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Synthesis and Phytotoxicity Evaluation of Substituted *para*-Benzoquinones

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Sorgoleone (1) is one of the major constituents of sorghum root exudates. Sorgoleone is an allelochemical that reduces the growth of broad-leaf plants. The 3,5-dimethoxybenzylic alcohol (3) was used as starting material for the synthesis of 2-methoxy-6-(non-1-yl)benzo-1,4-quinone (9) in 69% yield. Acetylation of (9) with acetic anhydride gave the triacetate (10) in 82% yield. The triacetate (10) was then converted in two steps in 2-hydroxy-5-methoxy-3-(non-1-yl)benzo-1,4-quinone (11) and 2-acetoxy-5-methoxy-3-(non-1-yl)benzo-1,4-quinone (12) in 8% and 37% yield, respectively. Quinone (11) was obtained also by reaction of (12) with DBU in 63% yield. Alkylation of (3) and oxidation with chromic anhydride formed the new quinones (16) (17) and (18) in 23%, 16% and 12% overall yield, respectively. The effect of these quinones and sorgoleone (1) at concentrations of 5.5 $\mu g\ g^{-1}$ on the development of radicle and aerial parts of *Cucumis sativus*, *Brachiaria decumbens*, *Hyptis lophanta*, and *Euphorbia heterophylla* was tested.

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Introduction

The cultures of sorghum have been investigated since the early 1900s for their effects on plants succeeding them in the same cultivated area. Allelochemicals liberated by sorghum plants are produced during seed germination, and the production of these compounds continues during the growth of the plant.[1]

Sorghum root exudate contains many hydrophilic and hydrophobic organic compounds that produce allelopathic effects,[2,7] its major constituents being sorgoleone (1) and dihydrosorgoleone (2), Diagram 1. Dihydrosorgoleone is the initial exudate, but it is easily oxidized to the more stable sorgoleone.[3,4]

At a low concentration (10 μM), sorgoleone reduces the growth of broad-leaf plants in hydroponic biological assays[5,6] and its activity can even be compared with synthetic herbicides such as diuron, atrazine, and metribuzin.[6] The total synthesis of sorgoleone has been published by Sargent and Wangchareontrakul.[7] Although some other natural quinones have been synthesized, their phytotoxicity have not been investigated.[8,9,16] Because of its phytotoxicity, sorgoleone can therefore serve as an excellent model for the development of new synthetic herbicides. Thus, the aim of this work was to prepare several new quinones and evaluate their phytotoxicity in *Cucumis sativus*, *Brachiaria decumbens*, *Hyptis lophanta*, and *Euphorbia heterophylla*.

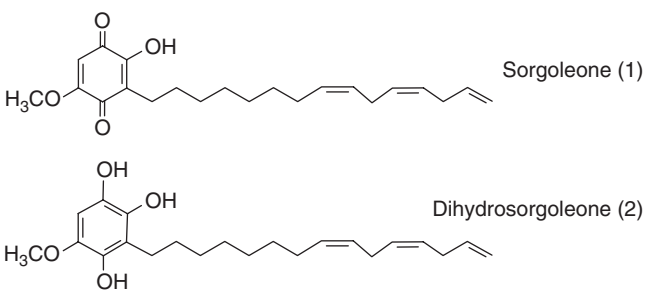

Diagram 1.

Results and Discussion

Commercially available 3,5-dimethoxybenzylic alcohol (3), used as starting material for the synthesis of new analogues of sorgoleone, was converted into aldehyde (4) in 88% by means of Swern oxidation[13] (Scheme 1). In order to extend the side chain, aldehyde (4) was converted into alcohol (5) in 88% yield by a Grignard reaction using 1-bromooctane.

The alcohol 1-(3,4-dimethoxyphenyl)pentan-1-ol has been deoxygenated in 77% yield by reaction with ZnI_2/$NaCNBH_3$,[13] according to literature methods.[15,16] Attempts to prepare hydrocarbon (8) in a one-pot reaction from the corresponding alcohol (5), following these methods, failed. There was no reaction even when the mixture was heated at 40°C for 2 h. A possible reason for this failure is that

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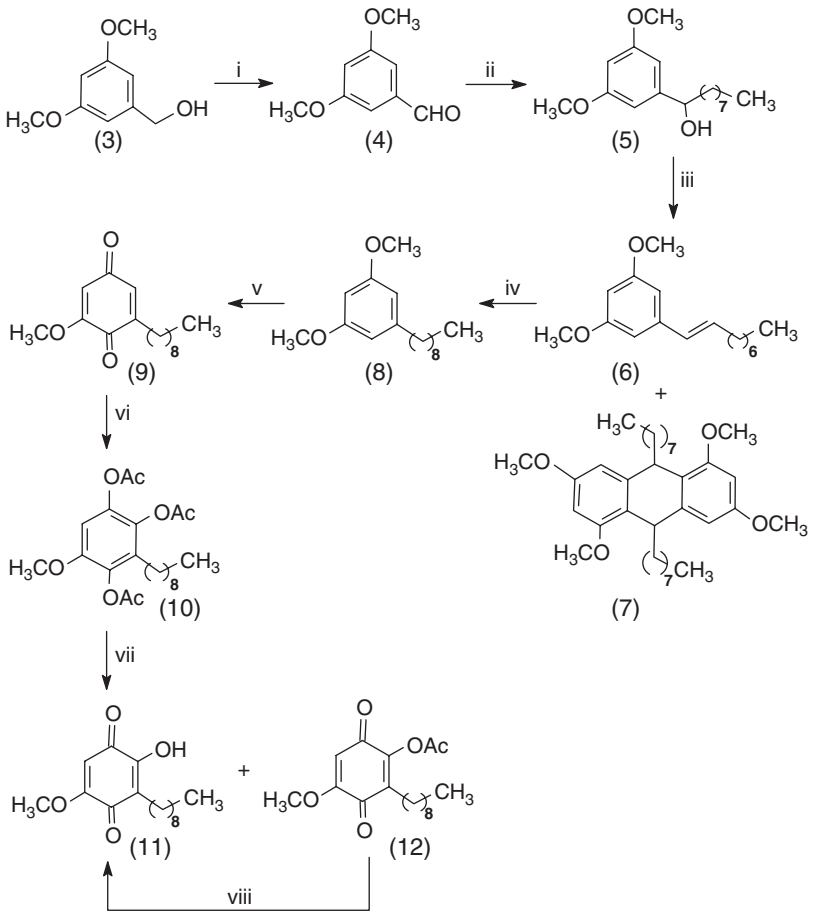


Scheme 1. Reagents and conditions: (i) $(CClO)_2$, CH_2Cl_2; DMSO, −78°C, 1.5 h; TEA, 25°C, 5 h; (ii) THF, $C_8H_{17}MgBr$, 2 h, 88%; (iii) PTSA, benzene, 60°C, 6 h, 74% of (6), 10% of (7); (iv) H_2, Pd/C 10%, ethyl acetate, 5 h, 93%; (v) CrO_3, AcOH, H_2O, 25°C, 2 d, 69%; (vi) Ac_2O, H_2SO_4, 25°C, 16 h, 82%; (vii) (a) $LiAlH_4$, THF, 70°C, 6 h; (b) $FeCl_3$, benzene, 25°C, 3 h, 8% of (11) and 37% of (12); (viii) DBU, THF, 25°C, 30 min, 64%.

none of the methoxy groups in alcohol (5) are located *para* to the alkyl chain, to facilitate the removal of the hydroxyl group.

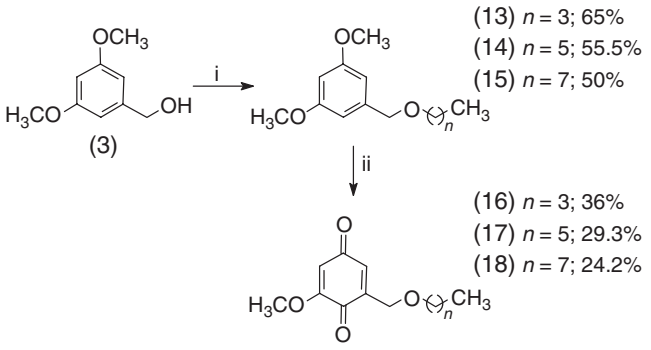
Alcohol (5) was then converted into hydrocarbon compound (8) via alkene (6). The *trans*-alkene (6), which is thermodynamically more stable than the *cis*-alkene, was prepared in 74% yield by reaction of the alcohol (5) with *p*-toluenesulphonic acid.[17] The *trans* geometry was confirmed by the ^1H coupling constant of H1′ and H2′ (J 15.7 Hz). Also isolated was the dimer (7) in 10% yield. The structures of these compounds were elucidated by IR, ^1H and ^{13}C NMR, and EIMS.

The ^1H NMR spectrum of the dimer (7) showed two doublets at the aromatic region. One at δ 6.34 (J 2.1 Hz) was assigned to H2 and H6, and one at δ 6.44 (J 2.1 Hz) to H4 and H8. Atoms H9 and H10 gave a triplet at δ 4.33 (J 3.9 Hz). This symmetric molecule showed 17 signals in its ^{13}C NMR spectrum, which corresponds to half the number of carbon atoms in its structure.

Hydrogenation of alkene (6) in the presence of 10% palladium on carbon afforded (8) in 93% yield. Compound (8) was oxidized by chromic anhydride in acetic acid and after flash column chromatography followed by recrystallization; quinone (9) was obtained as yellow crystals in 69% yield.[18,19] Thiele acetoxylation[18,19] of quinone (9) gave the triacetate (10) in 82% yield.

In the synthesis of metachromin A all three acetate groups were removed,[19] in good yield, from 1,2,4-triacetoxy-5-methoxy-3-[3-methyl-5-(1,3-dimethyl-2-methylene cyclohex-1-yl)-pent-2-enyl]benzene by $LiAlH_4$ reduction followed by $FeCl_3$ oxidation. Attempts to convert triacetate (10) into quinone (11) following this procedure afforded the required product (11) in only 8% yield and the unexpected acetylated quinone (12) in 37% yield. The saturated hydrocarbon chain in the triacetate (10) is probably hindering the acetoxy group from attack by the hydride, whereas the triacetate precursor of metachromin A, completely reduced by $LiAlH_4$, has a more rigid (*E*)-alkene geometry which could not hinder any acetoxy group.

As the yield for the synthesis of the quinone (11) from (10) was low, the conversion of the acetate (12) into (11) was attempted. Compound (12) was then treated with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in THF under nitrogen to give (11) in 64% yield.[19] Thus the overall yield for the synthesis of (11) from the triacetate (10) increased from 8% to 32%.



Scheme 2. Reagents and conditions: (i) alkyl bromide: 1-bromobutane ($n = 3$), 1-bromohexane ($n = 5$), or 1-bromooctane ($n = 7$), THF, NaH, imidazole, reflux, 6 h, 65% of (13), 56% of (14), and 50% of (15) respectively; (ii) CrO_3, AcOH, H_2O, 0°C, 30 min, 36% of (16), 29% of (17), and 24% of (18), respectively.

We envisaged that the benzylic alcohol (3) could be used to prepare more polar quinones, analogues of sorgoleone, for biological evaluation. This alcohol (3) was then converted, in good yields, into the ethers (13)–(15) according to the procedures described[21] (Scheme 2). These ethers were converted into the corresponding quinones (16)–(18) using the same methods described for the synthesis of (9).[18,19] As for the ethers, the spectroscopic data of these quinones differ from each other only by the aliphatic chain.

Bioassays

The effect of compounds (1), (9), (11), (12), and (16)–(18) at 5.5 μg g^{-1} on the development of the aerial parts and roots of *Cucumis sativus*, *Euphorbia heterophylla*, *Hyptis lophanta*, and *Brachiaria decumbens* were evaluated, and the results are shown in Table 1.

For *Cucumis sativus*, compound (9) was the only one that caused a significant inhibition (8.52%) on the development of the aerial parts; it was even more active than sorgoleone. For the roots of this plant, compounds (1), (11), (12), and (17) caused a significant growth inhibition. In this case only the acetate (12) was more active than sorgoleone. A small stimulatory effect (4.14%) was caused by compound (18).

For *Euphorbia heterophylla* only (9) showed activity with a significant root inhibition (11.86%). All the other compounds, including the natural quinone sorgoleone, were not active under the tested conditions.

For *Hyptis lophanta* none of the compounds had any effect on the root development, but compounds (9) and (11) caused a significant inhibition (8.47% in both cases) on the development of the aerial parts, although this was not significantly different from the inhibition caused by sorgoleone (1.69%). Compound (16) caused a small (8.47%) but significant stimulatory growth on the aerial parts.

For *Brachiaria decumbens* only compound (9) caused a significant inhibition (18.92%) on root development.

Although under the tested conditions none of the compounds caused a very high inhibition on the development of the roots or aerial parts of the plants, it is very important to note that some of them, especially (9), were more active than the natural herbicide sorgoleone.[6]

These results show that the triene unit in the side-chain of sorgoleone, which is difficult to prepare, is not required for biological activity. In general, the introduction of the oxygen atom at the side-chain, compounds (16)–(18), had little effect on the activity.

Table 1. Effect of quinones (1), (9), (11), (12), (16)–(18) at 5.5 μg g^{-1} on the development of roots and aerial parts of four plant species
Plants in plastic pots, using sand as substrate

Treatment (products)	Aerial parts Mass [mg][A]	Aerial parts Inhibition [%]	Roots Mass [mg][A]	Roots Inhibition [%]
Cucumis sativus				
Control	5.40^{ab}	0.00	1.69^{bc}	0.00
1	5.32^{ab}	1.48	1.58^{ef}	6.51
9	4.94^{c}	8.52	1.73^{ab}	−2.36
11	5.06^{bc}	6.29	1.55^{fg}	8.28
12	5.62^{a}	−4.07	1.53^{g}	9.47
16	5.14^{bc}	4.81	1.65^{cd}	2.36
17	5.66^{a}	−4.81	1.61^{de}	4.73
18	5.20^{bc}	3.70	1.76^{a}	−4.14
CV [%]	3.43	–	1.33	–
Euphorbia heterophylla				
Control	1.51^{a}	0.00	0.59^{a}	0.00
1	1.50^{a}	0.66	0.59^{a}	0.00
9	1.49^{a}	1.32	0.52^{b}	11.86
11	1.53^{a}	−1.32	0.61^{a}	−3.38
12	1.52^{a}	−0.66	0.62^{a}	−5.08
16	1.50^{a}	0.66	0.57^{a}	3.39
17	1.51^{a}	0.00	0.58^{a}	1.69
18	1.56^{a}	−3.31	0.58^{a}	1.69
CV [%]	1.59	–	4.15	–
Hyptis lophanta				
Control	0.59^{bc}	0.00	0.50^{a}	0.0
1	0.58^{cd}	1.69	0.48^{a}	4.0
9	0.54^{d}	8.47	0.54^{a}	−8.0
11	0.54^{d}	8.47	0.50^{a}	0.0
12	0.57^{cd}	3.39	0.47^{a}	6.0
16	0.64^{a}	−8.47	0.48^{a}	4.0
17	0.63^{ab}	−6.78	0.55^{a}	−1.0
18	0.58^{cd}	1.69	0.49^{a}	2.0
CV [%]	3.74	–	7.48	–
Brachiaria decumbens				
Control	1.40^{a}	0.00	0.74^{ab}	0.00
1	1.36^{a}	2.86	0.76^{a}	−2.70
9	1.32^{a}	5.71	0.60^{b}	18.92
11	1.32^{a}	5.71	0.74^{ab}	0.00
12	1.48^{a}	−5.71	0.74^{ab}	0.00
16	1.34^{a}	4.28	0.70^{ab}	5.40
17	1.26^{a}	10.00	0.66^{ab}	10.81
18	1.28^{a}	8.57	0.76^{a}	−2.70
CV [%]	7.83	–	9.99	–

[A] Means appearing in the same column with the same letter are not significantly different at $P = 0.05\%$ according to Tukey's test.

Conclusion

The biological tests showed that quinones like (9), which are easier to synthesize than the natural sorgoleone, showed better

activity. The chemistry described here can be used for the preparation of a larger number of quinones for structure–activity relationship studies directed towards the discovery of new compounds with potential commercial use as herbicides.

Experimental

Reagents and solvents were purified, when necessary, according to literature procedures.[11] Flash column chromatography was performed using Crosfield Sorbil C60 (32–63 μm) apparatus. The melting points were determined on a electrothermal digital apparatus with correction. Infrared spectra were recorded on a Perkin–Elmer Spectrum 1000 grating spectrometer, employing KBr disks or liquid film on NaCl. ^{1}H and ^{13}C NMR spectra were recorded in a Bruker DPX 200 (200 MHz) and Varian Mercury 300 (300 MHz) spectrometers. Tetramethylsilane was used as internal standard ($\delta = 0$) and $CDCl_3$ as solvent.

3,5-Dimethoxybenzaldehyde (4)

To a round-bottomed flask equipped with a $CaCl_2$ tube, dry CH_2Cl_2 (30 mL) and oxallyl chloride (0.60 mL, 6.5 mmol) were added. The solution was kept at −78°C and dimethyl sulfoxide (DMSO; 1 mL, 13 mmol) in dry dichloromethane (1 mL) was added. The reaction mixture was stirred for 30 min and 3,5-dimethoxybenzylic alcohol (3) (1.0 g, 6.0 mmol) was added. After 1 h, triethylamine (TEA; 4.2 mL, 30 mmol) was added and the reaction mixture stirred at room temperature for 5 h. After this time, water (40 mL) was added and the mixture extracted with CH_2Cl_2 (5 × 20 mL). The organic phase was washed with an aqueous solution of HCl (1 M, 2 × 20 mL), 5% aqueous $NaHCO_3$ (2 × 20 mL), and brine (20 mL), dried over $MgSO_4$, and concentrated under reduced pressure to yield an yellow oil. This oil was purified by flash chromatography (hexane/diethyl ether, 3 : 1 v/v) to afford the required *aldehyde* (4). White solid, 868 mg, 88% yield, mp 54–55°C. ν_{max} (film)/cm^{-1} 3525, 3500, 3400, 3000, 2800, 1710, 1600, 1475, 1375, 1350, 1300, 1200, 1060, 950, 900, 825, 700. δ_H (300 MHz) 3.80 (s, 2 × OCH_3), 6.70 (t, *J* 2.4, H4), 7.00 (d, *J* 2.4, H2, H6), 9.90 (s, CHO). δ_C (75 MHz) 55.6 (2 × OCH_3), 107.1 (C2, C6), 107.2 (C4), 138.4 (C1), 161.3 (C3, C5), 191.9 (C═O). *m*/*z* 166 ($M^{+\bullet}$, 100%), 165 (70), 137 (9), 135 (35), 95 (20), 63 (20).

1-(3,5-Dimethoxyphenyl)nonan-1-ol (5)

To a three-neck round-bottomed flask, magnesium (80 mg, 3.3 mmol) and some crystals of iodine in dry THF (2 mL) were added. The system was stirred under nitrogen for 20 min, when 1-bromooctane (0.5 mL, 3.0 mmol) dissolved in dry THF (10 mL) was added. When half of this solution had been added, it was diluted with a further 10 mL of THF before completing the addition of 1-bromooctane. The formation of the Grignard reagent was indicated when the reaction mixture changed from yellow to grey. After 20 min, 3,5-dimethoxybenzaldehyde (4) (100 mg, 0.60 mmol) in dry THF (2 mL) was added. Saturated NH_4Cl (15 mL) was added to the reaction mixture after 2 h, and the organic solvent evaporated in the rotary evaporator. The residue was extracted with CH_2Cl_2 (4 × 20 mL), and the combined organic layers were washed with brine (2 × 20 mL). The dichloromethane solution was dried with anhydrous $MgSO_4$ and concentrated in the rotary evaporator giving an yellow oil. This oil was purified by flash column chromatography eluting with hexane/diethyl ether (2 : 1 v/v) affording the desired *alcohol* (5). 149 mg, 88% yield. ν_{max} (film)/cm^{-1} 3380, 2930, 2850, 1600, 1450, 1375, 1200, 1150, 1060, 850. δ_H (300 MHz) 0.87 (t, *J* 7.2, CH_3), 1.21–1.28 (m, 6 × CH_2), 1.52 (q, *J* 6.6, H2), 1.75 (sl, OH), 3.77 (s, 2 × OCH_3), 4.59 (t, *J* 6.4, H1), 6.35 (t, *J* 2.1, H4′), 6.48 (d, *J* 2.1, H2′, H6′). δ_C (75 MHz) 14.3 (C9), 22.9 (C8), 26.0 (C3), 29.5 (C5*), 29.6 (C4*), 32.1 (C6), 33.0 (C7), 39.2 (C2), 55.5 (2 × OCH_3), 77.9 (C1), 99.3 (C4′), 104.0 (C2′, C6′), 147.6 (C1′), 160.8 (C3′, C5′). * The assignments could be inverted. *m*/*z* 97 (4%), 84 (20), 69 (50), 56 (100).

1,3-Dimethoxy-5-[(E)-non-1-en-1-yl]benzene (6) and 1,3,5,7-Tetramethoxy-9,10-(dioct–1-yl)-9,10-dihydroanthracene (7)

To a two-neck round-bottomed flask, 1-(3,5-dimethoxyphenyl)nonan-1-ol (5) (500 mg, 1.78 mmol) dissolved in benzene (20 mL) was added, followed by *p*-toluenesulphonic acid (PTSA; ∼50 mg). The mixture was stirred at 60°C for 6 h, diluted with ethyl acetate (20 mL), then washed with distilled water (2 × 15 mL) and brine (2 × 15 mL). The organic layer was dried with anhydrous $MgSO_4$, filtered, and the filtrate concentrated to give an oil. This oily residue was purified by flash column chromatography eluting with a mixture of hexane/diethyl ether (40 : 1 v/v) to afford the *alkene* (6) (yellow oil, 345 mg, 74% yield) and the *dimer* (7) (white crystals, 47.8 mg, 10% yield).

(6) ν_{max} (film)/cm^{-1} 2998, 2925, 2853, 1594, 1450, 1426, 1340, 1270, 1200, 1150, 1068, 850. δ_H (200 MHz) 0.88 (t, *J* 6.7, CH_3), 1.28–1.45 (m, 5 × CH_2), 2.19 (ql, *J* 6.1, H3′), 3.85 (s, 2 × OCH_3), 6.19 (dt, *J* 15.7, 6.1, H2′), 6.31 (d, *J* 15.7, H1′), 6.32 (t, *J* 2.3, H2), 6.5 (d, *J* 2.3, H4, H6). δ_C (50 MHz) 14.1 (C9′), 22.7 (C7′, C8′), 29.2 (C5′*), 29.3 (C6′*), 31.9 (C4′), 33.0 (C3′), 55.3 (2 × OCH_3), 99.1 (C2), 103.1 (C4*), 104.0 (C6*), 129.7 (C2′), 131.9 (C1′), 140.0 (C5), 160.8 (C1, C3). * The assignments could be inverted. *m*/*z* 262 ($M^{+\bullet}$, 10%), 191 (20), 177 (20), 164 (10), 152 (100), 121 (8), 91 (40).

(7) mp 116–116.5°C (found: C, 77.71; H, 10.14%; $C_{32}H_{48}O_4$ requires C, 77.38; H, 9.74%). ν_{max} (KBr)/cm^{-1} 2995, 2949, 2922, 2854, 1607, 1585, 1486, 1435, 1350, 1270, 1220, 1150, 1100, 950, 850. δ_H (300 MHz) 0.45–0.56 (m, 2 × CH_2, H3′), 0.82 (t, *J* 6.8, 2 × CH_3), 0.9–1.7 (m, 12 × CH_2), 2.0–2.2 (m, 2 × CH_2, H1′), 3.83 (s, 3-OCH_3, 7-OCH_3*), 3.86 (s, 1-OCH_3, 5-OCH_3*), 4.33 (t, *J* 3.7, H9, H10), 6.34 (d, *J* 2.1, H2, H6), 6.44 (d, *J* 2.1, H4, H8). δ_C (75 MHz) 14.1 (C8′), 22.6 (C7′*), 23.4 (C3′*), 29.2 (C4′*), 29.2 (C2′*), 29.8 (C5′*), 31.8 (C6′*), 37.4 (C9, C10), 38.4 (C1′), 55.1 (2 × OCH_3*), 55.2 (2 × OCH_3*), 96.2 (C2, C6), 103.1 (C4, C8), 119.2 (C12, C13), 140.5 (C11, C14), 157.2 (C1, C5), 158.2 (C3, C7). * The assignments could be inverted.

1,3-Dimethoxy-5-(non-1-yl)benzene (8)

The alkene (6) (100 mg, 0.38 mmol) was dissolved in ethyl acetate (6 mL) in a round-bottomed flask followed by addition of 10% Pd/C (10 mg). The mixture was stirred magnetically under an H_2 atmosphere for 5 h. The catalyst was filtered and the solution concentrated in a rotary evaporator to give (8) as an yellow oil (93.3 mg, 93% yield). ν_{max} (film)/cm^{-1} 2930, 2880, 1600, 1420, 1380, 1300, 1200, 1160, 1120, 1060, 820. δ_H (200 MHz) 0.87 (t, *J* 6.7, CH_3), 1.26–1.40 (m, 6 × CH_2), 1.55–1.59 (m, H2′), 2.54 (dd, *J* 7.3, 8.0, H1′), 3.73 (s, 2×OCH_3), 6.28 (t, *J* 2.2, H2), 6.34 (d, *J* 2.2, H4, H6). δ_C (50 MHz) 14.1 (C9′), 22.7 (C8′), 29.4 (C3′*), 29.6 (C4′*), 29.6 (C5′, C6′*), 31.3 (C2′), 31.9 (C7′), 36.3 (C1′), 55.2 (2 × OCH_3), 97.5 (C2), 106.5 (C4, C6), 145.4 (C5), 160.7 (C1, C3. * The assignments could be inverted. *m*/*z* 264 ($M^{+\bullet}$, 3%), 194 (2), 165 (10), 152 (100), 91 (10), 77 (15).

2-Methoxy-6-(non-1-yl)-benzo-1,4-quinone (9)

To a round-bottomed flask chromic anhydride (773 mg, 7.57 mmol), acetic acid (15 mL) and a few drops of distilled water was added, up to complete dissolution. The oxidizing mixture was stirred at 0°C for 30 min. This mixture was then transferred to another round-bottomed flask containing (8) (1.0 g, 3.78 mmol) dissolved in acetic acid (6 mL). The reaction mixture was stirred at room temperature for 2 d. The mixture was diluted with distilled water (20 mL) and extracted with CH_2Cl_2 (4 × 20 mL). The combined organic layers were washed with brine (2 × 20 mL), dried with anhydrous magnesium sulfate, filtered, and concentrated in the rotary evaporator. The yellow oil was purified by flash column chromatography (hexane/diethyl ether, 5 : 1) to give the *quinone* (9), which was recrystallized in a mixture of dichloromethane/hexane (yellow crystals, 690 mg, 69% yield). mp 69.0–69.8°C. ν_{max} (KBr)/cm^{-1} 2912, 2850, 1681, 1653, 1602, 1473, 1241, 1177, 1042, 906. δ_H (200 MHz) 0.87 (t, *J* 6.7, CH_3), 1.26–1.66 (m, 7 × CH_2), 2.46 (dt, *J* 1.3, 6.8, H1′), 3.81 (s, OCH_3), 5.88 (d, *J* 2.3, H3), 6.48 (dt, *J* 2.3, 1.3, H5). δ_C (50 MHz) 14.1 (C9′), 22.7 (C8′), 27.7 (C2′*), 28.7 (C3′*), 29.2 (C1′*), 29.3 (C4′*), 29.3 (C6′*), 29.4 (C5′*), 31.9 (C7′), 56.3 (OCH_3), 107.1 (C3), 132.9 (C5), 147.6 (C6), 158.9

(C2), 182.1 (C4), 187.7 (C1). * The assignments could be inverted. m/z 264 ($M^{+\bullet}$, 5%), 179 (10), 158 (50), 124 (15), 109 (15), 69 (100), 53 (80).

1,2,4-Triacetoxy-5-methoxy-3-(non-1-yl)benzene (10)

To a round-bottomed flask, quinone (9) (500 mg, 1.89 mmol), acetic anhydride (10 mL), and concentrated sulfuric acid (5 drops) was added. The reaction mixture was stirred at room temperature for 16 h. The mixture was cooled to 0°C, diluted with distilled water (20 mL) and extracted with diethyl ether (4 × 20 mL). The combined organic layers was washed with distilled water (2 × 15 mL) and $NaHCO_3$ 5% (2 × 15 mL). The ethereal solution was dried with anhydrous $MgSO_4$, filtered, and concentrated in the rotary evaporator. The residue was purified by flash column chromatography (hexane/diethyl ether, 3 : 2 v/v) to afford (10) as an yellow oil (633 mg, 82% yield). ν_{max} (film)/cm^{-1} 2926, 2926, 2854, 1770, 1598, 1480, 1380, 1270, 1100, 1000, 930. δ_H (200 MHz) 0.87 (t, J 6.5, CH_3), 1.25–1.41 (m, 7 × CH_2), 2.26 (s, 1-CH_3*), 2.29 (s, 2-CH_3*), 2.31 (s, 4-CH_3*), 2.41 (dd, J 7.0, 8.3, H1′), 3.78 (s, OCH_3), 6.79 (s, H6). δ_C (50 MHz) 14.0 (C9′), 20.2 (C8′), 20.4 (1-CH_3*), 20.7 (4-CH_3*), 22.6 (2-CH_3), 25.3 (C8′), 28.9 (C2′*), 29.2 (C3′*), 29.3 (C4′), 29.4 (C5′*), 29.6 (C6′*), 31.9 (C7′), 56.2 (OCH_3), 104.8 (C6), 130.2 (C3), 135.9 (C4), 140.2 (C2), 149.2 (C1, C5), 168.1 (1-C═O*), 168.3 (2-C═O*), 168.4 (4-C═O). * The assignments could be inverted.

2-Hydroxy-5-methoxy-3-(non-1-yl)benzo-1,4-quinone (11) and 2-Acetoxy-5-methoxy-3-(non-1-yl)benzo-1,4-quinone (12)

To a two-neck round-bottomed flask $LiAlH_4$ (85 mg, 2.12 mmol) and dry THF (20 mL) were added and stirred under an N_2 atmosphere. To this mixture was added (10) (300 mg, 1.06 mmol) dissolved in dry THF (5 mL). The reaction mixture was stirred at 70°C for 6 h. The heating source was removed and ethyl acetate (5 mL) was added to the reaction mixture to destroy the unreacted $LiAlH_4$. The mixture was diluted with distilled water (15 mL) and the organic solvents were removed in the rotary evaporator. The aqueous residue was extracted with CH_2Cl_2 (4 × 10 mL) and the combined organic layers was washed with brine (2 × 10 mL). The CH_2Cl_2 solution was dried with anhydrous $MgSO_4$, filtered, and concentrated in the rotary evaporator yielding an yellow solid (89% yield).

To a solution of this solid in benzene (5 mL), 1% $FeCl_3$ (3.0 mL) was added. The reaction mixture was stirred at room temperature for 3 h, and then extracted with ethyl acetate (4 × 10 mL). The combined organic layers was washed with brine (2 × 10 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated in the rotary evaporator. The residue obtained was purified by flash column chromatography (hexane/diethyl ether, 1 : 2 v/v) giving (11) as yellow crystals (17.3 mg, 8% yield) and (12) as orange crystals (88.9 mg, 37% yield).

Conversion of (12) into (11)

A mixture of the monoacetate (12) (80 mg, 0.24 mmol) and DBU (3 drops) dissolved in dry THF (10 mL) was stirred at room temperature for 30 min. The reaction was quenched with 2 M HCl (5 mL). The mixture was extracted with CH_2Cl_2 (3 × 20 mL), dried over anhydrous $MgSO_4$, and filtered. The filtrate was concentrated in the rotary evaporator and the residue was purified by flash column chromatography (hexane/diethyl ether, 1 : 1 v/v) to give (11) as yellow crystals (43.8 mg, 63% yield).

(11) mp 89.5–90.9°C. ν_{max} (KBr)/cm^{-1} 3344, 2920, 2851, 1661, 1635, 1597, 1443, 1384, 1312, 1205, 1115, 1067. δ_H (300 MHz) 0.87 (t, J 6.6, CH_3), 1.25–1.68 (m, 7 × CH_2), 1.44–1.59 (s, OH), 2.44 (dd, J 6.9, 7.8, H1′), 3.86 (s, OCH_3), 5.99 (s, H6). δ_C (75 MHz) 14.1 (C9′), 22.6 (C1′), 22.7 (C8′), 28.1 (C2′), 29.3 (C3′), 29.4 (C4′*), 29.5 (C5′*), 29.6 (C6′*), 31.9 (C7′), 56.8 (OCH_3), 102.2 (C6), 119.3 (C3), 151.6 (C5), 161.1 (C2), 181.7 (C1), 182.9 (C4). * The assignments could be inverted.

Compound (12) mp 115.7–117.4°C. ν_{max} (KBr)/cm^{-1} 3064, 2949, 2917, 2850, 1763, 1684, 1654, 1588, 1369, 1233, 1194, 1161. δ_H (300 MHz) 0.87 (t, J 6.7, H9′), 1.17–1.48 (m, 7 × CH_2), 2.33 (s, O_2CCH_3), 2.38 (dd, J 7.0, 7.7, H1′), 3.85 (s, OCH_3), 5.73 (s, H6). δ_C (75 MHz) 14.1 (C9′), 20.2 (O_2CCH_3), 22.7 (C2′), 23.9 (C8′), 28.2 (C1′), 29.2 (C3′*), 29.3 (C4′*), 29.4 (C5′*), 29.5 (C6′*), 31.9 (C7′), 57.1 (OCH_3), 101.1 (C6), 133.1 (C3), 151.1 (C5), 164.2 (C2), 167.7 (C1), 178.1 (O_2CCH_3), 179.4 (C4). * The assignments could be inverted.

1-(Butoxymethyl)-3,5-dimethoxybenzene (13)

A mixture of 3,5-dimethoxybenzylic alcohol (400 mg, 2.37 mmol), imidazole (80 mg), and NaH 80% (213 mg, 7.11 mmol) in dry THF (20 mL) was refluxed under an N_2 atmosphere for 6 h. KI (0.05 g) and 1-bromobutane (649 g, 4.74 mmol) were added to the reaction mixture. The reaction mixture was stirred at 70°C for a further 3 h and then for 12 h at room temperature. Distilled water (20 mL) was added to the mixture and it was extracted with CH_2Cl_2 (4 × 20 mL). The combined organic layers was washed with brine (2 × 20 mL), dried over anhydrous $MgSO_4$, and filtered. The filtrate was concentrated in the rotary evaporator and the residue was purified by flash column chromatography eluting with hexane/diethyl ether (20 : 1 v/v) to give the *ether* (13) as an yellow oil (345 mg, 65% yield). ν_{max} (film)/cm^{-1} 2957, 2934, 2865, 2800, 1598, 1464, 1430, 1361, 1320, 1205, 1155, 1103, 1067, 823. δ_H (300 MHz) 0.83 (t, J 7.0, CH_3), 1.2–1.6 (m, 2 × CH_2), 3.47 (t, J 6.6, H2′), 3.81 (s, 2 × OCH_3), 4.42 (s, H1′), 6.38 (t, J 2.1, H2), 6.51 (d, J 2.4, H4, H6). δ_C (75 MHz) 14.0 (C5′), 19.4 (C4′), 31.9 (C3′), 55.3 (2 × OCH_3), 70.2 (C2′), 72.8 (C1′), 99.5 (C2), 105.2 (C4, C6), 148.0 (C5), 160.8 (C1, C3). m/z 224 ($M^{+\bullet}$, 2%), 167 (2), 152 (100), 139 (5), 123 (5), 91 (20), 77 (30).

1-[(Hexyloxy)methyl]-3,5-dimethoxybenzene (14)

As described above in the synthesis of (13), the reaction of (3) (600 mg, 3.55 mmol), 80% NaH (333 mg, 8.88 mmol), and 1-bromohexane (1.46 g, 8.85 mmol) afforded (14) as an yellow oil (497 mg, 56% yield). ν_{max} (film)/cm^{-1} 2956, 2931, 2857, 1597, 1458, 1429, 1298, 1205, 1155, 1104, 1066, 832. δ_H (300 MHz) 0.88 (t, J 7.2, CH_3), 1.25–1.66 (m, 4 × CH_2), 3.45 (t, J 6.6, H2′), 3.82 (s, 2 × OCH_3), 4.40 (s, H1′), 6.37 (t, J 2.1, H2), 6.50 (d, J 2.1, H4, H6). δ_C (75 MHz) 14.3 (C7′), 22.9 (C6′), 26.2 (C4′), 30.0 (C3′), 32.0 (C5′), 55.6 (2 × OCH_3), 70.8 (C2′), 73.0 (C1′), 99.8 (C2), 105.5 (C4, C6), 141.4 (C5), 161.0 (C1, C3). m/z 166 (2%), 152 (100), 139 (5), 123 (5), 91 (20), 77 (30).

1,3-Dimethoxy-5-[(octyloxy)methyl]benzene (15)

As described above in the synthesis of (13), the reaction of (3) (500 mg, 2.96 mmol), 80% NaH (222 mg, 7.41 mmol), and 1-bromooctane (1.40 g, 7.41 mmol) gave (15) as an yellow oil (416 mg, 50% yield). ν_{max} (film)/cm^{-1} 2998, 2927, 2854, 1598, 1464, 1429, 1359, 1295, 1204, 1155, 1105, 1067, 832. δ_H (300 MHz) 0.87 (t, J 6.9, CH_3), 1.26–1.67 (m, 6 × CH_2), 3.45 (t, J 6.8, H2′), 3.82 (s, 2 × OCH_3), 4.40 (s, H1′), 6.37 (t, J 2.4, H2), 6.50 (d, J 2.1, H4, H6). δ_C (75 MHz) 14.1 (C9′), 22.7 (C8′), 26.2 (C4′), 29.3 (C6′*), 29.4 (C3′*), 29.8 (C5′*), 31.8 (C7′), 55.3 (2 × OCH_3), 70.5 (C2′), 72.7 (C1′), 99.5 (C2), 105.2 (C4, C6), 141.2 (C5), 160.8 (C1, C3). * The assignments could be inverted. m/z 280 ($M^{+\bullet}$, 2%), 152 (100), 91 (20), 77 (25).

2-(Butoxymethyl)-6-methoxybenzo-1,4-quinone (16)

To a round-bottomed flask chromic anhydride (340 mg, 3.33 mmol), acetic acid (10 mL), and a few drops of distilled water were added up to complete dissolution of the chromic anhydride. The mixture was stirred at 0°C for 30 min. This mixture was transferred to another round-bottomed flask containing (13) (300 mg, 1.33 mmol) dissolved in acetic acid (10 mL). The reaction mixture was stirred at room temperature for 30 h. Distilled water (20 mL) was added to the mixture and it was extracted with CH_2Cl_2 (4 × 20 mL). The combined organic layers was washed with brine (2 × 10 mL), dried over anhydrous $MgSO_4$, and filtered. The filtrate was concentrated in the rotary evaporator and the residue purified by flash column chromatography (hexane/diethyl ether 3 : 1 v/v) to give the *quinone* (16) as an yellow oil (108 mg, 36% yield). ν_{max} (film)/cm^{-1} 2958, 2870, 1677, 1652, 1602, 1458, 1293, 1244, 1183, 1053, 904. δ_H (300 MHz) 0.94 (t, J 7.2, CH_3), 1.26–1.64 (m, 2 × CH_2), 3.55 (t, J 6.6, H2′), 3.83 (s, OCH_3), 4.35 (d, J 2.1, H1′), 5.90 (d, J 2.4, H3), 6.77 (q, J 2.1, H5). δ_C (75 MHz) 13.7 (C5′), 19.3 (C4′), 31.7 (C3′), 56.3 (OCH_3), 65.8 (C2′), 71.4 (C1′), 107.3 (C3), 132.0

(C5), 144.0 (C6), 158.7 (C2), 181.6 (C4), 187.3 (C1. m/z 168 (50%), 152 (10), 140 (20), 123 (30), 95 (20), 69 (100), 57 (80).

2-[(Hexyloxy)methyl]-6-methoxybenzo-1,4-quinone (17)

As described above in the synthesis of (16), the reaction of (14) (500 mg, 1.98 mmol) and chromic anhydride (398 mg, 3.90 mmol) afforded (17) as an yellow oil (147 mg, 29% yield). ν_{max} (film)/cm^{-1} 3068, 2933, 2860, 1676, 1652, 1626, 1600, 1466, 1353, 1322, 1237, 1181, 1137, 1041, 910. δ_H (300 MHz) 0.88 (t, J 7.0, CH_3), 1.22–1.41 (m, 3 × CH_2), 1.58–1.64 (m, H3′), 3.53 (t, J 6.3, H2′), 3.83 (s, OCH_3), 4.35 (d, J 2.1, H1′), 5.90 (d, J 2.1, H3), 6.76 (q, J 2.1, H5). δ_C (75 MHz) 14.0 (C7′), 22.6 (C6′), 25.8 (C4′*), 29.6 (C3′*), 31.6 (C5′*), 56.3 (OCH_3), 65.7 (C2′), 71.7 (C1′), 107.3 (C3), 132.0 (C5), 144.0 (C6), 158.6 (C2), 181.6 (C4), 187.3 (C1). * The assignments could be inverted. m/z 168 (75%), 152 (20), 140 (17), 123 (30), 95 (25), 80 (30), 69 (100), 55 (90).

2-Methoxy-6-[(octyloxy)methyl]benzo-1,4-quinone (18)

As described above in the synthesis of (16), the reaction of (15) (389 mg, 1.38 mmol) and chromic anhydride (353 mg, 3.46 mmol) afforded (18) as yellow crystals (94 mg, 24% yield). mp 44.8–45.9°C. ν_{max} (KBr)/cm^{-1} 2927, 2854, 1678, 1653, 1604, 1465, 1354, 1314, 1233, 1183, 1127, 1052, 906. δ_H (300 MHz) 0.88 (t, J 7.2, CH_3), 1.21–1.40 (m, 5 × CH_2), 1.57–1.68 (m, H3′), 3.53 (t, J 6.6, H2′), 3.82 (s, OCH_3), 4.35 (d, J 2.1, H1′), 5.90 (d, J 2.4, H3), 6.76 (q, J 2.4, H5). δ_C (75 MHz) 14.1 (C9′), 22.6 (C8′), 26.1 (C7′*), 29.2 (C4′*), 29.6, (C6′*), 29.7 (C5′*), 31.8 (C3′*), 56.3 (OCH_3), 65.7 (C2′), 71.7 (C1′), 107.3 (C3), 132.0 (C5), 144.0 (C6), 158.6 (C2), 181.6 (C4), 187.4 (C1). * The assignments could be inverted. m/z 168 (40%), 152 (30), 124 (35), 95 (30), 69 (80), 55 (100), 56 (60).

Bioassays

The experiments were carried out in a greenhouse with *Cucumis sativus*, *Brachiaria decumbens*, *Hyptis lophanta*, and *Euphorbia heterophylla*. The bioassays for herbicide activity were carried out for quinones (1), (9), (11), (12), and (16)–(18) using plastic pots, and the total growth of the test plants evaluated.

The test solution was prepared by dissolving 5.0 mg of each quinone in a mixture of xylene (60 μL), pentan-3-one (20 μL), and Tween 40 (2 drops). The volume of the resulting mixture was diluted to 100 mL with distilled water.[11] A solution with the same composition described above, but without the test compound, was used as a control.

To plastic pots, of 0.10 dm^3 volume containing 165 g of washed sand soaked in 20 mL of the test solution, ten seeds of each test plant were placed at 0.5–1.0 cm depth. The pots were kept in a greenhouse at 25°C, watered regularly to maintain the humidity at 12% w/w, and, three times a week, a solution containing the required nutrients was applied.

The test plants *Cucumis sativus*, *Brachiaria decumbens*, and *Euphorbia heterophylla* were harvested 15 days after sowing. *Hyptis lophanta* was harvested 20 days after sowing. The harvest was done by separating the radicle from the aerial parts. These parts were kept separately in paper bags and dried at 75°C until constant weight and the mass of the dried matter determined. The data were analyzed using Tukey's test at 0.05 probability levels. All treatments were replicated six times in a completely randomized design. The percentage of roots and aerial parts growth inhibition were calculated in relation to the mass of the roots and aerial parts growth inhibition of the control, respectively.

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