HETEROCYCLES, Vol. 102, No. 4, 2021, pp. -. © 2021 The Japan Institute of Heterocyclic Chemistry
Received, 22nd December, 2020, Accepted, 8th February, 2021, Published online, 18th February, 2021
DOI: 10.3987/COM-20-14398

SYNTHESIS OF 4-HYDROXYAURONES AND THEIR HERBICIDAL ACTIVITIES

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Abstract – A series of 4-hydroxyaurone derivatives **4a**-**4v** were synthesized and characterized by ^{1}H NMR, ^{13}C NMR, and elemental analysis. Their herbicidal activities against four species of plants were evaluated in a greenhouse by both pre- and post-emergence treatments at a dosage of 750 g a.i. ha^{-1}. The bioassay revealed that 4-hydroxyaurones exhibited moderate to good herbicidal activities against dicotyledons plants for post-emergence treatment. For instance, (*Z*)-4-hydroxy-2-(4-nitrobenzylidene)benzofuran-3(2*H*)-one (**4m**), demonstrated 74.5% inhibitory activity against *Amaranthus retroflexus* L., higher than that of the positive control herbicide acetochlor. Thus, compound **4m** may serve as a new possible leading compound for the discovery of post-emergence herbicide.

INTRODUCTION

Aurones, the derivatives of 2-benzylidene-3(2*H*)-benzofuranone, which belong to natural flavonoid compounds, mainly distribute in fruits and flowers, making them emerge bright yellow. Recent studies had shown that aurones possessed extensive biological activities, such as anti-cancer activity, anti-viral activity, anti-inflammatory activity, and herbicidal activity.[1-4] However, the herbicidal activities of aurones are greatly underexplored, according to the literature we have investigated. Our group has been engaged in the synthesis and herbicidal activities of aurones including 4,6-dihydroxyaurones, 6-hydroxyaurones, and their derivatives. The results showed that most of those aurones owned considerable herbicidal activities against dicotyledonous plants.[4-6] Further study on the relationship between structure and herbicidal activities of aurones necessitate the design, synthesis, and bioassay of new 2-benzylidene-3(2*H*)-benzofuranone, e.g., 4-hydroxyaurones.

To date, only a few of literatures concerning 4-hydroxyaurones had been reported, which described several application potentials including anti-viral activity and the inhibition of human tyrosinase activity.[7-11] Research also proved that the introduction of a hydroxyl group at 4-position of aurone ring A was beneficial to improving biological activity in comparison with unsubstituented aurones or at other site of this scaffold.[7,9,10] More interestingly, 4-hydroxyaurones may inhibit 4-hydroxyphenylpyruvate dioxygenase (HPPD), a non-heme oxidase with Fe^{2+} as the active center,[12] because the oxygens of 3, 4-positions of 4-hydroxyaurones may form coordination interactions with Fe^{2+},[13] and the ring B may be involved in π-π stacking interaction with phenylalanine residue (Figure 1).[14]

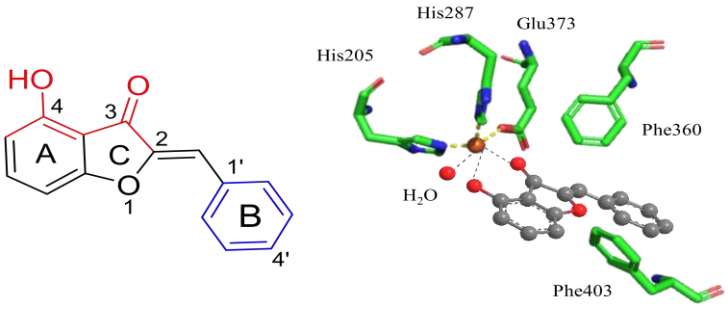


Figure 1. 4-Hydroxyaurone and simulated binding model of 4-hydroxyaurone with *At*HPPD

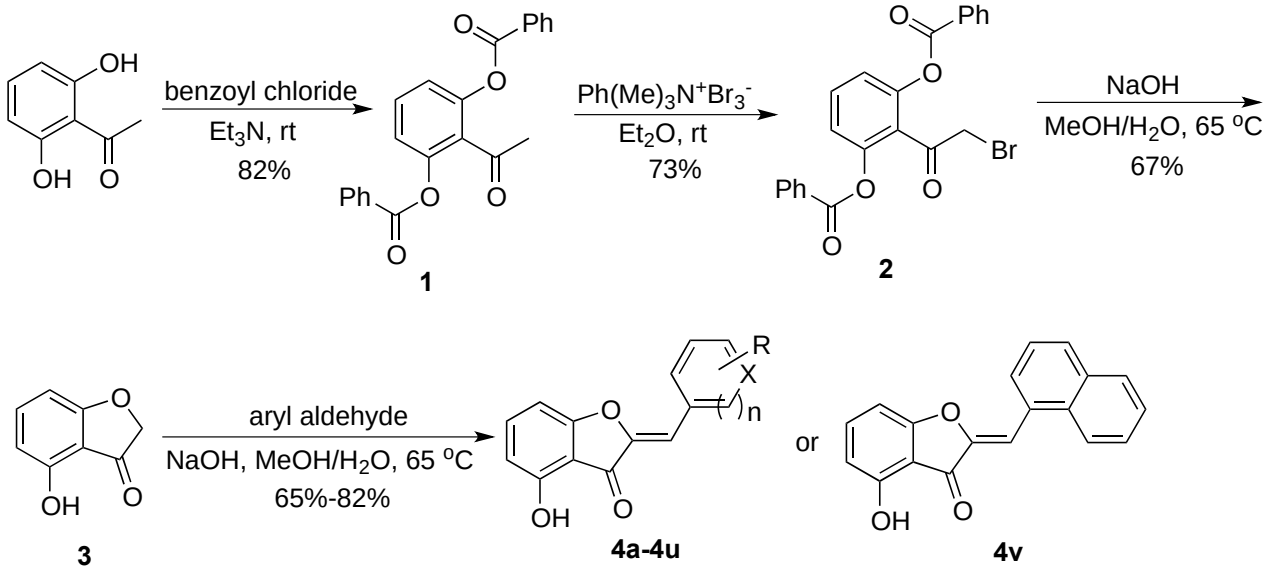
In this paper, the synthesis of 4-hydroxyaurones with different substituents on B ring was described and their herbicidal activities were evaluated through greenhouse tests against four species of plants in both post- and pre- emergence treatments using the previous research methods.[4]

RESULTS AND DISCUSSION

Synthesis.

As shown in Scheme 1, compound **1** was prepared from 1-(2,6-dihydroxyphenyl)ethan-1-one using benzoyl chloride in the presence of dry triethylamine,[15,16] followed by bromination of the α-position of the carbonyl with phenyltrimethylammonium tribromide to give intermediate **2**, then hydrolysis and cyclization in MeOH/H_2O in the presence of sodium hydroxide at 65 °C to give the key intermediate, 4-hydroxybenzofuran-3(2*H*)-one **3**.[17,18] The target aurones **4a**-**4v** were achieved by the condensation of **3** and aryl aldehydes under the alkaline condition.[8,19-21] Most of the target compounds were characterized by ^{1}H NMR, ^{13}C NMR, and elementel analysis. The ^{1}H chemical shifts of exocyclic =CH protons in all compounds appeared at δ 6.40-6.78 ppm except **4t** and **4v**, which were consistent with the reported values

for (*Z*)-aurones.[4,6,22] However, compounds **4t** and **4v** had chemical shifts of δ 6.96 and 7.29 ppm for their exocyclic =CH protons, respectively, and were also assigned *Z* configuration, for the down field shift of exocyclic =CH protons may be due to the anomalous ortho effect.[23]



Compds	n	X	R	Compds	n	X	R
4a	1	CH	H	**4l**	1	CH	3′ -Br
4b	1	CH	4′ -OMe	**4m**	1	CH	4′ -NO_2
4c	1	CH	3′ ,4′ -$(OMe)_2$	**4n**	1	CH	4′ -CN
4d	1	CH	2′ -Me	**4o**	1	CH	4′ -$N(Me)_2$
4e	1	CH	3′ -Me	**4p**	1	CH	4′ -OH
4f	1	CH	4′ -Me	**4q**	1	CH	4′ -F
4g	1	CH	4′ -$CH(Me)_2$	**4r**	1	CH	3′ -F
4h	1	CH	5′ -Br-2′ -OMe	**4s**	1	N	H
4i	1	CH	2′ -Cl-6′ -F	**4t**	0	S	H
4j	1	CH	2′ ,4′ -Cl_2	**4u**	0	O	5'-Me
4k	1	CH	4′ -Cl				

Scheme 1. Syntheses of 4-hydroxyaurones

Herbicidal activity.

The herbicidal activities of the title aurones were evaluated by both pre- and post-emergence treatments in greenhouse with *Echinochloa crusgalli* L. (*E. crusgalli*) and *Digitaria sanguinalis* L. (*D. sanguinalis*) as monocotyledons species, and *Brassica campestris* L. (*B. campestris*) and *Amaranthus retroflexus* L. (*A.*

retroflexus) as dicotyledons species at the dosage of 750 g a.i. ha^{-1} according to the reported procedure.[4] The results are listed in Table 1.

Table 1. Effects of 4-hydroxyaurones against 4 plants with pre- and post-emergence treatments

Compds	Pre-emergence treatment				Post-emergence treatment			
	B. campestris	*A. retroflexus*	*E. crusgalli*	*D. sanguinalis*	*B. campestris*	*A. retroflexus*	*E. crusgalli*	*D. sanguinalis*
4a	3.5	0	0	0	0	53.5	39.7	0
4b	3.2	0	54.4	21.7	0	0	17.9	15.7
4c	24.5	0	36.0	0	0	35.2	31.0	0
4d	10.5	0	24.4	6.1	0	26.3	14.7	4.3
4e	6.2	0	0.5	0	0	31.7	0	0
4f	31.2	0	2.0	0	10.0	11.6	0	0
4g	36.7	8.1	20.7	0	0	22.0	0	16.4
4h	34.2	36.1	7.4	1.3	0	29.1	7.6	0.9
4i	30.3	0	21.1	8.4	0	16.8	20.8	0
4j	36.7	34.0	26.1	1.3	0	10.5	0	0
4k	0	0	2.5	0	0	51.5	0	16.2
4l	0	20.7	6.0	0	0	34.0	12.4	18.9
4m	8.7	0.0	35.1	0	0	74.5	0	5.5
4n	8.7	11.9	3.0	0	39.4	0	0	0
4o	0	0	7.1	0	37.8	15.5	4.2	0
4p	16.8	10.0	20.0	0	26.7	7.2	0	0
4q	0.2	11.9	0	0	51.8	8.5	0	0
4r	8.7	11.9	12.3	0	29.9	0	0	0
4s	4.1	0.6	30.9	0	40.5	16.1	0	0
4t	0	0	19.4	1.2	19.8	14.0	24.6	0
4u	3.8	0	11.3	6.6	18.5	9.1	28.6	0
4v	0	28.8	12.7	0	43.2	35.2	0	0
Acetochlor	38.5	100	100	100	24.6	55.8	57.7	28.0
Mesotrione[a]	100	100	100	100	100	100	87.0	96.6

[a] Application rate: 250 g a.i. ha^{-1}

As shown in Table 1, most of 4-hydroxyaurones were active to inhibit the growth of monocotyledons and dicotyledons plants for pre- and post-emergence treatments. For instance, the inhibitory activity of compound **4b** reached 54.4% against *E. crusgalli* for pre-emergence treatment, and that of **4m** against *A. retroflexus* for post-emergence treatment was 74.5%. Moreover, it was also found that the target compounds had higher inhibitory effects on dicotyledonous plants than on monocotyledons plants, especially for post-emergence treatment. Compounds **4k**-**4v** exhibited moderate to good herbicidal activities against dicotyledonous plants for post-emergence treatment. Among them, compound **4q** (51.8%), **4n** (39.4%), **4s** (40.5%), and **4v** (43.2%) presented better herbicidal activity against *B. campestris* than commercial herbicide acetochlor (24.6%). Moreover, some of the title compounds displayed better inhibition activity against *A. retroflexus* for post-emergence treatment than other three plants, for example, the inhibition rate of compounds **4a** and **4k** were 53.5% and 51.5%, respectively, equal to that of acetochlor. Interestingly, the inhibition rate of **4m** against *A. retroflexus* for

post-emergence treatment was 74.5%, significantly higher than that of acetochlor (55.8%). Furthermore, the herbicidal activity of **4m** was better than 6-hydroxyaurones and 4,6-disubstituted aurones,[4,5] and the most active compound of them only exhibited 42.2% inhibition for *A. retroflexus* at the dosage of 1500 g a.i. ha^{-1}. However, when compared with mesotrione, a broad-spectrum selective herbicide for inhibiting HPPD,[24] the title aurones showed weak herbicidal activity, indicating that the target compounds might not be the effective HPPD inhibitors.

From Table 1, it was also found that the substituent on ring B could influence the herbicidal activity. The herbicidal activities for 4-hydroxyaurones against *A. retroflexus* for post-emergence treatment with 4'-substituent on ring B was NO_2 (**4m**, 74.5%) > H (**4a**, 53.5%) ≈ Cl (**4k**, 51.5%) > $CH(Me)_2$ (**4g**, 22.0%) > Me (**4f**, 11.6%) > OMe (**4b**, 0), which might reveal that the introduction of electron-withdrawing group was helpful to enhance the herbicidal activity, especially strong electron-withdrawing group such as nitro. In the case of the same substituent, the substituted position on ring B also affect herbicidal activity. It could be clearly found that the 4'-substituted aurone **4f** (R = 4'-Me, 31.2%) demonstrated higher herbicidal activity than **4d** (R = 2'-Me, 10.5%) and **4e** (R = 3'-Me, 6.2%) against *B. campestris* for pre-emergence treatment. In addition, the installment of a heterocyclic ring of ring B improved the herbicidal activities slightly against *A. retroflexus* for post-emergence treatment.

In summary, 22 kinds of 4-hydroxyaurones were synthesized and characterized, and their herbicidal activities against 4 target plants were tested in a greenhouse. The results of the bioassay indicated that several of the title compounds exhibited moderate to good herbicidal activity against dicotyledonous plants for post-emergence treatment. Specifically, compound **4m** showed 74.5% inhibition against *A. retroflexus* for post-emergence treatment at the dosage of 750 g a.i. ha^{-1}, significantly higher than that of acetochlor (55.8%). Our investigation suggests that compound **4m** possesses the potential to be as a new leading compound for post-emergence herbicide.

EXPERIMENTAL

Melting points were determined on an X-4 binocular microscope melting point apparatus (Beijing Tech Instruments Co., Beijing, China) and are uncorrected. Nuclear magnetic resonance (NMR) spectra were recorded on a Bruker AVANCEII400 MHz instrument (400 MHz for ^{1}H, 100 MHz for ^{13}C). Elemental analysis was carried out with a FLASH1112A analyzer (CE Instruments Ltd, Milan, Italy).

Synthesis of 4-hydroxybenzofuran-3(2*H*)-one (3).

To a solution of 1-(2,6-dihydroxyphenyl)ethan-1-one (0.61 g, 4.0 mmol) in anhydrous CH_2Cl_2 (DCM, 20 mL) were added benzoyl chloride (1.69 g, 12.0 mmol) and dry triethylamine (1.5 mL). The mixture was stirred at room temperature until 1-(2,6-dihydroxyphenyl)ethan-1-one could no longer be detected by TLC analysis. The solvent was then removed by rotary evaporation to yield a brown solid. The solid was

washed by distilled water until neutral, dried to obtain a crude product which was recrystallized from EtOH to yield pure **1** as colorless needles (1.18 g, 82%).

To a solution of compound **1** (1.08 g, 3.0 mmol) in Et_2O (20 mL) was added phenyltrimethylammonium tribromide (1.35 g, 3.6 mmol) in portions within half an hour. The mixture was stirred at room temperature for 8 h. The white precipitate was then filtered off and washed by saturated sodium bicarbonate solution and saline solution three times, respectively. The organic phase was collected and dried by anhydrous magnesium sulfate. The crude product was obtained after removing the solvent, and recrystallized from EtOH and water to give **2** (0.96 g, 73%).

The solution of compound **2** in MeOH (20 mL) was stirred at 65 °C until **2** was dissolved completely. Freshly prepared NaOH solution (0.32 g, 20 mL) was added dropwise to the solution. The reaction was stirred at 65 °C for 4 h. The solvent was removed in vacuum and then 20 mL water was poured into the residue. The mixture was acidified with dilute HCl (1.0 mol/L) until pH<6 and stood for 2 h at room temperature. The precipitate was reserved by suction filtration, washed by water, and dried at 50 °C, which was recrystallized from MeOH to yield 4-hydroxybenzofuran-3(2*H*)-one **3** (0.20 g, 67%).

Synthesis of 4-hydroxyaurone analogues (4a-4v).

To a mixture of compound **3** (0.15 g, 1.0 mmol) in MeOH (10 mL) were added 10% NaOH (10 mL) and aryl aldehyde (1.5 mmol) dropwise. The reaction was stirred at 65 °C until abundant precipitate was generated. After cooling, the solid was collected by filtration, washed with water until neutral pH, which was recrystallized with *N*, *N*-dimethylformamide (DMF) and water to yield 4-hydroxyaurone analogues (**4a-4v**).

(*Z*)-2-Benzylidene-4-hydroxybenzofuran-3(2*H*)-one[8] (4a): Yellow solid; yield 80%; mp 168-169 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.25 (br s, 1H), 7.96 (d, *J* = 7.6 Hz, 2H), 7.58-7.42 (m, 4H), 6.88 (d, *J* = 8.0 Hz, 1H), 6.78 (s, 1H), 6.68 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 181.8, 166.5, 157.7, 147.0, 139.2, 132.6, 131.4 (2C), 130.0, 129.4 (2C), 111.2, 110.3, 109.5, 102.9. Anal. Calcd for $C_{15}H_{10}O_3$; C, 75.62; H, 4.23. Found: C, 75.35; H, 4.54.

(*Z*)-4-Hydroxy-2-(4-methoxybenzylidene)benzofuran-3(2*H*)-one[25] (4b): Yellow solid; yield 82%; mp >250 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.87 (d, *J* = 8.4 Hz, 2H), 7.28 (t, *J* = 8.0 Hz, 1H), 7.05 (d, *J* = 8.4 Hz, 2H), 6.56 (s, 1H), 6.34 (d, *J* = 7.6 Hz, 1H), 6.30 (d, *J* = 8.4 Hz, 1H), 3.82 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 181.8, 166.5, 166.1, 160.3, 147.0, 137.9, 132.7 (2C), 125.8, 115.0 (2C), 114.8, 110.2, 108.0, 96.3, 55.8. Anal. Calcd for $C_{16}H_{12}O_4$; C, 71.64; H, 4.51. Found: C, 71.82; H, 4.28.

(*Z*)-2-(3,4-Dimethoxybenzylidene)-4-hydroxybenzofuran-3(2*H*)-one (4c): Yellow solid; yield 77%; mp >250 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.52-7.49 (m, 2H), 7.25 (t, *J* = 8.0 Hz, 1H), 7.06 (d, *J* = 8.4 Hz, 1H), 6.53 (s, 1H), 6.31 (d, *J* = 7.6 Hz, 1H), 6.25 (d, *J* = 8.4 Hz, 1H), 3.82 (s, 3H), 3.81 (s, 3H). Anal. Calcd for $C_{17}H_{14}O_5$; C, 68.45; H, 4.73. Found: C, 68.69; H, 5.02.

(*Z*)-4-Hydroxy-2-(2-methylbenzylidene)benzofuran-3(2*H*)-one (4d): Red solid; yield 67%; mp 188-189 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.12-8.10 (m, 1H), 7.40-7.31 (m, 4H), 6.72 (s, 1H), 6.53-6.44 (m, 2H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 181.8, 166.6, 163.4, 148.0, 138.6, 138.4, 131.4, 131.0, 130.5, 129.5, 126.8, 113.7, 109.8, 105.2, 98.6, 20.2. Anal. Calcd for $C_{16}H_{12}O_3$; C, 76.18; H, 4.79. Found: C, 75.95; H, 4.52.

(*Z*)-4-Hydroxy-2-(3-methylbenzylidene)benzofuran-3(2*H*)-one (4e): Yellow solid; yield 67%; mp 193-194 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.72 (d, *J* = 8.0 Hz, 1H), 7.69 (s, 1H), 7.36 (t, *J* = 7.6 Hz, 1H), 7.31-7.27 (m, 1H), 7.20 (d, *J* = 7.6 Hz, 1H), 6.51 (s, 1H), 6.35 (d, *J* = 7.6 Hz, 1H), 6.30 (d, *J* = 8.4 Hz, 1H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 182.1, 166.5, 166.2, 148.2, 138.4, 138.3, 133.1, 131.5, 130.1, 129.2, 128.1, 115.0, 110.0, 108.0, 96.6, 21.5. Anal. Calcd for $C_{16}H_{12}O_3$; C, 76.18; H, 4.79. Found: C, 76.45; H, 4.48.

(*Z*)-4-Hydroxy-2-(4-methylbenzylidene)benzofuran-3(2*H*)-one[26] (4f): Yellow solid; yield 71%; mp >250 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.80 (d, *J* = 8.0 Hz, 2H), 7.31-7.27 (m, 3H), 6.55 (s, 1H), 6.36 (d, *J* = 7.6 Hz, 1H), 6.31 (d, *J* = 8.4 Hz, 1H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 182.0, 166.5, 166.1, 147.8, 139.2, 138.1, 131.0 (2C), 130.4, 130.0 (2C), 114.9, 110.0, 108.0, 96.5, 21.6. Anal. Calcd for $C_{16}H_{12}O_3$; C, 76.18; H, 4.79. Found: C, 75.97; H, 4.93.

(*Z*)-4-Hydroxy-2-(4-isopropylbenzylidene)benzofuran-3(2*H*)-one[8] (4g): Yellow solid; yield 75%; mp >250 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.82 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 7.29-7.25 (m, 1H), 6.53 (s, 1H), 6.31-6.27 (m, 2H), 2.97-2.87 (m, 1H), 1.23-1.20 (m, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 182.0, 167.0, 166.5, 149.9, 148.0, 138.1, 131.0 (2C), 130.9, 127.3 (2C), 115.3, 110.1, 107.7, 95.8, 33.8, 24.1 (2C). Anal. Calcd for $C_{18}H_{16}O_3$; C, 77.12; H, 5.75. Found: 77.40; H, 5.54.

(*Z*)-2-(5-Bromo-2-methoxybenzylidene)-4-hydroxybenzofuran-3(2*H*)-one (4h): Yellow solid; yield 72%; mp >250 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.18 (d, *J* = 2.8 Hz, 1H), 7.53 (dd, *J* = 8.8, 2.8 Hz, 1H), 7.30-7.26 (m, 1H), 7.08 (d, *J* = 8.8 Hz, 1H), 6.77 (s, 1H), 6.36 (d, *J* = 7.6 Hz, 1H), 6.30 (d, *J* = 8.8 Hz, 1H), 3.80 (s, 3H). Anal. Calcd for $C_{16}H_{11}BrO_4$; C, 55.36; H, 3.19. Found: C, 55.09; H, 3.00.

(*Z*)-2-(2-Chloro-6-fluorobenzylidene)-4-hydroxybenzofuran-3(2*H*)-one (4i): Yellow solid; yield 72%; mp 210-211 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.49-7.43 (m, 2H), 7.36-7.32 (m, 1H), 7.23-7.19 (m, 1H), 6.40 (s, 1H), 6.21 (d, *J* = 8.4 Hz, 1H), 6.10 (d, *J* = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 180.8, 168.2, 166.4, 160.2 (d, *J* = 250.6 Hz), 150.8, 138.7, 134.6 (d, *J* = 5.2 Hz), 131.4 (d, *J* = 9.4 Hz), 125.9 (d, *J* = 3.4 Hz), 120.4 (d, *J* = 19.6 Hz), 116.2, 115.4 (d, *J* = 22.3 Hz), 109.9, 97.3, 95.1. Anal. Calcd for $C_{15}H_8ClFO_3$; C, 61.98; H, 2.77. Found: C, 61.73; H, 3.03.

(*Z*)-2-(2,4-Dichlorobenzylidene)-4-hydroxybenzofuran-3(2*H*)-one (4j): Yellow solid; yield 68%; mp 237-238 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.23 (d, *J* = 8.4 Hz, 1H), 7.73 (d, *J* = 2.0 Hz, 1H), 7.57 (dd, *J* = 8.8, 2.0 Hz, 1H), 7.12 (dd, *J* = 8.8, 7.2 Hz, 1H), 6.62 (s, 1H), 6.06 (d, *J* = 8.8 Hz, 1H), 6.00 (d, *J* = 7.2

Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 189.3, 181.2, 166.2, 150.9, 137.8, 134.4, 133.5, 132.3, 130.3, 129.7, 128.4, 118.8, 109.8, 98.9, 92.1. Anal. Calcd for $C_{15}H_8Cl_2O_3$; C, 58.66; H, 2.63. Found: C, 58.85; H, 2.86.

(*Z*)-2-(4-Chlorobenzylidene)-4-hydroxybenzofuran-3(2*H*)-one (4k): Yellow solid; yield 81%; mp 172-173 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.93-7.89 (m, 2H), 7.55-7.52 (m, 2H), 7.30-7.25 (m, 1H), 6.56 (s, 1H), 6.32 (d, *J* = 7.6 Hz, 1H), 6.28 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 181.8, 166.4, 166.3, 148.6, 138.4, 133.8, 132.5 (2C), 132.2, 129.4 (2C), 115.2, 109.9, 106.5, 96.5. Anal. Calcd for $C_{15}H_9ClO_3$; C, 66.07; H, 3.33. Found: C, 66.29; H, 3.02.

(*Z*)-2-(3-Bromobenzylidene)-4-hydroxybenzofuran-3(2*H*)-one (4l): Yellow solid; yield 73%; mp 178-179 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.08-8.07 (m, 1H), 7.93-7.90 (m, 1H), 7.58-7.55 (m, 1H), 7.45-7.41 (m, 1H), 7.31-7.27 (m, 1H), 6.56 (s, 1H), 6.35 (d, *J* = 7.6 Hz, 1H), 6.30 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 181.7, 166.5, 166.4, 149.1, 138.4, 135.8, 133.0, 131.8, 131.4, 129.7, 122. 6, 115.5, 109.8, 105.9, 96.4. Anal. Calcd for $C_{15}H_9BrO_3$; C, 56.81; H, 2.86. Found: C, 57.09; H, 3.19.

(*Z*)-4-Hydroxy-2-(4-nitrobenzylidene)benzofuran-3(2*H*)-one (4m): Yellow solid; yield 81%; mp 177-178 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.32-8.29 (m, 2H), 8.15-8.11 (m, 2H), 7.35-7.30 (m, 1H), 6.69 (s, 1H), 6.39 (d, *J* = 7.6 Hz, 1H), 6.34 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 181.5, 166.8, 166.4, 150.4, 146.9, 140.2, 138.6, 131.5 (2C), 124.4 (2C), 115.9, 109.6, 104.9, 96.5. Anal. Calcd for $C_{15}H_9NO_5$; C, 63.61; H, 3.20; N, 4.95. Found: C, 63.35; H, 3.51; N, 5.14.

(*Z*)-4-((4-Hydroxy-3-oxobenzofuran-2(3*H*)-ylidene)methyl)benzonitrile[27] (4n): Yellow solid; yield 65%; mp >250 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.04-8.01 (m, 2H), 7.91-7.89 (m, 2H), 7.15 (dd, *J* = 8.4, 7.2 Hz, 1H), 6.51 (s, 1H), 6.10 (d, *J* = 8.8 Hz, 1H), 6.05 (d, *J* = 7.2 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 181.5, 171.6, 166.3, 151.0, 138.5, 138.0, 133.0 (2C), 130.9 (2C), 119.4, 118.2, 110.4, 109.9, 104.1, 92.8. Anal. Calcd for $C_{16}H_9NO_3$; C, 73.00; H, 3.45; N, 5.32. Found: C, 72.79; H, 3.17; N, 5.59.

(*Z*)-2-(4-(Dimethylamino)benzylidene)-4-hydroxybenzofuran-3(2*H*)-one[28] (4o): Yellow solid; yield 74%; mp >250 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.78-7.74 (m, 2H), 7.33-7.28 (m, 1H), 6.81-6.77 (m, 2H), 6.56 (s, 1H), 6.44 (d, *J* = 7.6 Hz, 1H), 6.36 (d, *J* = 8.4 Hz, 1H), 3.00 (s, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 181.9, 166.1, 165.6, 151.1, 145.7, 137.6, 132.7 (2C), 120.4, 114.1, 112.5 (2C), 111.5, 110.7, 110.1, 96.6. Anal. Calcd for $C_{17}H_{15}NO_3$; C, 72.58; H, 5.37; N, 4.98. Found: C, 72.84; H, 5.12; N, 4.70.

(*Z*)-4-Hydroxy-2-(4-hydroxybenzylidene)benzofuran-3(2*H*)-one[8-10] (4p): Yellow solid; yield 71%; mp >250 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.78-7.74 (m, 2H), 7.30-7.26 (m, 1H), 6.88-6.85 (m, 2H), 6.52 (s, 1H), 6.36 (d, *J* = 8.0 Hz, 1H), 6.30 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 182.2, 166.4, 165.5, 159.4, 146.3, 138.0, 133.1 (2C), 123.9, 116.5 (2C), 114.2, 110.4, 109.3, 97.0. Anal. Calcd for $C_{15}H_{10}O_4$; C, 70.86; H, 3.96. Found: C, 71.15; H, 3.58.

(*Z*)-2-(4-Fluorobenzylidene)-4-hydroxybenzofuran-3(2*H*)-one (4q): Yellow solid; yield 66%; mp >250 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.99-7.94 (m, 2H), 7.35-7.28 (m, 3H), 6.61 (s, 1H), 6.36 (d, *J* = 8.0 Hz, 1H), 6.32 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 181.9, 166.5, 165.8, 162.5 (d, *J* = 247.0 Hz), 147.9, 138.3, 133.2 (d, *J* = 8.0 Hz, 2C), 129.9 (d, *J* = 3.0 Hz), 116.4 (d, *J* = 21.0 Hz, 2C), 114.9, 109.9, 106.8, 96.7. Anal. Calcd for $C_{15}H_9FO_3$; C, 70.31; H, 3.54. Found: C, 70.05; H, 3.81.

(*Z*)-2-(3-Fluorobenzylidene)-4-hydroxybenzofuran-3(2*H*)-one (4r): Yellow solid; yield 70%; mp 227-228 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.76-7.72 (m, 2H), 7.55-7.49 (m, 1H), 7.36-7.32 (m, 1H), 7.26-7.21 (m, 1H), 6.63 (s, 1H), 6.47 (d, *J* = 8.0 Hz, 1H), 6.38 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 181.8, 166.5, 164.6, 162.7 (d, *J* = 241.7 Hz), 148.6, 138.7, 135.5 (d, *J* = 8.4 Hz), 131.3 (d, *J* =8.4 Hz), 127.2 (d, *J* = 2.7 Hz), 117.0 (d, *J* = 22.2 Hz), 116.2 (d, *J* = 20.9 Hz), 114.5, 109.7, 106.9, 97.9. Anal. Calcd for $C_{15}H_9FO_3$; C, 70.31; H, 3.54. Found: C, 70.10; H, 3.23.

(*Z*)-4-Hydroxy-2-(pyridin-3-ylmethylene)benzofuran-3(2*H*)-one (4s): Yellow solid; yield 71%; mp >250 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.97 (s, 1H), 8.51-8.50 (m, 1H), 8.28 (d, *J* = 9.2 Hz, 1H), 7.50-7.46 (m, 1H), 7.14 (t, *J* = 8.8 Hz, 1H), 6.47 (s, 1H), 6.09-6.04 (m, 2H). Anal. Calcd for $C_{14}H_9NO_3$; C, 70.29; H, 3.79; N, 5.86. Found: C, 70.46; H, 3.41; N, 6.13.

(*Z*)-4-Hydroxy-2-(thiophen-2-ylmethylene)benzofuran-3(2*H*)-one (4t): Yellow solid; yield 74%; mp >250 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.81-7.80 (m, 1H), 7.59-7.58 (m, 1H), 7.30-7.26 (m, 1H), 7.19 (dd, *J* = 4.8, 3.6 Hz, 1H), 6.96 (s, 1H), 6.32 (d, *J* = 7.6 Hz, 1H), 6.31 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 181.3, 166.9, 166.1, 146.6, 138.0, 136.1, 132.3, 131.2, 128.4, 115.4, 110.7, 102.4, 95.9. Anal. Calcd for $C_{13}H_8O_3S$; C, 63.92; H, 3.30. Found: C, 64.21; H, 3.58.

(*Z*)-4-Hydroxy-2-((5-methylfuran-2-yl)methylene)benzofuran-3(2*H*)-one (4u): Yellow solid; yield 70%; mp 186-187 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.25-7.21 (m, 1H), 6.92 (d, *J* = 3.6 Hz, 1H), 6.42 (s, 1H), 6.34 (d, *J* = 3.2 Hz, 1H), 6.24-6.22 (m, 2H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 181.5, 166.1, 165.4, 155.2, 147.6, 145.5, 138.1, 117.3, 114.5, 110.5, 110.2, 97.5, 97.1, 14.1. Anal. Calcd for $C_{14}H_{10}O_4$; C, 69.42; H, 4.16. Found: C, 69.67; H, 3.45.

(*Z*)-4-Hydroxy-2-(naphthalen-1-ylmethylene)benzofuran-3(2*H*)-one (4v): Yellow solid; yield 69%; mp 215-216 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.35-8.32 (m, 1H), 8.28 (d, *J* = 8.4 Hz, 1H), 8.03-7.99 (m, 2H), 7.69-7.64 (m, 2H), 7.63-7.59 (m, 1H), 7.37-7.33 (m, 1H), 7.29 (s, 1H), 6.44 (d, *J* = 7.6 Hz, 1H), 6.40 (d, *J* = 8.4 Hz, 1H). Anal. Calcd for $C_{19}H_{12}O_3$; C, 79.16; H, 4.20. Found: C, 78.93; H, 3.97.

Herbicidal Activity Assays.

The herbicidal activities of the title compounds against dicotyledonous plants such as *B. campestris* and *A. retroflexus*, and monocotyledonous plants such as *E. crusgalli*, *D. sanguinalis* were evaluated in a greenhouse at Nankai University according to a previously reported procedure.[4]

All test compounds were dissolved in DMF with the addition of a little Tween-20, and then were sprayed with a laboratory belt sprayer. The mixture of the same amount of water, DMF, and Tween 20 was sprayed as the negative control. Activity numbers represent percent displaying herbicidal damage as compared to the control. Mesotrione and acetochlor were used as positive controls.

Pre-emergence treatment.

Sandy clay (100 g) in a plastic box (11 cm × 7 cm × 7 cm) was wetted with water. Then, 15 germinated seeds of the tested plants (*E. crusgalli*, *D. sanguinalis*, *B. campestris*, and *A. retroflexus*) were planted at a depth of 0.6 cm in a glasshouse, and the soil was sprayed at a test compound concentration of 750 g a.i. ha^{-1}.

Post-emergence treatment.

Seedlings (one leaf and one stem) of the plants were sprayed with the test compound at the same rate as used for the pre-emergence test.

For both methods, fresh weights were determined 21 days later and the percentage inhibition relative to the controls was calculated.

ACKNOWLEDGEMENTS

We are very grateful for the financial support by the National Natural Science Foundation of China (No. 31501686).

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