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Synthesis of 4,5-diaryl-1,2,3-benzenetricarboxylates by reaction of 4-hydroxycyclopent-2-en-1-one-2-carboxylates with dimethyl acetylenedicarboxylate

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Abstract—4,5-Diaryl-1,2,3-benzenetricarboxylates were prepared by cycloaddition of 4-hydroxycyclo-2-penten-1-one-2-carboxylates with dimethyl acetylenedicarboxylate.

1. Introduction

Functionalized arenes represent important building blocks in organic and medicinal chemistry.[1] An important strategy for the synthesis of functionalized benzene derivatives relies on the [4+2] cycloaddition of 1,3-dienes with alkynes and subsequent oxidation.[2] It is known for a long time that the reaction of alkynes with heterocyclic dienes such as furans results in the formation of bridged oxacycles, which can be transformed into functionalized benzene derivatives by acidic hydrolysis.[3] A related strategy has been reported for the cycloaddition of cyclopentadienones (fulvenones) with alkynes.[4] These reactions proceed by cycloaddition and subsequent extrusion of carbon monoxide. The acid-mediated reaction of alkynes with 4-hydroxycyclo-2-penten-1-ones, which represents precursors of highly reactive fulvenones, has been reported to give benzene derivatives.[5] We have recently reported[6] the synthesis of 4-hydroxycyclo-2-penten-1-one-2-carboxylates[7] by cyclization of 1,2-diketones with 1,3-dicarbonyl dianions or 1,3-bis(silyl enol ethers) (masked dianions). Herein, we report the synthesis of a variety of new 4-hydroxycyclo-2-penten-1-one-2-carboxylates and their transformation into novel 4,5-diaryl-1,2,3-benzenetricarboxylates by acid-mediated cycloaddition.

Keywords: Arenes; Cyclizations; Diels–Alder reactions; Dianions; Diketones.
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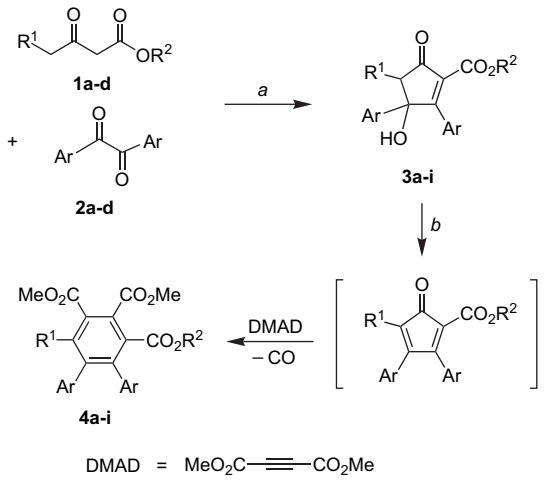
2. Results and discussion

The reaction of the dianion of methyl acetoacetate **1a** with benzil (**2a**) regioselectively afforded the 3-hydroxy-5-oxo-2,3-diphenylcyclopent-1-ene-1-carboxylate **3a**. The reactions were carried as one-pot transformations: the condensation of the dianion with **2a** gave an open-chained product, which underwent cyclization upon addition of silica gel to the reaction mixture and reflux. Notably, the cyclization exclusively afforded the hydroxylated product **3a** and not the corresponding fulvenone (by elimination of a second equivalent of water). This can be explained by the unstable nature of the fulvenone, due to its antiaromatic character.

The reaction of **3a** with dimethyl acetylenedicarboxylate (DMAD), in the presence of catalytic amounts of *p*-toluenesulfonic acid (PTSA, 5 mol %), afforded 4,5-diphenyl-1,2,3-benzenetricarboxylate **4a** (Scheme 1, Table 1). The reactions were carried out according to a known procedure.[5d] The choice of the acid played an important role. The use of concd sulfuric acid or Lewis acids ($BF_3 \cdot OEt_2$, $TiCl_4$) resulted in decomposition. The formation of **4a** can be explained[5d] by PTSA-catalyzed elimination of water from **3a** to give a highly reactive fulvenone. The [4+2] cycloaddition of the latter with DMAD afforded a bridged cycloadduct, which underwent extrusion of carbon monoxide and aromatization to give the final product.

The scope of the reaction was studied (Table 1). The reaction of the dianions of β-ketoesters **1a–d** with 1,2-diketones **2a–d** regioselectively afforded the 3-hydroxy-5-oxo-2,3-diarylcyclopent-1-ene-1-carboxylates **3a–i**. The reaction of



Scheme 1. Synthesis of 4,5-diaryl-1,2,3-benzenetricarboxylates **4a**–**i**, (a): (1) LDA (2.3 equiv), THF, 0 °C, 1 h; (2) **2**, −78→20 °C, 12 h; (3) addition of SiO_2, THF, reflux, 19–26 h and (b): DMAD (8.0 equiv), PTSA (5 mol %), toluene, 100 °C.

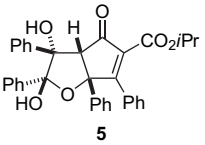
cyclopentenones **3** with dimethyl acetylenedicarboxylate (DMAD), in the presence of catalytic amounts of *p*-toluenesulfonic acid (PTSA, 5 mol %), afforded the 4,5-diaryl-1,2,3-benzenetricarboxylates **4a**–**i** (Scheme 1, Table 1). These experiments show that the presence of bromide or methoxy groups located at the aryl groups is compatible with the reaction conditions. All reactions proceeded in moderate to good yields. The PTSA mediated reaction of DMAD with methyl 3-hydroxy-5-oxo-2,3-dimethylcyclopent-1-ene-1-carboxylate, prepared from butane-2,3-dione, resulted in the formation of a complex mixture. Likewise, the reaction of **3a** with maleic anhydride proved to be unsuccessful (decomposition).

The structures of **3b** and **4c** were independently confirmed by X-ray crystal structure analysis (Figs. 1 and 2).[8] In case of **3c**, the interesting side-product **5** was isolated in low yield. The formation of **5**, the structure of which was also confirmed by X-ray crystal structure analysis (Fig. 3),[8] can be explained by cyclization of **3c** with benzil (**2a**) based on the aldol reaction and formation of a semi-ketal.

Table 1. Products and yields

1	2	3 and 4	R^1	R^2	Ar	Yield[a] of **3** (%)	Yield[a] of **4** (%)
a	**a**	**a**	H	Me	Ph	51	46
b	**a**	**b**	H	Et	Ph	60	46
c	**a**	**c**	H	*i*-Pr	Ph	41[b]	46
d	**a**	**d**	Et	Et	Ph	55[c]	33[d]
a	**b**	**e**	H	Me	4-MeC_6H_4	36	86
c	**b**	**f**	H	*i*-Pr	4-MeC_6H_4	52	40
a	**c**	**g**	H	Me	4-$(MeO)C_6H_4$	32	40
c	**c**	**h**	H	*i*-Pr	4-$(MeO)C_6H_4$	47	46
b	**d**	**i**	H	Et	4-BrC_6H_4	42	68

[a] Isolated yields.
[b] Besides, a small amount of **5** was isolated (vide infra).
[c] Mixture of diastereomers: dr=1:1.
[d] A small amount of impurity could not be separated.



5

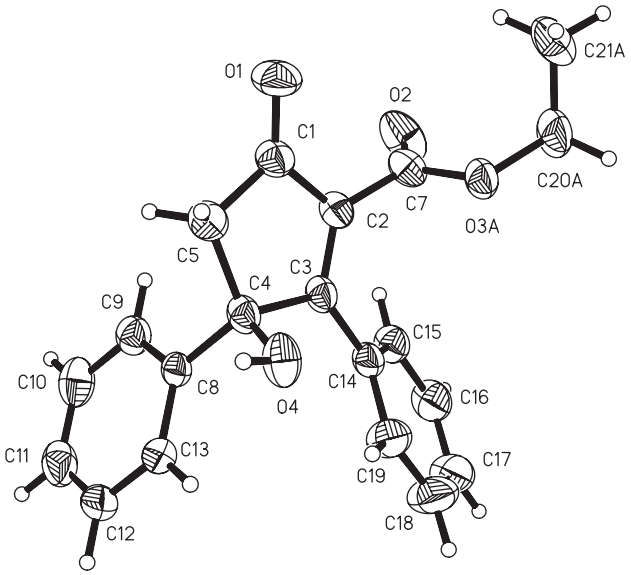


Figure 1. ORTEP plot of **3b**.

The reaction of the dianion of *N*,*N*-diethyl-acetylacetic amide (**1e**) with **2a** afforded the 3-hydroxycyclo-4-penten-1-one-2-carboxylic amide **6** and not a 4-hydroxycyclo-2-penten-1-one-2-carboxylic amide (as observed for **3a**–**i**) (Scheme 2). The formation of the different positional isomers can be explained by the steric interaction between the phenyl and the (rather rigid) amide group and by the relatively low electron-withdrawing effect of the amide (compared to the ester). The PTSA mediated cycloaddition of **6** with DMAD afforded phthalate **7**.

In conclusion, an efficient synthesis of 4,5-diaryl-1,2,3-benzenetricarboxylates by cycloaddition of 4-hydroxycyclo-2-penten-1-one-2-carboxylates with dimethyl acetylenedicarboxylate was reported.

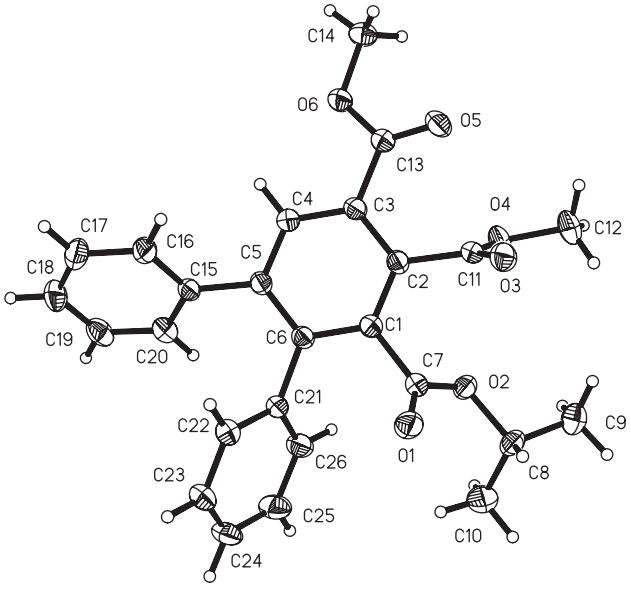


Figure 2. ORTEP plot of **4c**.

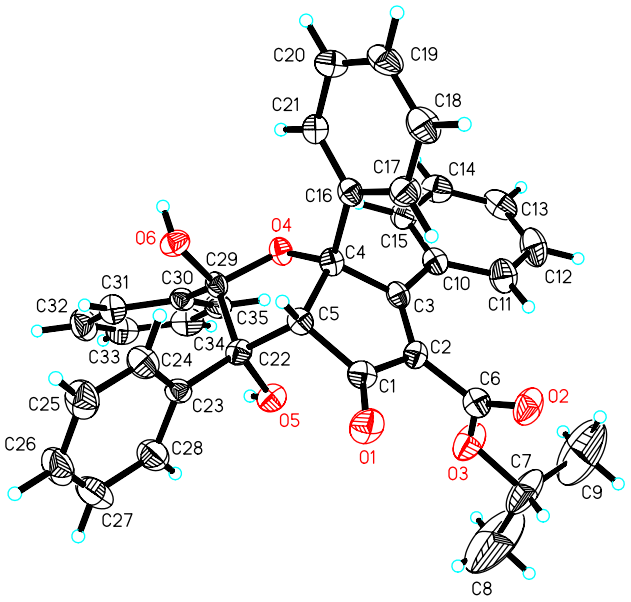
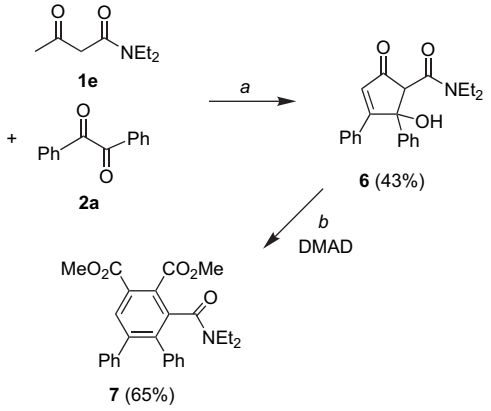


Figure 3. ORTEP plot of **5**.



Scheme 2. Synthesis of phthalate **7**, (a): (1) 2.3 LDA, THF, 0 °C, 1 h; (2) **2a**, −78→20 °C, 12 h, (3) addition of SiO_2, THF, reflux, 17 h and (b): PTSA (5 mol %), toluene, 100 °C, 10 h.

3. Experimental section

3.1. General procedure for the synthesis of functionalized 4-hydroxycyclopent-2-en-1-one-2-carboxylates 3a–i and 6

A THF solution (2.5 mL $mmol^{-1}$ of LDA) of diisopropylamine (2.5 equiv) and *n*-butyllithium (2.5 equiv, solution in *n*-hexane) was stirred at 0 °C for 30 min. The 1,3-dicarbonyl compound was added (1.1 equiv) and the mixture was stirred for 1 h. To the solution was added the 1,2-diketone (1.0 equiv) at −78 °C. The solution was stirred for 1 h and was then slowly warmed to 20 °C with stirring. To the solution was added silica gel (0.5 g $mmol^{-1}$ of 1,2-diketone) and the mixture was heated to reflux (TLC control). After cooling of the mixture to 20 °C, hydrochloric acid (5 mL, 10%), a saturated aqueous solution of sodium chloride (10 mL), and diethyl ether (50 mL) were added. The organic and aqueous layers were separated and the latter was repeatedly extracted with diethyl ether. The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, EtOAc and heptane).

3.1.1. Methyl 3-hydroxy-5-oxo-2,3-diphenylcyclopent-1-ene-1-carboxylate (3a). Starting with methyl acetoacetate (1.12 mL, 10.46 mmol, 1.1 equiv), diisopropylamine (3.21 mL, 22.82 mmol, 2.5 equiv), *n*-butyllithium (8.74 mL, 22.82 mmol, 2.5 equiv) and benzil (2.00 g, 9.51 mmol), **3a** was isolated by chromatography (heptane/ethyl acetate) as a slightly yellow solid (1.50 g, 51%). Reaction time: 24 h; mp 129–130 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ=2.98 (d, 1H, ^2J=18 Hz, HCH–CO), 3.11 (d, 1H, J=18 Hz, HCH–CO), 3.76 (s, 3H, OCH_3), 7.17–7.44 (m, 10H, Ph); ^{13}C NMR (62 MHz, $CDCl_3$): δ=52.4 (CH_3), 55.0 (CH_2–CO), 80.7 (COH), 124.5 ($2CH_{Ph}$), 128.6 (CH_{Ph}), 128.2 ($2CH_{Ph}$), 128.6 ($2CH_{Ph}$), 128.8 ($2CH_{Ph}$), 130.5 (CH_{Ph}), 131.2, 134.3, 142.3, 164.7, 174.1, 200.0 (C); IR (KBr): $\tilde{\nu}$=3357 (w), 3060 (w), 2951 (m), 1735 (s), 1686 (s), 1434 (m), 1343 (s), 1229 (s), 1059 (m), 779 (s), 704 (s), 513 (m) cm^{-1}; MS (EI, 70 eV): *m*/*z* (%): 308.1 (M^+, 22), 276.1 (100), 208 (18), 129 (27), 105 (56); elemental analysis: calcd (%) for $C_{19}H_{16}O_4$ (308.327): C 74.01, H 5.23; found: C 73.90, H 5.23.

3.1.2. Ethyl 3-hydroxy-5-oxo-2,3-diphenylcyclopent-1-ene-1-carboxylate (3b). Starting with ethyl acetoacetate (1.32 mL, 10.46 mmol, 1.1 equiv), diisopropylamine (3.35 mL, 23.77 mmol, 2.5 equiv), *n*-butyllithium (9.51 mL, 23.77 mmol, 2.5 equiv) and benzil (2.00 g, 9.51 mmol), **3b** was isolated by chromatography (heptane/ethyl acetate) as a slightly yellow solid (1.82 g, 60%); mp 78–80 °C. Reaction time: 26 h. ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.12 (t, 3H, ^3J=7.1 Hz, CH_3), 2.95 (d, 1H, ^2J=18.4 Hz, HCH–CO), 3.07 (d, 1H, ^2J=18.4 Hz, HCH–CO), 4.19 (q, 2H, ^3J=7.0 Hz, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ=13.8 (CH_3), 55.0 (CO–CH_2), 61.6 (OCH_2), 80.8 (COH), 124.5 ($2CH_{Ph}$), 127.7 (CH_{Ph}), 128.3 ($2CH_{Ph}$), 128.6 ($2CH_{Ph}$), 128.8 ($2CH_{Ph}$), 130.4 (CH_{Ph}), 131.2, 134.2, 142.5, 163.8, 173.9, 199.9 (C); IR (KBr): $\tilde{\nu}$=3463 (s), 3062 (w), 2979 (m), 1737 (s), 1712 (s), 1618 (m), 1447 (m), 1461 (m), 1373 (m), 1336 (s), 1211 (s), 1102 (m), 772 (m) cm^{-1}; MS (EI, 70 eV): *m*/*z* (%): 322 (M^+, 59), 276 (100), 105 (59); elemental analysis: calcd (%) for $C_{20}H_{18}O_4$ (322.36): C 74.52, H 5.63; found: C 74.43, H 5.36.

3.1.3. Isopropyl 3-hydroxy-5-oxo-2,3-diphenylcyclopent-1-ene-1-carboxylate (3c). Starting with isopropyl acetoacetate (1.14 mL, 7.84 mmol, 1.1 equiv), diisopropylamine (2.51 mL, 17.82 mmol, 2.5 equiv), *n*-butyllithium (7.13 mL, 17.82 mmol, 2.5 equiv) and benzil (1.50 g, 7.13 mmol), **3c** was isolated by chromatography (heptane/ethyl acetate) as a yellow solid (0.97 g, 41%); mp 110–111 °C. Besides, a small amount of **5** (10 mg) was isolated. Reaction time: 20 h. ^{1}H NMR (250 MHz, $CDCl_3$): δ=1.10 (d, 3H, J=6.7 Hz, CH_3), 1.16 (d, 3H, J=6.7 Hz, CH_3), 2.98 (d, 1H, J=18 Hz, HCH–CO), 3.10 (d, 1H, J=18 Hz, HCH–CO), 5.11 (sept, 1H, J=6.7 Hz, OCH), 5.30 (s, 1H, OH), 7.10–7.24 (m, 10H, Ph); ^{13}C NMR (75 MHz, $CDCl_3$): δ=21.2, 21.4 (CH_3), 55.0 (CH_2), 69.5 (CH), 80.7 (COH), 124.5 ($2CH_{Ph}$), 127.7 (CH_{Ph}), 128.2 ($2CH_{Ph}$), 128.6 ($2CH_{Ph}$), 128.8 ($2CH_{Ph}$), 130.2 (CH_{Ph}), 131.2, 134.3, 142.5, 163.4, 173.5, 199.8 (C); IR (KBr): $\tilde{\nu}$=3373 (w),

2983 (m), 1718 (s), 1679 (s), 1610 (s), 1450 (m), 1371 (s), 1323 (s), 1228 (m), 1095 (s), 1005 (s), 773 (m), 510 (m) cm^{-1}; GC–MS (EI, 70 eV): *m/z* (%): 336.2 (M^+, 24), 276.1 (100), 129.1 (33), 105.1 (76), 77.1 (26); HRMS (EI): calcd for $C_{21}H_{20}O_4$ $[M]^+$: 336.135023; found: 336.13561.

Compound **5**: was isolated as a side-product during the synthesis of **3c**. ^1H NMR (300 MHz, $CDCl_3$): δ=1.12 (d, 3H, ^3J=6.2 Hz, CH_3), 1.14 (d, 3H, ^3J=6.2 Hz, CH_3), 2.11 (s, 1H, OH), 2.75 (s, 1H, CH), 4.37 (s, 1H, OH), 5.11 (sept, 1H, ^3J=6.2 Hz, CH), 7.29–7.52 (m, 20H, Ph); MS (CI): 547.3 ($[M+1]^+$); elemental analysis: calcd (%) for $C_{35}H_{30}O_6$ (546.619): C 76.90, H 5.54; found: C 76.81, H 5.49.

3.1.4. Ethyl 4-ethyl-3-hydroxy-5-oxo-2,3-diphenylcyclopent-1-ene-1-carboxylate (3d). Starting with ethyl 3-oxohexanoate (1.68 mL, 10.46 mmol, 1.1 equiv), diisopropylamine (3.35 mL, 23.77 mmol, 2.5 equiv), *n*-butyllithium (9.51 mL, 23.77 mmol, 2.5 equiv) and benzil (2.00 g, 9.51 mmol), **3d** was isolated by chromatography (heptane/ethyl acetate) as a colourless solid (1.82 g, 55%). Reaction time: 24 h; mp 104–105 °C. ^1H NMR (250 MHz, $CDCl_3$): δ=1.01 (t, 3H, ^3J=8.2 Hz, CH_3), 1.18 (t, 3H, ^3J=7.3 Hz, CH_3), 1.81 (m, 2H, CH_2), 2.68 (t, 1H, ^3J=7.9 Hz, CH), 4.25 (q, 2H, ^3J=6.1 Hz, OCH_2), 7.22–7.27 (m, 10H, Ph); ^{13}C NMR (75 MHz, $CDCl_3$): δ=12.9, 14.5 (CH_3), 19.8 (CH_2), 61.9 (CH_2), 64.2 (CH), 84.9 (COH), 126.0 ($2CH_{Ph}$), 128.5 (CH_{Ph}), 128.7 ($2CH_{Ph}$), 129.1 ($2CH_{Ar}$), 129.2 ($2CH_{Ph}$), 130.8 (CH_{Ph}), 131.4, 134.0, 143.8, 164.6, 173.1, 201.1 (C); IR (KBr): $\tilde{\nu}$=3390 (w), 2978 (m), 1719 (s), 1687 (s), 1629 (m), 1447 (s), 1373 (s), 1341 (s), 1247 (s), 1183 (m), 1019 (s), 963 (m), 699 (s) cm^{-1}; GC–MS (EI, 70 eV): *m/z* (%): 350.2, (M^+, 7), 321.1 (31), 304.1 (100), 275.1 (38), 129.1 (24), 105.1 (54), 77 (23); HRMS (EI): calcd for $C_{22}H_{22}O_4$ $[M]^+$: 350.150583; found: 350.15126.

3.1.5. Methyl 3-hydroxy-5-oxo-2,3-di(*p*-methylphenyl)-cyclopent-1-ene-1-carboxylate (3e). Starting with methyl acetoacetate (0.74 mL, 6.92 mmol, 1.1 equiv), diisopropylamine (2.21 mL, 15.72 mmol, 2.5 equiv), *n*-butyllithium (6.29 mL, 15.72 mmol, 2.5 equiv) and 4,4-dimethylbenzil (1.50 g, 6.29 mmol), **3e** was isolated by chromatography (heptane/ethyl acetate) as a slightly yellow solid (0.75 g, 36%). Reaction time: 20 h; mp 41–49 °C. ^1H NMR (400 MHz, $CDCl_3$): δ=2.30 (s, 3H, CH_3), 2.34 (s, 3H, CH_3), 2.94 (d, 1H, ^2J=18 Hz, HCH–CO), 3.07 (d, 1H, ^2J=18 Hz, HCH–CO), 3.78 (s, 3H, OCH_3), 7.07 (d, 2H, ^3J=8.5 Hz, ArH), 7.10 (d, 2H, ^3J=8.5 Hz, ArH), 7.17 (d, 2H, ^3J=8.0 Hz, ArH), 7.30 (d, 2H, ^3J=8.2 Hz, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ=21.0, 21.4 (CH_3), 52.5 (OCH_3), 55.3 (OCH_2), 80.8 (COH), 124.3 ($2CH_{Ar}$), 128.1 (C), 128.8 ($2CH_{Ar}$), 129.3 ($2CH_{Ar}$), 129.6 ($2CH_{Ar}$), 133.4, 137.6, 139.9, 141.3, 164.5, 173.9, 199.6 (C); IR (KBr): $\tilde{\nu}$=1739 (s), 1608 (s), 1511 (m), 1435 (m), 1341 (s), 1216 (s), 1015 (m), 820 (s) cm^{-1}; MS (EI, 70 eV): *m/z* (%): 336 (M^+, 44), 304 (98), 236 (37), 206 (48), 143 (40), 119 (100), 91 (38); elemental analysis: calcd (%) for $C_{21}H_{20}O_4$ (360.387): C 74.94, H 5.99; found: C 74.56, H 6.08.

3.1.6. Isopropyl 3-hydroxy-5-oxo-2,3-di(*p*-methylphenyl)-cyclopent-1-ene-1-carboxylate (3f). Starting with isopropyl acetoacetate (1.0 mL, 6.92 mmol, 1.1 equiv), diisopropylamine (2.44 mL, 17.31 mmol, 2.5 equiv), *n*-butyllithium (6.92 mL, 17.31 mmol, 2.5 equiv) and 4,4-dimethylbenzil (1.50 g, 6.29 mmol), **3f** was isolated by chromatography (heptane/ethyl acetate) as a slightly yellow solid (1.20 g, 53%). Reaction time: 22 h; mp 118–119 °C. ^1H NMR (400 MHz, $CDCl_3$): δ=1.16 (d, 3H, ^3J=7.6 Hz, CH_3), 1.20 (d, 3H, ^3J=6.2 Hz, CH_3), 2.29 (s, 3H, CH_3), 2.33 (s, 3H, CH_3), 2.92 (d, 1H, ^2J=18.4 Hz, HCH–CO), 3.04 (d, 1H, ^2J=18.4 Hz, HCH–CO), 5.11–5.18 (m, 1H, OCH), 7.05 (d, 2H, ^3J=7.7 Hz, ArH), 7.12 (d, 2H, ^3J=8.3 Hz, ArH), 7.15 (d, 2H, ^3J=8.0 Hz, ArH), 7.29 (d, 2H, ^3J=8.3 Hz, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ=21.1, 21.44, 21.48, 21.6 (CH_3), 55.3 (CH_2), 69.4 (CH), 80.7 (COH), 124.4 ($2CH_{Ar}$), 128.3 (C), 128.8 ($2CH_{Ar}$), 129.0 ($2CH_{Ar}$), 129.5 ($2CH_{Ar}$), 134.1, 137.3, 140.0, 140.9, 163.7, 172.9, 199.9 (C); IR (KBr): $\tilde{\nu}$=3428 (w), 2978 (m), 1727 (s), 1693 (s), 1601 (s), 1512 (m), 1326 (s), 1224 (s), 1100 (s) cm^{-1}; GC–MS (EI, 70 eV): *m/z* (%): 364.2 (M^+, 36), 304.1 (98), 236.1 (35), 206.1 (48), 119.1 (100), 91.1 (39); elemental analysis: calcd (%) for $C_{23}H_{24}O_4$ (364.44): C 75.80, H 6.63; found: C 75.74, H 6.74.

3.1.7. Methyl 3-hydroxy-5-oxo-2,3-di(*p*-methoxyphenyl)-cyclopent-1-ene-1-carboxylate (3g). Starting with methyl acetoacetate (0.87 mL, 8.13 mmol, 1.1 equiv), diisopropylamine (2.60 mL, 18.47 mmol, 2.5 equiv), *n*-butyllithium (7.38 mL, 18.47 mmol, 2.5 equiv) and 4,4-dimethoxybenzil (2.00 g, 7.39 mmol), **3g** was isolated by chromatography (heptane/ethyl acetate) as a slightly yellow solid (0.85 g, 32%). Reaction time: 20 h; mp 50–52 °C. ^1H NMR (250 MHz, $CDCl_3$): δ=2.91 (d, 1H, *J*=18 Hz, HCH–CO), 3.06 (d, 1H, *J*=18 Hz, HCH–CO), 3.77 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 3.81 (s, 3H, OCH_3), 6.78 (d, 2H, *J*=8.8 Hz, ArH), 6.88 (d, 2H, *J*=9.1 Hz, ArH), 7.24 (d, 2H, *J*=8.2 Hz, ArH), 7.34 (d, 2H, *J*=9.1 Hz, ArH); ^{13}C NMR (62 MHz, $CDCl_3$): δ=52.4 (OCH_3), 55.2 (2C, OCH_3), 55.5 (CH_2–CO), 80.6 (COH), 114.0 ($2CH_{Ar}$), 114.2 ($2CH_{Ar}$), 123.2 (C), 125.6 ($2CH_{Ar}$), 131.1, 132.1 (CH_{Ar}) ($2CH_{Ar}$), 135.3, 158.6, 161.6, 164.9, 173.1, 199.5 (C); IR (KBr): $\tilde{\nu}$=3451 (w), 2839 (m), 1735 (s), 1603 (s), 1437 (m), 1137 (s), 1029 (s), 835 (s), 779 (m) cm^{-1}; MS (EI, 70 eV): *m/z* (%): 368.1 (M^+, 22), 336.1 (27), 219.0 (21), 152.0 (78), 135 (100), 77 (29); HRMS (EI): calcd for $C_{21}H_{20}O_6$ $[M]^+$: 368.125102; found: 368.12544.

3.1.8. Isopropyl 3-hydroxy-5-oxo-2,3-di(*p*-methoxyphenyl)-cyclopent-1-ene-1-carboxylate (3h). Starting with isopropyl acetoacetate (1.18 mL, 8.13 mmol, 1.1 equiv), diisopropylamine (2.60 mL, 18.47 mmol, 2.5 equiv), *n*-butyllithium (7.38 mL, 18.47 mmol, 2.5 equiv) and 4,4-dimethoxybenzil (2.00 g, 7.39 mmol), **3h** was isolated by chromatography (heptane/ethyl acetate) as a slightly yellow solid (1.36 g, 47%). Reaction time: 20 h; mp 117–118 °C. ^1H NMR (400 MHz, $CDCl_3$): δ=1.13 (d, 3H, ^3J=6.2 Hz, CH_3), 1.17 (d, ^3J=6.2 Hz, 3H, CH_3), 2.82 (d, 1H, ^2J=18.4 Hz, HCH–CO), 2.95 (d, 1H, ^2J=18.4 Hz, HCH–CO), 3.68 (s, 3H, OCH_3), 3.71 (s, 3H, OCH_3), 5.07–5.14 (m, 1H), 6.68 (d, 2H, ^3J=9.0 Hz, ArH), 6.79 (d, 2H, ^3J=8.9 Hz, ArH), 7.19 (d, 2H, ^3J=9.0 Hz, ArH), 7.26 (d, 2H, ^3J=8.9 Hz, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ=21.4, 21.6 (CH_3), 55.2, 55.3 (OCH_3), 55.4 (CH_2), 69.4 (OCH), 80.5 (COH), 113.8 ($2CH_{Ar}$), 114.1 ($2CH_{Ar}$), 123.4 (C), 125.7 ($2CH_{Ar}$), 131.19 ($2CH_{Ar}$), 133.2, 135.3, 158.9, 161.4, 164.2, 171.8, 199.8 (C); IR (KBr):

$\tilde{\nu}$=3431 (w), 2984 (m), 1740 (s), 1724 (s), 1516 (m), 1264 (s), 1242 (s), 1108 (s), 1063 (m), 817 (s), 788 (m) cm^{-1}; MS (CI): 397 [(M+1)$^+$]; elemental analysis: calcd (%) for $C_{23}H_{24}O_6$ (396.439): C 69.68, H 6.10; found: C 59.56, H 6.29.

3.1.9. Ethyl 3-hydroxy-5-oxo-2,3-di(*p*-bromophenyl)cyclopent-1-ene-1-carboxylate (3i). Starting with ethyl acetoacetate (583 mg, 4.48 mmol, 1.1 equiv), diisopropylamine (1.43 mL, 10.2 mmol, 2.5 equiv), *n*-butyllithium (4.1 mL, 10.2 mmol, 2.5 equiv) and 4,4-dibromobenzil (1.50 g, 4.1 mmol), **3i** was isolated by chromatography (heptane/ethyl acetate) as a slightly yellow solid (810 mg, 42%). Reaction time: 24 h; mp 139–149 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ=1.20 (t, 3H, ^3J=7.6 Hz, CH_3), 2.97 (d, 1H, ^2J=18 Hz, HCH–CO), 3.07 (d, 1H, ^2J=18 Hz, HCH–CO), 4.25 (q, 2H, ^3J=7.6 Hz, CH_2), 7.13 (d, 2H, ^3J=9.1 Hz, ArH), 7.26 (d, 2H, ^3J=8.5 Hz, ArH), 7.41 (d, 2H, ^3J=8.5 Hz, ArH), 7.48 (d, 2H, ^3J=8.8 Hz, ArH); ^{13}C NMR (75 MHz, $CDCl_3$): δ=14.3 (CH_3), 55.3 (CH_2), 62.4 (OCH_2), 80.9 (COH), 122.4, 125.8 (C), 126.8 ($2CH_{Ar}$), 130.3 (C), 130.6 ($2CH_{Ar}$), 132.1 ($2CH_{Ar}$), 132.4 ($2CH_{Ar}$), 134.9, 141.7, 164.1, 199.8 (C); IR (KBr): $\tilde{\nu}$=3481 (w), 1744 (s), 1486 (m), 1336 (s), 1217 (m), 1072 (s), 1010 (s), 825 (m) cm^{-1}; GC–MS (EI, 70 eV): *m*/*z* (%): 482 (M$^+$, ^{81}Br, 10), 479.9 (M$^+$, ^{79}Br, 17), 433.9 (57), 281.1 (42), 207 (100), 185 (49); elemental analysis: calcd (%) for $C_{20}H_{16}O_4Br_2$ (479.95): C 50.01, H 3.36; found: C 49.67, H 3.40.

3.1.10. 3-Hydroxy-5-oxo-2,3-diphenylcyclopent-1-ene-1-*N*,*N*-diethylacetoacetamide (6). Starting with *N*,*N*-diethylacetamide (0.82 mL, 5.22 mmol, 1.1 equiv), diisopropylamine (1.61 mL, 11.41 mmol, 2.5 equiv), *n*-butyllithium (4.36 mL, 11.4 mmol, 2.5 equiv) and benzil (1.00 g, 4.75 mmol), **6** was isolated by chromatography (heptane/ethyl acetate) as a slightly yellow solid (725 mg, 43%). Reaction time: 17 h; mp 117–118 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ=1.00 (t, 3H, ^3J=6.4 Hz, CH_3), 1.16 (t, 3H, ^3J=7.3 Hz, CH_3), 3.11–3.50 (m, 2H), 3.55–3.85 (m, 2H), 3.85 (s, 1H, CH–C=O), 6.77 (s, 1H, CH=C), 7.25–7.68 (m, 10H, Ph); ^{13}C NMR (62 MHz, $CDCl_3$): δ=12.9, 14.3 (CH_3), 41.3, 42.7 (CH_2), 63.4 (CH), 82.3 (COH), 124.6 ($2CH_{Ph}$), 127.5 (CH_{Ph}), 127.8 (CH_{Ph}), 128.4 ($2CH_{Ph}$), 128.8 ($2CH_{Ph}$), 129.7 ($2CH_{Ph}$), 130.9 (CH_{Ph}), 131.2 (CH), 144.2, 167.7, 176.6, 199.7 (C); IR (KBr): $\tilde{\nu}$=3399 (w), 2978 (m), 1691 (s), 1624 (s), 1571 (m), 1449 (s), 1309 (s), 1223 (s), 1339 (m), 772 (s), 6004 (s) cm^{-1}; MS (EI, 70 eV): *m*/*z* (%): 349.2 (M$^+$, 33), 331.1 (23), 249.1 (100), 105.0 (43), 72.1 (26); HRMS (EI): calcd for $C_{22}H_{23}O_3N_1$ [M]$^+$: 349.166663; found: 349.16725.

3.2. General procedure for the cyclization of functionalized 4-hydroxycyclopent-2-en-1-ones with dimethyl acetylenedicarboxylate (DMAD)

To a toluene solution (25 mL) of the 4-hydroxycyclopent-2-en-1-one (1.0 equiv) were added dimethyl acetylenedicarboxylate (DMAD, 8.0 equiv) and *p*-toluenesulfonic acid (PTSA, 5 mol %). The mixture was heated at reflux (TLC control). After cooling of the reaction mixture to 20 °C, a saturated aqueous solution of $NaHCO_3$ (10 mL) was added. The organic and aqueous layers were separated and the latter was extracted with diethyl ether (3×20 mL). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, EtOAc and heptane).

3.2.1. 1,2,3-Trimethyl-4,5-diphenylbenzene-1,2,3-tricarboxylate (4a). Starting with **3a** (500 mg, 1.62 mmol), DMAD (1.60 mL, 12.96 mmol) and PTSA (12 mg, 5 mol %), **4a** was isolated by chromatography (heptane/ethyl acetate) as a yellow solid (302 mg, 46%); mp 143–144 °C. Reflux time: 8 h. ^{1}H NMR (250 MHz, $CDCl_3$): δ=3.48 (s, 3H, OCH_3), 3.92 (s, 3H, OCH_3), 3.93 (s, 3H, OCH_3), 7.0–7.21 (m, 10H, Ph), 8.03 (s, 1H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$): δ=50.8, 50.9, 51.0 (OCH_3), 125.9, 126.0 (CH_{Ph}), 126.1 ($2CH_{Ph}$), 126.6 ($2CH_{Ph}$), 126.7 ($2CH_{Ph}$), 127.6 ($2CH_{Ph}$), 130.1, 130.8 (C), 132.3 (CH_{Ph}), 135.4, 137.0, 139.1, 140.6, 141.7, 163.9, 165.8, 166.9 (C); IR (KBr): $\tilde{\nu}$=1743 (s), 1728 (s), 1588 (m), 1429 (s), 1299 (s), 1244 (s), 1156 (m), 1008 (s), 765 (m), 703 (s) cm^{-1}; MS (EI, 70 eV): *m*/*z* (%): 404.1 (M$^+$, 68), 373.1 (100), 226.0 (11), 105 (22); HRMS (EI): calcd for $C_{24}H_{20}O_6$ [M]$^+$: 404.125328; found: 404.12544.

3.2.2. 3-Ethyl-1,2-dimethyl-4,5-diphenylbenzene-1,2,3-tricarboxylate (4b). Starting with **3b** (400 mg, 1.24 mmol), DMAD (1.21 mL, 11.84 mmol, 8 equiv) and PTSA (5 mol %), **4b** was isolated by chromatography (heptane/ethyl acetate) as a yellow solid (293 mg, 46%); mp 135–137 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=0.88 (t, 3H, ^3J=7.1 Hz), 3.92 (s, 6H, OCH_3), 3.95 (q, 2H, ^3J=7.1 Hz), 7.01–7.21 (m, 10H, Ph), 8.03 (s, 1H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$): δ=13.3 (CH_3), 52.7, 52.8 (OCH_3), 61.6 (OCH_2), 127.2, 127.5 (CH_{Ph}), 127.7 ($2CH_{Ph}$), 127.8 ($2CH_{Ph}$), 128.3 (C), 129.4 ($2CH_{Ph}$), 125.5 ($2CH_{Ph}$), 132.1 (CH_{Ph}), 132.6, 134.3, 137.4, 138.9, 142.5, 143.5, 165.7, 167.3, 167.8 (C); IR (KBr): $\tilde{\nu}$=1745 (s), 1726 (s), 1429 (m), 1337 (m), 1243 (s), 1161 (m), 1022 (m), 765 (m), 703 (s) cm^{-1}; MS (EI, 70 eV): *m*/*z* (%): 418 (M$^+$, 100), 373 (73), 327 (63), 306 (26), 226 (38), 133 (59), 57 (33); elemental analysis: calcd (%) for $C_{25}H_{22}O_6$ (418.445): C 71.75, H 5.29; found: C 71.64, H 5.04.

3.2.3. 3-Isopropyl-1,2-dimethyl-4,5-diphenylbenzene-1,2,3-tricarboxylate (4c). Starting with **3c** (500 mg, 1.48 mmol), DMAD (1.23 mL, 11.84 mmol) and PTSA (5 mol %), **4c** was isolated by chromatography (heptane/ethyl acetate) as a yellow solid (293 mg, 46%). Reflux time: 12 h; mp 161–162 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ=0.91 (d, 6H, ^3J=5.8 Hz), 3.92 (s, 3H, OCH_3), 3.93 (s, 3H, OCH_3), 4.83 (sept, 1H, ^3J=7.6 Hz), 6.99–7.20 (m, 10H, Ph), 8.02 (s, 1H, ArH); ^{13}C NMR (62 MHz, $CDCl_3$): δ=21.1 (2C, CH_3), 52.7, 52.8, (OCH_3), 69.5 (CH), 127.2 ($2CH_{Ph}$), 127.5 (CH_{Ph}), 127.7 (C), 127.8 ($2CH_{Ph}$), 128.3 (CH_{Ph}), 129.4 ($2CH_{Ph}$), 129.7 ($2CH_{Ph}$), 129.9 (C), 132.5 (CH_{Ph}), 134.5, 137.6, 139.1, 142.1, 143.8, 165.7, 167.0, 168.0 (C); IR (KBr): $\tilde{\nu}$=1740 (s), 1723 (s), 1550 (m), 1499 (m), 1429 (s), 1326 (s), 1241 (s), 1109 (s), 1000 (s), 910 (m), 700 (s), 552 (m) cm^{-1}; GC–MS (EI, 70 eV): *m*/*z* (%): 432.2 (M$^+$, 100), 373.1 (54), 359.1 (28), 327.1 (55), 256.1 (35), 226.1 (62); elemental analysis: calcd (%) for $C_{26}H_{24}O_6$ (432.47): C 72.20, H 5.59; found: C 72.21, H 5.56.

Compound **4d**: starting with **3d** (400 mg, 1.14 mmol), DMAD (0.95 mL, 9.13 mmol) and PTSA (5%), **4d** was isolated by chromatography (heptane/ethyl acetate) as a yellow solid (165 mg, 33%); mp 51–53 °C. Reflux time: 11 h.

A small amount of impurity could not be separated. ^{1}H NMR (250 MHz, $CDCl_3$): δ=0.92 (t, 3H, ^3J=7.6 Hz, CH_3), 1.17 (t, 3H, ^3J=7.3 Hz, CH_3), 2.53 (q, 2H, ^3J=6.4 Hz, CH_2), 3.86 (s, 3H, OCH_3), 3.92 (s, 3H, OCH_3), 4.24 (q, 2H, ^3J=6.5 Hz, OCH_2), 6.95–7.18 (m, 10H, Ph); ^{13}C NMR (62 MHz, $CDCl_3$): δ=12.2, 13.9 (CH_3), 19.1 (CH_2), 52.6, 52.9 (OCH_3), 61.5 (OCH_2), 125.5 ($2CH_{Ph}$), 126.9 (CH_{Ph}), 127.5 (C), 128.0 ($2CH_{Ph}$), 128.8 ($2CH_{Ph}$), 129.6 ($2CH_{Ph}$), 129.7 (C), 130.4 (CH_{Ph}), 131.0, 133.3, 133.7, 137.6, 139.4, 141.8, 163.8, 166.5, 171.8 (C); IR (KBr): $\tilde{\nu}$=2950 (m), 1797 (s), 1646 (m), 1541 (s), 1331 (s), 1282 (w), 1232 (s), 1171 (m), 1062 (s), 966 (m), 778 (m), 698 (s) cm^{-1}; GC–MS (EI, 70 eV): *m*/*z* (%): 446.2 (M^+, 7), 400.1 (46), 353.1 (100), 239.1 (28).

3.2.4. 1,2,3-Trimethyl-4,5-di(*p*-methylphenyl)-benzene-1,2,3-tricarboxylate (4e). Starting with **3e** (400 mg, 1.18 mmol), DMAD (1.16 mL, 9.51 mmol, 8 equiv) and PTSA (12 mg, 5 mol %), **4e** was isolated by chromatography (heptane/ethyl acetate) as a yellow solid (340 mg, 86%); mp 167–169 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ=2.27 (s, 3H, CH_3), 2.28 (s, 3H, CH_3), 3.49 (s, 3H, OCH_3), 3.90 (s, 3H, OCH_3), 3.91 (s, 3H, OCH_3), 6.90 (d, 2H, ^3J=8.2 Hz, ArH), 6.91 (d, 2H, ^3J=8.2 Hz, ArH), 6.98 (d, 2H, ^3J=7.8 Hz, ArH), 6.99 (d, 2H, ^3J=7.8 Hz, ArH), 7.24 (s, 1H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$): δ=21.0, 21.2 (CH_3), 52.3, 52.7, 52.9 (OCH_3), 128.3 (C), 128.5 ($2CH_{Ar}$), 128.6 ($2CH_{Ar}$), 129.4 ($4CH_{Ar}$), 131.6 (C), 132.7 (CH_{Ar}), 134.3, 134.4, 136.1, 137.0, 137.2, 142.5, 143.6, 165.9, 167.9, 167.0; IR (KBr): $\tilde{\nu}$=1738 (s), 1515 (m), 1433 (s), 1297 (s), 1265 (s), 1222 (s), 1159 (m), 1065 (m), 1000 (s), 779 (m) cm^{-1}; MS (EI, 70 eV): *m*/*z* (%): 432 (M^+, 100), 401 (82), 385 (21); elemental analysis: calcd (%) for $C_{26}H_{24}O_6$ (432.46): C 72.21, H 5.59; found: C 72.25, H 6.00.

3.2.5. 3-Isopropyl-1,2-dimethyl-4,5-di(*p*-methylphenyl)-benzene-1,2,3-tricarboxylate (4f). Starting with **3f** (500 mg, 1.37 mmol), DMAD (1.34 mL, 10.97 mmol, 8 equiv) and PTSA (5 mol %), **4f** was isolated by chromatography (heptane/ethyl acetate) as a yellow solid (250 mg, 40%); mp 155–157 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ=0.93 (d, 6H, ^3J=6.2 Hz, CH_3), 2.27 (s, 6H, CH_3), 3.90 (s, 3H, OCH_3), 3.91 (s, 3H, OCH_3), 4.80–4.87 (m, 1H, OCH), 6.46 (d, 2H, ^3J=8.2 Hz, ArH), 6.94 (d, 2H, ^3J=8.2 Hz, ArH), 6.98 (d, 2H, ^3J=7.8 Hz, ArH), 7.99 (d, 2H, ^3J=7.8 Hz, ArH), 7.98 (s, 1H, Ar); ^{13}C NMR (100 MHz, $CDCl_3$): δ=20.08 (2C, CH_3), 20.09 (CH_3), 20.16 (CH_3), 51.7 (OCH_3), 51.8 (OCH_3), 68.3 (CH), 127.1, 127.5, 127.6 (C), 128.4 ($2CH_{Ar}$), 128.6 ($2CH_{Ar}$), 130.6 ($2CH_{Ar}$), 131.5 ($2CH_{Ar}$), 133.5 (CH_{Ar}), 133.7, 135.2, 135.9, 136.2, 141.3, 142.5, 164.9, 166.0, 166.9 (C); IR (KBr): $\tilde{\nu}$=2980 (m), 1725 (s), 1687 (s), 1598 (s), 1513 (s), 1457 (m), 1327 (m), 1251 (s), 835 (m) cm^{-1}; MS (EI, 70 eV): *m*/*z* (%): 460.2 (M^+, 100), 401.1 (24), 355.1 (35), 239.1 (20), 131 (26), 69 (75); elemental analysis: calcd (%) for $C_{28}H_{28}O_6$ (460.526): C 73.62, H 6.12; found: C 73.73, H 6.34.

3.2.6. 1,2,3-Trimethyl-4,5-di(*p*-methoxyphenyl)-benzene-1,2,3-tricarboxylate (4g). Starting with **3g** (500 mg, 1.35 mmol), DMAD (1.13 mL, 10.85 mmol, 8 equiv) and PTSA (5 mol %), **4g** was isolated by chromatography (heptane/ethyl acetate) as a yellow solid (250 mg, 40%); mp 143–144 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ=3.52 (s, 3H, OCH_3), 3.76 (s, 3H, OCH_3), 3.77 (s, 3H, OCH_3), 3.92 (s, 6H, OCH_3), 6.72 (d, 2H, ^3J=9.1 Hz, ArH), 6.74 (d, 2H, ^3J=8.8 Hz, ArH), 6.95 (d, 2H, ^3J=8.5 Hz, ArH), 6.96 (d, 2H, ^3J=8.5 Hz, ArH), 7.98 (s, 1H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$): δ=52.4, 52.7, 52.9, 55.0, 55.1 (OCH_3), 113.3 ($2CH_{Ar}$), 113.4 ($2CH_{Ar}$), 128.3, 129.6 (C), 130.7 ($2CH_{Ar}$), 131.4 (2C), 132.6 (CH_{Ar}), 134.4, 142.0, 143.3, 158.8, 158.9, 165.9, 167.8, 168.0 (C); IR (KBr): $\tilde{\nu}$=1745 (s), 1608 (s), 1575 (m), 1516 (s), 1458 (m), 1435 (s), 1339 (s), 1248 (s), 1067 (m), 843 (m) cm^{-1}; GC–MS (EI, 70 eV): *m*/*z* (%): 464.2, (M^+, 100), 433.1 (16), 401.1 (11); elemental analysis: calcd (%) for $C_{26}H_{24}O_8$ (464.47): C 67.23, H 5.21; found: C 66.89, H 5.20.

3.2.7. 3-Isopropyl-1,2-dimethyl-4,5-di(*p*-methoxyphenyl)-benzene-1,2,3-tricarboxylate 4h. Starting with **3h** (500 mg, 1.26 mmol), DMAD (1.23 mL, 10.08 mmol, 8 equiv) and PTSA (5%), **4h** was isolated by chromatography (heptane/ethyl acetate) as a yellow solid (290 mg, 46%); mp 130–132 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ=0.95 (d, 6H, ^3J=6.2 Hz, CH_3), 3.74 (s, 6H, OCH_3), 3.88 (s, 3H, OCH_3), 3.89 (s, 3H, OCH_3), 4.89 (sept, 1H, ^3J=6.2 Hz, OCH), 6.70 (d, 2H, ^3J=6.4 Hz, ArH), 6.72 (d, 2H, ^3J=6.3 Hz, ArH), 6.92 (d, 2H, ^3J=8.8 Hz, ArH), 6.95 (d, 2H, ^3J=8.8 Hz, ArH), 7.24 (s, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ=20.2 ($2CH_3$), 51.7, 51.8, 54.1, 54.2 (OCH_3), 68.3 (CH),112.3 ($2CH_{Ar}$), 112.4 ($2CH_{Ar}$), 127.1, 128.9, 129.9, 130.4 (C), 130.5 ($2CH_{Ar}$), 131.3 ($2CH_{Ar}$), 133.9 (CH_{Ar}), 140.8, 142.3, 157.7, 158.0, 164.9, 166.0, 166.9 (C); IR (KBr): $\tilde{\nu}$=1741 (s), 1727 (s), 1608 (s), 1516 (s), 1461 (m), 1351 (m), 1251 (m), 1160 (s), 1065 (s), 833 (m) cm^{-1}; MS (EI, 70 eV): *m*/*z* (%): 492 (M^+, 100), 450 (20), 418 (25), 387 (19); HRMS (EI): calcd for $C_{28}H_{28}O_8$ $[M]^+$: 492.177507; found: 492.17787.

3.2.8. 3-Ethyl-1,2-dimethyl-4,5-di(*p*-bromophenyl)-benzene-1,2,3-tricarboxylate (4i). Starting with **3i** (400 mg, 0.83 mmol), DMAD (0.81 mL, 6.66 mmol, 8 equiv) and PTSA (5 mol %), **4i** was isolated by chromatography (heptane/ethyl acetate) as a yellow solid (325 mg, 68%); mp 171–173 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ=0.96 (t, 3H, ^3J=7.1 Hz, CH_3), 3.92 (s, 6H, OCH_3), 3.99 (q, 2H, ^3J=7.1 Hz, OCH_2CH_3), 6.88 (d, 2H, ^3J=8.4 Hz, ArH), 6.92 (d, 2H, ^3J=8.4 Hz, ArH), 7.35 (d, 2H, ^3J=8.4 Hz, ArH), 7.36 (d, 2H, ^3J=8.4 Hz, ArH), 7.98 (s, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ=13.4 (CH_3), 52.8, 52.9 (OCH_3), 61.4 (OCH_2), 122.0, 122.2, 128.9 (C), 131.0 ($2CH_{Ar}$), 131.1 ($2CH_{Ar}$), 131.2 ($2CH_{Ar}$), 131.3 ($2CH_{Ar}$), 132.5 (CH_{Ar}), 132.6, 136.0, 137.5, 141.0, 142.2, 165.4, 166.8, 167.5 (C); IR (KBr): $\tilde{\nu}$=2950 (m), 1742 (s), 1493 (m), 1249 (s), 1202 (s), 1073 (m), 835 (m), 701 (m) cm^{-1}; MS (EI, 70 eV): *m*/*z* (%): 578.9 (M^+, ^{81}Br, 12), 575.9 (M^+, ^{79}Br, 100), 530.9 (37), 484.9 (33), 229 (31), 121.1 (36), 91 (29); elemental analysis: calcd (%) for $C_{25}H_{20}O_6Br_2$ (576.237): C 52.11, H 3.52; found: C 52.16, H 3.54.

Compound **7**: starting with **6** (200 mg, 0.57 mmol), DMAD (0.65 mL, 4.58 mmol) and PTSA (5 mol %), **7** was isolated by chromatography (heptane/ethyl acetate) as a yellow solid (165 mg, 65%); mp 143–144 °C. Reflux time: 10 h. ^{1}H NMR (250 MHz, $CDCl_3$): δ=0.68 (t, 3H, ^3J=7.3 Hz, CH_3), 0.84 (t,

3H, ^{3}J=7.3 Hz, CH_3), 2.51–2.65 (1H), 2.90–3.06 (2H), 3.40–3.49 (1H), 3.88 (s, 3H, OCH_3), 3.91 (s, 3H, OCH_3), 7.01–7.60 (m, 10H, Ph), 8.02 (s, 1H, ArH); ^{13}C NMR (62 MHz, $CDCl_3$): δ=11.5, 12.5 (CH_3), 37.6, 42.5 (CH_2), 52.73, 52.75 (OCH_3), 127.2, 127.3 (C), 127.6 ($2CH_{Ph}$), 127.9 (CH_{Ph}), 128.5 ($2CH_{Ph}$), 129.6 ($2CH_{Ph}$), 130.1 ($2CH_{Ph}$), 131.7 (CH_{Ph}), 131.8 (CH_{Ar}), 136.6, 137.2, 139.4, 140.7, 143.2, 166.0, 167.0, 168.1 (C); IR (KBr): $\tilde{\nu}$=2951 (w), 1731 (s), 1628 (s), 1437 (m), 1267 (s), 1163 (m), 1092 (m), 761 (s), 702 (s) cm^{-1}; MS (EI, 70 eV): *m*/*z* (%): 445.1 (M^+, 2), 386.1 (91), 373.0 (100), 342.0 (17), 226.0 (33), 72.0 (54); HRMS (EI): calcd for $C_{27}H_{27}O_5N_1$ $[M]^+$: 445.188455; found: 445.18837.

3.3. X-ray crystallographic study

Crystallographic data were collected at 173 K with a Bruker X8Apex diffractometer and CCD area-detector, with the use of graphite-monochromatized Mo Kα radiation (λ 0.71073 Å). The data collection was performed with ϕ and ω scans. The structures were solved by direct methods with use of the Bruker SHELXTL software package and full-matrix, least-squares refinements on F^2 were performed with the SHELXL-97 program. In all cases, all heavy atoms were refined anisotropically. The hydrogen atoms were included at fixed distances from their host atoms, with fixed displacement parameters. Figures were drawn with Bruker XP, all at 50% level for the thermal ellipsoids.

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8. CCDC-628559 (**3b**), CCDC-628560 (**4c**) and CCDC-628561 (**5**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (internet) +44 1223336033; e-mail: deposit@ccdc.cam.ac.uk).