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One-pot reactions of 2,4-(dioxobutylidene)phosphoranes. Efficient synthesis of 4-(2-hydroxybenzoyl)salicylic acid derivatives and buta-1,3-diene-1,4-dicarboxylates

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Abstract—4-(2-Hydroxybenzoyl)salicylic esters and amides were prepared by domino 'Michael-Retro-Michael-Wittig' reactions of (2,4-dioxobutylidene)triphenylphosphoranes with 3-formylchromones.

1. Introduction

Functionalized benzophenones occur in a variety of natural products and represent important core structures for the development of pharmaceuticals.[1] For example, the benzophenone phenstatin and related 2-hydroxy- and 2-aminobenzophenones are of considerable relevance in anticancer therapy as they represent potent antitubulin agents.[2,3] We have recently shown that 4-(2-hydroxybenzoyl)salicylic esters represent potent E-, P- and L-selectin antagonists and are, thus, interesting compounds for medical applications against inflammatory disorders.[4] Benzophenones are widely used as photosensitizers and represent one of the most important substance classes in photochemistry.[5] 2-Hydroxybenzophenones are also widely used as UV filters[6] and we have recently reported that 4-(2-hydroxybenzoyl)salicylic esters represent promising candidates for the development of novel UV filters.[4]

Classic syntheses of benzophenones rely on reactions of aryllithium or magnesium reagents with aldehydes and subsequent oxidation[3a,7] and on Friedel–Crafts acylations.[8] The application of these methods to the synthesis of *functionalized* benzophenones (e.g., containing a hydroxy, halide or ester group) can result in competing side reactions. Recently, we reported[4] the synthesis of 4-(2-hydroxybenzoyl)salicylates by domino 'Michael-retro-Michael-Mukaiyama-aldol' reactions of 3-formylchromones with 1,3-bis(silyl enol ethers). The preparative scope of this method is relatively broad and most of the products were isolated in moderate to good yields (42–63%). Notably, the method is limited by the availability of the 1,3-bis(silyl enol ethers). For example, 4-(2-hydroxybenzoyl)salicylic amides could not be prepared, since the corresponding β-ketoamide derived 1,3-bis(silyl enol ethers) are not available.[9] Some years ago, we reported[10] an alternative approach to 4-(2-hydroxybenzoyl)salicylic derivatives based on domino 'Michael-Retro-Michael-Wittig' reactions of 3-formylchromones[11] with (2,4-dioxobutylidene)triphenylphosphoranes.[12,13] Herein, we report full details of these reactions, which allow inter alia the synthesis of 4-(2-hydroxybenzoyl)salicylic amides. In addition, we report, for the first time, the synthesis of buta-1,3-diene-1,4-dicarboxylates by the reaction of (2,4-dioxobutylidene)triphenylphosphoranes with α-ketoesters.

2. Results and discussion

The reaction of 3-formylchromone with phosphorane **2a** afforded 4-(2-hydroxybenzoyl)salicylic ester **3a** (Scheme 1). During optimization of the reaction the following parameters proved important (Table 1): (a) the presence of sodium hydride (NaH), (b) employment of THF as the solvent and (c) the reaction time (24 h) and temperature (reflux). Extension of the reaction time to 48 h did not result in any increase of the yield. The formation of **3a** can be explained by a domino 'Michael-Retro-Michael-Wittig' reaction. Michael reaction of **1a** with the central carbon atom of **2a** afforded intermediate **A**, which underwent a Retro-Michael reaction to give intermediate **B**. The latter underwent an intramolecular Wittig reaction to give **3a** (Scheme 1). The reaction proceeded with very good regioselectivity, which can be explained as follows: (a) In the first step, the Michael reaction predominated over any aldol or Wittig pathway; (b) the 2-hydroxybenzoyl moiety of **3a** was regiospecifically

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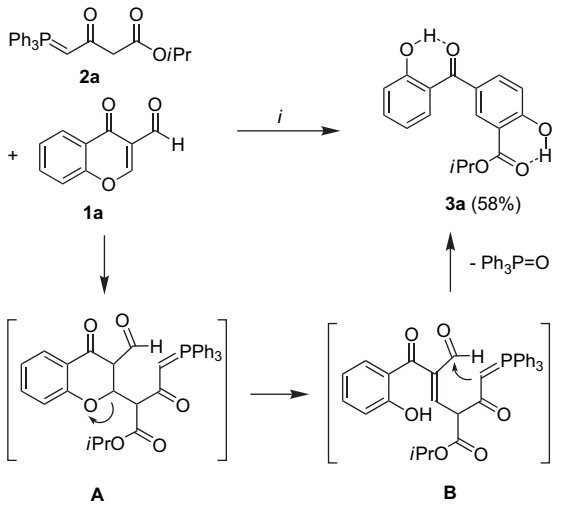


Scheme 1. Synthesis of 4-(2-hydroxybenzoyl)salicylate **3a**. Reagents: (i) NaH, THF, reflux.

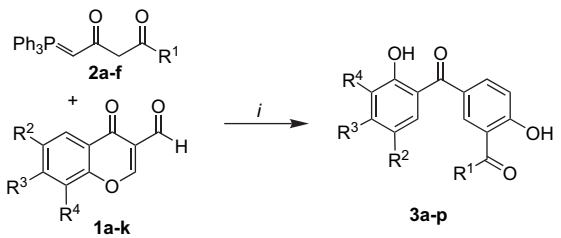
Table 1. Products and yields

1	2	3	R^1	R^2	R^3	R^4	%[a]
a	**a**	**a**	O-*i*-Pr	H	H	H	58
a	**b**	**b**	OEt	H	H	H	52
a	**c**	**c**	OMe	H	H	H	55
a	**d**	**d**	NH_2	H	H	H	18
a	**e**	**e**	$N(CH_2)_4$	H	H	H	54
a	**f**	**f**	$N(CH_2)_5$	H	H	H	25
b	**c**	**g**	OMe	Me	H	H	53
c	**c**	**h**	OMe	Et	H	H	55
d	**c**	**i**	OMe	*i*-Pr	H	H	64
e	**c**	**j**	OMe	Me	H	Me	60
f	**c**	**k**	OMe	Cl	H	H	53
g	**c**	**l**	OMe	Br	H	H	56
h	**c**	**m**	OMe	Cl	H	Cl	55
i	**c**	**n**	OMe	Br	H	Br	51[b]
j	**c**	**o**	OMe	Cl	Me	H	58
k	**c**	**p**	OMe	NO_2	H	H	16[c]

[a] Isolated yields.
[b] Isolated in form of the free acid.
[c] Reaction time—4 h: 16%, 24 h: 0%.

formed by cleavage of the chromone system; (c) the salicylic moiety was formed by regioselective cyclization.

To study the preparative scope of our methodology, the substituents of the starting materials were systematically varied (Scheme 2, Table 1). The cyclization of 3-formylchromone (**1a**) with ethoxy and methoxy substituted phosphanes **2b** and **2c** gave the corresponding salicylic esters **3b** and **3c**, respectively. The cyclization of **1a** with amino-substituted phosphanes **2d–f** afforded the salicylic amides **3d–f**.



Scheme 2. Synthesis of 4-(2-hydroxybenzoyl)salicylic acid derivatives **3a–p**. Reagents: (i) NaH, THF, reflux.

Variation of the chromone moiety was next studied. The reaction of phosphane **2c** with alkyl substituted formylchromones **1b–e** afforded 4-(2′-hydroxybenzoyl)salicylic esters **3g–j**. Salicylic esters **3k–o** were prepared by the reaction of **2c** with chloro and bromo substituted chromones **1f–j**. Starting with **1k**, nitro substituted salicylic ester **3p** was obtained, albeit, in low yield.

The structures of **3a–p** were established by spectroscopic methods. The two intramolecular hydrogen bonds O–H···O could be detected by ^{1}H NMR. The structures of **3e** and **3o** were independently confirmed by X-ray crystal structure analyses (Figs. 1 and 2).[14]

Buta-1,3-diene-1,4-dicarboxylates represent potentially useful synthetic building blocks, which have only scarcely been reported in the literature to date. Known syntheses rely on the hydrolysis of γ-alkylidenebutenolides,[15] on the reaction of malonates with fumaric acid derivatives, and on addition reactions to diynoates.[16] Ketipinates (2,3-di(hydroxyl)hexa-1,3-diene-1,4-dicarboxylates) are available by the reaction of dimethyl malonate with oxalyl chloride and related reactions.[17] Herein, we report a new and efficient approach to 2-(hydroxy)buta-1,3-diene-1,4-dicarboxylates by the reaction of (2,4-dioxobutylidene)phosphoranes with α-ketoesters.

The reaction of ethyl 2-oxopropionate (**4**) with phosphoranes **2c**, **2b**, **2e** and **2g** afforded the buta-1,3-diene-1,4-dicarboxylates **5a–d** in moderate to good yields, respectively

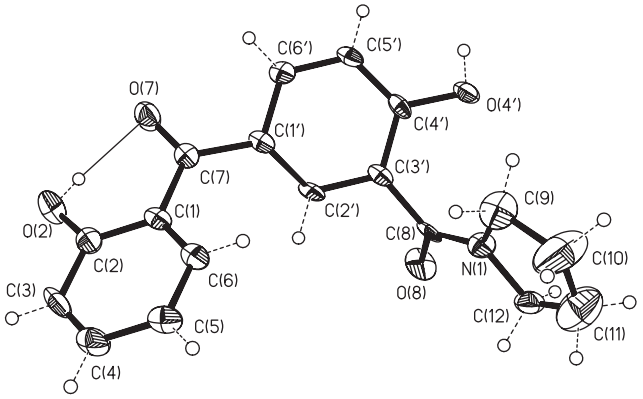


Figure 1. ORTEP plot of **3e**.

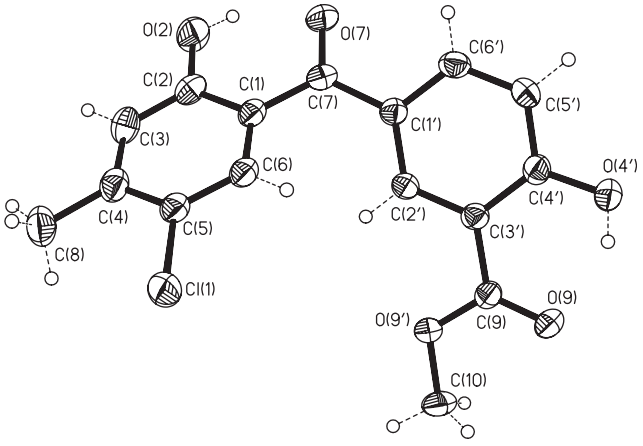
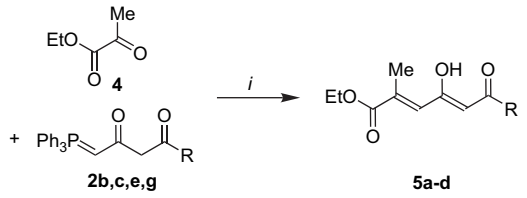


Figure 2. ORTEP plot of **3o**.

(Scheme 3, Table 2). All products were isolated as a single *E*/*Z*-diastereomer. They exclusively exist in their enol tautomeric form.



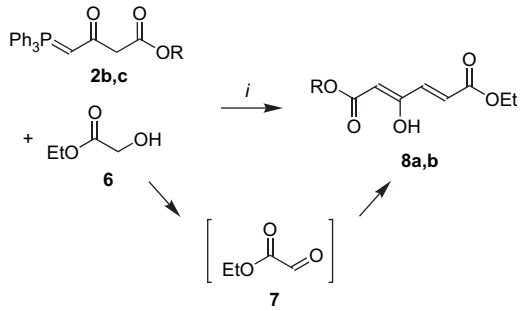
Scheme 3. Synthesis of hexa-2,4-diene-1,6-dicarboxylates **5a–d**. Conditions: (i) 80 °C, 2 h.

Table 2. Products and yields

2	5	R	%[a] (A)	%[a] (B)	Keto/enol[c]
c	**a**	OMe	76	50	1:2
b	**b**	OEt	80	50	1:1
e	**c**	NC_4H_8	—[b]	48	1:2
g	**d**	Ph	—[b]	49	>2:98

[a] Isolated yields; method A: neat, 80 °C; method B: toluene or benzene, reflux, 5 h.
[b] Experiment not carried out.
[c] By ^{1}H NMR ($CDCl_3$).

The condensation of phosphoranes **2** with ethyl glyoxylate was next studied. Ethyl glyoxylate is available by oxidative cleavage of diethyl tartrate. However, in our hands, **6** could not be prepared with sufficient purity. Recently, a one-pot synthesis of alkenes by in situ oxidation of primary alcohols and subsequent Wittig reaction has been reported.[18] We studied the application of this procedure to the reaction of ethyl 2-hydroxyacetate (**6**) with phosphorane **2c**. Initial results showed that the reaction of **2c** with ethyl glyoxylate (**7**), in situ generated by Swern oxidation of **6**, resulted in the formation of the desired diene **8a**. Optimal results were obtained when MnO_2 (10 equiv) was used as an oxidizing agent (CH_2Cl_2, 20 °C, 24 h). Following this procedure, hexa-2,4-dienes **8a** and **8b** were prepared in 52 and 51% yield, respectively (Scheme 4, Table 3). Again, all products were isolated as a single *E*/*Z*-diastereomer and exclusively exist in their enol tautomeric form.



Scheme 4. Synthesis of hexa-2,4-dienes **8a**,**b**. Reagents and conditions: MnO_2 (10 equiv), CH_2Cl_2, 20 °C, 24 h.

Table 3. Synthesis of hexa-2,4-dienes **8a**,**b**

2	8	R	%[a]	keto/enol[b]
c	**a**	OMe	52	>2:98
b	**b**	OEt	51	>2:98

[a] Isolated yields.
[b] By ^{1}H NMR ($CDCl_3$).

3. Experimental section

3.1. General

3.1.1. Methyl 4-(triphenylphosphoranylidene)acetoacetate (2c). The synthesis of **2c** has been previously reported.[19] To the best of our knowledge, NMR spectroscopic data have not yet been reported. A benzene solution (50 mL) of triphenylphosphane (20.30 g, 77.0 mmol) and of methyl 4-chloroacetoacetate (12.80 g, 85.0 mmol) was stirred at 50 °C for 24 h. After cooling, the precipitate formed was filtered off, washed with benzene and dissolved in water. A saturated aqueous solution of sodium bicarbonate was added and the precipitate formed was filtered off, washed with water and dried in vacuo to give **2c** (20.80 g, 72%) as a colourless solid. ^{1}H NMR (250 MHz, $CDCl_3$): δ=3.37 (s, 2H, CH_2), 3.73 (s, 3H, CH_3), 3.80–3.95 (br s, 1H, P=CH), 7.40–7.70 (m, 15H, CH, Ph). ^{13}C NMR (50.3 MHz, $CDCl_3$): δ=48.0 (d, $^3J_{C-P}$= 16 Hz, CH_2, O=C–*C*H_2), 51.8 (CH_3), 52.5 (d, $^1J_{C-P}$= 108 Hz, P=CH), 126.5 (d, $^1J_{C-P}$=91 Hz, C, Ph), 128.8 (d, $^2J_{C-P}$=13 Hz, CH, Ph, *ortho*), 132.1 (d, $^4J_{C-P}$=3 Hz, CH, Ph, *para*), 133.1 (d, $^3J_{C-P}$=10 Hz, CH, Ph, *meta*), 171.1 (CO, ester), 183.7 (d, $^2J_{C-P}$=3 Hz, CO, ketone). MS (EI, 70 eV): 376 [M^+] (13), 304 (20), 303 (100).

3.1.2. 4-(Triphenylphosphoranylidene)acetoacetic acid amide (2d). The synthesis of **2d** has been previously reported.[20] To the best of our knowledge, spectroscopic data have not yet been reported. Compound **2b** (3.90 g, 10.0 mmol) was stirred for 10 days in a MeOH solution (10 mL) saturated with ammonia. The precipitated product was recrystallized from benzene to give **2d** (2.70 g, 74%) as a colourless solid. ^{1}H NMR (250 MHz, $CDCl_3$): δ=3.30 (s, 2H, O=C–CH_2), 3.87 (d, $^2J_{H-P}$=26 Hz, 1H, P=CH), 5.84 (br s, 1H, NH_2), 7.30–7.70 (m, 15H, CH, Ph), 8.19 (br, 1H, NH_2). ^{13}C NMR (50.3 MHz, $CDCl_3$): δ=47.2 (d, $^3J_{C-P}$= 16 Hz, CH_2, O=C–*C*H_2), 55.3 (d, $^1J_{C-P}$=107 Hz, P=CH), 125.9 (d, $^1J_{C-P}$=91 Hz, C, Ph), 129.0 (d, $^2J_{C-P}$=12 Hz, CH, Ph, *ortho*), 132.4 (d, $^4J_{C-P}$=3 Hz, CH, Ph, *para*), 132.9 (d, $^3J_{C-P}$=10 Hz, CH, Ph, *meta*), 172.2 (CO, amide), 186.1 (d, $^2J_{C-P}$=3 Hz, CO, ketone). MS (EI, 70 eV): 361 [M^+] (14), 303 (100). Anal. Calcd for $C_{22}H_{20}O_2NP$: C, 73.12; H, 5.58; N, 3.88. Found: C, 72.55; H, 5.38; N, 3.53.

3.1.3. 4-(Triphenylphosphoranylidene)acetoacetic acid pyrrolidide (2e). The synthesis of **2e** has been previously reported.[21] To the best of our knowledge, spectroscopic data have not yet been reported. A toluene solution (25 mL) of **2b** (5.80 g, 19.0 mmol), pyrrolidine (2.70 g, 38.0 mmol) and DMAP (0.69 g, 6.0 mmol, 30 mol %) was stirred under reflux for 10 h. The solution was concentrated and cooled to 0 °C to give a precipitate. The latter was recrystallized from EtOH to give **2e** (6.20 g, 79%) as a colourless solid. ^{1}H NMR (250 MHz, $CDCl_3$): δ=1.80–1.90 (m, 4H, CH_2), 3.36 (s, 2H, O=C–CH_2), 3.48 (t, ^3J=7 Hz, 3H, N–CH_2), 3.56 (t, ^3J=6 Hz, 3H, N–CH_2), 3.91 (d, $^2J_{H-P}$=24 Hz, 1H, P=CH), 7.35–7.70 (m, 15H, CH, Ph). ^{13}C NMR (50.3 MHz, $CDCl_3$): δ=24.5, 26.0 (CH_2), 45.7, 47.3 (N–CH_2), 50.0 (d, $^3J_{C-P}$=15 Hz, CH_2, O=C–*C*H_2), 51.9 (d, $^1J_{C-P}$=108 Hz, P=CH), 126.6 (d, $^1J_{C-P}$=91 Hz, C, Ph), 128.7 (d, $^2J_{C-P}$=12 Hz, CH, Ph, *ortho*), 132.0 (d, $^4J_{C-P}$=3 Hz, CH, Ph, *para*), 133.0 (d, $^3J_{C-P}$=10 Hz, CH, Ph, *meta*), 168.9 (CO, amide), 185.4 (d,

$^2J_{C-P}$=3 Hz, CO, ketone). MS (70 eV, EI): 415 [M$^+$] (11), 303 (100), 262 (51). Anal. Calcd for $C_{22}H_{26}O_2NP$: C, 75.63; H, 6.53; N, 3.26. Found: C, 75.93; H, 6.95; N, 3.04.

3.1.4. 4-(Triphenylphosphoranylidene)acetoacetic acid piperidide (2f). A toluene solution (25 mL) of **2b** (5.90 g, 19.0 mmol), piperidine (3.20 g, 38.0 mmol) and DMAP (0.69 g, 6.0 mmol, 30 mol %) was stirred under reflux for 10 h. The solution was concentrated and cooled to 0 °C to give a precipitate. The latter was recrystallized from EtOH to give **2f** (6.40 g, 79%) as a colourless solid. ^{1}H NMR (250 MHz, $CDCl_3$): δ=1.40–1.60 (m, 6H, CH_2), 3.42 (s, 2H, O=C–CH_2), 3.50–3.60 (m, 4H, N–CH_2), 3.88 (d, $^2J_{H-P}$=24 Hz, 1H, P=CH), 7.35–7.70 (m, 15H, CH, Ph). ^{13}C NMR (50.3 MHz, $CDCl_3$): δ=24.5, 25.6, 26.1 (CH_2), 42.7, 47.5 (N–CH_2), 49.5 (d, $^3J_{C-P}$=15 Hz, CH_2, O=C–*C*H$_2$), 51.5 (d, $^1J_{C-P}$=109 Hz, P=CH), 126.6 (d, $^1J_{C-P}$=91 Hz, C, Ph), 128.7 (d, $^2J_{C-P}$=12 Hz, CH, Ph, *ortho*), 132.0 (d, $^4J_{C-P}$=3 Hz, CH, Ph, *para*), 132.98, 133.99 (d, $^3J_{C-P}$=10 Hz, CH, Ph, *meta*), 168.9 (CO, amide), 185.3 (d, $^2J_{C-P}$=3 Hz, CO, ketone). IR (KBr, cm^{-1}): $\tilde{\nu}$=2945 (m), 2856 (w), 16.28 (s), 1548 (s), 1440 (s), 1384 (s), 1271 (m), 1106 (s), 861 (m), 760 (m), 718 (m), 696 (m), 540 (m), 527 (m). MS (70 eV, EI): 429 [M$^+$] (12), 318 (27), 303 (100), 262 (40). HRMS (EI, 70 eV): calcd for $C_{23}H_{28}O_2NP$ (M$^+$): 429.1858; found: 429.1858±3 ppm.

3.2. General procedure for the synthesis of the 4-(2′-hydroxybenzoyl)salicylic acid derivatives 3a–p

A THF suspension (5 mL) of NaH (2.6–5.1 equiv) and of phosphorane **2** (1.3–1.4 equiv) was stirred under nitrogen atmosphere at 0 °C for 30 min. Then a THF solution (10 mL) of the formylchromone **1** (1.0 equiv) was added and the resulting solution was stirred for further 60 min at 0 °C. Thereafter the reaction mixture was refluxed for the specified time, cooled to room temperature and stirred for 12 h at 20 °C. To the mixture was added an aqueous solution of hydrochloric acid (5 mL, 1 M), a saturated solution of NaCl (10 mL) and ether (30 mL). The aqueous layer was separated and extracted with CH_2Cl_2 (3×10 mL). The combined organic layers were dried ($MgSO_4$), filtered and the solvent of the filtrate was removed in vacuo. Purification of the residue was performed by column chromatography.

3.2.1. 2-Hydroxy-5-(2-hydroxybenzoyl)benzoic acid isopropyl ester (3a). Phosphorane **2a** (638.4 mg, 1.58 mmol, 1.3 equiv), formylchromone **1a** (210.8 mg, 1.21 mmol) and NaH (111.5 mg, 4.65 mmol, 3.8 equiv) were reacted according to the general procedure (reflux time 27 h). After column chromatography (silica gel, petroleum ether/ether=20:1), **3a** could be isolated as a yellow solid (209.5 mg, 58%); R_f=0.50. ^{1}H NMR (250 MHz, $CDCl_3$): δ=1.40 (d, ^3J=6 Hz, 6H, 2×CH_3), 5.32 (sept, ^3J=6 Hz, 1H, OC*H*$(CH_3)_2$), 6.90 (dd, ^3J=7, 8 Hz, 1H, Ar), 7.07 (d, ^3J=7 Hz, 1H, Ar), 7.08 (d, ^3J=8 Hz, 1H, Ar), 7.47–7.60 (m, 2H, Ar), 7.82 (dd, ^3J=9 Hz, ^4J=2 Hz, 1H, Ar), 8.29 (d, ^4J=2 Hz, 1H, Ar), 11.44 (s, 1H, OH), 11.88 (s, 1H, OH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=21.77 (2×CH_3), 70.12 (O*C*H$(CH_3)_2$), 112.9 (C, Ar), 117.6, 118.5, 118.6 (CH, Ar), 119.0, 128.9 (C, Ar), 132.3, 132.9, 136.2, 136.5 (CH, Ar), 163.0, 164.7, 169.2 (COH, COOR), 199.2 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$=3396 (w), 3350 (w), 3069 (m), 2984 (m), 2936 (m), 1672 (s), 1629 (s), 1588 (s), 1485 (s), 1338 (s), 1296 (s), 1217 (s), 1106 (m), 799 (m), 759 (s), 632 (m). MS (70 eV, EI): *m*/*z* (%)=300 [M$^+$] (80), 121 (100), 120 (94). Anal. Calcd for $C_{17}H_{16}O_5$ (300.31): C, 67.99; H, 5.37. Found: C, 68.13; H, 5.18.

3.2.2. 2-Hydroxy-5-(2-hydroxybenzoyl)benzoic acid ethyl ester (3b). Phosphorane **2b** (556.4 mg, 1.43 mmol, 1.3 equiv), formylchromone **1a** (189.5 mg, 1.09 mmol) and NaH (77.9 mg, 3.25 mmol, 3.0 equiv) were reacted according to the general procedure (reflux time 5 h). After column chromatography (silica gel, petroleum ether/ether=20:1), **3b** could be isolated as a yellow solid (130 mg, 42%); R_f=0.36. ^{1}H NMR (250 MHz, $CDCl_3$): δ=1.42 (t, ^3J=7 Hz, 3H, CH_3), 4.45 (q, ^3J=7 Hz, 2H, CH_2), 6.91 (dd, ^3J=7, 8 Hz, 1H, Ar), 7.08 (d, ^3J=8 Hz, 1H, Ar), 7.09 (d, ^3J=8 Hz, 1H, Ar), 7.53 (dd, ^3J=7, 8 Hz, 1H, Ar), 7.59 (d, ^3J=8 Hz, 1H, Ar), 7.84 (d, ^3J=8 Hz, 1H, Ar), 8.30 (s, 1H, Ar), 11.34 (s, 1H, OH), 11.87 (s, 1H, OH). ^{13}C NMR (50.3 MHz, $CDCl_3$): δ=14.1 (CH_3), 62.1 (CH_2), 112.5 (C, Ar), 117.7, 118.5, 118.7 (CH, Ar), 119.0, 129.0 (C, Ar), 132.4, 132.9, 136.2, 136.6 (CH, Ar), 163.0, 164.7, 169.6 (COH, COOR), 199.1 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$=3187 (w), 3087 (w), 2987 (w), 2966 (w), 1683 (s), 1629 (s), 1589 (s), 1467 (m), 1444 (m), 1397 (m), 1343 (s), 1293 (s), 1242 (s), 1216 (s), 1176 (m), 1084 (m), 759 (s). MS (70 eV, EI): *m*/*z* (%)=286 [M$^+$] (100), 121 (94), 120 (86). Anal. Calcd for $C_{16}H_{14}O_5$ (286.28): C, 67.31; H, 4.93. Found: C, 66.88; H, 5.18.

3.2.3. 2-Hydroxy-5-(2-hydroxybenzoyl)benzoic acid methyl ester (3c). Phosphorane **2c** (519.5 mg, 1.38 mmol, 1.3 equiv), formylchromone **1a** (184.8 mg, 1.06 mmol) and NaH (127.6 mg, 5.31 mmol, 5.0 equiv) were reacted according to the general procedure (reflux time 14 h). After column chromatography (silica gel, petroleum ether/ether=10:1), **3c** could be isolated as a yellow solid (155 mg, 54%); R_f=0.51. ^{1}H NMR (250 MHz, $CDCl_3$): δ=3.98 (s, 3H, CH_3), 6.90 (dd, ^3J=7, 8 Hz, 1H, Ar), 7.08 (d, ^3J=8 Hz, 1H, Ar), 7.10 (d, ^3J=9 Hz, 1H, Ar), 7.45–7.60 (m, 2H, Ar), 7.86 (d, ^3J=9 Hz, 1H, Ar), 8.28 (s, 1H, Ar), 11.23 (s, 1H, OH), 11.84 (s, 1H, OH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=52.7 (CH_3), 112.1 (C, Ar), 117.8, 118.5, 118.7 (CH, Ar), 119.0, 129.0 (C, Ar), 132.4, 132.9, 136.1, 136.7 (CH, Ar), 162.9, 164.6, 169.9 (COH, COOR), 198.96 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$=3079 (w), 3045 (w), 2957 (w), 2923 (w), 1687 (s), 1628 (s), 1588 (s), 1445 (s), 1352 (s), 1292 (s), 1241 (s), 1221 (s), 1168 (m), 1088 (m), 757 (s). MS (70 eV, EI): *m*/*z* (%)=272 [M$^+$] (100), 147 (31), 121 (95), 120 (94). HRMS (EI, 70 eV): calcd for $C_{15}H_{12}O_5$ (M$^+$): 272.0685; found: 272.0685±3 ppm. Anal. Calcd for $C_{15}H_{12}O_5$ (272.26): C, 66.17; H, 4.44. Found: C, 66.35; H, 4.38.

3.2.4. 2-Hydroxy-5-(2-hydroxybenzoyl)benzamide (3d). Phosphorane **2d** (536.5 mg, 148 mmol, 1.3 equiv), formylchromone **1a** (199.3 mg, 1.14 mmol) and NaH (85.9 mg, 3.58 mmol, 3.1 equiv) were reacted according to the general procedure (reflux time 25 h). After column chromatography (silica gel, petroleum ether/ether=1:1), **3d** could be isolated as a pale yellow solid (49.0 mg, 17%); R_f=0.31. ^{1}H NMR (200 MHz, acetone-d_6): δ=2.83 (br s, 2H, NH_2), 6.90–7.10 (m, 2H, Ar), 7.07 (d, ^3J=9 Hz, 1H, Ar), 7.57 (dd, ^3J=9 Hz, ^3J=8 Hz, 1H, Ar), 7.66 (d, ^3J=9 Hz, 1H, Ar),

7.85 (dd, ^3J=8 Hz, ^4J=2 Hz, 1H, Ar), 8.28 (d, ^4J=2 Hz, 1H, Ar), 11.10–11.30 (br s, 1H, OH), 11.62 (s, 1H, OH). ^{13}C NMR (50.3 MHz, pyridine-d_5): δ=115.6 (C, Ar), 118.1, 118.3, 119.3 (CH, Ar), 129.1 (C, Ar), 131.39, 132.41, 134.8 (CH, Ar), 135.8 (C, Ar), 136.2 (CH, Ar), 160.8, 166.3, 173.0 (COH, COOR), 197.9 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$=3400 (s), 3191 (s), 2925 (m), 1699 (s), 1637 (s), 1626 (s), 1597 (s), 1490 (s), 1337 (s), 1245 (s), 1158 (m), 979 (m), 833 (m), 761 (s). MS (70 eV, EI): *m/z* (%)=257 [M$^+$] (100), 121 (70), 120 (83). HRMS (EI, 70 eV): calcd for $C_{14}H_{11}NO_4$ (M$^+$): 257.0688; found: 257.0688±3 ppm.

3.2.5. [2-Hydroxy-5-(2-hydroxybenzoyl)phenyl]pyrrolidin-1-yl-methanone (3e). Phosphorane **2e** (438.1 mg, 1.06 mmol, 1.3 equiv), formylchromone **1a** (438.1 mg, 1.06 mmol, 1.3 equiv) and NaH (77.4 mg, 3.23 mmol, 3.9 equiv) were reacted according to the general procedure (reflux time 25 h). After column chromatography (silica gel, petroleum ether/ether=1:1), **3e** could be isolated as a pale yellow solid (113.9 mg, 44%); R_f=0.23. ^{1}H NMR (250 MHz, $CDCl_3$) δ=1.90–2.05 (m, 4H, 2×CH_2), 3.60–3.90 (m, 4H, 2×NCH_2), 6.90 (dd, ^3J=8, 7 Hz, 1H, Ar), 7.07 (d, ^3J=9 Hz, 2H, CH, Ar), 7.51 (dd, ^3J=8, 7 Hz, 1H, Ar), 7.59 (d, ^3J=8 Hz, 1H, Ar), 7.75 (dd, ^3J=9 Hz, ^4J=2 Hz, 1H, Ar), 7.96 (d, ^4J=2 Hz, 1H, Ar), 11.81 (s, 1H, OH), 12.10 (s, 1H, OH). ^{13}C NMR (50.3 MHz, $CDCl_3$) δ=24.1, 26.9 (2×CH_2), 47.9, 50.5 (2×NCH_2), 116.8 (C, Ar), 117.7, 118.5, 118.6 (CH, Ar), 119.1, 127.7 (C, Ar), 130.7, 132.8, 134.5, 136.0 (CH, Ar), 162.8, 164.3, 169.2 (COH, COOR), 199.1 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$=3427 (m), 3128 (s), 2974 (m), 2885 (m), 1618 (s), 1588 (s), 1483 (s), 1455 (s), 1293 (s), 1256 (s), 1170 (m), 846 (m), 762 (s), 626 (m). MS (70 eV, EI): *m/z* (%)=311 [M$^+$] (100), 241 (29), 70 (50). Anal. Calcd for $C_{18}H_{17}NO_4$ (311.34): C, 69.44; H, 5.50. Found: C, 69.21; H, 5.75.

3.2.6. [2-Hydroxy-5-(2-hydroxybenzoyl)phenyl]piperidin-1-yl-methanone (3f). Phosphorane **2f** (567 mg, 1.33 mmol, 1.3 equiv), formylchromone **1a** (173 mg, 0.99 mmol) and NaH (78.6 mg, 3.25 mmol, 3.3 equiv) were reacted according to the general procedure (reflux time 25 h). After column chromatography (silica gel, petroleum ether/ether=2:1), **3f** could be isolated as a pale yellow solid (79.3 mg, 25%); R_f=0.24. ^{1}H NMR (250 MHz, $CDCl_3$): δ=1.55–1.80 (m, 6H, 3×CH_2), 3.60–3.75 (m, 4H, 2×NCH_2), 6.90 (dd, ^3J=8, 7 Hz, 1H, Ar), 7.08 (d, ^3J=8 Hz, 1H, Ar), 7.11 (d, ^3J=8 Hz, 1H, Ar), 7.52 (dd, ^3J=9, 7 Hz, 1H, Ar), 7.59 (dd, ^3J=8 Hz, 1H, ^4J=2 Hz, 1H, Ar), 7.69 (d, ^4J=2 Hz, 1H, Ar), 7.75 (dd, ^3J=9 Hz, ^4J=2 Hz, 1H, Ar), 10.47 (s, 1H, OH), 11.83 (s, 1H, OH). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ=14.4, 26.1 (CH_2), 47.1 (CH_2, NCH_2), 116.9 (C, Ar), 118.0, 118.6, 118.6 (CH, Ar), 119.2, 128.3 (C, Ar), 130.6, 132.8, 134.1, 136.1 (CH, Ar), 163.0, 163.1, 169.8 (COH, COOR), 199.1 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$=3431 (m), 3020 (m), 2935 (s), 2859 (s), 1629 (s), 1562 (s), 1480 (s), 1449 (s), 1289 (s), 1242 (s), 1137 (s), 967 (m), 765 (m), 655 (m). MS (EI, 70 eV): *m/z* (%)=325 (87), 324 (33), 121 (37), 84 (100). HRMS (EI, 70 eV): calcd for $C_{19}H_{19}NO_4$ (M$^+$): 325.1314; found: 325.1314±3 ppm.

3.2.7. 2-Hydroxy-5-(2-hydroxy-5-methylbenzoyl)benzoic acid methyl ester (3g). Phosphorane **2c** (523.8 mg, 1.39 mmol, 1.4 equiv), formylchromone **1b** (189.9 mg, 1.01 mmol) and NaH (82.3 mg, 3.42 mmol, 3.4 equiv) were reacted according to the general procedure (reflux time 8 h). After column chromatography (silica gel, petroleum ether/ether=20:1), **3g** could be isolated as a yellow solid (154.6 mg, 53%); R_f=0.22. ^{1}H NMR (250 MHz, $CDCl_3$): δ=2.28 (s, 3H, CH_3), 3.98 (s, 3H, OCH_3), 6.99 (d, ^3J=9 Hz, 1H, Ar), 7.10 (d, ^3J=9 Hz, 1H, Ar), 7.30–7.40 (m, 2H, Ar), 7.84 (dd, ^3J=9 Hz, ^4J=2 Hz, 1H, Ar), 8.27 (d, ^4J=2 Hz, 1H, Ar), 11.22 (s, 1H, OH), 11.64 (s, 1H, OH). ^{13}C NMR (50.3 MHz, $CDCl_3$): δ=23.9 (CH_3), 52.72 (OCH_3), 112.2 (C, Ar), 117.7, 118.3 (CH, Ar), 118.7, 127.9, 129.2 (C, Ar), 132.3, 132.6, 136.6, 137.2 (CH, Ar), 160.9, 164.5, 170.0 (COH, COOR), 199.0 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$=3064 (m), 2961 (m), 2925 (w), 1677 (s), 1584 (s), 1481 (s), 1358 (s), 1295 (s), 1220 (s), 1204 (s), 1088 (m), 955 (w), 794 (s), 640 (m). MS (70 eV, EI): *m/z* (%)=286 [M$^+$] (54), 135 (48), 134 (100). Anal. Calcd for $C_{16}H_{14}O_5$ (286.28): C, 67.31; H, 4.93. Found: C, 66.99; H, 5.00.

3.2.8. 5-(5-Ethyl-2-hydroxybenzoyl)-2-hydroxybenzoic acid methyl ester (3h). Phosphorane **2c** (458.7 mg, 1.22 mmol, 1.4 equiv), formylchromone **1c** (180.5 mg, 0.89 mmol) and NaH (71.3 mg, 2.97 mmol, 3.3 equiv) were reacted according to the general procedure (reflux time 14 h). After column chromatography (silica gel, petroleum ether/ether=10:1), **3h** could be isolated as yellow solid (146 mg, 55%); R_f=0.30. ^{1}H NMR (250 MHz, $CDCl_3$): δ=1.19 (t, ^3J=8 Hz, 3H, CH_3), 2.57 (q, ^3J=8 Hz, 2H, CH_2), 3.98 (s, 3H, OCH_3), 7.01 (d, ^3J=9 Hz, 1H, Ar), 7.11 (d, ^3J=9 Hz, 1H, Ar), 7.30–7.40 (m, 2H, Ar), 7.87 (dd, ^3J=9 Hz, ^4J=2 Hz, 1H, Ar), 8.29 (d, ^4J=2 Hz, 1H, Ar), 11.22 (s, 1H, OH), 11.64 (s, 1H, OH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=15.8 (CH_3), 27.9 (CH_2), 52.7 (OCH_3), 112.1 (C, Ar), 117.8, 118.3 (CH, Ar), 118.7, 129.2 (C, Ar), 131.5, 132.6 (CH, Ar), 134.3 (C, Ar), 136.1, 136.7 (CH, Ar), 161.0, 164.5, 170.0 (COH, COOR), 198.9 (C, CO). IR (KBr, cm^{-1}): $\tilde{\nu}$=3407 (w), 3098 (m), 3070 (m), 2965 (m), 1676 (s), 1585 (s), 1356 (s), 1291 (s), 1216 (s), 1200 (s), 1085 (m), 984 (m), 795 (s), 639 (m). MS (70 eV, EI): *m/z* (%)=300 [M$^+$] (59), 149 (36), 148 (100), 133 (31). HRMS (EI, 70 eV): calcd for $C_{17}H_{16}O_5$ (M$^+$): 300.0998; found: 300.0998±3 ppm.

3.2.9. 2-Hydroxy-5-(2-hydroxy-5-isopropylbenzoyl)benzoic acid methyl ester (3i). Phosphorane **2c** (512.1 mg, 1.36 mmol, 1.4 equiv), formylchromone **1d** (211.6 mg, 0.98 mmol) and NaH (120.3 mg, 5.01 mmol, 5.1 equiv) were reacted according to the general procedure (reflux time 4 h). After column chromatography (silica gel, petroleum ether/ether=20:1), **3i** could be isolated as a yellow oil (197.1 mg, 64%); R_f=0.35. ^{1}H NMR (250 MHz, $CDCl_3$): δ=1.20 (d, ^3J=7 Hz, 6H, 2×CH_3), 2.85 (sept, ^3J=7 Hz, 1H, $CH(Me)_2$), 3.97 (s, 3H, OCH_3), 7.01 (d, ^3J=9 Hz, 1H, Ar), 7.11 (d, ^3J=9 Hz, 1H, Ar), 7.35–7.45 (m, 2H, Ar), 7.89 (dd, ^3J=9 Hz, ^4J=2 Hz, 1H, Ar), 8.31 (d, ^4J=2 Hz, 1H, Ar), 11.21 (s, 1H, OH), 11.62 (s, 1H, OH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=23.9 (CH_3), 33.2 (CH), 52.7 (OCH_3), 112.0 (C, Ar), 117.9, 118.2 (CH, Ar), 118.2, 129.1 (C, Ar), 130.2, 132.8, 134.7, 136.7 (CH, Ar), 139.0 (C, Ar), 161.0, 164.6, 167.0 (COH, COOR), 198.8 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$=3144 (w), 2959 (m), 1681 (s),

1631 (s), 1484 (s), 1443 (m), 1354 (s), 1296 (s), 1213 (s), 1088 (m), 959 (w), 794 (m), 638 (m). MS (70 eV, EI): *m/z* (%)=314 [M^+] (89), 299 (27), 163 (21), 162 (50), 147 (100). HRMS (EI, 70 eV): calcd for $C_{18}H_{18}O_5$ (M^+): 314.1154; found: 314.1154±3 ppm.

3.2.10. 2-Hydroxy-5-(2-hydroxy-3,5-dimethylbenzoyl)-benzoic acid methyl ester (3j). Phosphorane **2c** (467.3 mg, 1.24 mmol, 1.3 equiv), formylchromone **1e** (188.6 mg, 0.93 mmol) and NaH (57.2 mg, 2.38 mmol, 2.6 equiv) were reacted according to the general procedure (reflux time 5 h). After column chromatography (silica gel, petroleum ether/ether=20:1), **3j** could be isolated as a yellow solid (168.7 mg, 60%); R_f=0.49. ^{1}H NMR (250 MHz, $CDCl_3$): δ=2.24 (s, 3H, CH_3), 2.29 (s, 3H, CH_3), 3.98 (s, 3H, OCH_3), 7.08 (d, ^3J=9 Hz, 1H, Ar), 7.17 (s, 1H, Ar), 7.21 (s, 1H, Ar), 7.83 (dd, ^3J=9 Hz, ^4J=2 Hz, 1H, Ar), 8.26 (d, ^4J=2 Hz, 1H, Ar), 11.20 (s, 1H, OH), 11.94 (s, 1H, OH). ^{13}C NMR (50.3 MHz, $CDCl_3$): δ=15.6, 20.5 (CH_3), 52.7 (OCH_3), 112.1 (C, Ar), 117.6 (CH, Ar), 118.0, 127.0, 127.3, 129.5 (C, Ar), 130.2, 132.3, 136.6, 138.2 (CH, Ar), 159.3, 164.4, 170.0 (COH, COOR), 199.3 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$=3148 (w), 2960 (w), 2363 (w), 1688 (s), 1624 (s), 1585 (s), 1440 (m), 1356 (s), 1289 (s), 1214 (s), 1091 (m), 798 (m), 717 (w). MS (70 eV, EI): *m/z* (%)=300 [M^+] (40), 148 (100), 120 (29). HRMS (EI, 70 eV): calcd for $C_{17}H_{16}O_5$ (M^+): 300.0998; found: 300.0998±3 ppm.

3.2.11. 5-(5-Chloro-2-hydroxybenzoyl)-2-hydroxybenzoic acid methyl ester (3k). Phosphorane **2c** (492.3 mg, 1.31 mmol, 1.3 equiv), formylchromone **1f** (209.2 mg, 1.00 mmol) and NaH (83.2 mg, 3.47 mmol, 3.5 equiv) were reacted according to the general procedure (reflux time 4 h). After column chromatography (silica gel, petroleum ether/ether=20:1), **3k** could be isolated as a yellow solid (154.4, 50%); R_f=0.25. ^{1}H NMR (250 MHz, $CDCl_3$): δ=4.00 (s, 1H, OCH_3), 7.04 (d, ^3J=9 Hz, 1H, Ar), 7.12 (d, ^3J=9 Hz, 1H, Ar), 7.46 (dd, ^3J=9 Hz, ^4J=3 Hz, 1H), 7.53 (d, ^4J=3 Hz, 1H, Ar), 7.84 (dd, ^3J=9 Hz, ^4J=2 Hz, 1H, Ar), 8.27 (d, ^4J=2 Hz, 1H, Ar), 11.27 (s, 1H, OH), 11.69 (s, 1H, OH). ^{13}C NMR (50.3 MHz, $CDCl_3$): δ=52.8 (OCH_3), 112.3 (C, Ar), 118.1 (CH, Ar), 119.7 (C, Ar), 120.2 (CH, Ar), 123.5, 128.4 (C, Ar), 131.8, 132.4, 136.0, 136.5 (CH, Ar), 161.4, 164.9, 169.9 (COH, COOR), 197.9 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$=3430 (m), 3180 (w), 3116 (w), 1680 (s), 1627 (s), 1583 (s), 1467 (s), 1356 (s), 1291 (s), 1207 (s), 1089 (m), 794 (m), 643 (m). MS (70 eV, EI): *m/z* (%)=306 ([M^+], ^{35}Cl) (100), 155 (51), 154 (67), 147 (38), 120 (51). Anal. Calcd for $C_{15}H_{11}O_5Cl$ (306.70): C, 58.74; H, 3.62. Found: C, 58.60; H, 3.54.

3.2.12. 5-(5-Bromo-2-hydroxybenzoyl)-2-hydroxybenzoic acid methyl ester (3l). Phosphorane **2c** (458.9 mg, 1.22 mmol, 1.3 equiv), formylchromone **1g** (236.1 mg, 0.93 mmol) and NaH (58.8 mg, 2.45 mmol, 2.6 equiv) were reacted according to the general procedure (reflux time 4 h). After column chromatography (silica gel, petroleum ether/ether=20:1), **3l** could be isolated as a yellow solid (182.3 mg, 56%); R_f=0.28. ^{1}H NMR (250 MHz, $CDCl_3$): δ=4.00 (s, 1H, OCH_3), 6.99 (d, ^3J=9 Hz, 1H, Ar), 7.12 (d, ^3J=9 Hz, 1H, Ar), 7.59 (dd, ^3J=9 Hz, ^4J= 2 Hz, 1H, Ar), 7.61 (d, ^4J=2 Hz, 1H, Ar), 7.84 (dd, ^3J=9 Hz, ^4J=2 Hz, 1H, Ar), 8.27 (d, ^4J=2 Hz, 1H, Ar), 11.29 (s, 1H, OH), 11.72 (s, 1H, OH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=52.8 (OCH_3), 110.3, 112.4 (C, Ar), 118.1 (CH, Ar), 120.3 (C, Ar), 120.5 (CH, Ar), 128.4 (C, Ar), 132.4, 134.8, 136.5, 138.7 (CH, Ar), 161.8, 164.9, 169.8 (COH, COOR), 197.7 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$=3429 (w), 3111 (w), 2959 (w), 1686 (s), 1625 (s), 1585 (m), 1469 (m), 1357 (s), 1288 (m), 1216 (s), 1088 (w), 801 (m), 636 (w). MS (70 eV, EI): *m/z* (%)=352 ([M^+], ^{81}Br) (100), 350 ([M^+], ^{79}Br) (100), 200 (71), 198 (69), 147 (48), 120 (66). Anal. Calcd for $C_{15}H_{11}O_5Br$ (351.15): C, 51.31; H, 3.16. Found: C, 51.17, H, 3.30.

3.2.13. 5-(3,5-Dichloro-2-hydroxybenzoyl)-2-hydroxybenzoic acid methyl ester (3m). Phosphorane **2c** (570.9 mg, 1.52 mmol, 1.3 equiv), formylchromone **1h** (275.2 mg, 1.13 mmol) and NaH (68.2 mg, 2.84 mmol, 2.5 equiv) were reacted according to the general procedure (reflux time 12 h). After column chromatography (silica gel, petroleum ether/ether=20:1), **3m** could be isolated as a yellow solid (211.4 mg, 55%); R_f=0.28. ^{1}H NMR (250 MHz, $CDCl_3$): δ=4.00 (s, 3H, OCH_3), 7.13 (d, ^3J=9 Hz, 1H, Ar), 7.48 (d, ^4J=2 Hz, 1H, Ar), 7.61 (d, ^4J=2 Hz, 1H, Ar), 7.85 (dd, ^3J=9 Hz, ^4J=2 Hz, 1H, Ar), 8.27 (d, ^4J=2 Hz, 1H, Ar), 11.33 (s, 1H, OH), 12.10–12.20 (br s, 1H, OH). ^{13}C NMR (50.3 MHz, $CDCl_3$): δ=52.9 (OCH_3), 112.4 (C, Ar), 118.3 (CH, Ar), 120.3, 123.3, 124.14, 127.9 (C, Ar), 130.3, 132.6, 135.6, 136.6 (CH, Ar), 157.2, 165.2, 169.8 (COH, COOR), 197.6 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$=3103 (w), 3077 (w), 2958 (w), 2927 (w), 1693 (s), 1580 (m), 1437 (s), 1356 (s), 1299 (s), 1222 (s), 1089 (w), 801 (w). MS (70 eV, EI): *m/z* (%)=342 ([M^+], ^{37}Cl, ^{35}Cl) (57), 340 ([M^+], ^{35}Cl, ^{35}Cl) (87), 190 (54), 188 (83), 152 (86), 147 (58), 120 (100). HRMS (EI, 70 eV): calcd for $C_{15}H_{10}Cl_2O_5$ (M^+): 339.9905; found: 339.9905±3 ppm.

3.2.14. 5-(3,5-Dibromo-2-hydroxybenzoyl)-2-hydroxybenzoic acid methyl ester (3n). Phosphorane **2c** (488.5 mg, 1.30 mmol, 1.3 equiv), formylchromone **1i** (329.2 mg, 0.99 mmol) and NaH (97.7 mg, 4.07 mmol, 4.1 equiv) were reacted according to the general procedure (reflux time 14 h). After column chromatography (silica gel, petroleum ether/ether=1:2), **3n** could be isolated as a yellow solid (170.9 mg, 51%); R_f=0.12–0.39. ^{1}H NMR (300 MHz, pyridine-d_5): δ=7.19 (d, ^3J=12 Hz, 1H, Ar), 7.80 (d, ^4J=2 Hz, 1H, Ar), 7.97 (d, ^4J=2 Hz, 1H, Ar), 8.07 (dd, ^3J=12 Hz, ^4J=2 Hz, 1H, Ar), 8.91 (d, ^4J=2 Hz, 1H, Ar), 11.80–12.10 (m, 3H, 2×OH, COOH). ^{13}C NMR (75.5 MHz, pyridine-d_5): δ=111.3, 114.4, 116.6 (C, Ar), 117.9 (CH, Ar), 127.9, 128.67 (C, Ar), 132.6, 134.5, 136.2, 138.5 (CH, Ar), 154.9, 167.5, 174.2 (COH, COOH), 194.6 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$=3430 (m), 3067 (w), 1625 (m), 1584 (m), 1425 (m), 1319 (m), 1223 (m), 1178 (m), 784 (m), 756 (m), 694 (m), 634 (m). MS (EI, 70 eV): *m/z* (%)=416 ([M^+], ^{79}Br, ^{81}Br) (52), 280 (54), 279 (79), 278 (100), 276 (51), 147 (77), 121 (82), 120 (54).

3.2.15. 5-(5-Chloro-2-hydroxy-4-methylbenzoyl)-2-hydroxybenzoic acid methyl ester (3o). Phosphorane **2c** (436.5 mg, 1.16 mmol, 1.3 equiv), formylchromone **1j** (195.3 mg, 0.88 mmol) and NaH (77.4 mg, 3.23 mmol, 3.7 equiv) were reacted according to the general procedure (reflux time 5 h). After column chromatography (silica gel, petroleum ether/ether=20:1), **3o** could be isolated as a

yellow solid (135.5 mg, 48%); R_f=0.32. ^{1}H NMR (250 MHz, $CDCl_3$): δ=2.40 (s, 3H, CH_3), 3.99 (s, 3H, OCH_3), 6.96 (s, 1H, Ar), 7.10 (d, ^3J=9 Hz, 1H, Ar), 7.52 (s, 1H, Ar), 7.82 (dd, ^3J=9 Hz, ^4J=2 Hz, 1H, Ar), 8.24 (d, ^4J=2 Hz, 1H, Ar), 11.25 (s, 1H, OH), 11.73 (s, 1H, OH). ^{13}C NMR (50.3 MHz, $CDCl_3$): δ=20.8 (CH_3), 52.8 (OCH_3), 112.2, 117.9 (C, Ar), 118.0, 120.5 (CH, Ar), 124.1, 128.6 (C, Ar), 132.16, 132.24, 136.4 (CH, Ar), 145.4 (C, Ar), 161.4, 164.7, 169.9 (COH, COOR), 197.6 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$=3109 (m), 3068 (m), 1676 (s), 1629 (s), 1581 (s), 1441 (s), 1357 (s), 1328 (s), 1214 (s), 1208 (s), 794 (s). MS (70 eV, EI): *m/z* (%)=320 ([M$^+$], ^{35}Cl) (75), 169 (61), 168 (100). HRMS (EI, 70 eV): calcd for $C_{16}H_{13}ClO_5$ (M$^+$): 320.0451; found: 320.0451±3 ppm.

3.2.16. 5-(5-Nitro-2-hydroxybenzoyl)-2-hydroxybenzoic acid methyl ester (3p). Phosphorane **2c** (466.4 mg, 1.24 mmol, 1.4 equiv), formylchromone **1k** (201.8 mg, 0.92 mmol) and NaH (77.8 mg, 3.24 mmol, 3.5 equiv) were reacted according to the general procedure (reflux time 4 h). After column chromatography (silica gel, petroleum ether/ether=5:1), **3p** could be isolated as a white solid (46.2 mg, 16%); R_f=0.21. ^{1}H NMR (250 MHz, $CDCl_3$): δ=4.00 (s, 3H, OCH_3), 7.17 (d, ^3J=9 Hz, 1H, Ar), 7.19 (d, ^3J=9 Hz, 1H, Ar), 7.90 (dd, ^3J=9 Hz, ^4J=2 Hz, 1H, Ar), 8.30 (d, ^4J=2 Hz, 1H, Ar), 8.40 (dd, ^3J=9 Hz, ^4J=3 Hz, 1H, Ar), 8.58 (d, ^4J=3 Hz, 1H, Ar), 11.37 (s, 1H, OH), 12.30–12.60 (br s, 1H, OH). ^{13}C NMR (50.3 MHz, $CDCl_3$): δ=52.9 (CH_3), 112.5, 117.9 (C, Ar), 118.7, 119.6 (CH, Ar), 127.5 (C, Ar), 128.9, 130.7, 132.7, 136.5 (CH, Ar), 139.4 (C, Ar), 165.5, 167.8, 169.7 (COH, COOR), 197.75 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$=3434 (m), 3236 (m), 2923 (m), 2852 (m), 1699 (s), 1632 (s), 1576 (s), 1477 (s), 1345 (s), 1241 (s), 1199 (s), 1098 (m), 677 (m), 640 (m). MS (70 eV, EI): *m/z* (%)=317 [M$^+$] (100), 285 (43), 152 (24), 147 (28), 120 (52). HRMS (EI, 70 eV): calcd for $C_{15}H_{11}NO_7$ (M$^+$): 317.0536; found: 317.0536±3 ppm.

3.3. General procedure A for the synthesis of 2-hydroxy-1,3-hexadiene-1,4-dicarboxylates 5a–d

A suspension of phosphorane **2** and of ethyl pyruvate (**4**) was stirred for 1 h at 80 °C. After cooling to 20 °C, the residue was purified by chromatography (silica gel, *n*-hexane/CH_2Cl_2=1:1).

3.4. General procedure B for the synthesis of 2-hydroxy-1,3-butadiene-1,4-dicarboxylates 5a–d

A benzene or toluene solution of phosphorane **2** and of ethyl pyruvate (**4**) was refluxed for 5 h. After cooling to 20 °C, the solvent was removed in vacuo and the residue was purified by chromatography (silica gel, *n*-hexane/CH_2Cl_2=1:1).

3.4.1. (2*E*,4*Z*)-1-Ethoxy-6-methoxy-4-hydroxy-2-methyl-1,6-dioxo-2,4-hexadiene (5a). Procedure A: Starting with phosphorane **2c** (0.376 g, 1.0 mmol) and ethyl pyruvate (0.232 g, 2.0 mmol), **5a** was isolated (0.163 g, 76%) as a colourless oil.

Procedure B: Starting with phosphorane **2c** (1.81 g, 4.8 mmol) and ethyl pyruvate (0.464 g, 4.0 mmol), dissolved in benzene (40 mL), **5a** was isolated (0.426 g, 50%). Spectroscopic data of **5a**: ^{1}H NMR ($CDCl_3$, 250 MHz, keto/enol=1:2): δ=1.31 (t, ^3J=7 Hz, 3H, CH_3), 2.28 (s, 3H, CH_3), 3.75 (s, 3H, CH_3), 4.25 (q, ^3J=7 Hz, 2H, CH_2), 5.25 (s, 1H, CH), 6.78 (s, 1H, CH), 11.99 (s, 1H, CH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ=14.2, 14.6 (CH_3, keto, enol), 50.5 (CH_2, keto), 51.5, 52.1 (CH_3, keto, enol), 61.4, 61.8 (CH_2, keto, enol), 95.8 (CH, enol), 130.5, 130.5 (CH, keto, enol), 137.1, 143.6 (C), 167.3, 167.7, 169.4, 172.9, 193.0 (CO, keto, enol). IR (KBr, cm^{-1}): $\tilde{\nu}$=2968 (w), 2955 (w), 1714 (s), 1651 (s), 1589 (s), 1448 (s). MS (EI, 70 eV): *m/z*=214 (M$^+$, 9), 182 (7), 169 (8), 141 (100), 137 (20). HRMS (EI, 70 eV): calcd for $C_{10}H_{14}O_5$ (M$^+$) *m/z* (%)=214.0841; found: 214.0841±2 ppm.

3.4.2. (2*E*,4*Z*)-1,6-Diethoxy-4-hydroxy-2-methyl-1,6-dioxo-2,4-hexadiene (5b). Procedure A: Starting with phosphorane **2b** (0.390 g, 1.0 mmol) and ethyl pyruvate (0.232 g, 2.0 mmol), **5b** was isolated (0.181 g, 80%) as a colourless oil.

Procedure B: Starting with phosphoran **2b** (0.780 g, 2.0 mmol) and ethyl pyruvate (0.116 g, 1.0 mmol), dissolved in benzene (10 mL), **5b** was isolated (0.115 g, 50%) as a colourless oil.

Keto/enol=1:1. IR (KBr, cm^{-1}): $\tilde{\nu}$=2985 (w), 1791 (m), 1717 (s), 1653 (s), 1592 (m), 1427 (m). UV–vis/NIR (MeCN): λ_{max}(lg ε)=291.70 (4.07) nm.

3.4.3. (2*E*,4*Z*)-1-Ethoxy-4-hydroxy-2-methyl-1,6-dioxo-6-piperidyl-2,4-hexadiene (5c). Procedure B: Starting with phosphorane **2e** (0.866 g, 2.0 mmol) and ethyl pyruvate (0.232 g, 2.0 mmol), dissolved in toluene (10 mL), **5c** was isolated (0.254 g, 48%) as a colourless oil. ^{1}H NMR ($CDCl_3$, 300 MHz, keto/enol=1:2): δ=1.24 (t, ^3J=7 Hz, 3H, CH_3), 1.51–1.62 (m, 6H, CH_2), 3.43–3.51 (m, 4H, CH_2), 4.16 (q, ^3J=7 Hz, 2H, CH_2), 5.38 (s, 1H, CH), 6.73 (s, 1H, CH), 14.75 (s, 1H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ=14.1, 14.2, 14.4, 14.6 (CH_3, keto, enol), 24.4, 24.48, 25.48, 26.3, 42.9, 47.5, 50.6, 61.2, 61.7 (CH_2, keto, enol), 93.6, 131.1, 132.4 (CH, keto, enol), 135.2, 142.6, 164.6, 167.3, 168.1, 169.2, 170.0, 195.1 (C, keto, enol). IR (KBr, cm^{-1}): $\tilde{\nu}$=2981 (w), 2939 (s), 2860 (m), 1711 (s), 1644 (s), 1588 (s), 1485 (s), 1447 (m). UV–vis/NIR (MeCN): λ_{max}(lg ε)=313.42 (4.20) nm. MS (EI, 70 eV): *m/z*=267 (M$^+$, 49), 194 (18), 127 (22), 111 (42), 84 (100). HRMS (FT-ICR): calcd for $C_{14}H_{22}NO_4$ *m/z*=268.15433; found: *m/z*=268.15468.

3.4.4. (2*E*,5*Z*)-1-Ethoxy-6-hydroxy-2-methyl-1,6-dioxo-6-phenyl-2,5-hexadiene (5d). Procedure B: Starting with phosphorane **2g** (0.633 g, 1.5 mmol) and ethyl pyruvate (0.186 g, 1.6 mmol), dissolved in benzene (8 mL), **5d** was isolated (0.126 g, 49%) as a colourless solid. ^{1}H NMR ($CDCl_3$, 300 MHz, keto/enol <2:98): δ=1.34 (t, ^3J=7 Hz, 3H, CH_3), 2.34 (s, 3H, CH_3), 4.27 (q, ^3J=7 Hz, 2H, CH_3), 6.36 (s, 1H, CH), 6.96 (s, 1H, CH), 7.44–7.58 (m, 3H, CH), 7.92 (d, ^3J=7 Hz, 2H, CH), 16.09 (br s, 1H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ=14.6, 15.2 (CH_3), 61.9 (CH_2), 101.3, 127.9, 129.1, 132.0, 133.3 (CH), 140.0, 167.6, 179.6, 190.1 (C). IR (KBr, cm^{-1}): $\tilde{\nu}$=2983 (w), 1716 (s), 1684 (m), 1641 (s), 1599 (s), 1571 (s), 1456 (s). UV–vis/NIR (MeCN): λ_{max}(lg ε)=344.20 (4.20) nm. MS

(EI, 70 eV): m/z=260 (M^+, 8), 187 (30), 146 (17), 121 (9), 105 (47). Anal. Calcd for $C_{14}H_{14}O_4$: C, 68.28; H, 5.74. Found: C, 67.87; H, 5.52.

3.5. General procedure for the synthesis of buta-2,4-diene-1,6-dicarboxylates 8a,b

A CH_2Cl_2 suspension of phosphorane **2**, ethyl 2-hydroxyacetate (**6**) and MnO_2 was stirred for 16 h at 20 °C. The suspension was filtered and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, *n*-hexane/CH_2Cl_2=1:1).

3.5.1. (2*Z*,4*E*)-6-Ethoxy-1-methoxy-3-hydroxy-1,6-dioxo-2,4-hexadiene (8a). Starting with phosphorane **2c** (0.376 g, 1.0 mmol), **6** (0.208 g, 2.0 mmol) and MnO_2 (1.74 g, 20.0 mmol), dissolved in CH_2Cl_2 (20 mL), **8a** was isolated (0.104 g, 52%, keto/enol >2:98) as a colourless oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ=1.29 (t, ^3J=7 Hz, 3H, CH_3), 3.76 (s, 3H, CH_3), 4.22 (q, ^3J=7 Hz, 2H, CH_2), 5.29 (s, 1H, CH), 6.61 (d, $^3J_{trans}$=16 Hz, 1H, CH), 6.90 (d, $^3J_{trans}$=16 Hz, 1H, CH), 11.56 (s, 1H, OH). IR (KBr, cm^{-1}): $\tilde{\nu}$=3436 (s), 2986 (w), 2956 (w), 1718 (s), 1663 (s), 1599 (s), 1452 (s), 1402 (w). UV–vis/NIR (MeCN): λ_{max}(lg ε)=291.96 (4.13) nm. MS (EI, 70 eV): m/z=200 (M^+, 5), 155 (9), 127 (100), 123 (21), 99 (15). Anal. Calcd for $C_9H_{12}O_5$: C, 54.00; H, 6.04. Found: C, 54.42; H, 6.35.

3.5.2. (2*Z*,4*E*)-1,6-Diethyl-3-hydroxy-2,4-hexadiene-1,6-dicarboxylate (8b). Starting with phosphorane **2b** (0.390 g, 1.0 mmol), **6** (0.208 g, 2.0 mmol) and MnO_2 (1.74 g, 20.0 mmol), dissolved in CH_2Cl_2 (20 mL), **8b** was isolated (0.110 g, 51%, keto/enol >2:98) as a colourless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.15–1.34 (m, 6H, CH_3), 4.15–4.29 (m, 4H, CH_2), 5.29 (s, 1H, CH), 6.64 (d, ^3J=16 Hz, 1H, CH), 6.91 (d, ^3J=16 Hz, 1H, CH), 11.66 (s, 1H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ=14.1, 14.2 (CH_3), 60.8, 61.0 (CH_2), 96.6, 125.8, 137.3 (CH), 165.9, 166.0, 172.0 (C). MS (EI, 70 eV): m/z=214 (M^+, 12), 169 (22), 141 (100), 127 (44), 112 (64). HRMS (EI, 70 eV): calcd for $C_{10}H_{14}O_5$ (M^+): 214.0841; found: m/z (%)=214.0841±2 ppm. IR (KBr, cm^{-1}): $\tilde{\nu}$=3106 (w), 2985 (m), 2940 (w), 2912 (w), 1722 (s), 1695 (w), 1659 (s), 1600 (s), 1470 (w), 1448 (w), 1423 (m). UV–vis/NIR (MeCN): λ_{max}(lg ε)=292.79 (4.23) nm.

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