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Synthesis of Malononitrile-Substituted Diarylmethines via 1,6-Addition of Masked Acyl Cyanides to *para*-Quinone Methides

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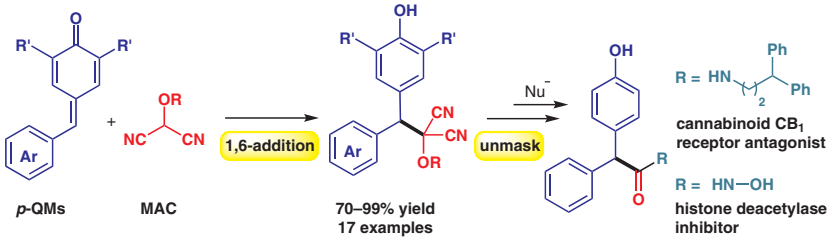

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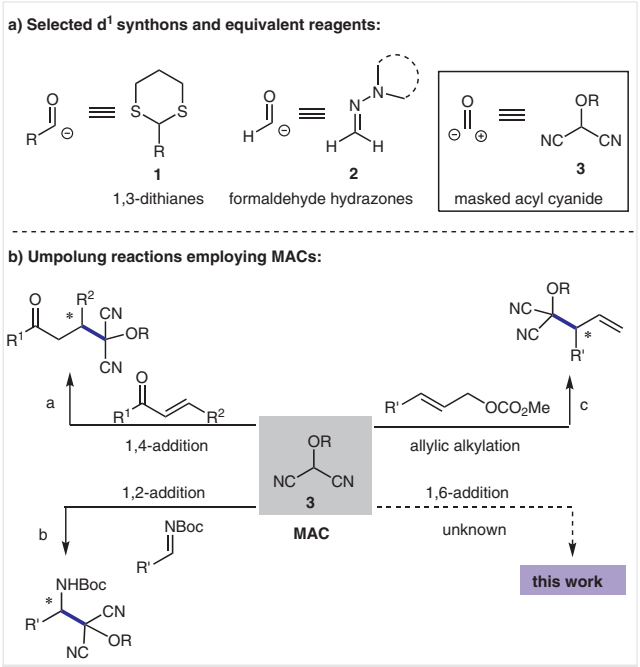
Abstract An efficient method for the synthesis of malononitrile-substituted diarylmethines through 1,6-conjugate addition of *para*-quinone methides with masked acyl cyanide (MAC) reagents has been developed. Under mild conditions, the scalable reaction occurs in good to excellent yields providing a straightforward access to a series of malononitrile-substituted diarylmethines. The synthetic utility of this protocol has been demonstrated in the synthesis of bioactive compounds.

Key words diarylmethines, 1,6-addition, masked acyl cyanides, *para*-quinone methides, malononitrile-substituted diarylmethines

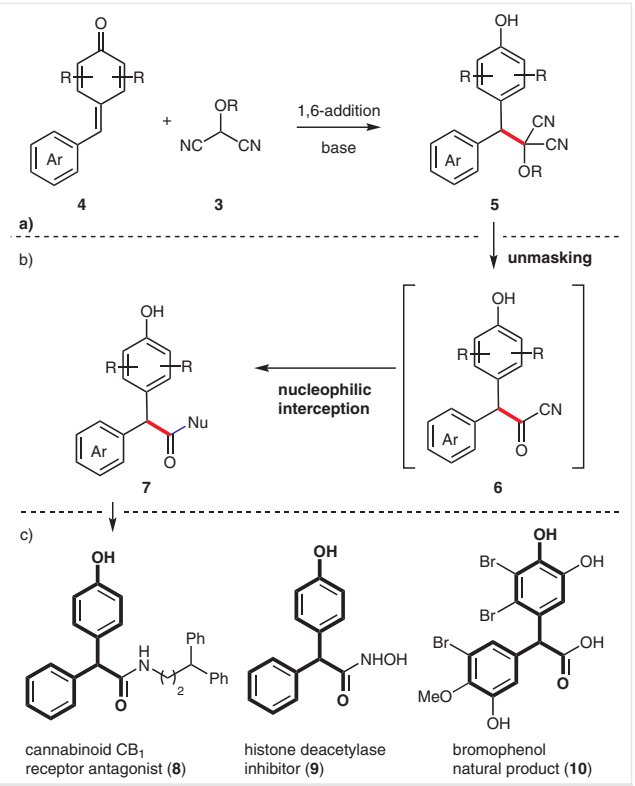
The umpolung of the natural reactivity of functional groups is a powerful concept in chemistry and of enormous value in the synthesis strategy of organic molecules.[1] Since the pioneering work of Corey and Seebach in the mid 1960s,[2] significant attention has been paid to this basic research field and several acyl anion equivalents, such as 1,3-dithianes **1**[3] and aldehyde *N*,*N*-dialkylhydrazones **2**,[4] have been developed and employed in a large number of chemical transformations (Scheme 1, a). Meanwhile, much effort has also been devoted to the use of alkoxymalononitriles **3** in umpolung reactions, termed masked acyl cyanide (MAC) reagents.[5] Compared with the common acyl anion equivalents, MACs can exhibit both nucleophilic (d^1) and electrophilic (a^1) reactivity, thus serving as carbon monoxide equivalents. Not surprising this unique property has attracted much interest among chemists.[6] In 2013, the Rawal group disclosed a squaramide-catalyzed 1,4-addition reaction between masked acyl cyanides and α,β-unsaturated aryl ketones.[6e] In 2014, the same group reported an organocatalytic 1,2-addition of MAC reagents to *N*-Boc-aldimines.[6f] Very recently, the iridium-catalyzed allylic alkylation reaction of masked acyl cyanides was achieved by Stoltz and co-workers (Scheme 1, b).[6h] Despite the fact that masked acyl cyanides have been used successfully in reactions as described above, it is still desirable to explore the reactivity of MAC reagents as nucleophiles with novel electrophiles, such as 1,6-Michael acceptors.[7]



Scheme 1 Selected d^1 synthons and reports based on MAC reagents

During the past several years, *para*-quinone methides (*p*-QMs)[8] have emerged as important vinylogous Michael acceptors due to their intrinsic reactivities,[9,10] and applications of *p*-QMs in domino reactions have also been achieved. However, to the best of our knowledge, the reaction between *p*-QMs and MAC reagents has not been

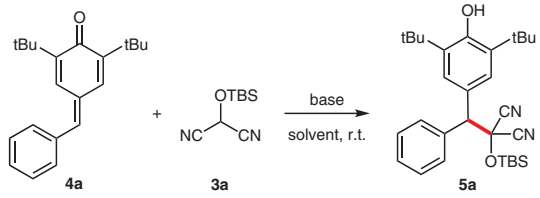
reported so far. We envisioned that a 1,6-addition of MAC reagents **3** to *p*-QMs **4** might occur in the presence of a suitable base (Scheme 2, a). This reaction could provide a facile access to malononitrile-substituted diarylmethines **5**, which after unmasking would deliver acyl cyanide intermediates **6**, amenable to interception by a wide range of nucleophiles to afford the products **7** (Scheme 2, b). Furthermore, based on this proposed strategy the synthesis of several bioactive compounds (**8** and **9**)[11] and natural products (**10**)[12] should be possible (Scheme 2, c).



Scheme 2 Project design and selected bioactive and natural products

To test our hypothesis, we chose the readily available *para*-quinone methide **4a** and TBS-MAC **3a** as the standard substrates to carry out the screening of the reaction conditions (Table 1). The initial experiment was done using sodium carbonate (0.2 equiv) as base in dichloromethane at room temperature. To our delight, the proposed 1,6-addition occurred and the expected adduct **5a** was isolated in a good yield of 69% (Table 1, entry 1). It turned out that the choice of an ideal base is crucial for the success of this 1,6-addition, and therefore a systematic screening of the base was conducted. First, several commonly used inorganic bases (e.g., K_2CO_3, Cs_2CO_3, K_3PO_4, NaOH) were examined, and all of them afforded the desired product **5a** in comparable yields (entries 2–5). Especially, when 20 mol% of NaOH was used, a very clean reaction was observed and the adduct **5a** was obtained in 98% yield (entry 5). Further optimization with a series of organic bases (e.g., Et_3N, DIPEA, DBU) revealed that organic bases had a negative influence on the efficiency of this 1,6-addition, delivering **5a** in 32–44% yields (entries 6–8). Once the best base was established, the effect of the solvent was investigated and we found that other solvents failed to further improve the yield of this transformation (entries 10–15).

Table 1 Optimization of the Reaction Conditions[a]



4a 3a 5a

Entry	Base	Solvent	Time (h)	Yield(%)[b]
1	Na_2CO_3	CH_2Cl_2	48	69
2	K_2CO_3	CH_2Cl_2	48	88
3	Cs_2CO_3	CH_2Cl_2	4	97
4	K_3PO_4	CH_2Cl_2	12	96
5	**NaOH**	**CH_2Cl_2**	**1**	**98**
6	Et_3N	CH_2Cl_2	24	32
7	DIPEA	CH_2Cl_2	24	44
8	DBU	CH_2Cl_2	2	39
9	NaOH	toluene	48	46
10	NaOH	Et_2O	24	94
11	NaOH	CCl_4	48	51
12	NaOH	$CHCl_3$	12	62
13	NaOH	DCE	2	97
14	NaOH	MeOH	2	45
15	NaOH	1,4-dioxane	24	88

[a] All reactions were conducted with 0.2 mmol of **4a**, 0.24 mmol of **3a**, and 20 mol% of base in 2 mL of solvent at r.t.
[b] Yield of isolated **5a** after column chromatography.

With the optimal conditions found (Table 1, entry 5), the substrate scope of this 1,6-addition was investigated and the results are shown in Scheme 3. First, we evaluated the scope of the *p*-QM component. Generally, a broad range of *p*-quinone methides reacted with **3a** to afford the corresponding adducts **5a–o** in good to excellent yields (70–99%). In detail, *p*-QMs bearing electron-neutral (R = H), electron-donating (R = Me, OMe), or electron-withdrawing groups (R = Cl, Br, NO_2) in the *para* and *ortho* positions of the benzene ring easily underwent this 1,6-addition reaction furnishing the desired products **5a–h** in 88–99% yields. A bulky substituent (2-OTBS) was well tolerated and the expected product **5i** could be isolated in 97% yield. Furthermore, the disubstituted *p*-QMs were suitable substrates for this transformation, and the corresponding adducts **5j,k**

were obtained with excellent results. Moreover, we found that *p*-quinone methides, containing furyl and naphthyl moieties, could be processed to deliver the products **5l** and **5m** in 70% and 95% yield, respectively. Replacing the bulky *tert*-butyl R′ substituents of the *p*-QMs by isopropyl or methyl groups did not influence the efficiency of this 1,6-addition reaction (**5n**, **o**). In terms of the MAC reagents, the MOM-MAC **3b** displays a similar reactivity in this reaction providing the product **5p** in nearly quantitative yield. Notably, the *p*-quinone methide derived from ferrocene carboxaldehyde also underwent this reaction smoothly to its corresponding adduct **5q**, and the structure of **5q** was confirmed by NMR as well as X-ray crystallographic analysis.[13] A gram-scale reaction using the standard conditions worked very well with the same efficiency, and the desired compound **5a** was obtained in 96% yield.

Because MAC adducts can be considered as versatile precursors for the synthesis of carboxylic acid derivatives, we turned our attention to this issue (Scheme 4, a). Unmasking compound **5k** and addition of methylamine provided the amide **7a** in 94% yield. Similarly, the methyl ester **7b** could be synthesized via methanolysis of adduct **5a**. Treatment of **7b** with $AlCl_3$ in benzene (60 °C) for 1 hour successfully removed the *tert*-butyl groups, delivering product **7c** in 96% yield. Furthermore, the utility of this novel 1,6-addition was demonstrated with the synthesis of bioactive compounds (Scheme 4, b). First, the cannabinoid CB_1 receptor inverse agonist **8** and histone deacetylase inhibitor **9** could be efficiently synthesized from **7c** in 71% and 68% yield, respectively. The unmasking of adduct **5a** with AcOH-buffered TBAF gave the carboxylic acid **7d** reflecting the basic α-phenolic phenyl acetic acid skeleton of natural products, such as the bromophenol derivative **10**.

In conclusion, we have developed a novel 1,6-conjugate addition reaction between *p*-QMs and MAC reagents. With this new scalable protocol a variety of diarylmethine derivatives could be easily synthesized in good to excellent yields. Based on this method, we accomplished the synthesis of the cannabinoid CB_1 receptor antagonist **8** and the histone deacetylase inhibitor **9**.

Commercially available compounds were used without further purification. Solvents were distilled using standard procedures. Flash column chromatography was performed with silica gel SIL G-25 UV254 (size 0.040–0.063 mm) from Machery & Nagel. For the TLC silica gel 60 F254 plates from Merck, Darmstadt, were used. The compounds on the TLC plates were identified under UV light (254 nm) and by staining with anisaldehyde staining reagent. ^1H and ^{13}C NMR spectra were recorded on Varian Gemini 300, Varian Mercury 300, Varian Inova 400, and Varian Inova 600 instruments at r.t. Mass spectra were recorded on the spectrometer SSQ7000 from Finnigan at 70 eV, whereas HRMS data (ESI) were collected with a ThermoFisher Scientific LTQ-Orbitrap XL apparatus. IR spectra were recorded using the ATR technique on a PerkinElmer FT-IR Spectrum 100 spectrophotometer. Melting points were measured with a Büchi 510 instrument.

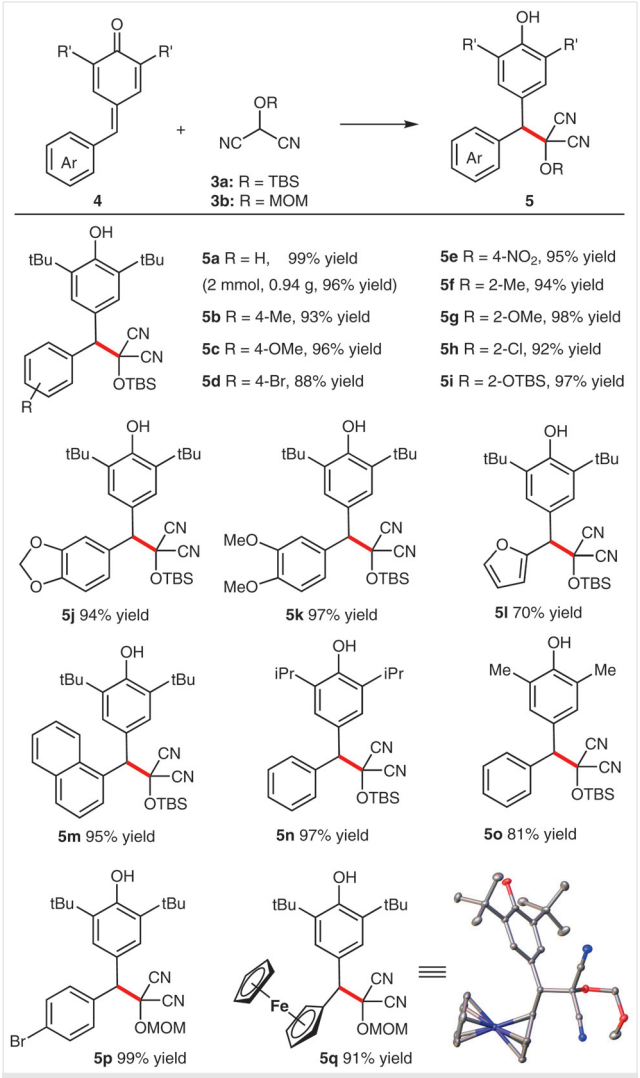
Malononitrile-Substituted Diarylmethines 5; General Procedure

A 10 mL glass tube equipped with a stirring bar was charged with *p*-QMs **4** (0.40 mmol, 1.0 equiv), MAC reagents **3** (0.48 mmol, 1.2 equiv), NaOH (0.08 mmol, 20 mol%), and CH_2Cl_2 (4.0 mL). The resulting solution was stirred at r.t. for 1 h. The solvent was evaporated under reduced pressure and the crude product was directly purified by flash column chromatography (PE/EtOAc from 50:1 to 30:1) to provide the desired products **5a–q**.

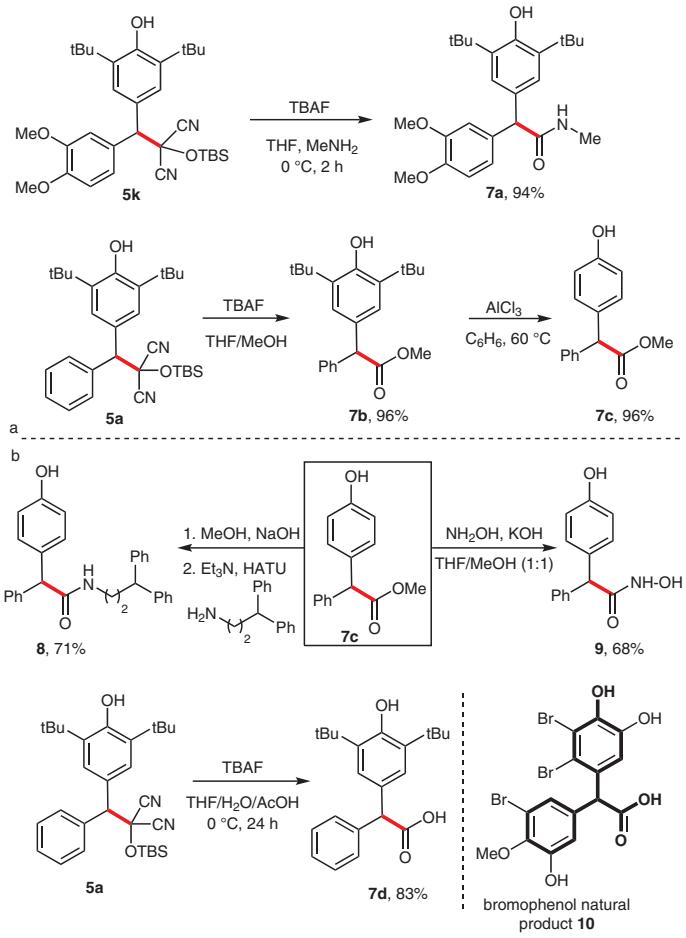
2-[(*tert*-Butyldimethylsilyl)oxy]-2-[(3,5-di-tert-butyl-4-hydroxyphenyl)(phenyl)methyl]malononitrile (5a)

According to the general procedure, **5a** was obtained as a light yellow wax (0.194 g, 99%).

IR (ATR): 3630, 2954, 2240, 2056, 1955, 1735, 1596, 1439, 1366, 1317, 1253, 1128, 1008, 840, 786, 696 cm^{-1}.



Scheme 3 Evaluation of the substrate scope. *Reagents and conditions*: Unless otherwise noted, the reactions were conducted with 0.4 mmol of **4** (1.0 equiv), 0.48 mmol of **3** (1.2 equiv), and 20 mol % of NaOH in CH_2Cl_2 (4.0 mL) at r.t. Yields are those of the isolated products **5** after column chromatography.



Scheme 4 Unmasking of MAC adducts and synthesis of bioactive compounds; HATU: 1-[bis(dimethylamino)methylene]-1*H*-1,2,3-triazolo[4,5-*b*]pyridinium 3-oxide hexafluorophosphate

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.57 (d, *J* = 7.8 Hz, 2 H), 7.39–7.36 (m, 2 H), 7.33 (d, *J* = 7.2 Hz, 1 H), 7.31 (s, 2 H), 5.24 (s, 1 H), 4.44 (s, 1 H), 1.42 (s, 18 H), 0.79 (s, 9 H), 0.22 (s, 3 H), 0.21 (s, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 153.9 (2 C), 136.2, 135.9 (2 C), 129.5 (2 C), 128.7 (2 C), 128.2, 126.4 (2 C), 125.8, 115.3, 67.7, 61.7, 34.4 (2 C), 30.2 (6 C), 25.2 (3 C), 18.0, –4.7 (2 C).

MS (EI): *m*/*z* (%) = 295.2 (100) $[M - C_9H_{15}N_2OSi]^+ = [C_{21}H_{27}O]^+$.

HRMS (EI): *m*/*z* $[M - C_9H_{15}N_2OSi]^+$ calcd for $C_{21}H_{27}O$: 295.2056; found: 295.2057.

2-[(*tert*-Butyldimethylsilyl)oxy]-2-[(3,5-di-*tert*-butyl-4-hydroxyphenyl)(*p*-tolyl)methyl]malononitrile (5b)

According to the general procedure, **5b** was obtained as a wax (0.187 g, 93%).

IR (ATR): 3625, 3459, 2943, 2338, 2094, 1741, 1378, 1218, 1129, 827 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.46 (d, *J* = 8.4 Hz, 2 H), 7.31 (s, 2 H), 7.18 (d, *J* = 8.4 Hz, 2 H), 5.21 (s, 1 H), 4.39 (s, 1 H), 2.33 (s, 3 H), 1.42 (s, 18 H), 0.80 (s, 9 H), 0.22 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.8 (2 C), 138.0, 135.8, 133.2, 129.4 (2 C), 129.3 (2 C), 126.3 (2 C), 126.1, 115.4, 115.3, 67.8, 61.5, 34.4 (2 C), 30.2 (6 C), 25.2 (3 C), 21.1, 18.0, –4.7 (2 C).

MS (EI): *m*/*z* (%) = 309.2 (100) $[M - C_9H_{15}N_2OSi]^+ = [C_{22}H_{29}O]^+$.

HRMS (EI): *m*/*z* $[M - C_9H_{15}N_2OSi]^+$ calcd for $C_{22}H_{29}O$: 309.2213; found: 309.2216.

2-[(*tert*-Butyldimethylsilyl)oxy]-2-[(3,5-di-*tert*-butyl-4-hydroxyphenyl)(4-methoxyphenyl)methyl]malononitrile (5c)

According to the general procedure, **5c** was obtained as a light yellow solid (0.200 g, 96%); mp 103–105 °C.

IR (ATR): 3623, 3464, 2946, 2328, 2066, 1741, 1609, 1438, 1233, 1133, 824 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.50 (d, *J* = 8.4 Hz, 2 H), 7.30 (s, 2 H), 6.91 (d, *J* = 8.4 Hz, 2 H), 5.23 (s, 1 H), 4.39 (s, 1 H), 3.81 (s, 3 H), 1.42 (s, 18 H), 0.80 (s, 9 H), 0.22 (s, 3 H), 0.22 (s, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 159.5 (2 C), 153.8, 135.9 (2 C), 130.6 (2 C), 128.2, 126.3 (2 C), 126.2, 115.4, 115.3, 114.0 (2 C), 67.9, 61.0, 55.3, 34.4 (2 C), 30.2 (6 C), 25.2 (3 C), 18.0, –4.7 (2 C).

MS (EI): *m*/*z* (%) = 325.2 (100) $[M - C_9H_{15}N_2OSi]^+ = [C_{22}H_{29}O_2]^+$.

HRMS (EI): *m*/*z* [M – $C_9H_{15}N_2OSi]^+$ calcd for $C_{22}H_{29}O_2$: 325.2162; found: 325.2158.

2-[(4-Bromophenyl)(3,5-di-*tert*-butyl-4-hydroxyphenyl)methyl]-2-[(*tert*-butyldimethylsilyl)oxy]malononitrile (5d)

According to the general procedure, **5d** was obtained as a wax (0.201 g, 88%).

IR (ATR): 3518, 2939, 2317, 2099, 1740, 1605, 1467, 1369, 1130, 827, 701 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.51 (d, *J* = 8.4 Hz, 2 H), 7.43 (d, *J* = 8.4 Hz, 2 H), 7.25 (s, 2 H), 5.25 (s, 1 H), 4.40 (s, 1 H), 1.41 (s, 18 H), 0.80 (s, 9 H), 0.24 (s, 3 H), 0.21 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.0 (2 C), 136.1, 135.3, 131.8 (2 C), 131.1 (2 C), 126.3 (2 C), 125.3, 122.5, 115.1, 115.0, 67.4, 61.1, 34.4 (2 C), 30.1 (6 C), 25.2 (3 C), 18.0, –4.7 (2 C).

MS (EI): *m*/*z* (%) = 373.1 (100) [M – $C_9H_{15}N_2OSi]^+$ = $[C_{21}H_{26}BrO]^+$.

HRMS (EI): *m*/*z* [M – $C_9H_{15}N_2OSi]^+$ calcd for $C_{21}H_{26}BrO$: 373.1162; found: 373.1160.

2-[(*tert*-Butyldimethylsilyl)oxy]-2-[(3,5-di-*tert*-butyl-4-hydroxyphenyl)(4-nitrophenyl)methyl]malononitrile (5e)

According to the general procedure, **5e** was obtained as a light yellow solid (0.203 g, 95%); mp 115–116 °C.

IR (ATR): 3554, 2938, 2324, 2228, 2186, 2047, 1993, 1948, 1739, 1600, 1525, 1434, 1351, 1223, 1122, 995, 840, 792, 695 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.24 (d, *J* = 8.8 Hz, 2 H), 7.74 (d, *J* = 8.8 Hz, 2 H), 7.23 (s, 2 H), 5.31 (s, 1 H), 4.58 (s, 1 H), 1.40 (s, 18 H), 0.80 (s, 9 H), 0.27 (s, 3 H), 0.22 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.4 (2 C), 147.6, 143.5, 136.4, 130.4 (2 C), 126.3 (2 C), 124.3, 123.7 (2 C), 114.9, 114.8, 67.1, 61.1, 34.5 (2 C), 30.1 (6 C), 25.1 (3 C), 18.0, –4.6, –4.7.

MS (EI): *m*/*z* (%) = 340.3 (100) [M – $C_9H_{15}N_2OSi]^+$ = $[C_{21}H_{26}NO_3]^+$.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{30}H_{41}N_3O_4SiNa^+$: 558.2759; found: 558.2744.

2-[(*tert*-Butyldimethylsilyl)oxy]-2-[(3,5-di-*tert*-butyl-4-hydroxyphenyl)(*o*-tolyl)methyl]malononitrile (5f)

According to the general procedure, **5f** was obtained as a light yellow solid (0.190 g, 94%); mp 132–136 °C.

IR (ATR): 3627, 2937, 2325, 2088, 1739, 1613, 1443, 1125, 831 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.89 (d, *J* = 8.0 Hz, 1 H), 7.30–7.25 (m, 1 H), 7.22 (s, 2 H), 7.21–7.15 (m, 2 H), 5.20 (s, 1 H), 4.66 (s, 1 H), 2.29 (s, 3 H), 1.38 (s, 18 H), 0.80 (s, 9 H), 0.23 (s, 3 H), 0.21 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.8 (2 C), 136.7, 135.7, 135.3, 131.1, 127.8, 127.0 (2 C), 126.9, 126.1, 124.8, 115.6, 115.5, 67.6, 56.7, 34.3 (2 C), 30.1 (6 C), 25.2 (3 C), 20.2, 18.0, –4.6, –4.7.

MS (EI): *m*/*z* (%) = 309.3 (100) [M – $C_9H_{15}N_2OSi]^+$ = $[C_{22}H_{29}O]^+$.

HRMS (ESI): *m*/*z* [M + K]$^+$ calcd for $C_{31}H_{44}N_2O_2SiK^+$: 543.2804; found: 543.2792.

2-[(*tert*-Butyldimethylsilyl)oxy]-2-[(3,5-di-*tert*-butyl-4-hydroxyphenyl)(2-methoxyphenyl)methyl]malononitrile (5g)

According to the general procedure, **5g** was obtained as a light yellow solid (0.204 g, 98%); mp 123–125 °C.

IR (ATR): 3793, 3623, 3332, 2937, 2304, 2077, 1904, 1599, 1451, 1246, 1131, 1033, 783 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.80 (dd, *J* = 8.0, 1.6 Hz, 1 H), 7.32 (s, 2 H), 7.31–7.24 (m, 1 H), 7.03–6.97 (m, 1 H), 6.90 (d, *J* = 8.0 Hz, 1 H), 5.20 (s, 1 H), 5.13 (s, 1 H), 3.83 (s, 3 H), 1.41 (s, 18 H), 0.80 (s, 9 H), 0.22 (s, 3 H), 0.22 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.9 (2 C), 153.7, 135.6, 129.2, 129.0, 126.8 (2 C), 125.8, 125.2, 120.5, 115.6, 115.5, 111.1, 67.7, 55.5, 52.7, 34.4 (2 C), 30.2 (6 C), 25.2 (3 C), 18.0, –4.7, –4.8.

MS (EI): *m*/*z* (%) = 325.3 (100) [M – $C_9H_{15}N_2OSi]^+$ = $[C_{22}H_{29}O_2]^+$.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{31}H_{44}N_2O_3SiNa^+$: 543.3013; found: 543.3005.

2-[(*tert*-Butyldimethylsilyl)oxy]-2-[(2-chlorophenyl)(3,5-di-*tert*-butyl-4-hydroxyphenyl)methyl]malononitrile (5h)

According to the general procedure, **5h** was obtained as a wax (0.194 g, 92%).

IR (ATR): 3626, 2937, 2350, 1745, 1440, 1133, 797 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.00 (dd, *J* = 8.0, 1.6 Hz, 1 H), 7.41 (dd, *J* = 8.0, 1.2 Hz, 1 H), 7.38–7.31 (m, 1 H), 7.27 (s, 2 H), 7.26–7.23 (m, 1 H), 5.24 (s, 1 H), 5.15 (s, 1 H), 1.40 (s, 18 H), 0.80 (s, 9 H), 0.25 (s, 3 H), 0.22 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.0 (2 C), 135.8, 134.9, 134.6, 130.3, 129.1, 128.7, 126.9, 126.8 (2 C), 124.1, 115.3, 115.1, 67.3, 56.4, 34.4 (2 C), 30.1 (6 C), 25.2 (3 C), 18.0, –4.7, –4.8.

MS (EI): *m*/*z* (%) = 329.3 (100) [M – $C_9H_{15}N_2OSi]^+$ = $[C_{21}H_{26}ClO]^+$.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{30}H_{41}ClN_2O_2SiNa^+$: 547.2519; found: 547.2526.

2-[(*tert*-Butyldimethylsilyl)oxy]-2-({2-[(*tert*-butyldimethylsilyl)oxy]phenyl}(3,5-di-*tert*-butyl-4-hydroxyphenyl)methyl)malononitrile (5i)

According to the general procedure, **5i** was obtained as a brown solid (0.240 g, 97%); mp 130–132 °C.

IR (ATR): 3610, 2948, 2864, 2334, 2048, 1994, 1928, 1735, 1596, 1444, 1258, 1121, 919, 833, 781 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 7.90 (d, *J* = 7.2 Hz, 1 H), 7.32 (s, 2 H), 7.21–7.18 (m, 1 H), 7.04–7.01 (m, 1 H), 6.85 (d, *J* = 7.8 Hz, 1 H), 5.19 (s, 2 H), 1.40 (s, 18 H), 1.03 (s, 9 H), 0.80 (s, 9 H), 0.28 (s, 3 H), 0.23 (s, 3 H), 0.19 (s, 6 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 153.8, 153.5, 135.5 (2 C), 128.9, 128.7, 127.2, 127.0 (2 C), 125.5, 121.0, 118.5, 115.6, 115.4, 67.7, 52.2, 34.4 (2 C), 30.1 (6 C), 25.9 (3 C), 25.2 (3 C), 18.3, 18.0, –4.0, –4.3, –4.8, –4.9.

MS (EI): *m*/*z* (%) = 425.4 (100) [M – $C_9H_{15}N_2OSi]^+$ = $[C_{27}H_{41}O_2Si]^+$.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{36}H_{56}N_2O_3Si_2Na^+$: 643.3722; found: 643.3705.

2-[Benzo[*d*][1,3]dioxol-5-yl(3,5-di-*tert*-butyl-4-hydroxyphenyl)methyl]-2-[(*tert*-butyldimethylsilyl)oxy]malononitrile (5j)

According to the general procedure, **5j** was obtained as a colorless solid (0.200 g, 94%); mp 116–119 °C.

IR (ATR): 3629, 2931, 2324, 2093, 1740, 1453, 1241, 1121, 1035, 806, 696 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 7.30 (s, 2 H), 7.08–7.04 (m, 2 H), 6.82 (d, *J* = 9.0 Hz, 1 H), 5.97 (s, 2 H), 5.25 (s, 1 H), 4.37 (s, 1 H), 1.44 (s, 18 H), 0.82 (s, 9 H), 0.25 (s, 3 H), 0.24 (s, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 153.9 (2C), 147.9, 147.6, 136.0, 129.8, 126.2 (2 C), 126.0, 123.2, 115.3, 109.8, 108.3, 101.2, 67.8, 61.3 (2 C), 34.4 (2 C), 30.2 (6 C), 25.2 (3 C), 18.1, –4.6, –4.7.

MS (EI): *m*/*z* (%) = 339.3 (100) [M – $C_9H_{15}N_2OSi]^+$ = $[C_{22}H_{27}O_3]^+$.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{31}H_{42}N_2O_4SiNa^+$: 557.2806; found: 557.2797.

2-[(*tert*-Butyldimethylsilyl)oxy]-2-[(3,5-di-*tert*-butyl-4-hydroxyphenyl)(3,4-dimethoxyphenyl)methyl]malononitrile (5k)

According to the general procedure, **5k** was obtained as a wax (0.210 g, 97%).

IR (ATR): 3627, 2922, 2858, 2332, 2223, 2003, 1945, 1736, 1595, 1517, 1443, 1361, 1256, 1130, 1027, 935, 846, 784, 666 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.33 (s, 2 H), 7.15–7.10 (m, 2 H), 6.86 (d, *J* = 8.0 Hz, 1 H), 5.22 (s, 1 H), 4.37 (s, 1 H), 3.88 (s, 3 H), 3.86 (s, 3 H), 1.41 (s, 18 H), 0.78 (s, 9 H), 0.21 (s, 3 H), 0.20 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.8 (2 C), 149.0, 148.8, 135.9, 128.5, 126.3 (2 C), 126.0, 122.1, 115.5, 115.4, 112.5, 111.1, 68.0, 61.4, 55.8 (2 C), 34.4 (2 C), 30.2 (6 C), 25.2 (3 C), 18.0, –4.7 (2 C).

MS (EI): *m*/*z* (%) = 355.3 (100) [M – $C_9H_{15}N_2OSi]^+$ = $[C_{23}H_{31}O_3]^+$.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{32}H_{46}N_2O_4SiNa^+$: 573.3119; found: 573.3109.

2-[(*tert*-Butyldimethylsilyl)oxy)-2-[(3,5-di-*tert*-butyl-4-hydroxyphenyl)(furan-2-yl)methyl]malononitrile (5l)

According to the general procedure, **5l** was obtained as a dark yellow solid (0.134 g, 70%); mp 113–114 °C.

IR (ATR): 3629, 2941, 2326, 2087, 1973, 1740, 1579, 1439, 1226, 1138, 1037, 842 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.47 (d, *J* = 1.8 Hz, 1 H), 7.37 (s, 2 H), 6.53 (d, *J* = 3.0 Hz, 1 H), 6.40 (dd, *J* = 3.0, 1.8 Hz, 1 H), 5.29 (s, 1 H), 4.56 (s, 1 H), 1.44 (s, 18 H), 0.79 (s, 9 H), 0.24 (s, 3 H), 0.18 (s, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 154.4 (2 C), 149.1, 142.9, 135.9, 126.8 (2 C), 123.4, 114.9, 114.8, 110.7, 110.1, 67.2, 55.9, 34.4 (2 C), 30.1 (6 C), 25.1 (3 C), 18.0, –4.7, –4.9.

MS (EI): *m*/*z* (%) = 285.2 (100) [M – $C_9H_{15}N_2OSi]^+$ = $[C_{19}H_{25}O_2]^+$.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{28}H_{40}N_2O_3SiNa^+$: 503.2700; found 503.2693.

2-[(*tert*-Butyldimethylsilyl)oxy]-2-[(3,5-di-*tert*-butyl-4-hydroxyphenyl)(naphthalen-1-yl)methyl]malononitrile (5m)

According to the general procedure, **5m** was obtained as a colorless solid (0.205 g, 95%); mp 153–154 °C.

IR (ATR): 3625, 3459, 2943, 2323, 2099, 1740, 1599, 1372, 1220, 1125, 779 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.11 (d, *J* = 7.2 Hz, 1 H), 8.01 (d, *J* = 8.4 Hz, 1 H), 7.88–7.80 (m, 2 H), 7.59–7.42 (m, 3 H), 7.31 (s, 2 H), 5.32 (s, 1 H), 5.20 (s, 1 H), 1.37 (s, 18 H), 0.81 (s, 9 H), 0.24 (s, 3 H), 0.20 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.0 (2 C), 135.7, 134.1, 132.6, 131.6, 129.1, 128.8, 126.8 (2 C), 126.6, 125.7, 125.2, 125.1, 124.9, 122.8, 115.6, 115.5, 67.9, 56.1, 34.3 (2 C), 30.1 (6 C), 25.3 (3 C), 18.1, –4.6, –4.7.

MS (EI): *m*/*z* (%) = 345.2 (100) [M – $C_9H_{15}N_2OSi]^+$ = $[C_{25}H_{29}O]^+$.

HRMS (EI): *m*/*z* [M – $C_9H_{15}N_2OSi]^+$ calcd for $C_{25}H_{29}O$: 345.2213; found: 345.2205.

2-[(*tert*-Butyldimethylsilyl)oxy]-2-[(4-hydroxy-3,5-diisopropylphenyl)(phenyl)methyl]malononitrile (5n)

According to the general procedure, **5n** was obtained as a light yellow solid (0.179 g, 97%); mp 113–115 °C.

IR (ATR): 3518, 2950, 2864, 2322, 2101, 1739, 1599, 1461, 1364, 1303, 1263, 1199, 1125, 996, 943, 887, 831, 790, 697 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.56 (d, *J* = 7.8 Hz, 2 H), 7.39–7.36 (m, 2 H), 7.34–7.32 (m, 1 H), 7.22 (s, 2 H), 4.88 (s, 1 H), 4.48 (s, 1 H), 3.15 (hept, *J* = 6.8 Hz, 2 H), 1.27 (d, *J* = 7.0 Hz, 12 H), 0.86 (s, 9 H), 0.27 (s, 3 H), 0.26 (s, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 150.2 (2 C), 136.1, 133.8, 129.6 (2 C), 128.6 (2 C), 128.2, 127.4, 124.9 (2 C), 115.3, 115.2, 67.7, 61.4, 27.3 (2 C), 25.2 (4 C), 22.6 (3 C), 18.1, –4.6, –4.7.

MS (EI): *m*/*z* (%) = 267.2 (100) [M – $C_9H_{15}N_2OSi]^+$ = $[C_{19}H_{23}O]^+$.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{28}H_{38}N_2O_2SiNa^+$: 485.2595; found: 485.2580.

2-[(*tert*-Butyldimethylsilyl)oxy]-2-[(4-hydroxy-3,5-dimethylphenyl)(phenyl)methyl]malononitrile (5o)

According to the general procedure, **5o** was obtained as a light yellow solid (0.132 g, 81%); mp 93–95 °C.

IR (ATR): 3626, 2935, 2216, 1911, 1739, 1592, 1438, 1219, 1010, 793 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.51–7.49 (m, 2 H), 7.38–7.28 (m, 3 H), 7.12 (s, 2 H), 4.70 (s, 1 H), 4.38 (s, 1 H), 2.21 (s, 6 H), 0.87 (s, 9 H), 0.26 (s, 3 H), 0.25 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.4 (2 C), 136.1, 129.8 (2 C), 129.5 (2 C), 128.6 (2 C), 128.2, 127.1, 123.2, 115.1, 115.0, 67.4, 60.6, 25.1 (3 C), 18.1, 16.0 (2 C), –4.8 (2 C).

MS (EI): *m*/*z* (%) = 211.2 (100) [M – $C_9H_{15}N_2OSi]^+$ = $[C_{15}H_{15}O]^+$.

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{24}H_{30}N_2O_2Si$: 406.2071; found: 406.2050.

2-[(4-Bromophenyl)(3,5-di-*tert*-butyl-4-hydroxyphenyl)methyl]-2-(methoxymethoxy)malononitrile (5p)

According to the general procedure, **5p** was obtained as a yellow solid (0.197 g, 99%); mp 104–106 °C.

IR (ATR): 3622, 2956, 2647, 2256, 2163, 2006, 1920, 1730, 1589, 1439, 1312, 1237, 1160, 1109, 1022, 928, 831, 768 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.51 (d, *J* = 8.4 Hz, 2 H), 7.41 (d, *J* = 8.4 Hz, 2 H), 7.27 (s, 2 H), 5.29 (s, 1 H), 5.04 (s, 2 H), 4.53 (s, 1 H), 3.42 (s, 3 H), 1.43 (s, 18 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.1 (2 C), 136.2, 135.3, 131.9 (2 C), 131.1 (2 C), 126.2 (2 C), 125.2, 122.5, 113.0, 112.9, 96.4, 69.6, 59.1, 57.4, 34.5 (2 C), 30.2 (6 C).

MS (EI): *m*/*z* (%) = 373.2 (100) [M – $C_5H_5N_2O_2]^+$ = $[C_{21}H_{26}BrO]^+$.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{26}H_{31}N_2O_3BrNa^+$: 521.1410; found: 521.1397.

Cyclopenta-2,4-dien-1-yl{5-[2,2-dicyano-1-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-2-(methoxymeth-oxy)ethyl]cyclopenta-1,3-dien-1-yl}iron (5q)

According to the general procedure, **5q** was obtained as a dark red solid (0.229 g, 91%); mp 114–116 °C.

IR (ATR): 3592, 3096, 2955, 2246, 2053, 1735, 1662, 1439, 1304, 1234, 1157, 1119, 1046, 974, 918, 889, 820, 754, 666 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38 (s, 2 H), 5.30 (s, 1 H), 4.97–4.90 (m, 2 H), 4.42–4.40 (m, 1 H), 4.33–4.30 (m, 1 H), 4.22–4.18 (m, 2 H), 4.14 (s, 1 H), 3.80 (s, 5 H), 3.35 (s, 3 H), 1.50 (s, 18 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.9 (2 C), 135.8 (2 C), 127.1, 126.2 (2 C), 113.2, 96.1, 83.3, 71.3, 70.3, 69.2, 68.9 (5 C, Cp), 68.7, 67.9, 57.0, 56.0, 34.5 (2 C), 30.4 (6 C).

MS (ESI): *m*/*z* = 551.2 $[M + Na]^+$.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{30}H_{36}FeN_2O_3Na^+$: 551.1973; found: 551.1948.

2-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-2-(3,4-dimethoxyphenyl)-*N*-methylacetamide (7a)

In a 10 mL glass tube equipped with a stirring bar, **5k** (85 mg, 0.15 mmol) and $MeNH_2$ [100 mg, 0.6 mmol, 33% (w/w) in EtOH] were dissolved in THF (1.2 mL) in an ice bath. TBAF (0.17 mL, 0.17 mmol, 1 N in THF) was added dropwise to the solution at 0 °C. The reaction mixture was allowed to stir for 2 h and then quenched with sat. aq NH_4Cl (1 mL). The mixture was extracted with Et_2O (3 × 10 mL), the combined Et_2O layers were dried (anhyd Na_2SO_4), and the solvent was evaporated. The residue was purified by flash column chromatography (PE/Et_2O 4:1) to afford **7a** (86 mg, 94%) as a wax.

IR (ATR): 3313, 2916, 2854, 2333, 2088, 1923, 1733, 1649, 1515, 1459, 1375, 1234, 1177, 1104, 1046, 982, 884, 807, 725 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.03 (s, 2 H), 6.82 (d, *J* = 2.0 Hz, 1 H), 6.80–6.73 (m, 2 H), 5.69 (br s, 1 H), 5.14 (s, 1 H), 4.74 (s, 1 H), 3.82 (s, 3 H), 3.80 (s, 3 H), 2.78 (d, *J* = 4.8 Hz, 3 H), 1.37 (s, 18 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.5, 152.9, 148.9, 148.0, 135.9 (2 C), 132.6, 130.0, 125.3 (2 C), 120.9, 112.2, 111.1, 58.6, 55.9, 55.8, 34.3 (2 C), 30.2 (6 C), 26.6.

MS (EI): *m*/*z* (%) = 413.4 (7) $[M]^+ = [C_{25}H_{35}NO_4]^+$, 355.3 (100) $[M - C_2H_4NO]^+ = [C_{23}H_{31}O_3]^+$.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{25}H_{35}NO_4Na^+$: 436.2458; found: 436.2445.

Methyl 2-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-2-phenylacetate (7b)

In a 10 mL glass tube equipped with a stirring bar, **5a** (155 mg, 0.31 mmol) was dissolved in a mixture of THF (2.2 mL) and MeOH (1.1 mL) in an ice bath. TBAF (0.35 mL, 0.35 mmol, 1 N in THF) was added dropwise to the solution at 0 °C. The reaction mixture was allowed to stir for 2 h and then quenched with sat. aq NH_4Cl (1 mL). The mixture was extracted with Et_2O (3 × 10 mL), the combined Et_2O layers were dried (anhyd Na_2SO_4), and the solvent was evaporated. The residue was purified by flash column chromatography (PE/Et_2O 30:1) to afford **7b** (105 mg, 96%) as a wax.

IR (ATR): 3625, 2946, 2651, 2325, 2084, 1934, 1744, 1566, 1440, 1354, 1197, 703 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.35–7.30 (m, 4 H), 7.27–7.24 (m, 1 H), 7.13 (s, 2 H), 5.16 (s, 1 H), 4.94 (s, 1 H), 3.74 (s, 3 H), 1.41 (s, 18 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 173.5, 153.0, 139.2, 135.8, 129.0, 128.5 (2 C), 128.4 (2 C), 127.0 (2 C), 125.2 (2 C), 56.9, 52.2, 34.4 (2 C), 30.3 (6 C).

MS (EI): *m*/*z* (%) = 354.3 (35) $[M]^+ = [C_{23}H_{30}O_3]^+$, 295.2 (100) $[M - C_2H_3O_2]^+ = [C_{21}H_{27}O]^+$.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{23}H_{30}O_3Na^+$: 377.2087; found: 377.2082.

Methyl 2-(4-Hydroxyphenyl)-2-phenylacetate (7c)

A solution of alcohol **7b** (100 mg, 0.28 mmol) and $AlCl_3$ (224 mg, 1.68 mmol) in anhyd benzene (0.018 M, 16.0 mL) was stirred at 60 °C for 1 h. H_2O (3 mL) and EtOAc (3 mL) were added and the layers were separated. The aqueous layer was extracted with EtOAc (3 × 5 mL) and the combined organic layers were dried (anhyd Na_2SO_4) and filtered. The solvent was removed and the crude product was purified by flash chromatography (PE/Et_2O 25:1) to give **7c** (65 mg, 96%) as a colorless oil.

IR (ATR): 3421, 2969, 2324, 2096, 1733, 1610, 1361, 1209, 1003, 815, 707 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.34–7.26 (m, 5 H), 7.17 (d, *J* = 9.0 Hz, 2 H), 6.77 (d, *J* = 9.0 Hz, 2 H), 4.97 (s, 1 H), 4.82 (s, 1 H), 3.74 (s, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 173.3, 154.7, 138.8, 130.9, 129.9 (2 C), 128.6 (2 C), 128.4 (2 C), 127.2, 115.4 (2 C), 56.1, 52.3.

MS (EI): *m*/*z* (%) = 242.1 (20) $[M]^+ = [C_{15}H_{14}O_3]^+$, 183.1 (100) $[M - C_2H_3O_2]^+ = [C_{13}H_{11}O]^+$.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{15}H_{14}O_3Na^+$: 265.0835; found: 265.0827.

2-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-2-phenylacetic Acid (7d)

In a 10 mL glass tube equipped with a stirring bar, **5a** (49 mg, 0.1 mmol) was dissolved in a mixed solvent of H_2O (0.1 mL), THF (0.1 mL), and AcOH (0.2 mL) in an ice bath. In a separate vial, TBAF (0.12 mmol, 0.12 mL, 1 N in THF) was dissolved in a mixture of THF (0.48 mL) and H_2O (0.6 mL). The resulting solution of TBAF [0.1 M in THF/H_2O (1:1)] was added dropwise to the solution at 0 °C. The reaction mixture was allowed to stir for 24 h and then diluted with H_2O (0.5 mL). The mixture was extracted with Et_2O (2 × 5 mL), dried (anhyd Na_2SO_4), and the solvent was evaporated. The crude product was purified by flash column chromatography (PE/Et_2O 5:1) to afford **7d** (28 mg, 83%) as a colorless solid; mp 157–169 °C.

IR (ATR): 3625, 2942, 2092, 1714, 1432, 1209, 905, 703 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.37–7.31 (m, 4 H), 7.29–7.26 (m, 1 H), 7.15 (s, 2 H), 5.17 (s, 1 H), 4.95 (s, 1 H), 1.40 (s, 18 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 178.6, 153.2, 138.5, 135.9, 128.6 (2 C), 128.5 (2 C), 128.3, 127.3 (2 C), 125.4 (2 C), 56.8, 34.4 (2 C), 30.2 (6 C).

MS (ESI): *m*/*z* = 363.2 $[M + Na]^+$.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{22}H_{28}O_3Na^+$: 363.1931; found: 363.1927.

N-(3,3-Diphenylpropyl)-2-(4-hydroxyphenyl)-2-phenylacetamide (8)

To a solution of compound **7c** (42 mg, 0.17 mmol) in MeOH (1.7 mL) was added NaOH (21 mg, 0.52 mmol) and the reaction mixture was heated to 90 °C for 12 h. The solution was cooled to r.t. and concentrated. To the residue, H_2O (5 mL) was added and then extracted with Et_2O (3 × 10 mL). The aqueous phase was adjusted to pH 1 with aq 1 M HCl and extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with brine, dried (anhyd Na_2SO_4) and concentrated to give the acid compound, which was used directly in the next step without further purification.

In a glass tube, to a solution of the above obtained acid (23 mg, 0.1 mmol), Et_3N (50 mg, 0.5 mmol), 3,3-diphenylpropan-1-amine (42 mg, 0.2 mmol) in DMF (1 mL) was added HATU (76 mg, 0.2 mmol) at r.t. and the reaction mixture was stirred for 4 h. The reaction was quenched with aq $NaHCO_3$ and extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with brine, dried (anhyd

Na_2SO_4), and concentrated. The residue was purified by column chromatography over silica gel (CH_2Cl_2/MeOH 10:1) to give **8** (30 mg, 71%) as a colorless solid; mp 153–155 °C.

IR (ATR): 3852, 3621, 3537, 3319, 3031, 2923, 2870, 2473, 2297, 2184, 2125, 2068, 1974, 1888, 1739, 1614, 1516, 1444, 1363, 1230, 1085, 1029, 964, 834, 793, 740, 698 cm^{-1}.

^1H NMR (600 MHz, CD_3OD): δ = 7.30–7.20 (m, 9 H), 7.18–7.16 (m, 4 H), 7.13–7.09 (m, 4 H), 6.74 (d, *J* = 9.0 Hz, 2 H), 4.85 (s, 1 H), 3.87 (t, *J* = 7.8 Hz, 1 H), 3.13 (t, *J* = 7.2 Hz, 2 H), 2.25–2.22 (m, 2 H).

^{13}C NMR (151 MHz, CD_3OD): δ = 173.8, 156.2, 144.4, 140.2, 130.5 (2 C), 129.5 (2 C), 128.4 (2 C), 128.1 (4 C), 128.0 (2 C), 127.4 (4 C), 126.5, 125.8 (2 C), 114.8 (2 C), 57.0, 48.4, 37.9, 34.5.

MS (ESI): *m*/*z* = 422.2 $[M + H]^+$.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{29}H_{28}NO_2^+$: 422.2115; found: 422.2120.

N-Hydroxy-2-(4-hydroxyphenyl)-2-phenylacetamide (9)

To a solution of **7c** (24 mg, 0.1 mmol) and hydroxylamine (50% in H_2O, 0.1 mL) in THF/MeOH (1:1, 0.8 mL) was added KOH (23 mg, 0.4 mmol). The mixture was stirred at r.t. for 2 h, acidified to pH 7 with aq 1 M HCl, diluted with EtOAc (5 mL), and washed with H_2O (1 mL). The organic layer was separated, dried (anhyd Na_2SO_4), filtered, and concentrated. The residue was purified by flash column chromatography (CH_2Cl_2/MeOH 10:1) to afford **9** (17 mg, 68%) as a colorless solid; mp 157–160 °C.

IR (ATR): 3620, 3351, 3220, 2921, 2855, 2664, 2313, 2108, 1893, 1656, 1609, 1509, 1442, 1358, 1212, 1107, 1033, 984, 887, 836, 798, 726, 690 cm^{-1}.

^1H NMR (600 MHz, DMSO-d_6): δ = 10.83 (s, 1 H), 9.28 (s, 1 H), 8.89 (s, 1 H), 7.28–7.25 (m, 4 H), 7.22–7.16 (m, 1 H), 7.10 (d, *J* = 8.4 Hz, 2 H), 6.67 (d, *J* = 8.4 Hz, 2 H), 4.56 (s, 1 H).

^{13}C NMR (150 MHz, DMSO-d_6): δ = 168.9, 156.6, 141.0, 130.6, 129.9 (2 C), 128.7 (2 C), 128.6 (2 C), 127.0, 115.4 (2 C), 53.0.

MS (ESI): *m*/*z* = 266.1 $[M + Na]^+$.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{14}H_{13}NO_3Na^+$: 266.0788; found: 266.0792.

Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0036-1590947.

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(13) CCDC 1566735 contains the supplementary crystallographic data for this paper. The data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/getstructures.