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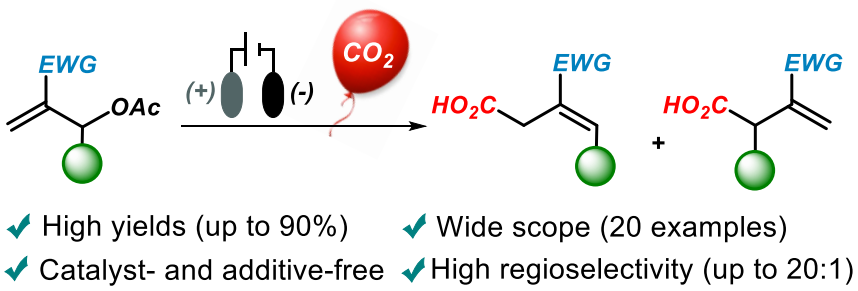


Abstract The electrochemical carboxylation of Morita-Baylis-Hillman (MBH) acetates with CO_2 is presented. The process proceeds in the absence of transition metal catalysts and relies on the cathodic reduction of MBH acetates to generate nucleophilic anions able to trap low-pressure CO_2. Valuable succinate derivatives are obtained (20 examples) in high yields (up to 90%) and high functional group tolerance. A remarkable substrate controlled (electronic nature) regioselectivity of the transformation was documented along with a mechanistic rationale based on control experiments.

Key words electrosynthesis, carbon dioxide, MBH acetates, cathodic reduction, catalyst-free.

The application of enabling technologies in organic chemistry plays a fundamental role in designing efficient and sustainable synthetic strategies, especially when the combination of different activation modes is explored. Among them, synthetic organic electrochemistry (eChem) opens access to redox based electrolytic processes by replacing stoichiometric oxidizing/reducing chemical agents with electricity.[1] In particular, by means of electrons as traceless redox equivalents, electrosynthesis has been shown to regulate chemical reactivity by easy and precise control of reaction parameters (*i.e.* applied current and potential) with extraordinary application also in the chemical valorization of raw materials.[2]

In this context, carbon dioxide (CO_2) is gaining growing credit by the synthetic chemical community as a valuable C_1 synthon in organic chemistry being abundant, non-toxic, non-flammable and inexpensive.[3] As a consequence, the fixation of CO_2 into organic frameworks for the formation of carboxylic acids is particularly attractive, given their use in the manufacture of cosmetics, soaps, detergents, rubbers, dyes, plastics, agrochemicals, and pharmaceuticals, among others.[4] Nucleophilic trapping of CO_2 is the most efficient strategy to implement carbon dioxide into synthetic organic reactions, with the use of metal catalysis (*in situ* generation of nucleophilic organometallic intermediates) amongst the most valuable alternatives.[5] These methodologies, although displaying very wide applicability, often rely on the concomitant use of metal-powder reductants and multiple stoichiometric additives that hamper the overall sustainability of the protocol. The use of eChem as a power supply for carboxylation reactions paves the way towards simpler, more efficient and more economical protocols for the valorization and fixation of CO_2.[6]

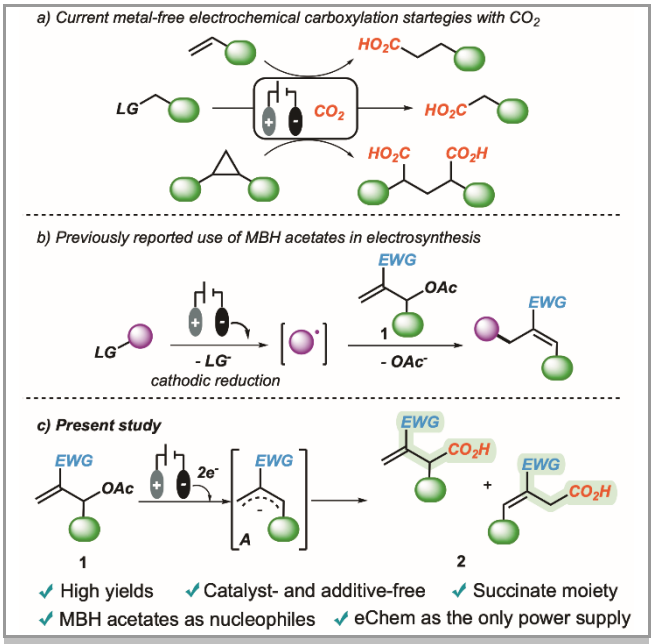


Figure 1 a) Examples of metal-free electrochemical carboxylation reactions with CO_2. b) Previous works of the group on the eChem-based manipulations of MBH derivatives. c) The present working hypothesis.

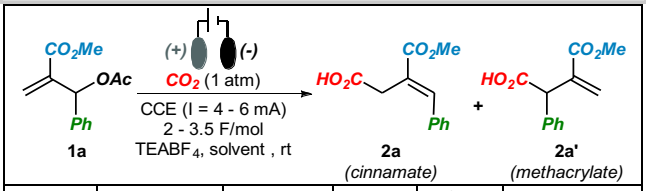
Indeed, eChem, using electricity alone as a sufficient power supply, can effectively generate transient nucleophilic species, capable of trapping CO_2 for the subsequent conversion into value-added functionalized carboxylic acids (Figure 1a).[7]

In continuation with our ongoing interest addressing the synthetic valorization of CO_2[8] and the electrochemical

manipulation of Morita-Baylis-Hillman (MBH) acetates **1**,[9] we envisioned the possibility to merge these approaches documenting a cathodic reduction[10] of MBH derivatives **1** and subsequent CO_2 trapping.[11] Therefore, the electrophilic profile of MBH acetates **1**, previously serving for the capture of nucleophilic radicals[12] generated by cathodic reduction (Figure 1b), is twisted into a nucleophilic character.[13] The interception of the resulting allyl anions (**A**) by CO_2 would lead to direct access to synthetically valuable succinates **2** (Figure 1c).[14]

At the outset of our investigation, we subjected acetate **1a** to galvanostatic electrolysis (5 mA, 2 F/mol$_{\mathbf{1a}}$) under CO_2 atmosphere (1 atm), in the presence of $TEABF_4$ as supporting electrolyte (DMF, 0.05 M in **1a**) and using $C_{graphite}$ and Zn rods as cathode and anode, respectively (Table 1). Importantly, the presence of a Zn anode avoids the use of organic reductants, following the sacrificial anode strategy. To our delight, the target succinate **2** was isolated in 38% yield as a 1:1.2 regioisomeric mixture comprising the cinnamate-like derivative **2a** and the methacrylate-like derivative **2a'**.

Table 1 Optimization of reaction conditions



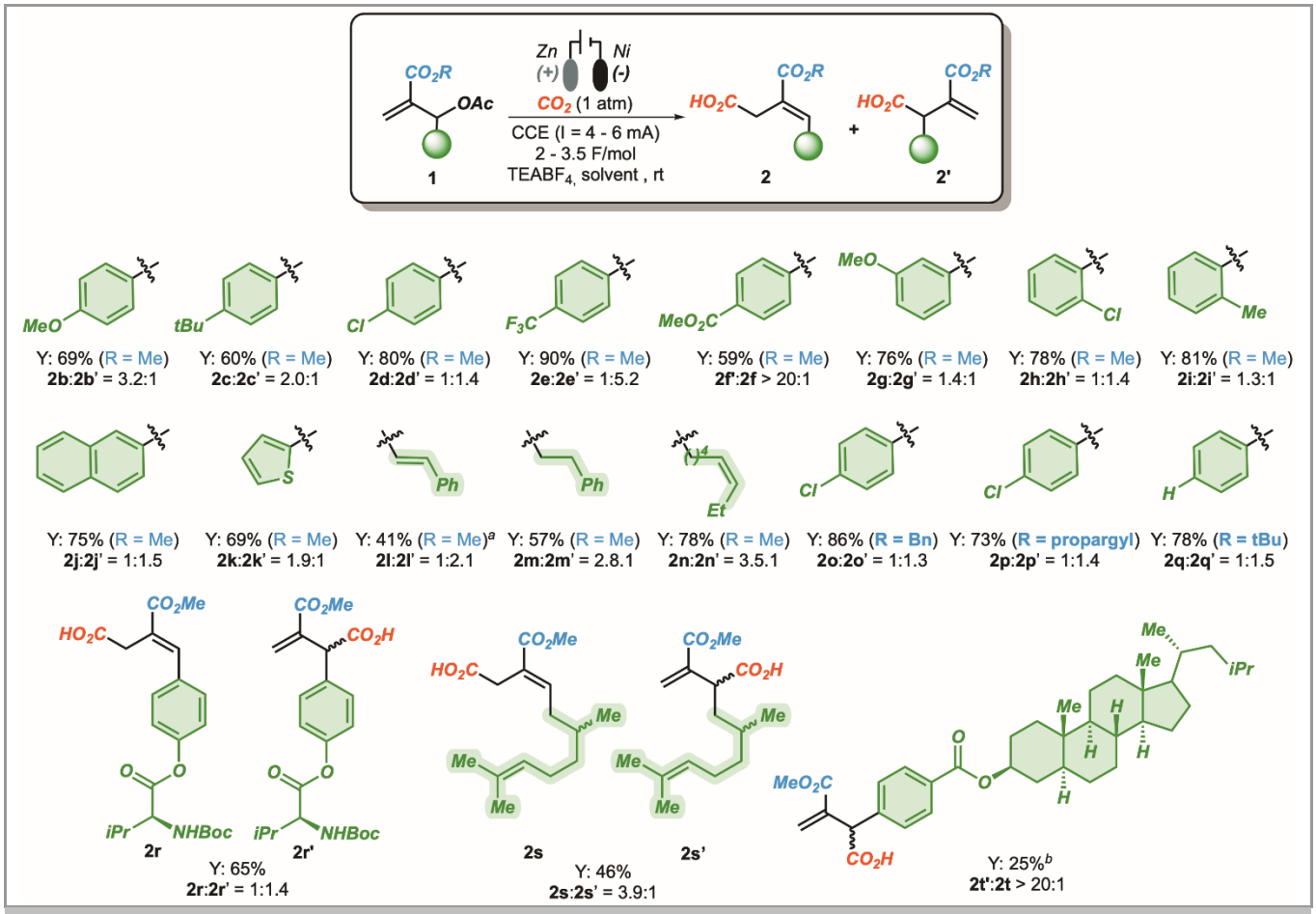
Entry[a]	C(-)||A(+)	Solvent	I [mA]	F/mol	Yield [%] (**2a**:**2a'**)[b]
1	$C_{graph.}$||Zn	DMF	5	2	38 (1.2:1)
2	SS||Zn	DMF	5	2	61 (1.4:1)
3	GC||Zn	DMF	5	2	48 (1.3:1)
4	Pt||Zn	DMF	5	2	51 (1.5:1)
5	Ni||Zn	DMF	5	2	63 (1.4:1)
6	Ni||Mg	DMF	5	2	57 (1.0:1)
7[c]	Ni||$C_{graph.}$	DMF	5	2	15 (1.0:1)
8	Ni||Zn	ACN	5	2	29 (1:1.2)
9	Ni||Zn	DMSO	5	2	61 (1.4:1)
10	Ni||Zn	DMA	5	2	60 (1.2:1)
11	Ni||Zn	DMF	4	2	50 (1.3:1)
12	Ni||Zn	DMF	6	2	70 (1.4:1)
13	Ni||Zn	DMF	5	3.5	79 (1.4:1)
14	Ni||Zn	DMF	6	3.5	83 (1.4:1)

[a] All reactions were carried in the Electrasyn 2.0 apparatus (undivided cell) under constant stirring and a net CO_2 atmosphere, [**1a**] = 0.05 M. [b] Isolated yields after flash chromatography. Regioisomeric ratios were determined via ^{1}H-NMR analysis on the reaction crude. [c] Triethanolamine (TEOA, 2 equiv) was used as a chemical reductant.

Then, we investigated a series of electrode couples. From a survey of cathodic materials, inert metals such as stainless steel (SS, entry 2), platinum (Pt, entry 4) and nickel (Ni, entry 5) were found to be superior to graphitic electrodes ($C_{graphite}$, entry 1 and GC, glassy carbon, entry 3). Having elected Ni as the best cathode (63% yield, entry 5), different anodes were also investigated. However, both sacrificial magnesium (Mg, entry 6, 57% yield) and $C_{graphite}$ coupled with the organic reductant triethanolamine (TEOA, 2 equiv, entry 7) were found less competent with respect to sacrificial Zn in delivering the target product. Then, other polar solvents (*i.e.* ACN, DMA and DMSO) were tested (entries 8-10) without recording improved outcomes with respect to DMF (yield up to 61%) and emphasizing the trend of less polar solvents (ACN) performing generally less effectively (29%). Finally, we reached high yields in the desired product (83%) by fine-tuning of the electrolytic parameters, such as the current intensity and the total charge (F/mol$_{\mathbf{1a}}$). In particular, convergence to optimal was obtained by running the process at a constant current of 6 mA and employing 3.5 F/mol$_{\mathbf{1a}}$ (entry 14) Interestingly, in all the optimization experiments (see also SI for an extensive overview) the **2a**/**2a'** ratio did not change significantly, suggesting a possible control exerted by the substrate on the overall regioselectivity of the process. Importantly, isomer **2a** was always obtained in the *E* configuration of the newly formed double bond.

With the optimal reaction conditions in hand, we moved to evaluate the generality of the disclosed methodology, showing a good tolerance towards functional groups and structural diversity (Scheme 1). Importantly, the regioselectivity of the carboxylation was found to be profoundly influenced by the electronic nature of the substituents of the carbon bearing the OAc group. Here, while a strong electron-donating group (*p*-OMe, **1b**) rendered predominantly cinnamate **2b** (3.2:1, 69% yield), a milder EDG such as *t*Bu (**1c**) impacted less significantly (**2c**:**2c'** = 2.0:1, 60% yield). Accordingly, MBH acetates bearing electron-withdrawing substituents such as -Cl (**1d**) and -CF_3 (**1e**) underwent eChem carboxylation with inverted regioselectivity and leading to methacrylate adducts **2d'** (**2d**:**2d'** = 1:1.4) and **2e'** (**2e**:**2e'** = 1:5.2) as the major isomers (combined yields up to 90%). Following the same trend, a conjugative electron-withdrawing group such as a methyl ester (**1f**) promoted the exclusive formation of methacrylate isomer **2f'** in 59% yield. Interestingly, the presence of a methoxy group at the *meta*-position did not bias the regiochemical outcome (**2g:2g'** = 1.4;1, 76% yield) as it was observed for the analogue **1b**, stressing the lower electronic perturbation of EDGs towards the relative *meta* positions of the arenes with respect to the *para* one. Additionally, the reaction was found not to be influenced by steric hinderance, as *ortho*-substituted **1h** and **1i** delivered the respective succinates **2** as balanced mixtures in high yield. Naphthalene (**1j**) and thiophene (**1k**) units were also tolerated.

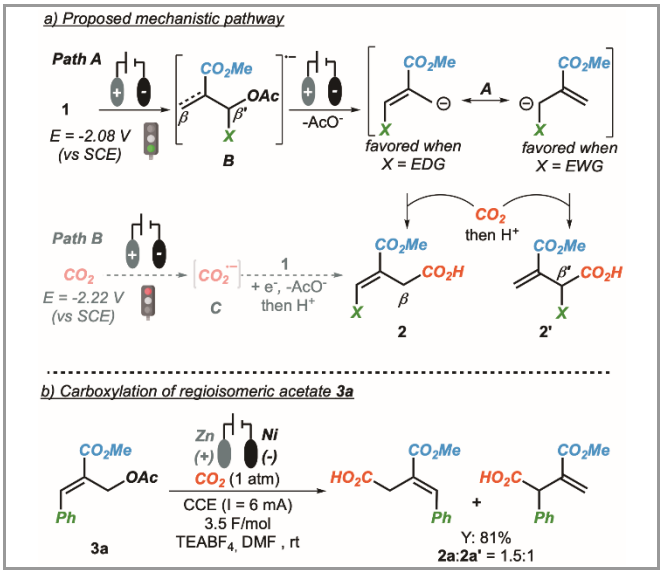
Importantly, non-aromatic MBH acetates **1** were found to be suitable platforms for the present electrochemical CO_2 fixation as well. Cinnamaldehyde-derived **1l** afforded the respective succinates in moderate yield (41%), favoring skipped diene **2l'** (**2l**:**2l'** = 1:2.1). In general, predominant formation of the regioisomer featuring higher substitution of the double bond was observed in alkyl MBH adducts **1m** and **1n**, delivering **2m** (57%, 2.8:1) and **2n** (78%, 3.5:1) as the major regioisomers, respectively.



Scheme 1 Scope of the present electrochemical carboxylation of MBH acetates **1**. Structural modifications were operated both on the MBH substituents and on the nature of the leaving group. In all cases compounds **2** were isolated as the *E*-isomer. [a] Partial decomposition of **1l** was observed during the reaction. [b] Partial recovering of unreacted **1t** was observed.

Different ester groups such as benzyl (**1o**), propargyl (**1p**) and *t*Bu (**1q**) were also excellently tolerated in the present eChem carboxylation. A regioselectivity switch was observed in the case of **2q** and **2q'** (1:1.5, 78% yield) compared to **2a**, indicating a certain influence of the steric size of the ester group in the outcome. Finally, MBH acetates deriving from naturally occurring or biologically relevant compounds such as *L*-valine (**1r**), citronellal (**1s**) and 5α-cholestanol (**1t**) showed that the present protocol can serve as a late-stage functionalization of complex molecular architectures by means of eChem CO_2 fixation. Compound **2r'** (**2r**:**2r'** = 1:1.4, 65% yield) was favored in the case of the carboxylation of **1r**, accounting for the lower electron-releasing effect of the substituent (*cfr.* **1b**). In accordance with previous observations, aliphatic product **2s** was isolated as the major regioisomer and **2t'** was obtained exclusively.

From the data collected in Scheme 1 and following literature precedents on the electrochemical reductive carboxylation of electron deficient olefins,[7i,j] the reaction machinery depicted in Scheme 2a is tentatively proposed. Cathodic reduction of **1** (**1a**: -2.08 V *vs* SCE, see SI) renders intermediate radical anion **B** that, upon successive reduction and loss of the acetate anion gives key intermediate **A** (path a). Allyl anion **A** displays a delocalized negative charge accounting for the observed presence of regioisomeric adducts **2** and **2'**. In particular, the regiocontrol dictated by the aryl ring of **1** might be explained by the tendency to stabilize or destabilize the negative charge in **A**.



Scheme 2 a) Proposed mechanistic sketch. b) Proving the preferential reduction of **1** *vs* CO_2 by control experiments.

As a matter of fact, while electron-withdrawing substituents will localize the anion predominantly at the β' carbon, resulting in products **2'** as the major regioisomers, the presence of electron-donating substituents, destabilizing the negative charge in **A**, will favor the β carbon functionalization.

On the contrary, the initial reduction of CO_2 to give highly reactive radical anion **C** ($CO_2^{\bullet-}$) followed by condensation on MBH acetates **1**, is deemed unlikely for the following reasons: first, CO_2 is more hardly reducible (-2.2 V *vs* SCE)[15] with respect to **1a** (-2.08 V *vs* SCE); and secondly, the condensation of **C** to **1** would result to **2** exclusively, as largely demonstrated in reactions featuring MBH acetates trapping nucleophilic radicals. In addition, to finally support the formation of allyl anion **A** as a key intermediate, acetate **3a** was synthetized and subjected to the optimized reaction conditions (Scheme 2b). A very similar yield and regiochemical outcome, compared to **1a**, was observed (81% yield, **2a**:**2a'** = 1.5:1), suggesting the two regioisomeric starting materials to be converted to the common reactive intermediate (**A**).

In conclusion, we have documented the competence of MBH acetates in electroreductive processes to deliver stabilized anionic species capable of trapping CO_2. The methodology enabled the synthesis of a variety of densely functionalized 1,4-dicarboxylic acids (20 examples, yields up to 90%) and does not require catalytic activation or the assistance of additives. A high regioselectivity – electronic nature of the substrate correlation was documented as well, and rationalized by the proposed reaction machinery.

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^{1}H-NMR spectra were recorded on Varian 400 (400 MHz) . Chemical shifts are reported in ppm from TMS with the solvent resonance as the internal standard ($CHCl_3$: 7.26 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, dd= double doublet, t = triplet, td = triple doublet, dt = double triplet, q = quartet, b = broad, m = multiplet), coupling constants (Hz). ^{13}C-NMR spectra were recorded on a Varian 400 (400 MHz) with complete proton decoupling. Chemical shifts are reported in ppm from TMS with the solvent as the internal standard ($CHCl_3$: 77.0 ppm). HRMS spectra were obtained with a G2XS QTof mass spectrometer using either ESI ionization techniques. Chromatographic purification was done with 240-400 mesh silica gel. Anhydrous solvents, including DMF and ACN for the electrochemical processes, were supplied by Merck in Sureseal® bottles and used without any further purification. All other commercially available starting materials and (non-anhydrous) solvents were purchased from Merck, TCI chemicals, Fluorochem or Alfa Aesar and were used as such without further purification. MBH acetates **1a-1q** and **1s** are known compounds and were synthesized according to literature procedures.[16] The preparation of **1s** and **1t** follows a modification of the same procedure and is reported in the SI. Acetate **3a** was prepared following a literature procedure.[17] Electrochemical reactions were carried out using the ElectraSyn 2.0 apparatus, purchased from IKA.

Electrochemical fixation of CO_2 into MBH acetates; General Procedure.

The ElectraSyn vial (5 mL), equipped with a stir bar, was charged with MBH acetate **1** (0.15 mmol), and $TEABF_4$ (0.30 mmol, 65.1 mg). The ElectraSyn vial cap, equipped with anode (Zn) and cathode (Ni), was inserted into the mixture, and closed with a rubber septum. The vessel was evacuated and backfilled with CO_2 (balloon) three times, then dry DMF (3.0 mL) was added, and the mixture stirred until complete dissolution of the solids occurred. Then, the solution bubbled with CO_2 (balloon) under stirring for 1 min. The reaction mixture was electrolyzed (under CO_2, balloon) at a constant current of 6.0 mA, until a total charge of 0.525 F (3.5 F/mol$_1$) was reached. The ElectraSyn vial cap was removed, and the electrodes and vial were rinsed with EtOAc (10 mL) and $HCl_{(aq)}$ (2M, 10 mL), which were combined with the crude mixture in a separatory funnel. Then, the organic layer was separated, and the aqueous layer was extracted with EtOAc (2 x 10 mL). The combined organic layers were washed with $HCl_{(aq)}$ (0.1 M, 3 x 10 mL), dried over Na_2SO_4 and concentrated *in vacuo*. The crude product was finally purified by FC to afford pure products **2**.

(*E*)-3-(methoxycarbonyl)-4-phenylbut-3-enoic acid (2a) and **3-(methoxycarbonyl)-2-phenylbut-3-enoic acid (2a')**.

White solid. FC eluent: from *n*Hex/EtOAc: 70:30 to *n*Hex/EtOAc/HCOOH: 69:30:1. Yield = 83%, (0.125 mmol, 27.4 mg). **2a**:**2a'** = 1.4:1, for **2a** *E*/*Z* > 20:1.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.91 (s, 1H **2a**), 7.43 – 7.26 (m, 5H **2a** + 5H **2a'**), 6.42 (s, 1H **2a'**), 5.45 (s, 1H **2a'**), 4.85 (s, 1H **2a'**), 3.83 (s, 3H **2a**), 3.77 (s, 3H **2a'**), 3.57 (s, 2H **2a**).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 174.6 (**2a'**), 174.2 (**2a**), 165.3 (**2a**), 164.1 (**2a'**), 140.1 (**2a**), 135.9 (**2a**), 132.6 (**2a'**), 132.1 (**2a**), 126.5 (2C **2a'** overlapped with C **2a'**), 126.4 (2C **2a**), 126.3 (2C **2a'**), 126.1 (2C **2a**), 125.8 (**2a'**), 125.4 (**2a**), 122.6 (**2a'**), 50.4 (**2a'**), 49.8 (**2a**), 49.7 (**2a'**), 31.0 (**2a**). **HRMS (ESI)** m/z: $[M-H]^-$ calcd. for $C_{12}H_{11}O_4$ 219.0663; found 219.0671.

(*E*)-3-(methoxycarbonyl)-4-(4-methoxyphenyl)but-3-enoic acid (2b) and **3-(methoxycarbonyl)-2-(4-methoxyphenyl)but-3-enoic acid (2b')**.

White solid. FC eluent: from *n*Hex/EtOAc: 70:30 to *n*Hex/EtOAc/HCOOH: 69:30:1. Yield = 69%, (0.104 mmol, 25.9 mg). **2b**:**2b'** = 3.2:1, for **2b** *E*/*Z* > 20:1.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.84 (s, 1H **2b**), 7.36 – 7.30 (m, 2H **2b**), 7.23 – 7.15 (m, 2H **2b'**), 6.95 – 6.90 (m, 2H **2b**), 6.90 – 6.86 (m, 2H **2b'**), 6.39 (s, 1H **2b'**), 5.46 (s, 1H **2b'**), 4.77 (s, 1H **2b'**), 3.81 (s, 6H **2b**), 3.78 (s, 3H **2b'**), 3.76 (s, 3H **2b'**), 3.59 (s, 2H **2b**).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 177.4 (**2b'**), 176.6 (**2b**), 168.4 (**2b**), 166.8 (**2b'**), 160.4 (**2b**), 159.3 (**2b'**), 142.4 (**2b**), 138.8 (**2b'**), 131.0 (2C **2b**), 130.2 (2C **2b'**), 128.1 (**2b'**), 127.2 (**2b'**), 127.1 (**2b**), 122.9 (**2b**), 114.3 (2C **2b'**), 114.2 (2C **2b**), 55.3 (**2b**), 55.2 (**2b'**), 52.3 (**2b**), 52.3 (**2b'**), 52.2 (**2b'**), 33.7 (**2b**).

HRMS (ESI) m/z: $[M-H]^-$ calcd. for $C_{13}H_{13}O_5$ 249.0768; found 249.0762.

(*E*)-4-(4-(*tert*-butyl)phenyl)-3-(methoxycarbonyl)but-3-enoic acid (2c) and **2-(4-(*tert*-butyl)phenyl)-3-(methoxycarbonyl)but-3-enoic acid (2c')**.

White solid. FC eluent: from *n*Hex/EtOAc: 70:30 to *n*Hex/EtOAc/HCOOH: 69:30:1. Yield = 60%, (0.090 mmol, 24.9 mg). **2c**:**2c'** = 2:1, for **2c** *E*/*Z* > 20:1.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.88 (s, 1H **2c**), 7.42 (m, 2H **2c**), 7.36 (m, 2H **2c'**), 7.30 (m, 2H **2c**), 7.21 (m, 2H **2c'**), 6.40 (s, 1H **2c'**), 5.47 (s, 1H **2c'**), 4.81 (s, 1H **2c'**), 3.82 (s, 3H **2c**), 3.77 (s, 3H **2c'**), 3.59 (s, 2H **2c**), 1.31 (s, 3H **2c**), 1.30 (s, 3H **2c'**).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 177.4 (**2c'**), 176.8 (**2c**), 168.2 (**2c**), 166.8 (**2c'**), 152.5 (**2c**), 150.8 (**2c'**), 142.6 (**2c**), 138.5 (**2c'**), 132.0 (**2c'**), 131.7 (**2c**), 129.0 (2C **2c**), 128.7 (2C **2c'**), 128.3 (**2c'**), 125.8 (2C **2c'**), 125.7 (2C **2c**), 124.3 (**2c**), 52.6 (**2c'**), 52.4 (**2c**), 52.2 (**2c'**), 34.8 (**2c**), 34.5 (**2c'**), 33.7 (**2c**), 31.3 (3C **2c'**), 31.2 (3C **2c**).

HRMS (ESI) m/z: $[M-H]^-$ calcd. for $C_{16}H_{19}O_4$ 275.1289; found 275.1283.

(*E*)-4-(4-chlorophenyl)-3-(methoxycarbonyl)but-3-enoic acid (2d) and **2-(4-chlorophenyl)-3-(methoxycarbonyl)but-3-enoic acid (2d')**.

White solid. FC eluent: from *n*Hex/EtOAc: 70:30 to *n*Hex/EtOAc/HCOOH: 69:30:1. Yield = 80%, (0.114 mmol, 30.5 mg). **2d**:**2d'** = 1:1.4, for **2d** *E*/*Z* > 20:1.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.05 (bs, 1H **2d** + 1H **2d'**), 7.84 (s, 1H **2d**), 7.39 – 7.34 (m, 2H **2d**), 7.34 – 7.30 (m, 2H **2d'**), 7.29 – 7.26 (m, 2H **2d**), 7.25 – 7.20 (m, 2H **2d'**), 6.41 (s, 1H **2d'**), 5.48 (s, 1H **2d'**), 4.81 (s, 1H **2d'**), 3.82 (s, 3H **2d**), 3.76 (s, 3H **2d'**), 3.52 (s, 2H **2d**).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 176.9 (**2d**), 176.6 (**2d'**), 167.6 (**2d**), 166.4 (**2d'**), 141.3 (**2d**), 138.0 (**2d'**), 135.2 (**2d**), 134.0 (**2d'**), 133.7 (**2d'**), 133.1 (**2d**), 130.4 (2C **2d'**), 130.3 (2C **2d**), 129.0 (2C **2d'**), 129.0 (2C **2d**), 128.3 (**2d'**), 125.7 (**2d**), 52.5 (**2d**), 52.4 (**2d'**), 33.5 (**2d'**), 22.0 (**2d**).

HRMS (ESI) m/z: $[M-H]^-$ calcd. for $C_{12}H_{10}{}^{(35)}ClO_4$ 253.0273; found 253.0280; calcd. for $C_{12}H_{10}{}^{(37)}ClO_4$ 255.0244; found 255.0249.

(*E*)-3-(methoxycarbonyl)-4-(4-(trifluoromethyl)phenyl)but-3-enoic acid (2e) and **3-(methoxycarbonyl)-2-(4-(trifluoromethyl)phenyl)but-3-enoic acid (2e')**.

White solid. FC eluent: from *n*Hex/EtOAc: 70:30 to *n*Hex/EtOAc/HCOOH: 69:30:1. Yield = 90%, (0.135 mmol, 40.7 mg). **2e**:**2e'** = 1:5.2, for **2e** *E*/*Z* > 20:1.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.90 (s, 1H **2e**), 7.65 (m, 2H **2e**), 7.61 (m, 2H **2e'**), 7.45 – 7.39 (m, 2H **2e** + 2H **2e'**), 6.44 (s, 1H **2e'**), 5.50 (s, 1H **2e'**), 4.91 (s, 1H **2e'**), 3.84 (s, 3H **2e**), 3.76 (s, 3H **2e'**), 3.51 (s, 2H **2e**).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 176.5, 166.3, 139.3 (d, J = 1.1 Hz), 137.7, 130.3 (d, J = 32.6 Hz), 129.5 (2C), 128.6, 125.8 (q, J = 3.8 Hz, 2C), 123.9 (d, J = 272.2 Hz), 52.7, 52.4; only the peaks relative to major isomer **2e'** are given.

HRMS (ESI) m/z: $[M-H]^-$ calcd. for $C_{13}H_{10}F_3O_4$ 287.0537; found 287.0541.

3-(methoxycarbonyl)-2-(4-(methoxycarbonyl)phenyl)but-3-enoic acid (2f').

White solid. FC eluent: from *n*Hex/EtOAc: 70:30 to *n*Hex/EtOAc/HCOOH: 69:30:1. Yield = 59%, (0.081 mmol, 20.2 mg). **2f'**: **2f** > 20:1. Mp = 150-152 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.01 (m, 1H), 7.36 (m, 2H), 6.42 (s, 1H), 5.45 (s, 1H), 4.90 (s, 1H), 3.89 (s, 3H), 3.75 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 176.3, 166.7, 166.4, 140.3, 137.8, 130.1 (2C), 129.8, 129.1 (2C), 128.5, 52.9, 52.4, 52.2.

HRMS (ESI) m/z: $[M-H]^-$ calcd. for $C_{14}H_{13}O_6$ 277.0718; found 277.0709.

(*E*)-3-(methoxycarbonyl)-4-(3-methoxyphenyl)but-3-enoic acid (2g) and **3-(methoxycarbonyl)-2-(3-methoxyphenyl)but-3-enoic acid (2g')**.

White solid. FC eluent: from *n*Hex/EtOAc: 70:30 to *n*Hex/EtOAc/HCOOH: 69:30:1. Yield = 76%, (0.115 mmol, 28.6 mg). **2g**:**2g'** = 1.4:1, for **2g** *E*/*Z* > 20:1.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.88 (s, 1H **2g**), 7.34 – 7.26 (m, 1H **2g** + 1H **2g'**), 6.96 – 6.80 (m, 3H **2g** + 3H **2g'**), 6.41 (s, 1H **2g'**), 5.49 (s, 1H **2g'**), 4.81 (s, 1H **2g'**), 3.83 (s, 3H **2g**), 3.79 (s, 3H **2g**), 3.78 (s, 3H **2g'**), 3.77 (s, 3H **2g'**), 3.57 (s, 2H **2g**).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 177.2 (**2g'**), 176.8 (**2g**), 167.9 (**2g**), 166.7 (**2g'**), 159.9 (**2g'**), 159.7 (**2g**), 142.6 (**2g**), 138.2 (**2g'**), 136.6 (**2g'**), 136.0 (**2g**), 129.8 (**2g'**), 129.8 (**2g**), 128.4 (**2g'**), 125.4 (**2g'**), 121.4 (**2g'**), 121.3 (**2g**), 115.0 (**2g**), 114.8 (**2g'**), 114.1 (**2g**), 113.4 (**2g**), 55.2 (**2g**), 55.2 (**2g'**), 53.0 (**2g'**), 52.4 (**2g**), 52.3 (**2g'**), 33.6 (**2g**).

HRMS (ESI) m/z: $[M-H]^-$ calcd. for $C_{13}H_{13}O_5$ 249.0768; found 249.0777.

(*E*)-4-(2-chlorophenyl)-3-(methoxycarbonyl)but-3-enoic acid (2h) and **2-(2-chlorophenyl)-3-(methoxycarbonyl)but-3-enoic acid (2h')**.

White solid. FC eluent: from *n*Hex/EtOAc: 70:30 to *n*Hex/EtOAc/HCOOH: 69:30:1. Yield = 78%, (0.117 mmol, 29.7 mg). **2h**:**2h'** = 1:1.4, for **2h** *E*/*Z* > 20:1.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.95 (s, 1H **2h**), 7.46 – 7.38 (m, 1H **2h** + 1H **2h'**), 7.36 – 7.25 (m, 3H **2h** + 3H **2h'**), 6.42 (s, 1H **2h'**), 5.39 (s, 1H **2h'**), 5.36 (s, 1H **2h'**), 3.85 (s, 3H **2h**), 3.78 (s, 3H **2h'**), 3.44 (s, 2H **2h**).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 176.7 (**2h** + **2h'** overlapped), 167.3 (**2h'**), 166.4 (**2h**), 139.8 (**2h**), 136.9 (**2h'**), 134.6 (**2h**), 134.0 (**2h**), 133.4 (**2h'**), 133.3 (**2h'**), 130.2 (**2h**), 130.0 (**2h'**), 129.9 (**2h**), 129.8 (**2h'**), 129.7 (**2h**), 129.3 (**2h'**), 128.4 (**2h'**), 127.2 (**2h'**), 127.0 (**2h**), 126.9 (**2h'**), 52.5 (**2h**), 52.4 (**2h'**), 49.8 (**2h'**), 33.7 (**2h**).

HRMS (ESI) m/z: $[M-H]^-$ calcd. for $C_{12}H_{10}{}^{(35)}ClO_4$ 253.0273; found 253.0280; calcd. for $C_{12}H_{10}{}^{(37)}ClO_4$ 255.0244; found 255.0248.

(*E*)-3-(methoxycarbonyl)-4-(*o*-tolyl)but-3-enoic acid (2i) and **3-(methoxycarbonyl)-2-(*o*-tolyl)but-3-enoic acid (2i')**.

White solid. FC eluent: from *n*Hex/EtOAc: 70:30 to *n*Hex/EtOAc/HCOOH: 69:30:1. Yield = 81%, (0.114 mmol, 28.3 mg). **2i**:**2i'** = 1.3:1, for **2i** *E*/*Z* > 20:1.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.95 (s, 1H **2i**), 7.29 – 7.14 (m, 4H **2i** + 4H **2i'**), 6.38 (s, 1H **2i'**), 5.31 (s, 1H **2i'**), 5.07 (s, 1H **2i'**), 3.83 (s, 3H **2i**), 3.79 (s, 3H **2i'**), 3.42 (s, 2H **2i**), 2.29 (s, 3H **2i'**), 2.27 (s, 3H **2i**).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 177.6 (**2i'**), 176.9 (**2i**), 167.6 (**2i**), 166.8 (**2i'**), 142.2 (**2i**), 137.6 (**2i'**), 136.9 (**2i**), 136.8 (**2i'**), 134.0 (**2i**), 133.7 (**2i'**), 130.9 (**2i'**), 130.2 (**2i**), 128.9 (**2i**), 128. (**2i**), 128.1 (**2i'**), 128.1 (**2i'**), 127.9 (**2i'**), 126.4 (**2i'**), 126.0 (**2i**), 52.3 (**2i**), 52.3 (**2i'**), 49.2 (**2i'**), 33.4 (**2i**), 19.8 (**2i**), 19.5 (**2i'**).

HRMS (ESI) m/z: $[M-H]^-$ calcd. for $C_{13}H_{13}O_4$ 233.0819; found 233.0827.

(*E*)-3-(methoxycarbonyl)-4-(naphthalen-2-yl)but-3-enoic acid (2j) and **3-(methoxycarbonyl)-2-(naphthalen-2-yl)but-3-enoic acid (2j')**

White solid. FC eluent: from *n*Hex/EtOAc: 70:30 to *n*Hex/EtOAc/HCOOH: 69:30:1. Yield = 75%, (0.099 mmol, 30.6 mg). **2j**:**2j'** = 1:1.5, for **2j** *E*/*Z* > 20:1.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.98 (bs, 1H **2j** + 1H **2j'**), 8.06 (s, 1H **2j**), 7.88 – 7.74 (m, 4H **2j** + 4H **2j'**), 7.54 – 7.35 (m, 3H **2j** + 3H **2j'**), 6.44 (s, 1H **2j'**), 5.49 (s, 1H **2j'**), 5.03 (s, 1H **2j'**), 3.85 (s, 3H **2j**), 3.78 (s, 3H **2j'**), 3.66 (s, 2H **2j**).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 177.3 (**2j'**), 176.9 (**2j**), 168.0 (**2j**), 166.7 (**2j'**), 142.7 (**2j**), 138.4 (**2j'**), 133.4 (**2j'**), 133.2 (**2j**), 133.0 (**2j**), 132.8 (**2j'**), 132.6 (**2j'**), 132.1 (**2j'**), 129.0 (**2j'**), 128.6 (**2j'**), 128.6 (**2j**), 128.4 (2 C **2j'**), 128.3 (**2j**), 127.9 (**2j**), 127.7 (**2j**), 127.6 (**2j'**), 127.0 (**2j**), 126.7 (**2j'**), 126.6 (**2j**), 126.4 (**2j'**), 126.3 (**2j**), 126.1 (**2j**), 125.3 (**2j**), 53.6 (**2j'**), 52.5 (**2j**), 52.3 (**2j'**), 33.7 (**2j**).

HRMS (ESI) m/z: $[M-H]^-$ calcd. for $C_{16}H_{13}O_4$ 269.0819; found 269.0811.

(*E*)-3-(methoxycarbonyl)-4-(thiophen-2-yl)but-3-enoic acid (2k) and **3-(methoxycarbonyl)-2-(thiophen-2-yl)but-3-enoic acid (2k')**

Yellow oil. FC eluent: from *n*Hex/EtOAc: 70:30 to *n*Hex/EtOAc/HCOOH: 69:30:1. Yield = 69%, (0.093 mmol, 21.2 mg). **2k**:**2k'** = 4.0:1, for **2k** *E*/*Z* > 20:1.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.99 (s, 1H **2k**), 7.52 – 7.48 (m, 1H **2k**), 7.33 – 7.29 (m, 1H **2k**), 7.12 – 7.08 (m, 1H **2k**), 7.02 – 6.96 (m, 2H **2k'**), 6.90 (m, 1H **2k'**), 6.45 (s, 1H **2k'**), 5.71 (d, *J* = 1.4 Hz, 1H **2k'**), 5.09 (s, 1H **2k'**), 3.82 (s, 3H **2k**), 3.80 (s, 2H **2k**), 3.78 (s, 3H **2k'**).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 176.1, 167.9, 137.4, 134.7, 132.9, 129.9, 127.8, 120.9, 52.5, 33.7; only the peaks relative to major isomer **2k'** are given.

HRMS (ESI) m/z: $[M-H]^-$ calcd. for $C_{10}H_9O_4S$ 225.0227; found 225.0222.

(3*E*,5*E*)-3-(methoxycarbonyl)-6-phenylhexa-3,5-dienoic (2l) acid and **(*E*)-2-(3-methoxy-3-oxoprop-1-en-2-yl)-4-phenylbut-3-enoic acid (2l')**

White solid. FC eluent: from *n*Hex/EtOAc: 70:30 to *n*Hex/EtOAc/HCOOH: 69:30:1. Yield = 41%, (0.062 mmol, 15 mg). **2l**:**2l'** = 1:2.1, for **2l** *E*/*Z* > 20:1.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.49 – 7.45 (m, 2H **2l**), 7.40 – 7.22 (m, 3H **2l** + 5H **2l'**), 6.97 (d, *J* = 3.7 Hz, 1H **2l**) partially overlapped with 6.96 (d, *J* = 0.9 Hz, 1H **2l**), 6.55 (d, *J* = 15.9 Hz, 1H **2l'**), 6.41 (s, 1H **2l'**), 6.35 (dd, 1H **2l'**), 5.85 (s, 1H **2l'**), 4.33 (d, *J* = 8.3 Hz, 1H **2l'**), 4.10 (q, 1H **2l**), 3.80 (s, 3H **2l**), 3.78 (s, 3H **2l'**), 3.59 (s, 2H **2l**).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 177.0 (**2l**), 176.8 (**2l'**), 166.9 (**2l**), 165.8 (**2l'**), 141.6 (**2l**), 138.1 (**2l'**), 135.6 (**2l**), 135.4 (**2l'**), 135.2 (**2l**), 134.0 (**2l**), 133.7 (**2l'**), 133.0 (**2l'**), 130.5 (**2l**), 130.3 (**2l'**), 129.1 (**2l**), 129.0 (**2l'**), 128.6 (**2l**), 128.6 (**2l'**), 128.3 (**2l'**), 128.3 (**2l**), 128.1 (**2l**), 128.1 (**2l'**), 125.8 (**2l**), 67.2 (**2l**), 67.1 (**2l'**), 52.4 (**2l'**), 33.5 (**2l'**), 20.8 (**2l**).

HRMS (ESI) m/z: $[M-H]^-$ calcd. for $C_{14}H_{13}O_4$ 245.0819; found 245.0808.

(*E*)-3-(methoxycarbonyl)-6-phenylhex-3-enoic acid (2m) and **3-(methoxycarbonyl)-2-phenethylbut-3-enoic acid (2m')**

Colourless sticky oil. FC eluent: from *n*Hex/EtOAc: 70:30 to *n*Hex/EtOAc/HCOOH: 69:30:1. Yield = 57%, (0.078 mmol, 19.3 mg). **2m**:**2m'** = 2.8:1, for **2m** *E*/*Z* > 20:1.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.30 – 7.23 (m, 2H **2m** + 2H **2m'**), 7.21 – 7.13 (m, 3H **2m** + 2H **2m'**), 7.01 (t, *J* = 7.6 Hz, 1H **2m**), 6.40 (s, 1H **2m'**), 5.77 (s, 1H **2m'**), 3.76 (s, 3H **2m'**), 3.74 (s, 3H **2m**), 3.52 (t, *J* = 7.3 Hz, 1H **2m'**), 3.30 (s, 2H **2m**), 2.76 (t, *J* = 7.7 Hz, 1H **2m**), 2.65 (t, *J* = 7.9 Hz, 2H **2m'**), 2.50 (q, *J* = 7.6 Hz, 2H **2m**), 2.35 – 2.21 (m, 1H **2m'**), 2.06 – 1.93 (m, 1H **2m'**).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 178.4 (**2m'**), 176.3 (**2m**), 167.3 (**2m**), 166.6 (**2m'**), 145.1 (**2m**), 140.9 (**2m'**), 140.6 (**2m'**), 137.6 (**2m**), 128.5 (2C **2m**), 128.4 (2C **2m'**), 128.4 (2C **2m'**), 128.3 (2C **2m**), 127.7 (**2m'**), 126.2 (**2m**), 126.1 (**2m'**), 125.4 (**2m**), 52.2 (**2m'**), 52.1 (**2m**), 46.3 (**2m'**), 34.5 (**2m**), 33.4 (**2m'**), 32.2 (**2m'**), 32.1 (**2m**), 30.8 (**2m**).

HRMS (ESI) m/z: $[M-H]^-$ calcd. for $C_{14}H_{15}O_4$ 247.0976; found 247.0988.

(3*E*,9*Z*)-3-(methoxycarbonyl)dodeca-3,9-dienoic acid (2n) and **(*Z*)-2-(3-methoxy-3-oxoprop-1-en-2-yl)dec-7-enoic acid (2n')**

Colourless sticky oil. FC eluent: from *n*Hex/EtOAc: 70:30 to *n*Hex/EtOAc/HCOOH: 69:30:1. Yield = 78%, (0.114 mmol, 26.0 mg). **2n**:**2n'** = 3.5:1, for **2n** *E*/*Z* > 20:1.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.97 (t, *J* = 7.6 Hz, 1H **2n**), 6.37 (s, 1H **2n'**), 5.76 (s, 1H **2n'**), 5.40 – 5.22 (m, 2H **2n** + 2H **2n'**), 3.76 (s, 3H **2n'**), 3.74 (s, 3H **2n**), 3.49 (t, *J* = 7.4 Hz, 1H **2n'**), 3.37 (s, 2H **2n**), 2.18 (q, *J* = 7.4 Hz, 2H **2n**), 2.06 – 1.96 (m, 6H **2n** + 4H **2n'**), 1.50 – 1.29 (m, 4H **2n** + 6H **2n'**), 0.93 (t, *J* = 7.5 Hz, 3H **2n** + 3H **2n'** partially overlapped).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 178.6 (**2n'**), 176.4 (**2n**), 167.5 (**2n**), 166.7 (**2n'**), 146.5 (**2n**), 137.7 (**2n'**), 132.0 (**2n**), 131.9 (**2n'**), 128.7 (**2n'**), 128.5 (**2n**), 127.3 (**2n'**), 124.7 (**2n**), 52.2 (**2n'**), 52.0 (**2n**), 46.7 (**2n'**), 32.2 (**2n**), 30.6 (**2n'**), 29.4 (**2n'**), 29.3 (**2n**), 28.9 (**2n**), 27.9 (**2n**), 27.0 (**2n'**), 26.8 (**2n'**), 26.7 (**2n**), 20.5 (**2n**), 20.4 (**2n'**), 14.3 (**2n** + **2n'** overlapped).

HRMS (ESI) m/z: $[M-H]^-$ calcd. for $C_{14}H_{21}O_4$ 253.1445; found 253.1456.

(*E*)-3-((benzyloxy)carbonyl)-4-(4-chlorophenyl)but-3-enoic acid (2o) and **3-((benzyloxy)carbonyl)-2-(4-chlorophenyl)but-3-enoic acid (2o')**.

White solid. FC eluent: from *n*Hex/EtOAc: 70:30 to *n*Hex/EtOAc/HCOOH: 69:30:1. Yield = 86%, (0.130 mmol, 42.7 mg). **2o**:**2o'** = 1:1.3, for **2o** *E*/*Z* > 20:1.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.88 (s, 1H **2o**), 7.44 – 7.17 (m, 9H **2o +** 9H **2o'**), 6.47 (s, 1H **2o'**), 5.50 (s, 1H **2o'**), 5.26 (s, 2H **2o**), 5.19 (s, 2H **2o**)', 4.83 (s, 1H **2o'**), 3.55 (s, 2H **2o**).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 177.0 (**2o**), 176.8 (**2o'**), 166.9 (**2o**), 165.8 (**2o'**), 141.6 (**2o**), 138.1 (**2o** + **2o'** overlapped), 135.6 (**2o**), 135.4 (**2o'**), 135.2 (**2o**), 134.0 (**2o**), 133.7 (**2o'**), 133.0 (**2o'**), 130.5 (2C **2o**), 130.3 (2C **2o'**), 129.1 (2C **2o**), 129.0 (2C **2o'**), 128.6 (2C **2o**), 128.6 (2C **2o'**), 128.3 (**2o'**), 128.3 (**2o**), 128.1 (2C **2o**), 128.1 (2C **2o'**), 125.8 (**2o'**), 67.2 (**2o**), 67.1 (**2o'**), 52.4 (**2o'**), 33.5 (**2o**).

HRMS (ESI) m/z: $[M-H]^-$ calcd. for $C_{18}H_{14}{}^{(35)}ClO_4$ 329.0586; found 329.0577; calcd. for $C_{18}H_{14}{}^{(37)}ClO_4$ 331.0557; found 331.0549.

(*E*)-4-(4-chlorophenyl)-3-((prop-2-yn-1-yloxy)carbonyl)but-3-enoic acid (2p) and **2-(4-chlorophenyl)-3-((prop-2-yn-1-yloxy)carbonyl)but-3-enoic acid (2p')**

White solid. FC eluent: from *n*Hex/EtOAc: 70:30 to *n*Hex/EtOAc/HCOOH: 69:30:1. Yield = 73%, (0.110 mmol, 30.3 mg). **2p**:**2p'** = 1:1.4, for **2p** *E*/*Z* > 20:1.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.88 (s, 1H **2p**), 7.39 – 7.35 (m, 2H **2p**), 7.34 – 7.31 (m, 2H **2p'**), 7.29 – 7.26 (m, 2H **2p**), 7.24 – 7.21 (m, 2H **2p'**), 6.48 (s, 1H **2p'**), 5.52 (d, J = 1.46 Hz, 1H **2p'**), 4.82 (d, *J* = 2.5 Hz, 2H **2p**), 4.80 (s, 1H **2p'**) partially overlapped with 4.79 (dd, *J* = 15.6, 2.5 Hz, 2H **2p'**), 4.72 (dd, *J* = 15.6, 2.5 Hz, 2H **2p'**), 3.54 (s, 2H **2p**), 2.49 (t, *J* = 2.5 Hz, 1H **2p**), 2.47 (t, *J* = 2.5 Hz, 1H **2p'**).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 176.8 (**2p'**), 176.5 (**2p**), 166.3 (**2p**), 165.2 (**2p'**), 142.2 (**2p**), 137.6 (**2p**), 135.4 (**2p**), 134.1 (**2p'**), 133.5 (**2p**), 132.8 (**2p'**), 130.5 (2C **2p'**), 130.3 (2C **2p**), 129.2 (**2p'**), 129.1 (**2p'**), 129.1 (**2p**), 125.2 (**2p'**) 77.2 (**2p**), 77.1 (**2p'**), 75.3 (**2p'**), 75.2 (**2p**), 52.9 (**2p**), 52.8 (**2p'**), 52.4 (**2p'**), 33.4 (**2p**).

HRMS (ESI) m/z: $[M-H]^-$ calcd. for $C_{14}H_{10}{}^{(35)}ClO_4$ 277.0273; found 277.0270; calcd. for $C_{14}H_{10}{}^{(37)}ClO_4$ 279.0244; found 279.0246.

(*E*)-3-(tert-butoxycarbonyl)-4-phenylbut-3-enoic acid (2q) and **3-(tert-butoxycarbonyl)-2-phenylbut-3-enoic acid (2q')**

White solid. FC eluent: from *n*Hex/EtOAc: 70:30 to *n*Hex/EtOAc/HCOOH: 69:30:1. Yield = 78%, (0.117 mmol, 30.7 mg). **2q**:**2q'** = 1:1.5, for **2q** *E*/*Z* > 20:1.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.81 (s, 1H **2q**), 7.41 – 7.25 (m, 5H **2q'** + 5H **2q**), 6.32 (t, *J* = 1.1 Hz, 1H **2q'**), 5.26 (dd, *J* = 1.8, 0.8 Hz, 1H **2q'**), 4.75 (s, 1H **2q'**), 3.50 (s, 2H **2q**), 1.51 (s, 9H **2q**), 1.45 (s, 9H **2q'**).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 178.1 (**2q**), 177.2 (**2q'**), 166.6 (**2q**), 165.3 (**2q'**), 141.5 (**2q**), 140.2 (**2q'**), 135.3 (**2q'**), 135.0 (**2q**), 129.1 (2C **2q'**), 129.0 (2C **2q**), 128.8 (2C **2q'**), 128.8 (**2q'**), 128.6 (2C **2q**), 127.9 (**2q'**), 127.4 (**2q**), 126.9 (**2q**), 81.8 (**2q'**), 81.7 (**2q**), 53.5 (**2q'**), 33.8 (**2q**), 28.0 (3C **2q**), 27.9 (3C **2q'**).

HRMS (ESI) m/z: $[M-H]^-$ calcd. for $C_{15}H_{17}O_4$ 261.1132; found 261.1139.

(*E*)-4-(4-(((tert-butoxycarbonyl)-*L*-valyl)oxy)phenyl)-3-(ethoxy carbonyl)but-3-enoic acid (2r) and **2-(4-(((tert-butoxycarbonyl)-*L*-valyl)oxy)phenyl)-3-(ethoxycarbonyl)but-3-enoic acid (2r')**

White solid. FC eluent: from *n*Hex/EtOAc: 70:30 to *n*Hex/EtOAc/HCOOH: 69:30:1. Yield = 65%, (0.098 mmol, 43.8 mg). **2r**:**2r'** = 1:1.4, for **2r** *E*/*Z* > 20:1; for **2r'** *dr* = 1:1.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.85 (s, 1H **2r**), 7.40 – 7.33 (m, 2H **2r**), 7.32 – 7.27 (m, 2H **2r'**), 7.14 – 7.09 (m, 2H **2r'**), 7.09 – 7.03 (m, 2H **2r**), 6.40 (s, 1H **2r'**), 5.48 (s, 1H **2r'**), 5.11 (d, *J* = 9.0 Hz, 1H **2r** + 1H **2r'** overlapped), 4.83 (s, 1H **2r'**), 4.48 – 4.38 (m, 1H **2r** + 1H **2r'**), 3.81 (s, 3H **2r'**), 3.74 (s, 3H **2r**), 3.53 (s, 2H **2r'**), 2.35 – 2.17 (m, 1H **2r** + 1H **2r'**), 1.44 (s, 9H **2r** + 9H **2r'** overlapped), 1.11 – 0.94 (6H **2r** + 6H **2r'**). The diastereoisomers of **2r'** overlap completely, appearing as a single compound.

^{13}C NMR (100 MHz, $CDCl_3$) δ = 176.2, 176.0, 174.4, 172.9, 171.0, 167.8, 166.6, 155.8, 150.8, 150.0, 141.4, 138.4, 134.3, 133.2, 132.6, 130.3, 130.3, 128.3, 125.7, 123.6, 121.8, 121.7, 115.8, 80.2, 80.2, 60.5, 58.7, 52.4, 52.4, 52.3, 33.5, 31.2, 28.3, 19.1, 17.7; all peaks are given, without assignment.

HRMS (ESI) m/z: $[M-H]^-$ calcd. for $C_{23}H_{30}NO_8$ 448.1977; found 448.1983.

(*E*)-3-(methoxycarbonyl)-6,10-dimethylundeca-3,9-dienoic acid (2s) and **2-(3-methoxy-3-oxoprop-1-en-2-yl)-4,8-dimethylnon-7-enoic acid (2s')**

Colorless sticky oil. FC eluent: from *n*Hex/EtOAc: 70:30 to *n*Hex/EtOAc/HCOOH: 69:30:1. Yield = 46%, (0.069 mmol, 18.5 mg). **2s**:**2s'** = 3.9:1, for **2s** *E*/*Z* > 20:1; for **2s'** *dr* = 1:1.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.99 (t, *J* = 7.6 Hz, 1H **2s**), 6.37 (d, *J* = 6.5 Hz, 1H **2s'**), 5.76 (d, *J* = 8.8 Hz, 1H **2s'**), 5.13 – 5.00 (m, 1H **2s** + 1H **2s'**), 3.76 (s, 3H **2s'**), 3.74 (s, 3H **2s**), 3.66 – 3.60 (m, 1H **2s'**), 3.37 (s, 2H **2s**), 2.24 – 2.14 (m, 1H **2s** + 1H **2s'**), 2.08 – 1.85 (m, 3H **2s** + 3H **2s'**), 1.75 – 1.61 (m, 1H **2s** + 1H **2s'**) partially overlapped with 1.66 (s, 3H **2s** + 3H **2s'** overlapped), 1.58 (s, 3H **2s** + 3H **2s'** overlapped), 1.40 – 1.29 (m, 1H **2s** + 1H **2s'**), 1.22 – 1.12 (m, 1H **2s** + 1H **2s'**), 0.89 (d, *J* = 6.7 Hz, 3H **2s** + 3H **2s'** overlapped).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 176.4, 167.5, 145.6, 131.5, 125.3, 124.3, 52.1, 36.7, 36.2, 32.5, 32.3, 25.7, 25.5, 19.6, 17.6; only the peaks relative to major isomer **2s** are given.

HRMS (ESI) m/z: $[M-H]^-$ calcd. for $C_{15}H_{23}O_4$ 267.1602; found 167.1611.

Cholestanol derivative (2t')

White solid. FC eluent: from *n*Hex/EtOAc: 70:30 to *n*Hex/EtOAc/HCOOH: 69:30:1. Yield = 25%, (0.038 mmol, 22.7 mg). **2t'**:**2t** > 20:1, *dr* = 1:1.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.02 – 7.98 (m, 2H), 7.36 – 7.32 (m, 2H), 6.41 (s, 1H), 5.45 (s, 1H), 4.97 – 4.84 (m, 2H), 3.76 (s, 3H), 2.01 – 1.86 (m, 2H), 1.86 – 1.42 (m, 10H), 1.40 – 1.18 (m, 8H), 1.17 – 0.92 (m, 8H), 0.89 (d, *J* = 6.5 Hz, 3H), 0.85 (d, *J* = 6.7 Hz, 3H), 0.85 (s, 3H), 0.84 (d, *J* = 6.6 Hz, 3H), 0.64 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 175.9, 166.5, 165.7, 140.0, 130.6, 130.0 (2C), 129.0 (2C), 128.5, 74.6, 56.4, 56.3, 54.2, 52.4, 44.7, 42.6, 40.0, 39.5, 36.8, 36.1, 35.8, 35.5, 35.5, 34.1, 32.0, 28.6, 28.2, 28.0, 27.5, 24.2, 23.8, 22.8, 22.5, 21.2, 18.7, 12.3, 12.1.

HRMS (ESI) m/z: $[M-H]^-$ calcd. for $C_{38}H_{53}O_6$ 605.3848; found 605.3855.

Funding Information

MB is also grateful to the PRIN-2017 project 2017W8KNZW

Acknowledgment

Acknowledgements are made to University of Bologna for financial support.

Supporting Information

YES (this text will be updated with links prior to publication)

Primary Data

NO.

Conflict of Interest

The authors declare no conflict of interest.

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