 2271–2277.
15. Lanners, S.; Norouzi-Arasi, H.; Khiri, N.; Hanquet, G. *Eur. J. Org. Chem.* **1980**, 4065–4075.
16. Hayes, R. N.; Bowie, J. H. *J. Chem. Soc. Perkin Trans. II* **1986**, 1827–1831.
17. Canney, D. J.; Lu, H.-F.; McKeon, A. C.; Yoon, K.-W.; Xu, K.; Holland, K. D.; Rothman, S. M.; Ferrendelli, J. A.; Covey, D. F. *Bioorg. Med. Chem.* **1998**, *6*, 43–45.
18. Mandal, P. K.; McMurray, J. S. *J. Org. Chem.* **2007**, *72*, 6599–6601.
19. Lee, H. S.; Kim, D. H. *Bioorg. Med. Chem.* **2003**, *11*, 4685–4691.
20. Endo, T.; Kakimoto, K.; Ochiai, B.; Nagai, D. *Macromolecules* **2005**, *38*, 8177–8182.
21. Doni, E.; Mondal, B.; O'Sullivan, S.; Tuttle, T.; Murphy, J. A. *J. Am. Chem. Soc.* **2013**, *135*, 10934–10937.
22. Niwayama, S.; Cho, H.; Lin, C. *Tetrahedron Lett.* **2008**, *49*, 4434–4436.
23. Bien, S.; Gillon, A.; Kohen, S. *J. Chem. Soc., Perkin Trans. 1* **1976**, *5*, 489–492.
24. Flipo, M.; Charton, J.; Hocine, A.; Dassoneville, S.; Deprez, B.; Deprez-Poulain, R. *J. Med. Chem.* **2009**, *52*, 6790–6802.
25. The spectroscopic information for several esters 3 perfectly matches with reported data, either from commercial sources (**3a**–**c, e, g**) or from literature (**3d, f, h, k**).
26. Kim, S.; Lim, C. J. *Angew. Chem., Int. Ed.* **2002**, *41*, 3265–3267.
27. Sakai, T.; Danheiser, R. L. *J. Am. Chem. Soc.* **2010**, *132*, 13203–13205.
28. Jost, M.; Sonke, B.; Broxterman, Q. B.; Sewald, N. *Synthesis* **2005**, 272–278.
29. Li, J.-Q.; Quan, X.; Anderson, P. G. *Chem.—Eur. J.* **2012**, *18*, 10609–10616.