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# Synthesis of Diketones, Ketoesters, and Tetraketones by Electrochemical Oxidative Decarboxylation of Malonic Acid Derivatives: Application to the Synthesis of *cis*-Jasmone

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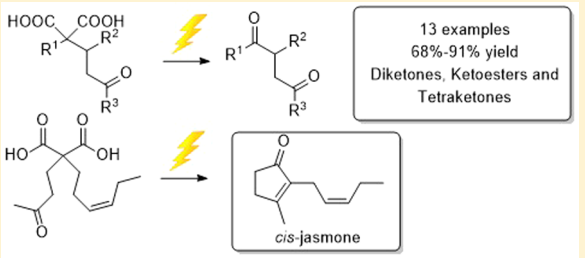
Supporting Information

**ABSTRACT:** Disubstituted malonic acid derivatives are smoothly converted into diketones and ketoesters in good to excellent yield (68% to 91%) under electrochemical conditions. The scope can be extended to transform trisubstituted bis-malonic acids into tetraketones in 77% to 86% yield. The new method was applied to the total synthesis of *cis*-jasmone.




## INTRODUCTION

Diketones, ketoesters, and polyketones are privileged building blocks for the construction of a wide range of useful carbo- and heterocyclic compounds. For example, 1,4-diketones are extensively used as synthetic precursors for the assembly of a variety of biologically active compounds embodying diols,[1] diamines,[2] cyclopentenones,[3] furans,[4] thiophenes,[5] pyrroles,[6] and pyridazines[7] (Figure 1). The 1,4-diketone motif is also featured in numerous natural products, such as herquline A (**6**),[8] amphidinolide F (**7**),[9] and maoecrystal V (**8**) (Figure 1).[10] In addition, 1,5-diketones and 1,5-ketoesters are commonly employed to assemble pyridines, dihydropyridines, and cyclohexenones.[11]

In view of the widespread occurrence of these key functional groups in numerous important products and their use as basic synthons for the construction of a wide variety of carbo- and heterocyclic structures, it is not surprising that many methods have been developed to access these valuable synthetic intermediates.[12] Among them, the conjugate addition of acyl equivalents to Michael acceptors is likely the most popular route to the construction of 1,4-diketones.

In sharp contrast to 1,5-dicarbonyls that are easily obtained by Michael addition of $\beta$-dicarbonyl nucleophiles to $\alpha,\beta$-unsaturated carbonyl derivatives, followed by acid- or base-promoted decarboxylation, the synthesis of 1,4-dicarbonyls by the same Michael addition stratagem requires the use of Umpolung strategies.[13] Accordingly, different acyl addition methods, using masked or unmasked carbonyl functions, were developed, including the Stetter reaction[13] and Sila-Stetter variant,[14] transition-metal-catalyzed CO insertion,[15] Sm-promoted coupling between aryl acyl chlorides and aromatic enones,[16] In−Pd catalyzed reactions between $\alpha,\beta$-unsaturated ketones and acyl chlorides,[17] and finally, Michael addition of nitro compounds, followed by a Nef reaction to convert the nitro group to a ketone (Scheme 1).[18] Though usually proceeding in good yields, these methods suffer from some limitations. For example, the selectivity of the Stetter reaction is highly dependent upon the reactivity of the aldehyde. While, in general, the addition of aromatic and heteroaromatic aldehydes proceeds smoothly, the use of the more reactive aliphatic aldehydes often results in large amounts of self-condensation or benzoin-type products.[14]

In some other cases, either greater than stoichiometric amounts of expensive metals or highly toxic organometallics, such as $Ni(CO)_4$, has to be used to catalyze or promote the reaction with limited substrate scope. Therefore, efficient and more ecologically benign methodologies for the assembly of these key-building blocks are still highly desired.

In the search for more environmentally friendly reduction and oxidation protocols, organic electrochemistry has attracted renewed interest. Indeed, instead of using stoichiometric (at least) quantities of reducing or oxidizing reagents, leading to a large amount of byproducts, simple electron transfer is employed to promote these redox processes, leading to sustainable organic synthetic methods.[19,20] Furthermore,

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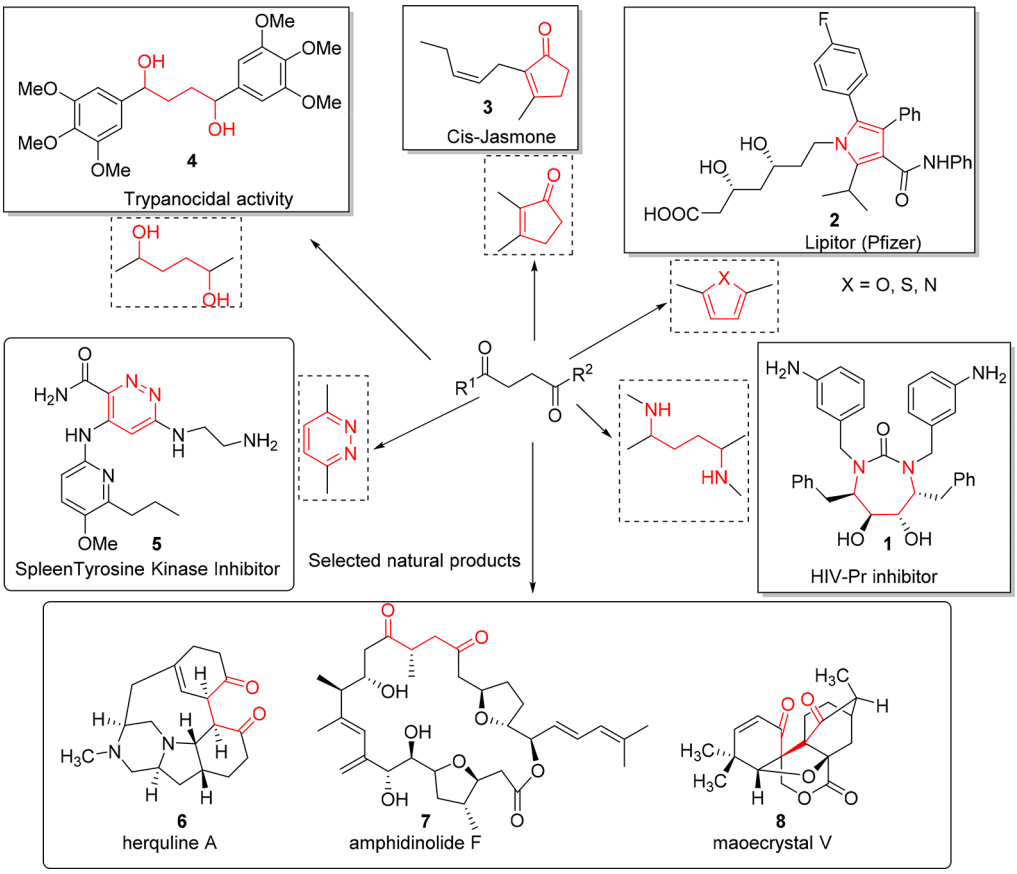
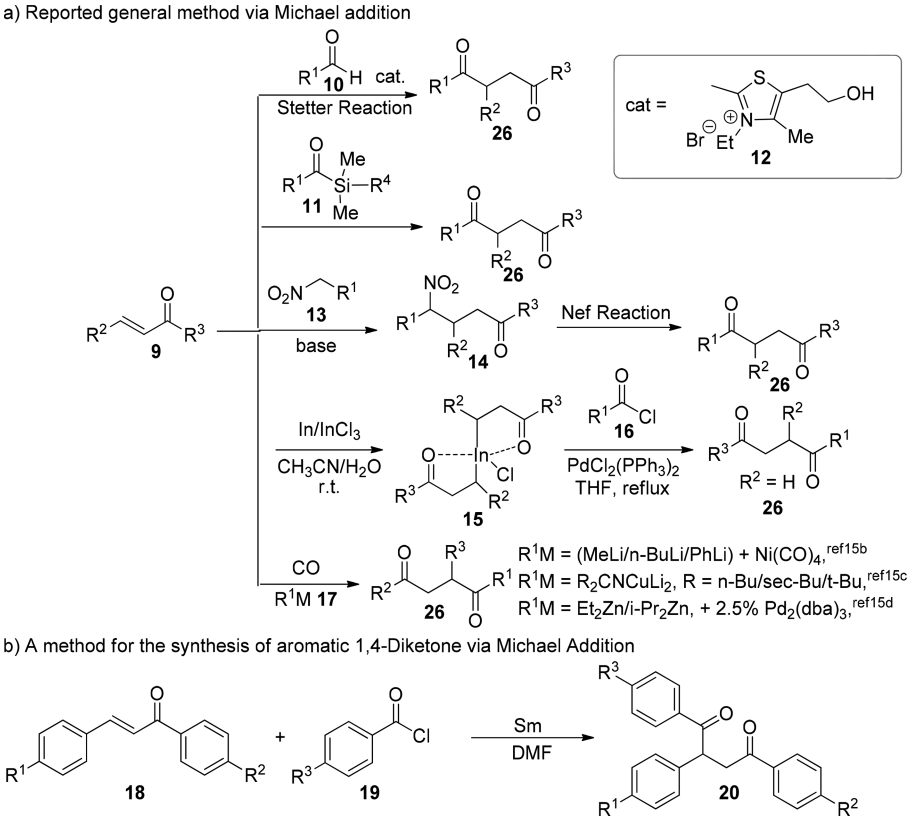



**Figure 1.** Selected application of 1,4-diketones.

**Scheme 1. Selected Examples of the Construction of 1,4-Diketones by Umpolung Michael Addition**



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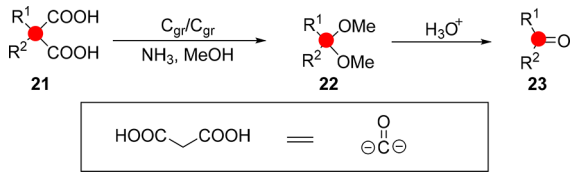
organic electrochemistry possesses other inherent advantages including, i.e., mild reaction conditions, large functional group tolerance, and easy scalability. Finally, electrolysis setups, such as Electrasyn 2.0, are now widely available, making electrosynthesis accessible to any organic synthetic laboratory.

Recently, we have disclosed that the treatment of a range of disubstituted malonic acids under electrochemical conditions[21] afforded a variety of ketals that could be isolated in excellent yields. Moreover, addition of an aqueous acid solution to the crude reaction mixture in the electrolytic cell directly generated the corresponding ketones (Scheme 2). Herein, we report the use of this last transformation for the synthesis of diketones, polyketones, and ketoesters as well as for the total synthesis of *cis*-jasmone.

**Scheme 2. Previous Results**

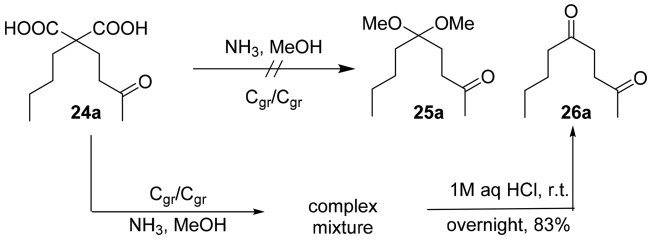



## RESULTS AND DISCUSSION

Our previously developed electrochemical oxidative decarboxylation reaction proved to be tolerant toward many different functional groups, such as alkenes, alkynes, aromatics, esters, and protected alcohols, to cite but a few. In this novel approach,[21,22] the malonic acid function is employed as an Umpolung equivalent of the formaldehyde dianion. A limited selection of some products obtained using this methodology is displayed in Table 1.

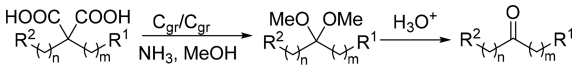
In an effort to extend the scope of this efficient and ecologically benign approach toward carbonyl functions, we envisioned the construction of dicarbonyl compounds and polycarbonyl products from cheap and readily available malonic acid derivatives as starting materials. Thus, malonic acid **24a**, bearing a $\gamma$-ketone function was readily prepared (see the SI) and treated under the standard reaction conditions. However, instead of the expected formation of the desired keto-ketal **25a**, a complex mixture of products was obtained (Scheme 3). Attempted tuning of the reaction conditions by altering several parameters, such as electrode material, concentration, and temperature, did not yield satisfactory results.

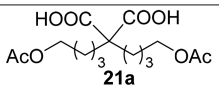
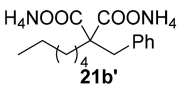
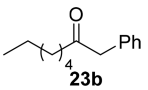
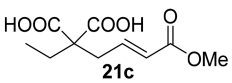
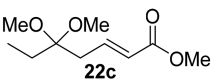
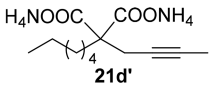
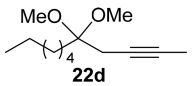
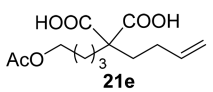
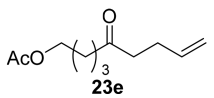
**Scheme 3. Initial Trial**




The analysis of the crude product, indicating the presence of several ketal and bis-ketal functions, coupled with a careful consideration of the reaction mechanism (vide infra) provided us with a plausible hypothesis regarding the nature of the complex mixture generated during this electrochemical transformation, offering us at the same time a possible solution to our predicament in the form of a prolong aqueous acid treatment. Much to our delight, when the complex reaction mixture was treated overnight with a 1 M aq HCl solution, a

**Table 1. Selected Examples of Previous Results**




| entry | starting material | product | yield (%)[b] | Faradic yield (%) |
|---|---|---|---|---|
| 1 |  **21a** |  **22a** | 80 | 16 |
| 2 |  **21b'** |  **23b** | 50 | 10 |
| 3 |  **21c** |  **22c** | 82 | 16 |
| 4 |  **21d'** |  **22d** | 56 | 11 |
| 5 |  **21e** |  **23e** | 72 | 14 |

[a]All reactions were carried out using 0.5 mmol of starting material with 2.1 equiv of $NH_3$ (7.0 M in MeOH) in MeOH at room temperature for 4.5 h. [b]Isolated yield.



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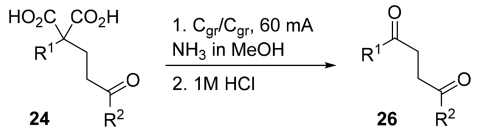
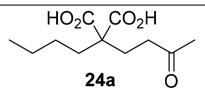
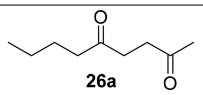
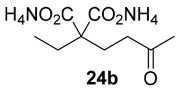
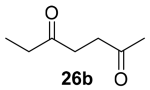
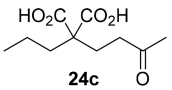
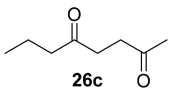
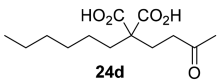
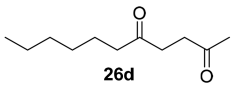
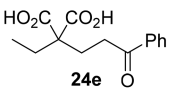
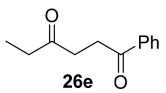
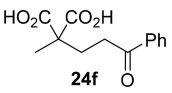
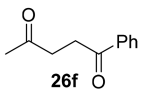
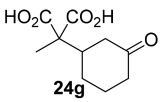
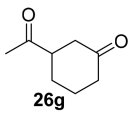
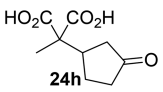
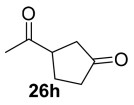
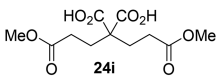
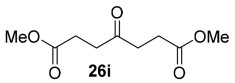
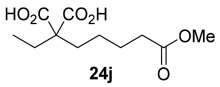
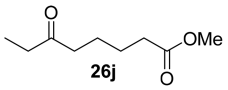
**Table 2. Scope of the Reaction**




| entry | starting material | product | yield (%)[b] | Faradic yield (%) |
|---|---|---|---|---|
| 1 |  **24a** |  **26a** | 83 | 15 |
| 2 |  **24b** |  **26b** | 86 | 15 |
| 3 |  **24c** |  **26c** | 91 | 16 |
| 4 |  **24d** |  **26d** | 85 | 15 |
| 5 |  **24e** |  **26e** | 84 | 15 |
| 6 |  **24f** |  **26f** | 81 | 14 |
| 7 |  **24g** |  **26g** | 83 | 15 |
| 8 |  **24h** |  **26h** | 77 | 14 |
| 9 |  **24i** |  **26i** | 72 | 13 |
| 10 |  **24j** |  **26j** | 68 | 12 |

[a]All reactions were carried out using 0.5 mmol of starting material with 2.1 equiv of $NH_3$ (7.0 M in MeOH) in MeOH at room temperature for 5 h. Then 1 M aq HCl was added, and the mixture was stirred at rt overnight. [b]Isolated yield.

single product was formed: the desired 1,4-diketone **26a** (83% isolated yield, Scheme 3).

Having delineated mild conditions for the conversion of ketone-containing malonic acid **24a** into the diketone **26a**, the scope and limitations of this novel approach to 1,4-diketones were investigated. A range of disubstituted malonic acids were synthesized by Michael addition of malonate esters to $\alpha,\beta$-unsaturated ketones and acrylates, followed by hydrolysis of the esters to form the desired malonic acids in good to excellent yields. Substrate **24j** was assembled by alkylation of the monosubstituted malonate with 5-iodoethyl pentanoate, followed by a subsequent hydrolysis of the malonic acid. The



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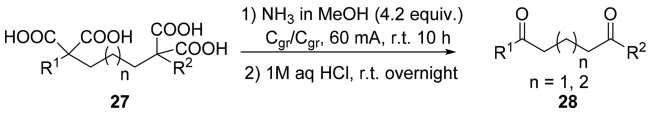
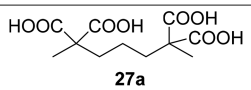
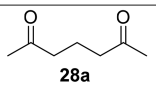
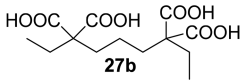
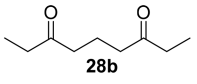
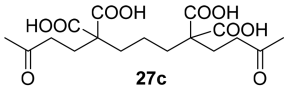
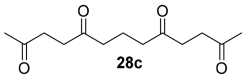
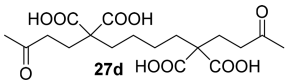
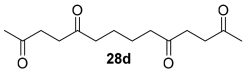
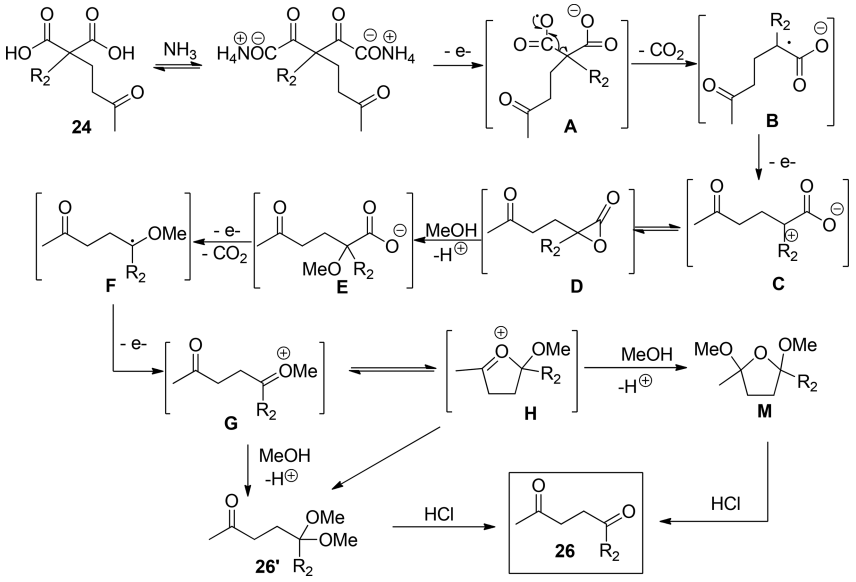
**Table 3. Electrochemical Oxidative Decarboxylation of Bis-malonic Acid Derivatives**




| entry | starting material | products | yield (%) [b] | Faradic yield (%) |
|---|---|---|---|---|
| 1 |  27a |  28a | 85 | 15 |
| 2 |  27b |  28b | 82 | 15 |
| 3 |  27c |  28c | 77 | 14 |
| 4 |  27d |  28d | 86 | 15 |

[a]All reactions were carried out using 0.5 mmol of starting material with 4.2 equiv of $NH_3$ (7.0 M in MeOH) in MeOH at room temperature for 10 h. Then, 1 M aq HCl was added, and the mixture was stirred at rt overnight. [b]Isolated yield.

**Scheme 4. Proposed Mechanism for the Formation of Diketone**




disubstituted malonic acids thus obtained were sufficiently pure to be directly subjected to the standard electrochemical reaction conditions without further purification. In some cases, pure malonic acids were submitted to the electrolytic step and the yields found to be essentially identical. Selected examples, highlighting the broad scope of the electrochemical decarboxylation of disubstituted ketomalonic acids, are collected in Table 2.

As can be seen in Table 2, changing the length of the aliphatic carbon chain of the starting substrate has essentially no effect on the yield of the corresponding diketones, which are isolated in excellent yield (86%−91%) (Table 2, entries 1−3). Remarkably, aromatic ketones are also tolerated in the substrates, and the corresponding diketones can be obtained in good yields (Table 2, entries 4 and 5). Cyclohexanone- and cyclopentanone-bearing malonic acids are smoothly converted into the desired diketones under the standard reaction conditions (Table 2, entries 6 and 7). Adducts **26g** and **26h**, corresponding to the Michael addition of an acetyl anion equivalent to cyclohexenone and cyclopentenone, are obtained in 83% and 77% yield, respectively. These yields compare favorably with those reported in the literature for the same products.

To expand the scope further, the preparation of ketoesters was also undertaken. Hence, double-Michael addition of di-*tert*-butyl malonate to methyl acrylate afforded the corresponding tris-ester. Selective removal of the *tert*-butyl substituents provided the desired ester-substituted malonic acid **24i**.



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Subjecting this substrate to the standard reaction conditions generated the tricarbonyl compound **26i** in 72% yield (Table 2, entry 8). Finally, an easy access to 1,6-ketoester **26j** is provided by oxidative decarboxylation of **24j** (Table 2, entry 9).

The power of our methodology was further demonstrated by the electrochemical decarboxylation of some representative tetracarboxylic acids (Table 3). Thus, electrolysis of **27a** and **27b** afforded the 1,5-diketones **28a** and **28b** in 85% and 82% yield, respectively. It is noteworthy that 1,5-diketone **28a** is a very important starting material for further transformations.[23] Interestingly, when the ketone-containing tetracarboxylic acids **27c** and **27d** were employed, the synthetically useful tetraketones **28c** and **28d** were isolated in 77% and 86% yield, respectively.

We have been successful in preparing, by electrochemical oxidative decarboxylation of malonic acid derivatives, a wide variety of the diketones, ketone esters, and tetraketones in high yields (up to 91% yield). The electrochemical setup is simple and consists of an undivided cell equipped with graphite electrodes, known to facilitate multielectron transfers. The electrolyses are then a carried out in methanol at room temperature without the need to add any wasteful additional supporting electrolyte. Today, such conditions could easily be replicated in any organic synthetic laboratory by using an Electrasyn 2.0. A minor inconvenience, which is common to most anodic decarboxylations, is the rather low current efficiency (10−16%) (Tables 1−3), which explains why long electrolysis times are required.

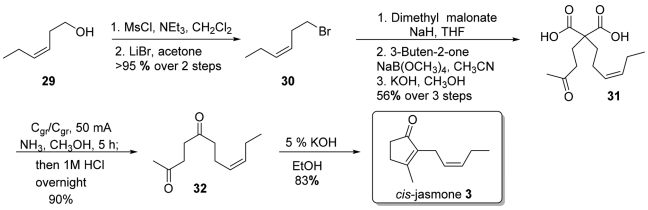
A plausible mechanism that rationalizes the formation of the diketones, ketoesters, and polyketones can be proposed (Scheme 4). After reaction with ammonia to form the corresponding ammonium salts, the malonic acid carboxylates can lose an electron to produce radical anion **A**. Elimination of $CO_2$ from **A** then forms the new radical anion **B**, which is oxidized a second time to generate either zwitterionic intermediate **C** or the $\alpha$-lactone **D**. These two species are in equilibrium, as previously demonstrated by Adams.[24]

At this point, with methanol either adding directly to the zwitterionic intermediate **C** or to the $\alpha$-lactone **D**, followed by loss of a proton to give anion **E**. A subsequent oxidation of carboxylate **E** takes place, and loss of $CO_2$ produces the radical intermediate **F**, which is further oxidized into cation **G**. Capture of species **G** by MeOH then gives **26′**, which is one of the products formed in the initial complex mixture. Alternatively, ionic species **G** can also be intramolecularly intercepted by the pendant ketone function, leading to the oxonium cation **H**. Addition of MeOH to **H** can either produce the bis-acetal **M** or generate adduct **26′** by reversion to cation **G** or direct addition onto **H**. In addition to these three products, some hemiacetal intermediates can also be formed, due to the presence of small amounts of $H_2O$ in the MeOH.

The situation is even more complicated in the case of polyketones such as **27c** since additional intermediates, i.e., tetrahydropyrans bis-ketals, can also be formed. Fortunately, this complex mixture of products, upon treatment with 1 M aq HCl, smoothly converges to the desired diketone **28c**.

The synthetic utility of our electrochemical reaction was then demonstrated via the total synthesis of *cis*-jasmone **3** (Scheme 5), the major fragrant component of jasmine flower oil.[25] This target was selected as its cyclization from key 1,4-diketone precursor **32** is well established in the literature.[26]

**Scheme 5. Total Synthesis of *cis*-Jasmone 3**




The synthesis began with the methanesulfonyl chloride activation of *cis*-3-hexenol **29** followed by a Finkelstein reaction, which afforded the corresponding bromide **30** in quantitative yield. After a first di-*tert*-butyl malonate alkylation, Echavarren sodium tetramethoxyborate catalyzed addition[27] using 3-buten-2-one and a classical ester cleavage led to malonic acid **31** in a good yield of 57% over three steps (Scheme 5).

Using our optimized electrochemical conditions, the latter was efficiently transformed into 1,4-diketone **32** with a remarkable 90% yield. This example furthermore extends the scope of our transformation to alkene-containing compounds. Eventually, precursor **32** was cyclized according to a described procedure into *cis*-jasmone **3**,[26] which had spectral data identical to those of the naturally occurring compound.

## CONCLUSIONS

In conclusion, we have developed a mild and efficient method for the construction of a variety of polyketones and ketoesters by electrochemical oxidative decarboxylation of the corresponding substituted malonic acid derivatives. The dicarbonyl and polycarbonyl products are important building blocks for the synthesis of a wide range of carbo- and heterocyclic compounds. Current efforts are directed at establishing the mechanism of these electrochemical oxidations, expanding their scope, and applying these transformations to the total synthesis of selected natural products.

## EXPERIMENTAL SECTION

**General Experimental Section.** Commercial-grade solvents were dried and purified by standard procedures as specified in *Purification of Laboratory Chemicals*.[28] NMR spectra were recorded at room temperature with a Bruker Avance 300 instrument operating at a frequency of 300 MHz for $^1$H and 75 MHz for $^{13}$C. Chemical shifts ($\delta$) are reported in ppm from $CDCl_3$ ($\delta$ = 7.27 ppm) or DMSO-$d_6$ ($\delta$ = 2.50 ppm) for $^1$H NMR and relative to $CDCl_3$ ($\delta$ = 77.2 ppm) or DMSO-$d_6$ ($\delta$ = 39.5 ppm) for $^{13}$C NMR. Column chromatography was performed over ROCC silica gel 60 (40−63 $\mu$m mesh) eluting with ethyl acetate (or diethyl ether) and petroleum ether. Mass spectra were recorded using Varian Matt 44S and Finnigan-Matt TSQ-70 spectrometers. High-resolution mass data were recorded on a Q-Extractive orbitrap from ThermoFisher. The instrument for electrolysis is Thurlby/Thandar PL320QMT 30 V, 2A Quad Mode Triple Output DC Power Supply.

Disubstituted malonic acids **24b**,[29] **24d**,[22a] **24g**,[30] and **24i**[31] were prepared according to literature procedures.

**Procedure for the Synthesis of Substituted Malonate.** All starting materials were purchased from commercial suppliers and used without further purification.

*General Procedure A.* The malonate was added dropwise to a stirring solution of NaH in a given volume of THF at 0 °C (ice−water bath). The reaction mixture was allowed to reach room temperature until no more $H_2$ emission was observed. To this mixture was added the electrophile, and the resulting solution was stirred at reflux overnight. The reaction was cooled to room temperature then quenched by the addition of brine and diethyl ether. The resulting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layers were separated, and the aqueous layer was extracted with diethyl ether 3 times. The combined organic layers were washed with brine, dried over $Na_2SO_4$, and filtered, and the solvents were evaporated under reduced pressure to give the crude product, which was purified by flash chromatography.

*Synthesis of Tetramethyl Nonane-3,3,7,7-tetracarboxylate (**S1**).* Prepared according to the general procedure starting from dimethyl 2-ethylmalonate (3.1 mL, 20 mmol, 2.2 equiv), NaH (0.84 g, 20.9 mmol, 2.3 equiv), NaI (0.4 g, 2.67 mmol, 0.29 equiv), and 1,3-dibromopropane (1.1 mL, 9.1 mmol, 1.0 equiv) in DMF (60 mL). The solution was stirred at 100 °C (oil bath temperature) for 48 h. The residue was purified by column chromatography over silica gel (ethyl acetate/petroleum ether 1:8−1:2) yielding the desired product **S1** (6.3 g, 87%) as a colorless oil. $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 3.69 (s, 12H), 2.06−1.66 (m, 9H), 1.08−0.94 (m, 2H), 0.78 (t, $J$ = 7.5 Hz, 6H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 172.1, 58.1, 52.4, 32.4, 25.8, 18.9, 8.6. HRMS (ESI): $m/z$ calcd for $C_{17}H_{29}O_8$ $[M + H]^+$ 361.1857, found 361.1856.

*Synthesis of tetramethyl 2,12-dioxotridecane-5,5,9,9-tetracarboxylate (**S2**).* Prepared according to the general procedure starting from dimethyl 2-(3-oxobutyl)malonate[32] (2.02 g, 10 mmol, 2.2 equiv), NaH (0.42 g, 10.45 mmol, 2.3 equiv), NaI (0.5 g, 3.3 mmol, 0.33 equiv), and 1,3-dibromopropane (0.46 mL, 4.5 mmol, 1.0equiv) in DMF (30 mL). The solution was stirred at 100 °C (oil bath temperature) for 48 h. The residue was purified by column chromatography over silica gel (ethyl acetate/petroleum ether 1:8 to 1:2) to yield a mixture that was further purified by column chromatography over silica gel ($Et_2O$/petroleum ether 3:1) to yield product **S2** (1.32 g, 66%) as a white solid. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 3.70 (s, 12H), 2.46−2.37 (m, 4H), 2.18−2.06 (m, 10H), 1.87−1.79 (m, 4H), 1.16−1.03 (m, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$): $\delta$ 207.2, 171.7, 56.9, 52.6, 38.8, 34.1, 30.1, 26.9, 19.3. HRMS (ESI): $m/z$ calcd for $C_{21}H_{33}O_{10}$[M + H]$^+$ 445.2069, found 445.2068.

*Synthesis of Tetramethyl 2,13-Dioxotetradecane-5,5,10,10-tetracarboxylate (**S3**).* Prepared according to general procedure A starting from dimethyl 2-(3-oxobutyl)malonate (2.02 g, 10 mmol, 2.2 equiv), NaH (0.42 g, 10.45 mmol, 2.3 equiv), NaI (0.5 g, 3.3 mmol, 0.33 equiv), and 1,4-dibromobutane (0.54 mL, 4.5 mmol, 1.0 equiv) in DMF (30 mL). The solution was stirred at 100 °C (oil bath temperature) for 48 h. The residue was purified by column chromatography over silica gel (ethyl acetate/petroleum ether 1:8−1:2) to yield the desired product **S3** (1.99 g, 95%) as a colorless oil. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 3.61 (s, 12H), 2.38−2.28 (m, 4H), 2.04 (s, 6H), 2.03−1.97 (m, 4H), 1.79−1.67 (m, 4H), 1.07 (dt, $J$ = 7.6, 3.6 Hz, 4H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 207.1, 171.6, 56.6, 52.4, 38.6, 33.3, 29.9, 26.6, 24.3. HRMS (ESI): $m/z$ calcd for $C_{22}H_{34}O_{10}Na$[M + Na]$^+$ 481.2044, found 481.2043.

**Synthesis of Disubstituted Malonic Acids.** *General Procedure A.* The disubstituted dimethyl malonate was added to a stirred solution of LiOH in methanol and water (v/v = 1:1). The resulting reaction mixture was stirred at reflux overnight. After being cooled to room temperature, the mixture was washed 3 times with diethyl ether. Hydrogen chloride (1 M) was then added until the pH reached 1. The acidified aqueous phase was then extracted with ethyl acetate. The combined organic layers were dried over $MgSO_4$ and filtered, and the solvents were evaporated under reduced pressure. The solid crude product was finally washed with pentane, filtrated, and dried under vacuum to give the desired disubstituted malonic acid as a solid.

*Synthesis of 2-Butyl-2-(3-oxobutyl)malonic acid (**24a**).* Prepared according to general procedure A, starting from dimethyl 2-butyl-2-(3-oxobutyl) malonate[33] (0.4 g, 1.55 mmol, 1 equiv) and LiOH·$H_2O$ (0.195 g, 4.64 mmol, 3 equiv) in 20 mL of MeOH and $H_2O$ (v/v = 1:1). The resulting solution was stirred was stirred at reflux overnight, after workup, to yield the desired product **24a** as a white solid (321 mg, 90%). $^1$H NMR (300 MHz, DMSO-$d_6$): $\delta$ 12.74 (s, br, 1H), 2.22 (dd, $J$ = 10.2, 6.1 Hz, 6H), 1.98 (dd, $J$ = 10.1, 6.1 Hz, 5H), 1.38 (d, $J$ = 2.9 Hz, 3H). $^{13}$C NMR (75 MHz, DMSO-$d_6$): $\delta$ 172.7, 172.2, 55.4, 51.5, 28.8, 28.6, 27.4, 27.1, 27.0. HRMS (ESI): $m/z$ calcd for $C_{11}H_{17}O_5$ $[M - H]^-$ 229.1082, found 229.1070.

*Synthesis of 2-(3-Oxobutyl)-2-propylmalonic Acid (**24c**).* Prepared according to general procedure A, starting from dimethyl 2-(3-oxobutyl)-2-propylmalonate[34] (0.81 g, 3.37 mmol, 1 equiv) and LiOH·$H_2O$ (0.424 g, 10.11 mmol, 3 equiv) in 30 mL of MeOH and $H_2O$ (v/v = 1:1). The resulting solution was stirred was stirred at reflux overnight, after workup, to yield the desired product **24c** as a white solid (633 mg, 87%). $^1$H NMR (300 MHz, DMSO-$d_6$): $\delta$ 2.40−2.23 (m, 2H), 2.07 (s, 3H), 1.97−1.81 (m, 2H), 1.66 (dd, $J$ = 10.3, 5.7 Hz, 2H), 1.11 (d, $J$ = 7.8 Hz, 2H), 0.86 (t, $J$ = 7.0 Hz, 3H). $^{13}$C NMR (75 MHz, DMSO-$d_6$): $\delta$ 207.6, 173.0, 55.9, 37.9, 34.4, 29.9, 25.8, 17.1, 14.4. HRMS (ESI): $m/z$ calcd for $C_{10}H_{15}O_5$ $[M - H]^-$ 215.0925, found 215.0920.

*Synthesis of 2-Ethyl-2-(3-oxo-3-phenylpropyl)malonic Acid (**24e**).* Prepared according to general procedure A, starting from 2-ethyl-2-(3-oxo-3-phenylpropyl)malonate[35] (0.62 g, 2.12 mmol, 1 equiv) and LiOH·$H_2O$ (0.267 g, 6.36 mmol, 3 equiv) in 20 mL of MeOH and $H_2O$ (v/v = 1:1). The resulting solution was stirred was stirred at reflux overnight, after workup, to yield the desired product **24f** as a white solid (500 mg, 89%). $^1$H NMR (300 MHz, DMSO-$d_6$): $\delta$ 8.01−7.84 (m, 2H), 7.70−7.57 (m, 1H), 7.51 (tt, $J$ = 7.3, 3.7 Hz, 2H), 2.98−2.81 (m, 2H), 2.25−1.97 (m, 2H), 1.94−1.76 (m, 2H), 0.89−0.67 (m, 3H). $^{13}$C NMR (75 MHz, DMSO-$d_6$): $\delta$ 199.2, 172.9, 136.5, 133.3, 128.8, 127.9, 56.6, 33.4, 25.8, 25.0, 8.6. HRMS (ESI): $m/z$ calcd for $C_{14}H_{15}O_5$ $[M - H]^-$ 263.0925, found 263.0919.

*Synthesis of 2-Methyl-2-(3-oxo-3-phenylpropyl)malonic Acid (**24f**).* Prepared according to general procedure A, starting from 2-methyl-2-(3-oxo-3-phenylpropyl)malonate[35] (2.16 g, 7.76 mmol, 1 equiv) and LiOH·$H_2O$ (0.977 g, 23.28 mmol, 3 equiv) in 60 mL of MeOH and $H_2O$ (v/v = 1:1). The resulting solution was stirred was stirred at reflux overnight, after workup, to yield the desired product **24e** as a white solid (1.80 g, 93%). $^1$H NMR (300 MHz, DMSO-$d_6$): $\delta$ 8.03−7.85 (m, 2H), 7.62 (t, $J$ = 7.3 Hz, 1H), 7.51 (t, $J$ = 7.4 Hz, 2H), 3.06−2.86 (m, 2H), 2.06 (d, $J$ = 5.0 Hz, 2H), 1.32 (s, 3H). $^{13}$C NMR (75 MHz, DMSO-$d_6$): $\delta$ 199.2, 173.5, 136.5, 133.2, 128.8, 127.9, 52.4, 52.3, 40.4, 40.1, 39.8, 39.5, 39.2, 39.0, 38.7, 33.8, 29.7, 19.9. HRMS (ESI): $m/z$ calcd for $C_{13}H_{13}O_5$ $[M - H]^-$ 249.0769, found 249.0764.

*Synthesis of 2-Methyl-2-(3-oxocyclohexyl)malonic Acid (**24g**).* Prepared according to general procedure A, starting from dimethyl 2-methyl-2-(3-oxocyclohexyl)malonate (3.40 g, 14.04 mmol, 1 equiv) and LiOH·$H_2O$ (1.77 g, 43.12 mmol, 3 equiv) in 60 mL of MeOH and $H_2O$ (v/v = 1:1). The resulting solution was stirred was stirred at reflux overnight, after workup, to yield the desired product **24g** as a light red solid (2.60 g, 86%). $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ 12.81 (s, 2H), 2.43−2.21 (m, 3H), 2.21−2.06 (m, 2H), 1.99 (ddd, $J$ = 12.4, 6.2, 2.9 Hz, 1H), 1.72 (d, $J$ = 12.1 Hz, 1H), 1.60−1.32 (m, 2H), 1.23 (s, 3H). $^{13}$C NMR (101 MHz, DMSO-$d_6$): $\delta$ 210.1, 172.5, 172.3, 56.1, 43.2, 41.8, 40.6, 26.0, 24.5, 15.7, 15.7.

*Synthesis of 2-Methyl-2-(3-oxocyclopentyl)malonic Acid (**24h**).* Prepared according to general procedure A, starting from dimethyl 2-methyl-2-(3-oxocyclopentyl)malonate[36] (1.1 g, 4.8 mmol, 1 equiv) and LiOH·$H_2O$ (607 mg, 14.46 mmol, 3 equiv) in 24 mL of MeOH and $H_2O$ (v/v = 1:1). The resulting solution was stirred was stirred at reflux for 20 h, after workup, to yield the desired product as a light red solid **24h** (0.53 g, 55%). $^1$H NMR (300 MHz, DMSO-$d_6$): $\delta$ 12.68 (s, 2H), 2.85−2.66 (m, 1H), 2.30−1.85 (m, 5H), 1.74−1.52 (m, 1H), 1.19 (s, 3H). $^{13}$C NMR (75 MHz, DMSO-$d_6$): $\delta$ 217.5, 173.1, 171.8, 54.9, 45.8, 38.1, 24.3, 17.2, 13.8. HRMS (ESI): $m/z$ calcd for $C_9H_{11}O_5$ $[M - H]^-$ 199.0612, found 199.0612.

*Synthesis of 2-(5-Ethoxy-5-oxopentyl)-2-ethylmalonic Acid (**24j**).* Prepared according to the general procedure (see the general procedure for the synthesis of substituted malonate) starting from di-*tert*-butyl ethyl malonate (2.0 g, 8.19 mmol, 1 equiv), NaH (0.393 g, 9.83 mmol, 1.2 equiv), and ethyl 5-bromopentanoate (1.57 mL, 9.83 mmol, 1.2 equiv) in THF (50 mL). The solution was stirred at 80 °C (oil bath temperature) overnight. After workup led to a crude product, which was then dissolved in 30 mL of $CH_2Cl_2$, TFA (3.8 mL, 49.1 mmol, 6.0 equiv) was added. The resulting reaction mixture was stirred at room temperature overnight. The solvent was then evaporated under reduced pressure, and the resulting solid was


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washed with hexane (50 mL) and dried under vacuum to give the desired malonic acid **24j** (0.90 g, 42%) as a white solid. $^1$H NMR (300 MHz, DMSO-$d_6$): $\delta$ 12.69 (s, 2H), 4.03 (q, $J$ = 7.1 Hz, 2H), 2.26 (t, $J$ = 7.2 Hz, 2H), 1.72 (p, $J$ = 9.6, 8.5 Hz, 4H), 1.50 (p, $J$ = 7.1 Hz, 2H), 1.22−1.03 (m, 5H), 0.73 (t, $J$ = 7.4 Hz, 3H). $^{13}$C NMR (75 MHz, DMSO-$d_6$): $\delta$ 173.2, 172.8, 59.7, 56.9, 33.4, 31.0, 30.8, 24.9, 24.7, 23.1, 14.2, 8.5. HRMS (ESI): $m/z$ calcd for $C_{12}H_{19}O_6[M - H]^-$ 259.1187, found 259.1188.

*Synthesis of 2,13-Dioxotetradecane-5,5,10,10-tetracarboxylic Acid (**27a**).* Prepared according to general procedure A (see the general procedure for the synthesis of substituted malonate), starting from dimethyl 2-ethylmalonate (2.7 mL, 20 mmol, 2.2 equiv), NaH (0.84 g, 20.9 mmol, 2.3 equiv), NaI (0.4 g, 2.67 mmol, 0.29 equiv), and 1,3-dibromopropane (1.1 mL, 9.1 mmol, 1.0 equiv) in DMF (60 mL). The solution was stirred at 100 °C (oil bath temperature) overnight, after workup obtain a crude product, which was dissolved in 45 mL of MeOH and $H_2O$ (v/v = 2:1), and treated with LiOH·$H_2O$ (1.52 g, 76.8 mmol, 6 equiv) at 70 °C overnight, after workup, to yield the desired product **27a** as a colorless solid (1.85 g, 33% after two steps). $^1$H NMR (300 MHz, DMSO-$d_6$): $\delta$ 12.62 (s, 4H), 1.68 (t, $J$ = 8.3 Hz, 4H), 1.26−1.08 (m, 8H). $^{13}$C NMR (75 MHz, DMSO-$d_6$): $\delta$ 173.6, 52.7, 40.4, 40.1, 39.8, 39.5, 39.2, 39.0, 38.7, 35.6, 19.8, 19.1. HRMS (ESI): $m/z$ calcd for $C_{11}H_{15}O_8$ $[M - H]^-$ 275.0772, found 275.0769.

*Synthesis of 2,13-Dioxotetradecane-5,5,10,10-tetracarboxylic Acid (**27b**).* Prepared according to general procedure A, starting from tetramethyl nonane-3,3,7,7-tetracarboxylate **S1** (4.6 g, 12.8 mmol, 1 equiv) and LiOH·$H_2O$ (3.2 g, 76.8 mmol, 6 equiv) in 60 mL of MeOH and $H_2O$ (v/v = 1:1). The resulting solution was stirred was stirred at reflux for 20 h. After workup, the desired product was obtained as a colorless solid **27b** (3.5 g, 91%). $^1$H NMR (300 MHz, DMSO-$d_6$): $\delta$ 12.62 (s, 2H), 1.85−1.56 (m, 8H), 0.98 (p, $J$ = 5.6 Hz, 2H), 0.73 (t, $J$ = 7.4 Hz, 6H). $^{13}$C NMR (75 MHz, DMSO-$d_6$): $\delta$ 172.9, 57.0, 40.4, 40.1, 39.8, 39.5, 39.2, 39.0, 38.7, 31.6, 24.7, 18.4, 8.5. HRMS (ESI): $m/z$ calcd for $C_{13}H_{19}O_8$ $[M - H]^-$ 303.1085, found 303.1077.

*Synthesis of 2,13-Dioxotetradecane-5,5,10,10-tetracarboxylic Acid (**27d**).* Prepared according to general procedure A, starting from tetramethyl 2,13-dioxotetradecane-5,5,10,10-tetracarboxylate **S3** (0.89 g, 2.0 mmol, 1 equiv) and LiOH·$H_2O$ (420 mg, 10 mmol, 5 equiv) in 50 mL of MeOH and $H_2O$ (v/v = 1:1). The resulting solution was stirred was stirred at reflux for 20 h, after workup, to yield the desired product as a colorless solid **27d** (0.68 g, 85%). $^1$H NMR (300 MHz, DMSO-$d_6$): $\delta$ 2.38−2.23 (m, 4H), 2.06 (d, $J$ = 4.8 Hz, 6H), 1.93−1.82 (m, 4H), 1.66 (s, 4H), 1.09 (s, 4H). $^{13}$C NMR (75 MHz, DMSO-$d_6$): $\delta$ 207.5, 172.8, 55.9, 37.9, 31.9, 29.9, 25.7, 24.0. HRMS (ESI): $m/z$ calcd for $C_{18}H_{25}O_{10}$ $[M - H]^-$ 401.1453, found 401.1455.

**General Procedure for the Electrochemical Oxidative Decarboxylation of Malonic Acid Derivatives.** To an undivided beaker-type cell (100 mL) equipped with two graphite electrodes (2 cm × 1.5 cm) was added disubstituted acid (0.5 mmol) dissolved in MeOH (40 mL). Then 150 $\mu$L (1.05 mmol, 2.1 equiv) of 7 M $NH_3$ in MeOH (for malonic acid derivatives) or 300 $\mu$L (2.1 mmol, 4.2 equiv) of 7 M $NH_3$ in MeOH (for tetracarboxylic acid) was added, and the resulting solution was stirred at room temperature for 10 min. The power was switched on to start the electrochemical reaction. The current was maintained at 60 mA. The reaction was monitored by TLC and stopped after 5 h (for diacid) or 10 h for (tetraacid). Then, 1 mL of 1 M HCl was added to the reaction mixture, and the resulting solution was stirred at room temperature overnight. The solvent was concentrated under reduced pressure to obtain a crude ketone product, which was further purified by flash chromatography on silica gel. (For the synthesis of ketals **22a**, **22c**, and **22d**: The reaction was stopped after 4−4.5 h. The solvent was concentrated under reduced pressure to obtain a crude ketal product, which was further purified by chromatography.)

*Synthesis of 5,5-dimethoxynonane-1,9-diyl diacetate (**22a**).* Purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 20:1). Colorless liquid, 121.8 mg, 80% yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 4.01 (t, $J$ = 6.6 Hz, 1H), 3.08 (s, 6H), 1.99 (s, 1H), 1.63−1.50 (m, 1H), 1.30−1.18 (m, 1H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 171.2, 102.9, 64.2, 64.0, 47.6, 32.0, 28.7, 21.0, 20.2. IR (film): $\nu$ (cm-1) = 2927 [w], 1731−1714 [s], 1461 [w], 1386−1367 [m], 1240 [s], 1120 [w], 1068−1035 [m], 887 [w], 724 [w]. HRMS (ESI): $m/z$ calcd for $C_{15}H_{28}O_6Na[M + Na]^+$: 327.1778, found 327.1782. MS (ESI): $m/z$ 327 (9) [$MNa^+$ ], 281 (100), 273 (9) [$M - CH_3O$].

*Synthesis of 1-Phenyloctan-2-one (**23b**).* Purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 50:1). Colorless liquid, 51.1 mg, 50% yield. The spectral data were in accordance with those reported in the literature.[37] $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.37−7.24 (m, 3H), 7.23−7.17 (m, 2H), 3.68 (s, 2H), 2.44 (t, $J$ = 7.4 Hz, 2H), 1.60−1.48 (m, 2H), 1.31−1.14 (m, 6H), 0.86 (t $J$ = 8.6 Hz, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 208.8, 134.5, 129.5, 128.8, 127.1, 50.3, 42.1, 31.7, 28.9, 23.8, 22.6, 14.1.

*Synthesis of (E)-Methyl 5,5-Dimethoxyhept-2-enoate (**22c**).* Purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 10:1). Colorless liquid, 82.9 mg, 82% yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 6.84 (dt, $J$ = 15.7, 7.5 Hz, 1H), 5.90 (dt, $J$ = 15.7, 1.5 Hz, 1H), 3.72 (s, 3H), 3.18 (s, 6H), 2.51 (dd, $J$ = 7.5, 1.5 Hz, 2H), 1.60 (q, $J$ = 7.5 Hz, 2H), 0.83 (t, $J$ = 7.5 Hz, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 166.8, 143.9, 123.6, 102.9, 51.6, 48.1, 35.4, 26.1, 7.9. IR (film): $\nu$ ($cm^{-1}$) = 2949 [w] (C−H), 2831 [w], 1724 [s], 1659 [m], 1460−1435 [w], 1344 [m], 922 [m], 737 [m]. HRMS (ESI): $m/z$ calcd for $C_{10}H_{18}O_4Na$ $[M + Na]^+$:225.1097, found 225.1098. MS ($ESI^+$): $m/z$ 279 (64) [$MNa^+$], 225 (100) [$MH^+$], 171 (61), 139 (24).

*Synthesis of 5,5-Dimethoxyundec-2-yne (**22d**).* Purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 50:1). Colorless liquid, 82.8 mg, 78% yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 3.18 (s, 6H), 2.43 (q, $J$ = 2.5 Hz, 2H), 1.78 (t, $J$ = 2.6 Hz, 3H), 1.76−1.68 (m, 2H), 1.29 (s, 8H), 0.87 (t, $J$ = 6.7 Hz, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 102.7, 77.6, 74.2, 48.3, 33.2, 31.8, 29.6, 24.4, 23.7, 22.7, 14.2, 3.8. IR (film): $\nu$ ($cm^{-1}$) = 2924 [w] (C−H), 1456−1429 [w], 1269 [m], 1090 [m], 1049 [m], 736 [s]. HRMS (ESI): $m/z$ calcd for $C_{13}H_{25}O_2$ $[M + H]^+$:213.1849, found 213.1851. MS ($ESI^+$): $m/z$ 213 (100) [$MH^+$], 181 (27), 159 (6).

*Synthesis of 5-Oxonon-8-en-1-yl Acetate (**23e**).* Purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 30:1). Pale yellow oil, 71.4 mg, 72% yield; The spectral data were in accordance with those reported in the literature.[38] $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 5.80 (ddt, $J$ = 16.8, 10.2, 6.4 Hz, 1H), 5.08−4.93 (m, 2H), 4.09−4.01 (m, 2H), 2.56−2.39 (m, 4H), 2.32 (tdd, $J$ = 7.8, 6.5, 1.6 Hz, 2H), 2.04 (s, 3H), 1.63 (td, $J$ = 8.4, 7.2, 4.4 Hz, 6H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 213.0, 171.3, 137.2, 115.4, 64.2, 42.3, 42.0, 28.2, 27.9, 21.1, 20.2.

*Synthesis of Nonane-2,5-dione (**26a**).* Purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 12:1). Colorless liquid, 64.8 mg, 83% yield. The spectral data were in accordance with those reported in the literature.[39] $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 2.67 (td, $J$ = 4.7, 1.9 Hz, 4H), 2.43 (t, $J$ = 7.5 Hz, 2H), 2.16 (s, 3H), 1.63−1.45 (m, 2H), 1.33−1.24 (m, 2H), 0.88 (t, $J$ = 7.3 Hz, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 209.8, 207.4, 42.6, 37.0, 36.1, 30.0, 26.0, 22.4, 13.9.

*Synthesis of Heptane-2,5-dione (**26b**).* Purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 12:1). Colorless liquid, 55.1 mg, 86% yield. The spectral data were in accordance with those reported in the literature.[40] $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 2.77−2.63 (m, 4H), 2.49 (q, $J$ = 7.3 Hz, 2H), 2.20 (s, 3H), 1.07 (t, $J$ = 7.3 Hz, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 210.2, 207.5, 37.1, 36.1, 35.8, 30.1, 7.9.

*Synthesis of Octane-2,5-dione (**26c**).* Purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 12:1). Colorless liquid, 58 mg, 91% yield. The spectral data were in accordance with those reported in the literature.[41] $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 2.72−2.62 (m, 4H), 2.42 (t, $J$ = 7.3 Hz, 2H), 2.17 (s, 3H), 1.58 (dt, $J$ = 14.7, 7.4 Hz, 2H), 0.90 (t, $J$ = 7.4 Hz, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 209.7, 207.5, 44.8, 37.0, 36.2, 30.1, 17.4, 13.8.


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*Synthesis of Undecane-2,5-dione (**26d**).* Purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 20:1). Colorless liquid, 78.3 mg, 85% yield. The spectral data were in accordance with those reported in the literature.[42] $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 2.72−2.62 (m, 4H), 2.43 (t, $J$ = 7.5 Hz, 2H), 2.16 (s, 3H), 1.60−1.50 (m, 2H), 1.33−1.19 (m, 6H), 0.85 (t, $J$ = 8.2 Hz, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 209.8, 207.4, 42.9, 37.0, 36.1, 31.7, 30.0, 28.9, 23.9, 22.6, 14.1.

*Synthesis of 1-Phenylpentane-1,4-dione (**26e**).* Purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 10:1). Colorless liquid, 71.4 mg, 81% yield. The spectral data were in accordance with those reported in the literature.[43] $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 8.00−7.89 (m, 2H), 7.58−7.50 (m, 1H), 7.49−7.38 (m, 2H), 3.26 (dd, $J$ = 6.8, 5.7 Hz, 2H), 2.87 (t, $J$ = 6.3 Hz, 2H), 2.24 (s, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 207.4, 198.6, 136.7, 133.2, 128.7, 128.1, 37.1, 32.5, 30.2.

*Synthesis of 1-Phenylhexane-1,4-dione (**26f**).* Purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 10:1). Colorless liquid, 80.3 mg, 84% yield. The spectral data were in accordance with those reported in the literature.[44] $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.97−7.96 (m, 2H), 7.61−7.51 (m, 1H), 7.50−7.39 (m, 2H), 3.34−3.18 (t, $J$ = 6.1 Hz, 2H), 2.85 (t, $J$ = 6.3 Hz, 2H), 2.56 (q, $J$ = 7.3 Hz, 2H), 1.09 (t, $J$ = 7.3 Hz, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 210.3, 199.0, 136.8, 133.3, 128.7, 128.2, 36.2, 35.9, 32.6, 8.0.

*Synthesis of 3-Acetylcyclohexanone (**26g**).* Purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 10:1). Colorless liquid, 58 mg, 83% yield; The spectral data were in accordance with those reported in the literature.[45] $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 2.89−2.82 (m, 1H), 2.54−2.22 (m, 4H), 2.17 (s, 3H), 2.13−2.01 (m, 2H), 1.80−1.60 (m, 2H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 210.1, 208.6, 51.0, 42.6, 41.0, 28.4, 27.3, 25.0.

*Synthesis of 3-Acetylcyclopentanone (**26h**).* Purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 5:1). Colorless liquid, 48 mg, 77% yield. The spectral data were in accordance with those reported in the literature.[46] $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 3.34−3.20 (m, 1H), 2.51 (dd, $J$ = 18.4, 8.9 Hz, 1H), 2.43−2.27 (m, 3H), 2.26 (s, 3H), 2.09−1.95 (m, 1H), 1.28−1.20 (m, 1H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 216.7, 208.4, 48.7, 40.0, 37.7, 28.8, 26.0.

*Synthesis of Dimethyl 4-oxoheptanedioate (**26i**).* Purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 10:1). Colorless liquid, 75 mg, 74% yield. The spectral data were in accordance with those reported in the literature.[47] $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 3.66 (s, 6H), 2.77 (t, $J$ = 6.5 Hz, 4H), 2.59 (t, $J$ = 6.5 Hz, 4H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 207.1, 173.3, 51.9, 37.1, 27.8.

*Synthesis of Ethyl 6-Oxooctanoate (**26j**).* Purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 15:1). Colorless liquid, 75 mg, 74% yield. The spectral data were in accordance with those reported in the literature.[48] $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 4.12 (q, $J$ = 7.1 Hz, 2H), 2.42 (q, $J$ = 7.4 Hz, 4H), 2.31 (ddd, $J$ = 7.0, 4.5, 2.2 Hz, 2H), 1.61 (p, $J$ = 3.4 Hz, 4H), 1.25 (t, $J$ = 7.1 Hz, 3H), 1.05 (t, $J$ = 7.3 Hz, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 211.4, 173.6, 60.4, 42.0, 36.0, 34.2, 24.6, 23.4, 14.4, 8.0.

*Synthesis of Heptane-2,6-dione (**28a**).* Purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 10:1 to 5:1). Colorless liquid, 54.5 mg, 85% yield. The spectral data were in accordance with those reported in the literature.[49] $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 2.47 (t, $J$ = 7.1 Hz, 4H), 2.13 (s, 6H), 1.83 (p, $J$ = 7.1 Hz, 2H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 208.5, 42.6, 30.0, 17.8.

*Synthesis of Nonane-3,7-dione (**28b**).* Purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 10:1 to 5:1). Colorless liquid, 69.5 mg, 89% yield. The spectral data were in accordance with those reported in the literature.[50] $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 2.42 (dt, $J$ = 12.4, 7.2 Hz, 8H), 1.84 (p, $J$ = 7.1 Hz, 2H), 1.04 (t, $J$ = 7.4 Hz, 6H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 211.3, 41.3, 36.0, 18.0, 7.9.

*Synthesis of Tridecane-2,5,9,12-tetraone (**28c**).* The tetramethyl 2,12-dioxotridecane-5,5,9,9-tetracarboxylate **S2** (303 mg, 0.68 mmol, 1 equiv) was added to a stirred solution of $LiOH{\cdot}H_2O$ (172 mg, 4.1 mmol, 6 equiv) in 30 mL of MeOH and $H_2O$ (v/v = 1:1). The resulting solution was stirred at reflux overnight, after workup, to yield the desired product as a colorless solid **27c** (0.20 g, 75%). The acid **27c** (0.20 g, 0.51 mmol) was added and dissolved in MeOH (40 mL). A 300 $\mu$L (2.1 mmol, 4.2 equiv) portion of 7 M $NH_3$ in MeOH was added, and the resulted solution was stirred at room temperature for 10 min. The power was switched on to start the electrochemical reaction, keeping the current at 60 mA. The reaction was monitored by TLC and stopped after 10 h. Then 1 mL of 1 M HCl was added to the reaction mixture, the resulting mixture was stirred at room temperature overnight, and the solvent was concentrated under reduced pressure to obtain a crude ketone product. The product was purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 10:1 to 5:1). Colorless liquid, 92 mg, 77% yield. The spectral data were in accordance with those reported in the literature.[51] $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 2.72−2.55 (m, 8H), 2.46 (t, $J$ = 7.1 Hz, 4H), 2.14 (s, 6H), 1.81 (t, $J$ = 7.0 Hz, 2H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 209.0, 207.3, 41.5, 37.0, 36.1, 29.9, 17.8.

*Synthesis of Tetradecane-2,5,10,13-tetraone (**28d**).* Purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 10:1 to 5:1). Colorless liquid, 109 mg, 86% yield. The spectral data were in accordance with those reported in the literature.[53] $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 2.81−2.59 (m, 8H), 2.52−2.38 (m, 4H), 2.18 (d, $J$ = 3.1 Hz, 6H), 1.64−1.49 (m, 4H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 209.3, 207.4, 42.6, 37.0, 36.2, 30.1, 23.3.

**Total Synthesis of *cis*-Jasmone.** *Synthesis of (Z)-2-(Hex-3-en-1-yl)-2-(3-oxobutyl)malonic Acid (**31**).* To a stirred suspension of sodium hydride (60% dispersion in mineral oil, 520 mg, 13.0 mmol, 2.6 equiv) in tetrahydrofuran (25 mL) was added dimethyl malonate (1.4 mL, 12.5 mmol, 2.5 equiv) at 0 °C. The resulting mixture was warmed to room temperature and stirred for 15 min. (Z)-1-Bromohex-3-ene[54] (**30**) was then added, and the reaction was further refluxed overnight. The reaction was monitored by TLC, and upon completion, the mixture was quenched with water (15 mL), the two layers were separated, and the aqueous phase was extracted with $Et_2O$ (3 × 20 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, and filtered, and the solvent was concentrated under reduced pressure. Purification by flash column chromatography (petroleum ether/diethyl ether 8:2) afforded dimethyl (Z)-2-(hex-3-en-1-yl)malonate (734 mg, 69%) as a colorless liquid. The spectral data were in accordance with those reported in the literature.[52] $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 5.47−5.37 (m, 1H), 5.32−5.21 (m, 1H), 3.73 (s, 6H), 3.38 (t, $J$ = 7.3 Hz, 1H), 2.13−1.91 (m, 6H), 0.94 (t, $J$ = 7.5 Hz, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 170.0, 133.6, 127.0, 52.6, 51.1, 28.9, 24.9, 20.6, 14.4.

To a stirred solution of (Z)-2-(hex-3-en-1-yl)malonate (3.0 g, 14.0 mmol, 1.0 equiv) and sodium tetramethoxyborate (222 mg, 1.4 mmol, 0.1 equiv) in acetonitrile (42 mL) was added dropwise 3-buten-2-one (2.3 mL, 28.0 mmol, 2.0 equiv) at room temperature. The reaction was monitored by TLC, and upon completion, the volatiles were removed under reduced pressure. Purification by flash column chromatography (petroleum ether/diethyl ether 7:3) afforded dimethyl (Z)-2-(hex-3-en-1-yl)-2-(3-oxobutyl)malonate (3.53 g, 89%) as a slightly yellow liquid. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 5.43−5.32 (m, 1H), 5.31−5.17 (m, 1H), 3.71 (m, 6H), 2.43 (dd, $J$ = 8.9 and 6.6 Hz, 2H), 2.22−2.12 (m, 5H), 2.06−1.86 (m, 6H), 0.95 (t, $J$ = 7.5 Hz, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 207.3, 171.9, 132.9, 127.4, 56.8, 52.6, 38.9, 33.9, 30.1, 26.8, 22.2, 20.6, 14.4. HRMS (ESI): $m/z$ calcd for $C_{15}H_{25}O_5[M + H]^+$ 285.1697, found 285.1696.

To a stirred solution of dimethyl (Z)-2-(hex-3-en-1-yl)-2-(3-oxobutyl)malonate (3.5 g, 12.3 mmol, 1.0 equiv) in methanol (60 mL) was added portionwise potassium hydroxide (6.9 g, 123.0 mmol, 10.0 equiv) at room temperature. The resulting mixture was refluxed overnight and then quenched with a 10% hydrochloric acid solution (50 mL). The two layers were separated, and the aqueous phase was extracted with AcOEt (3 × 40 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, and filtered, and the solvent was concentrated under reduced pressure. Crude (Z)-2-(hex-3-en-1-yl)-2-(3-oxobutyl)malonic acid (**31**) was obtained as a slightly


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yellow oil (2.9 g, 92%), which was used for the next step without purification. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 9.09 (bs, 2H), 5.48−5.32 (m, 1H), 5.31−5.16 (m, 1H), 2.55 (dd, $J$ = 8.8 and 6.6 Hz, 2H), 2.26−2.15 (m, 5H), 2.07−1.91 (m, 6H), 0.93 (t, $J$ = 7.5 Hz, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 208.9, 176.5, 133.4, 126.9, 56.7, 39.1, 35.2, 30.1, 28.5, 22.6, 20.6, 14.3. HRMS (ESI): $m/z$ calcd for $C_{13}H_{21}O_5$ $[M + H]^+$ 257.1384, found 257.1383.

*Synthesis of (Z)-Undec-8-ene-2,5-dione (**32**).* To an undivided beaker-type cell (100 mL) equipped with two graphite electrodes (2 cm × 1.5 cm) was added (*Z*)-2-(hex-3-en-1-yl)-2-(3-oxobutyl)-malonic acid (**31**) (142 mg, 0.5 mmol, 1.0 equiv) dissolved in MeOH (30 mL). Then 7 M $NH_3$ in MeOH (150 $\mu$L, 1.05 mmol, 2.1 equiv) was added, and the resulting solution was stirred at room temperature for 10 min. The power was switched on to start the electrochemical reaction. The current was maintained at 50 mA. The reaction was monitored by TLC and stopped after 4 h. Then 1 M HCl (2 mL) was added, and the resulting solution was stirred at room temperature overnight. Brine (20 mL) was added, the two layers were separated, and the aqueous phase was extracted with $Et_2O$ (3 × 25 mL). The combined organic layers were dried over $MgSO_4$ and filtered, and the solvent was concentrated under reduced pressure. Purification by flash column chromatography (petroleum ether/diethyl ether 95:5) afforded (*Z*)-undec-8-ene-2,5-dione (**32**) as a colorless liquid (82 mg, 90%). The spectral data were in accordance with those reported in the literature.[26] $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 5.44−5.33 (m, 1H), 5.31−5.21 (m, 1H), 2.74−2.63 (m, 4H), 2.50 (t, $J$ = 7.5 Hz, 2H), 2.35−2.25 (m, 2H), 2.18 (s, 3H), 2.04 (p, 7.1 Hz, 2H), 0.95 (t, $J$ = 7.5 Hz, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 209.1, 207.4, 133.0, 127.2, 42.9, 37.0, 36.3, 30.1, 21.7, 20.6, 14.4.

*Synthesis of cis-Jasmone (**3**).* To a stirred solution of (*Z*)-undec-8-ene-2,5-dione (**29**) (108 mg, 0.6 mmol, 1.0 equiv) in ethanol (2.5 mL) was added a 5% aqueous solution of potassium hydroxide (1 mL) at room temperature. The resulting mixture was then refluxed for 2 h and quenched with a 1 M aqueous solution of hydrochloric acid. The two layers were separated, and the aqueous phase was extracted with $Et_2O$ (3 × 5 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, and filtered, and the solvent was concentrated under reduced pressure. Purification by flash column chromatography (petroleum ether/diethyl ether 7:3) afforded *cis*-jasmone (**3**) (81 mg, 83%) as a slightly yellow oil. The spectral data were in accordance with those reported in the literature.[26] $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 5.38 (dtt, $J$ = 10.3, 6.9, and 1.6 Hz, 1H), 5.29−5.18 (m, 1H), 2.93 (d, $J$ = 7.1 Hz, 6H), 2.52−2.45 (m, 2H), 2.39−2.34 (m, 2H), 2.15 (p, $J$ = 7.0 Hz, 2H), 2.06 (s, 3H), 0.98 (t, $J$ = 7.5 Hz, 3H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 209.2, 170.5, 139.5, 132.5, 125.2, 34.4, 31.8, 21.3, 20.7, 17.4, 14.3.

## ■ ASSOCIATED CONTENT

### Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.8b01994.

Spectra of **24b**, **24d**, **24i**, **24j**, and their precursors as well as of all new compounds (PDF)

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### Notes

The authors declare no competing financial interest.

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## ■ DEDICATION

Dedicated to the memory of Professor István E. Markó.

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