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Michael addition approach for the synthesis of novel spiro compounds and 2-substituted malonic acid derivatives from Meldrum's acid

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Abstract—Novel routes for the synthesis of spiro derivatives of Meldrum's acid and 2-substituted malonic acid derivatives have been developed. Meldrum's acid was monoalkylated using a Michael addition reaction. Mono-Michael adducts were then alkylated using substituted haloalkanes, which on condensation gave spiro derivatives of Meldrum's acid. Bis Michael addition of Meldrum's acid with 1,5-diaryl-1,4-pentadien-3-one gave directly a spiro derivative of Meldrum's acid. These compounds and bis alkylated Meldrum's acid derivatives, on acidic methanolysis gave 2-substituted malonic acids.

2,2-Dimethyl-1,3-dioxane-4,6-dione (Meldrum's acid) **1**[1] is a versatile organic reagent[2] and its derivatives are very useful building blocks in synthetic organic chemistry. Because of its acidity (pK_a 4.83),[2] steric rigidness and notable tendency to regenerate acetone, Meldrum's acid is often employed with advantage over malonic ester.[3]

There are several methods for the synthesis of 5-mono and 5,5-disubstituted Meldrum's acids.[4] Although the Michael addition reaction[5] is widely recognized as one of the most important C–C bond forming reactions in organic chemistry and an important method for alkylation of active methylene compounds, there are only a few reports on the Michael addition of Meldrum's acid to electrophilic olefins.[6]

In continuation of our work on the synthesis of novel spiro compounds,[7] we report here, the utilization of Michael adducts of Meldrum's acid for constructing novel spiro molecules. Spiro systems are important in bio-organic chemistry and are present in many natural products and pharmaceuticals[8] and 2-substituted malonic acid derivatives are very useful reagents in organic synthesis.[9]

This letter focuses on a novel synthetic strategy, which provides versatile routes for the synthesis of spiro derivatives of Meldrum's acid **1** by Michael addition, and 2-substituted malonic acid derivatives, which are otherwise difficult or tedious to synthesize.

5-Monoalkyl derivatives of Meldrum's acid **3**,[6b] **8**,[6a] and **12**[6a] were prepared in high yields by Michael addition of **1** to methyl acrylate **2**, acrylonitrile **7**, and methyl vinyl ketone **11** in the presence of benzyltrimethylammonium hydroxide (Triton B), using K_2CO_3 as a base in acetonitrile as solvent. Formation of the double adduct was not observed even with 3 mol equiv of the Michael acceptor, probably for steric reasons (highly crowded carbanion).[6b]

Compound **3**[10] was prepared by heating anhydrous K_2CO_3, Meldrum's acid **1**, and methyl acrylate **2** in acetonitrile in the presence of Triton B at 50–60 °C. The presence of a triplet for the methine proton at δ 3.91 and a quartet and triplet for the two methylene protons at δ 2.39 and 2.65, respectively, in the ^{1}H NMR, clearly indicated the formation of a monoadduct. Compound **3** was then alkylated with ethyl bromoacetate to give the 5,5-dialkylated Meldrum's acid **4**.[11] Dieckmann cyclisation of **4** in the presence of sodium hydride in dry DMF gave the spiro derivative **5**[12] as a dark yellow liquid in good yield.

Substituted Meldrum's acids upon acid catalysed alcoholysis afford carboxylic esters.[13] Heating **5** in methanolic hydrochloric acid gave **6**[14] in 70% yield (Scheme 1,

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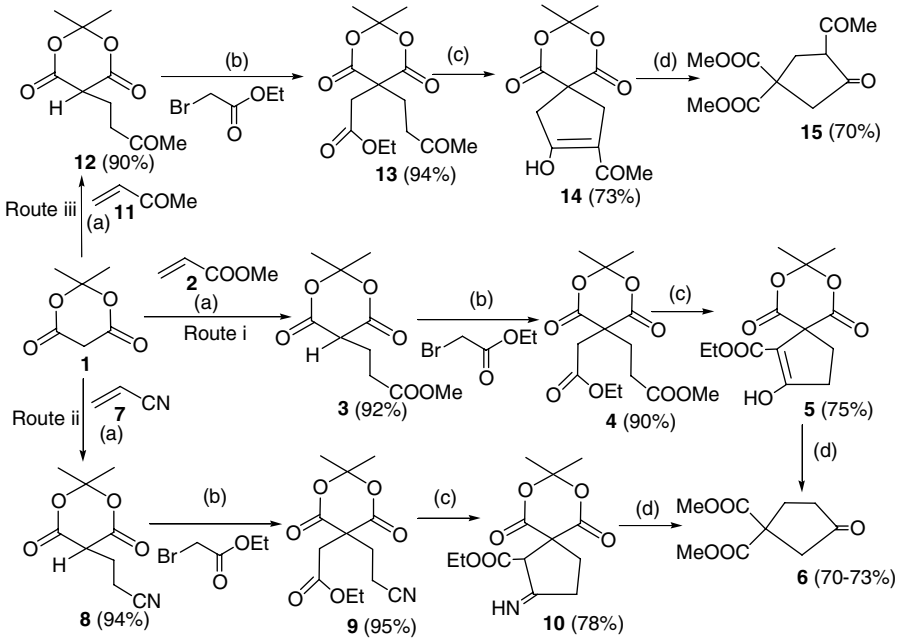


Scheme 1. Reagents and conditions: (a) Triton B/K_2CO_3/CH_3CN, 50–60 °C, 8 h; (b) K_2CO_3/$(CH_3)_2CO$, reflux, 4 h; (c) NaH/DMF, 10–15 °C, 5 h; (d) aq HCl/MeOH, reflux, 5 h.

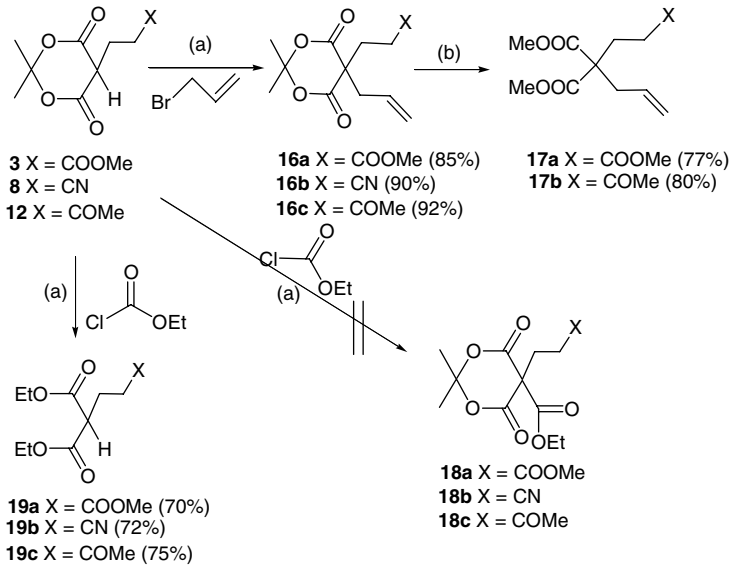
route i). However, reported procedures[15] for the diethyl analog of **6** have disadvantages like low yield, and longer reaction time. The procedure reported above represents a general method for the synthesis of **6**, with good yield and shorter reaction time, which is an intermediate in the synthesis of (*R*,*S*)-3-oxocyclopentanecarboxylic acid, a key intermediate in the synthesis of various biologically active products.[15b]

When Michael addition of **1** was extended to acrylnitrile **7**, under similar experimental conditions the mono adduct **8**[16] was obtained in excellent yield. The IR spectrum displayed a sharp band at 2251 cm^{-1} due to the nitrile group. Alkylation of **8** with ethyl bromoacetate gave **9**[17] in excellent yield, which on cyclisation furnished the desired spiro molecule **10**[18] in good yield. Compound **10** was easily converted into 1,1-di(methoxycarbonyl)cyclopentan-3-one **6** by heating in methanolic hydrochloric acid (Scheme 1, route ii).

5-Monoalkyl Meldrum's acid **12**[19] was prepared in 90% yield by Michael addition of **1** to methyl vinyl ketone **11**, which was then alkylated using ethyl bromoacetate to give 5,5-dialkylated Meldrum's acid **13**.[20] Intramolecular Claisen condensation of **13** in the presence of sodium hydride in dry DMF gave **14**[21] as a dark yellow liquid in good yield. 3-Acetyl-1,1-di(methoxycarbonyl)cyclopentan-4-one **15**[22] was produced by heating **14** in methanolic hydrochloric acid, in 70% yield (Scheme 1, route iii).

The reaction sequence shown in Scheme 2 further illustrates the usefulness of 5-monoalkylated Meldrum's acids **3**, **8** and **12**. These monoadducts were allylated by refluxing with allyl bromide in K_2CO_3/acetone to obtain 5,5-dialkylated Meldrum's acids **16**[23] in excellent yields. These were converted into 2,2-disubstituted malonic acid derivatives **17**[24] by refluxing in acidic methanol in good yields. It was observed that compounds **16a** and **16b** gave the same compound, dimethyl 2-allyl-2-methoxycarbonyl pentanedioate **17a** on acidic methanolysis, which was confirmed on the basis of IR spectra, which were superimposable. In contrast, **16c** gave compound **17b**.[25]

Monoadducts **3**, **8** and **12** were refluxed with equimolar quantities of ethyl chloroformate and K_2CO_3 in acetone in an effort to give 5,5-dialkylated Meldrum's acids **18a**–**c**, but when the reactions were monitored by TLC, they showed unconsumed starting material along with the new spot. Hence another mol equivalent of ethyl chloroformate was added to the reaction mixture along with 1 mol equiv of K_2CO_3, and within one hour the starting materials were fully consumed. The products obtained were not the expected 5,5-dialkylated Meldrum's acids **18a**–**c**, but 2-substituted malonic acids **19a**–**c**,[26] probably because of in situ dehydrohalogenation of the mono-Michael adducts with ethyl chloroformate followed by hydrolysis of **18** to **19**. Many research groups have prepared **19c**[27] from diethyl malonate, whereas **19b**[28] and **19a**[29] are not as well known as **19c** in the literature. 2-Substituted malonic acids can be synthesized using diethyl malonate as starting material, but the utility of this method is often hampered by the undesired addition of a second acceptor molecule because of the high acidity of the resulting dialkyl alkylmalonates. This side reaction becomes particularly pronounced with reactive acceptors such that monofunctionalized products cannot be obtained in this case.[5] Hence, our method can be a solution for the synthesis of 2-monosubstituted malonic acid derivatives. 2-Monosubstituted malonic acid derivatives can be alternatively prepared using the Michael addition on methanetricarboxylic esters.[30]

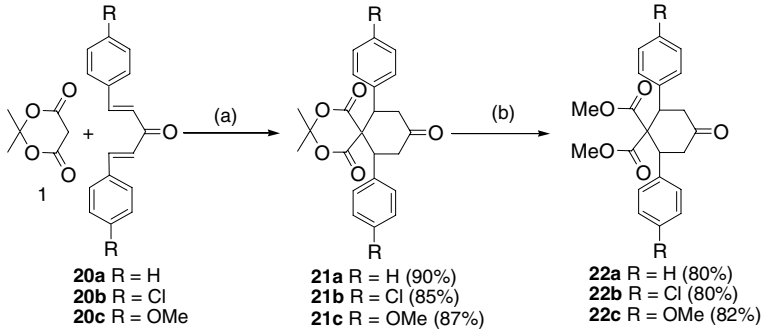


Scheme 2. Reagents and conditions: (a) $K_2CO_3/(CH_3)_2CO$, reflux, 4 h; (b) aq HCl/MeOH, reflux, 5 h.

The double Michael addition on Meldrum's acid **1** is very rare,[31] so we decided to carry out the reaction of dibenzylideneacetones with Meldrum's acid **1**. We tested organic bases such as triethylamine, pyridine, piperidine and K_2CO_3 along with Triton B in different solvent systems, but the attempts were unsuccessful. When the reaction was carried out using K_2CO_3 in dry DMF, it was complete after 24 h. However, the reaction proceeded smoothly in the presence of an equimolar amount of sodamide in dry DMF at 10–15 °C in 3 h. Thus spiro cyclohexanone **21**[32] was synthesized in a single step by bis Michael addition of Meldrum's acid **1** and 1,5-diaryl-1,4-pentadien-3-one **20** in more than 85% yield (Scheme 3). Cyclohexanones and spirocyclohexanones have been extensively studied for their stereochemistry.[33] The ^{1}H NMR spectrum of **21** displayed an AMX pattern for the methine (H_A) and methylene (H_M and H_X) protons of the cyclohexanone moiety. The axial methylene protons (H_M) at C-8 and C-10 lie in the direction of the π-orbitals of the oxygen of the carbonyl group at C-9, whereas the equatorial protons (H_X) at C-8 and C-10 form an angle of 60°. Thus, the axial methylene protons (H_M) fall in the deshielding zone of the carbonyl group at position 9. Hence, they absorb at distinctly different positions than the equatorial protons (H_X).[34] In **21a**, H_A exhibited a doublet of doublets at δ 3.98 (dd, $J = 3$, 11 Hz), while H_M and H_X exhibited a triplet and a doublet of doublets at δ 3.73 (t, $J = 11$ Hz) and δ 2.65 (dd, $J = 3$, 11 Hz). The coupling constants of H_A are in agreement with those of axial–axial and axial–equatorial H–H couplings of a cyclohexane chair conformation.

This confirmed the axial orientation for H_A and that the aryl substituents are in an equatorial orientation as shown in **I** (Fig. 1) and not in an axial–equatorial orientation as shown in **II** (Fig. 1). This was further confirmed by the ^{13}C NMR spectrum which highlighted the symmetry in the molecule, which could only occur when the aryl substituents are disposed in equatorial orientations as shown in **I** (Fig. 1). Hence, only the *cis* 1,3-diequatorial isomer of **21 I** (Fig. 1) had been produced, selectively, and in very good yield.

Koher and Dewey[35] has synthesized **22** from dimethyl malonate and benzylidene acetone and the same method has been used by other groups[33a,34b,36] to prepare **22**. Compounds **21** were refluxed in methanolic hydrochloric acid to give 1,1-di(methoxycarbonyl)2,6-diaryl-



Scheme 3. Reagents and conditions: (a) $NaNH_2$/DMF, 10–15 °C, 3 h; (b) aq HCl/ MeOH, reflux, 5 h.

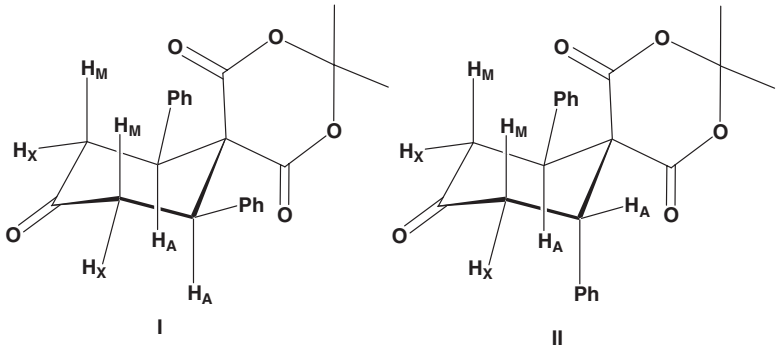


Figure 1. Compound **22a**.

cyclohexan-4-one **22**[37] (Scheme 3). So, thus our method is an alternative method for the synthesis of **22**.

In this letter, we have reported a novel synthetic strategy for the synthesis of spiro derivatives of Meldrum's acid using mono and bis Michael additions as well as a convenient route for the synthesis of 2-mono and bis-substituted malonic acid derivatives.

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10. Spectroscopic data for **3**: mp 76 °C; IR (KBr): 2995, 2952, 2893 (C–H str.), 1749 (C=O; ester) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 1.80$ (s, 3H, CH_3), 1.82 (s, 3H, CH_3), 2.39 (q, $J = 7$ Hz, 2H, CH_2), 2.65 (t, $J = 7$ Hz, 2H, CH_2), 3.68 (s, 3H, OCH_3), 3.91 (t, $J = 5$ Hz, 1H, CH); ^{13}C NMR (500 MHz, $CDCl_3$): $\delta = 21.2$, 26.4 ($2 \times CH_2$), 28.5, 30.0 ($2 \times CH_3$), 44.7 (CH), 57.7 (OCH_3), 105.1 (quaternary carbon), 165.1, 173.7 ($3 \times C$=O; esters). Anal. Calcd for $C_{10}H_{14}O_6$: C, 52.17; H, 6.13; O, 41.70. Found: C, 52.50; H, 6.20; O, 41.30.
11. Spectroscopic data for **4**: mp 57 °C; IR (KBr): 3024, 2952 (C–H str.), 1738 (C=O; ester) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 1.25$ (t, $J = 7$ Hz, 3H, CH_3), 1.89 (s, 3H, CH_3), 1.93 (s, 3H, CH_3), 2.26 (t, $J = 7.5$ Hz, 2H, CH_2), 2.47 (t, $J = 7$ Hz, 2H, CH_2), 3.08 (s, 2H, CH_2), 3.68 (s, 3H, OCH_3), 4.13 (q, $J = 7$ Hz, 2H, OCH_2); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 13.9$, 28.5, 28.9 ($3 \times CH_3$), 32.7, 39.3, 42.4 ($3 \times CH_2$), 49.3 (quaternary carbon), 51.7 (OCH_3), 61.6 (OCH_2), 107.1 (quaternary carbon), 167.8, 169.0, 170.8, 171.6 ($4 \times C$=O; esters). Anal. Calcd for $C_{14}H_{20}O_8$: C, 53.16; H, 6.37; O, 40.47. Found: C, 53.10; H, 6.30; O, 40.60.
12. Spectroscopic data for **5**: IR (CCl_4): 3468 (O–H str.), 2926, 2856 (C–H str.), 1741 (C=O; ester) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 1.24$ (t, $J = 7$ Hz, 3H, CH_3), 1.79 (s, 3H, CH_3), 1.81 (s, 3H, CH_3), 2.94 (t, $J = 8$ Hz, 2H, CH_2), 3.14 (t, $J = 8$ Hz, 2H, CH_2), 4.15 (q, $J = 7$ Hz, 2H, OCH_2), 5.10 (br, 1H, OH) (D_2O exchangeable); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 13.9$, 26.7, 28.7 ($3 \times CH_3$), 31.2, 42.4 ($2 \times CH_2$), 47.3 (quaternary carbon C_5), 61.5 (OCH_2), 94.6 (=*C*–COOEt), 105.3 (quaternary carbon C_8), 165.1 (C–OH of cyclopentanone), 168.2, 170.8, 171.5 ($3 \times C$=O, esters). Anal. Calcd for $C_{13}H_{16}O_7$: C, 54.93; H, 5.67; O, 39.40. Found: C, 54.85; H, 5.60; O, 39.55.

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14. Spectroscopic data for **6**: IR (CCl_4): 3000, 2953, 2852 (C–H str.), 1744 (C=O; ester) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 2.20$ (m, 2H, CH_2), 2.40 (m, 2H, CH_2), 2.65 (s, 2H, CH_2), 3.71 (s, 3H, OCH_3), 3.77 (s, 3H, OCH_3); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 26.7$, 31.4, 32.9 ($3 \times CH_2$), 47.4 (quaternary carbon), 52.1, 52.9 ($2 \times OCH_3$), 168.7, 171.2 ($2 \times C$=O, esters), 208.0 (C=O, cyclopentanone). Anal. Calcd $C_9H_{12}O_5$: C, 54.00; H, 6.04; O, 39.96. Found: C, 54.00; H, 6.10; O, 39.90.
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16. Spectroscopic data for **8**: mp 124 °C; IR (KBr): 3005, 2946, 2899 (C–H str.), 2251 (CN str.), 1740 (C=O; ester) cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$): $\delta = 1.74$ (s, 3H, CH_3), 1.82 (s, 3H, CH_3), 2.41 (q, $J = 7$ Hz, 2H, CH_2), 2.71 (t, $J = 7$ Hz, 2H, CH_2), 3.61 (t, $J = 5$ Hz, 1H, CH). Anal. Calcd $C_9H_{11}NO_4$: C, 54.82; H, 5.62; N, 7.10; O, 32.46. Found: C, 54.70; H, 5.73; N, 7.16; O, 32.47.
17. Spectroscopic data for **9**: mp 133 °C; IR (KBr): 2986 (C–H str.), 2253 (CN str.), 1739 (C=O; ester) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) $\delta = 1.23$ (t, $J = 7.5$ Hz, 3H, CH_3), 1.82 (s, 3H, CH_3), 1.86 (s, 3H, CH_3), 2.28 (t, $J = 7.5$ Hz, 2H, CH_2), 2.49 (t, $J = 7$ Hz, 2H, CH_2), 3.18 (s, 2H, CH_2), 4.13 (q, $J = 7.5$ Hz, 2H, OCH_2); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 13.9$ (CH_2CN), 13.1, 28.7, 29.2 ($3 \times CH_3$), 33.1, 38.7 ($2 \times CH_2$), 49.3 (quaternary carbon), 61.7 (OCH_2), 107.5 (quaternary carbon), 117.5 (CN), 167.0, 170.6 ($3 \times C$=O; esters). Anal. Calcd $C_{13}H_{17}NO_6$: C, 55.12; H, 6.05; N, 4.94; O, 33.89. Found: C, 55.10; H, 6.07; N, 4.93; O, 33.90.
18. Spectroscopic data for **10**: IR (CCl_4): 2938, 2931 (C–H str.), 1740 (C=O; ester) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 1.21$ (t, $J = 7$ Hz, 3H, CH_3), 1.79 (s, 3H, CH_3), 1.81 (s, 3H, CH_3), 2.88 (t, $J = 7$ Hz, 2H, CH_2), 2.97 (t, $J = 7$ Hz, 2H, CH_2), 3.14 (m, 1H, CH), 4.14 (q, $J = 7$ Hz, 2H, OCH_2), 6.97 (br, 1H, NH) (D_2O exchangeable); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 13.2$, 27.1, 28.1 ($3 \times CH_3$), 31.0, 37.0 ($2 \times CH_2$), 42.6 (CH), 46.9 (quaternary carbon C5), 61.1 (OCH_2), 105.3 (quaternary carbon C8), 163.7 (C=NH), 170.5, 171.1, 172.8 ($3 \times C$=O, esters). Anal. Calcd for $C_{13}H_{17}NO_6$: C, 55.12; H, 6.05; N, 4.94; O, 33.89. Found: C, 55.10; H, 6.03; N, 4.90; O, 33.97.
19. Spectroscopic data for **12**: mp 120 °C; 3004, 2955, 2893 (C–H str.), 1788, 1747 (C=O; ester), 1708 (C=O; ketone) cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$): $\delta = 1.76$ (s, 3H, CH_3), 1.83 (s, 3H, CH_3), 2.16 (s, 3H, CH_3), 2.30 (q, $J = 7$ Hz, 2H, CH_2), 2.73 (t, $J = 7$ Hz, 2H, CH_2), 3.86 (t, $J = 5$ Hz, 1H, CH). Anal. Calcd for $C_{10}H_{14}O_5$: C, 56.07; H, 6.59; O, 37.34. Found: C, 56.00; H, 6.60; O, 37.40.
20. Spectroscopic data for **13**: mp 110 °C; IR (KBr): 2928 (C–H str.), 1740 (C=O; ester) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 1.28$ (t, $J = 7$ Hz, 3H, CH_3), 1.89 (s, 3H, CH_3), 1.90 (s, 3H, CH_3), 2.16 (s, 3H, CH_3), 2.22 (t, $J = 7.5$ Hz, 2H, CH_2), 2.61 (t, $J = 7$ Hz, 2H, CH_2), 3.13 (s, 2H, CH_2), 4.12 (q, $J = 7$ Hz, 2H, OCH_2); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 8.7$, 23.7, 24.7, 25.7 ($4 \times CH_3$), 20.6, 32.5, 34.1 ($3 \times CH_2$), 43.7 (quaternary carbon), 56.3 (OCH_2), 101.8 (quaternary carbon), 162.8, 165.6 ($3 \times C$=O; esters) 200.1 (CO-CH_3). Anal. Calcd for $C_{14}H_{20}O_7$: C, 55.99; H, 6.71; O, 37.29. Found: C, 56.00; H, 6.70; O, 37.30.
21. Spectroscopic data for **14**: IR (CCl_4): 3425 (O–H str.), 2986 (C–H str.), 1721 (C=O; ester) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 1.81$ (s, 6H, $2 \times CH_3$), 1.82 (s, 3H, $COCH_3$), 3.17 (s, 2H, CH_2), 3.79 (s, 2H, CH_2), 6.00–7.00 (br, 1H, OH) (D_2O exchangeable); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 23.8$, 28.2 ($3 \times CH_3$), 26.9, 31.3 ($2 \times CH_2$), 42.6 (quaternary carbon), 105.3 (quaternary carbon), 120.5 (H_3COC=C), 165.0 (C=C–OH, esters), 170.4 ($2 \times C$=O, esters), 199.0 (CO–CH_3). Anal. Calcd for $C_{12}H_{14}O_6$: C, 56.69; H, 5.55; O, 37.76. Found: C, 56.70; H, 5.58; O, 37.72.
22. Spectroscopic data for **15**: IR (CCl_4): 3001, 2953, 2849 (C–H str.), 1745 (C=O; ester) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 2.14$ (s, 3H, $COCH_3$), 2.62 (s, 2H, CH_2), 2.92 (m, 2H, CH_2), 3.69 (s, 3H, OCH_3), 3.75 (s, 3H, OCH_3), 8.95 (m, 1H, CH); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 22.1$ (CH_3), 29.2, 32.8 ($2 \times CH_2$), 36.6 (CH), 47.4 (quaternary carbon), 52.1, 52.8 ($2 \times OCH_3$), 168.7, 171.2 ($2 \times C$=O, esters), 207.2, 208.2 ($2 \times C$=O). Anal. Calcd for $C_{11}H_{14}O_6$: C, 54.54; H, 5.83; O, 39.63. Found: C, 54.50; H, 5.87; O, 39.63.
23. Spectroscopic data for **16c**: mp 75 °C; IR (CCl_4): 3089, 3006, 2944 (C–H str.), 1774, 1737 (C=O; ester) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) $\delta = 1.71$ (s, 3H, CH_3), 1.79 (s, 3H, CH_3), 2.14 (s, 3H, CH_3), 2.29 (t, $J = 7.5$ Hz, 2H, CH_2), 2.56 (t, $J = 7.5$ Hz, 2H, CH_2), 2.73 (d, $J = 7.5$ Hz, 2H, CH_2), 5.21 (dd, $J = 9$, 7.5 Hz, 2H, =CH_2), 5.67 (m, 1H, =CH); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 24.5$, 26.7 ($3 \times CH_3$), 24.1, 33.0, 36.6 ($3 \times CH_2$), 48.0 (tetrahedral carbon), 100.5 (tetrahedral carbon), 116.2 (HC=CH_2), 125.5 (HC=CH_2), 163.2 ($2 \times C$=O; esters), 200.6 (C=O, ketone). Anal. Calcd for $C_{13}H_{18}O_5$: C, 61.40; H, 7.14; O, 31.46. Found: C, 61.45; H, 7.15; O, 31.4.
24. Spectroscopic data for **17b**: IR (CCl_4): 3080, 2950 (C–H str.), 1719 (C=O) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) $\delta = 2.00$ (s, 3H, CH_3), 2.25 (t, $J = 7.5$ Hz, 2H, CH_2), 2.48 (t, $J = 7.5$ Hz, 2H, CH_2), 2.70 (d, $J = 7.5$ Hz, 2H, CH_2), 3.69 (s, 6H, $2 \times OCH_3$), 5.51 (dd, $J = 9$, 7.5 Hz, 2H, =CH_2), 5.73 (m, 1H, =CH). Anal. Calcd for $C_{12}H_{18}O_5$: C, 59.49; H, 7.49; O, 33.02. Found: C, 59.45; H, 7.45; O, 33.1.
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32. Spectroscopic data for **21a**: mp 184 °C; IR (KBr): 3065, 3035, 2999, 2928 (C–H), 1762, 1730 (C═O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 0.58$ (s, 6H, $2 \times CH_3$), 2.65 (dd, $J = 3$, 11 Hz, $2H_X$), 3.75 (t, $J = 11$ Hz, $2H_M$), 3.98 (dd, $J = 3$, 11 Hz, $2H_A$), 7.15–7.38 (m, 10H, aromatic protons); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 28.4$, 28.7 ($2 \times CH_3$), 42.9 ($2 \times CH_2$), 50.1 ($2 \times CH$), 60.6 (quaternary carbon), 106.3 (quaternary carbon), 128.4–136.9 (aromatic carbons) 165.4, 168.2 ($2 \times C═O$; esters), 207.4 (C═O, ketone). Anal. Calcd for $C_{23}H_{22}O_5$: C, 73.00; H, 5.86; O, 21.14. Found: C, 73.10; H, 5.87; O, 21.03.
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37. Spectroscopic data for **22a**: mp 135 °C; IR (KBr): 1740 (C═O; ester) cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$): $\delta = 2.92$ (dd, $J = 3$, 11 Hz, $2H_X$), 3.40 (s, 6H, $–OCH_3$), 3.12 (t, $J = 11$ Hz, $2H_M$), 4.47 (dd, $J = 3$, 11 Hz, $2H_A$), 7.15–7.38 (m, 10H, aromatic protons). Anal. Calcd for $C_{22}H_{22}O_5$: C, 72.12; H, 6.05; O, 21.83. Found: C, 72.10; H, 6.02; O, 21.88.