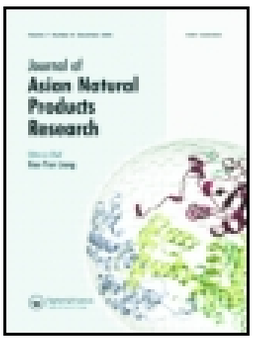

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Synthesis of sulfonate derivatives of maltol and their biological activity against *Phytophthora capsici* and *Bursaphelenchus xylophilus in vitro*

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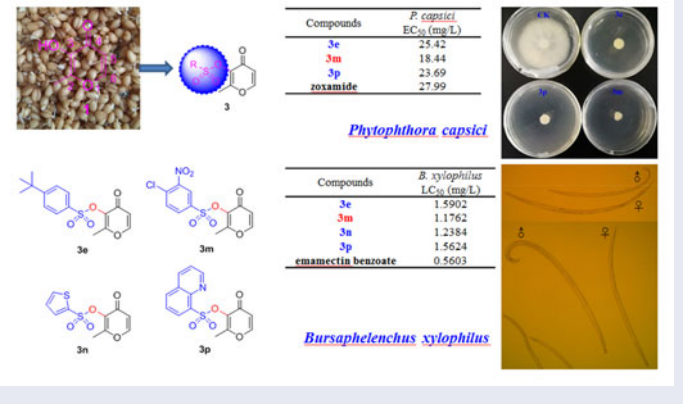
ABSTRACT

Sixteen sulfonate derivatives of maltol were synthesized and screened *in vitro* for their anti-oomycete and nematicidal activity against *Phytophthora capsici* and *Bursaphelenchus xylophilus*, respectively. Among all the compounds, **3e**, **3m**, and **3p** exhibited the most promising and pronounced anti-oomycete activity against *P. capsici* than zoxamide, and the EC_{50} values of 25.42, 18.44, 23.69, and 27.99 mg/L, respectively; compounds **3e**, **3m**, **3n**, and **3p** exhibited potent nematicidal activity with LC_{50} values ranging from 1 to 2 mg/L, especially **3m** and **3n** showed the best promising and pronounced nematicidal activity, with LC_{50} values of 1.1762 and 1.2384 mg/L, respectively.



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Maltol; sulfonate; semisynthesis; anti-oomycete activity; nematicidal activity

1. Introduction

The oomycete *Phytophthora capsici*, is a virulent, hemibiotrophic pathogen of vegetable crops, inflicting significant losses worldwide [1–3]. Its main hosts are pepper and cucurbits. The pathogen *P. capsici* has shown remarkable adaptation to

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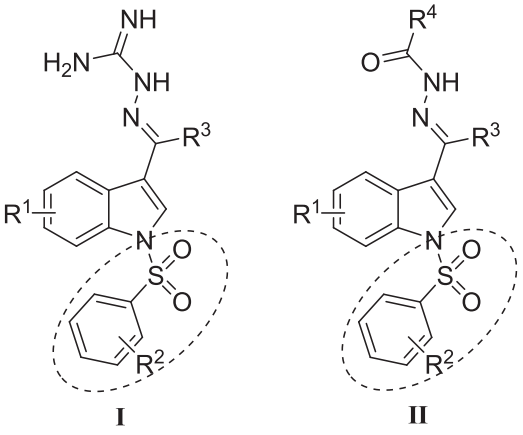
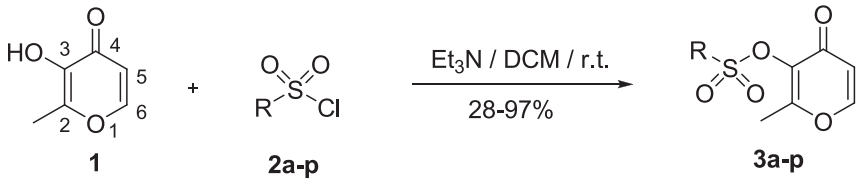


Figure 1. Structures of aminoguanidine derivatives of *N*-arylsulfonyl-3-acylindoles (**I**) and *N*-arylsulfonyl-3-acylindole arylcarbonyl hydrazine derivatives (**II**).

fungicides and new hosts [1–5]. Due to the lack of the resistant germplasm resources, chemical controlling is still the main way to reduce the incidence of *P. capsici* on main hosts though resistance is an inevitable result of evolution [6–8]. However, the oomycete *P. capsici*, which are hard to control, easily infect many crops, therefore development of new compounds that effectively inhibit those agricultural diseases is still highly desirable.

Pine wood nematode (*Bursaphelenchus xylophilus*), is the cause of pine wilt disease, which has been devastating forests worldwide [9]. Moreover, at present there are only a few commercial nematicides left in use, and their repeated applications over the years have led to the development of resistance [10]. To prevent pine wilt disease and overcome the problems of resistance development and environmental pollution, therefore, the research and development of efficacious nematicidal agents has received much attention internationally in recent years [11].

Plant secondary metabolites play an important role in novel pesticide discovery for their unique sources and potential target sites [12–16]. Maltol (**1**, 3-hydroxy-2-methyl-4-pyrone, Scheme 1), a commercial natural metabolite, is primarily extracted from germinated seeds of *Hordeum vulgare* L. and *Triticum aestivum* L. [17]. To the best of our knowledge, compound **1** is an excellent candidate for the study of antifungal activity [18], anticancer activity [19], antimycobacterial activity [20], antioxidant activity [21], neuroprotective effect [22], and liver protection effect [23]. Moreover, maltol is used extensively as a food preservative, flavor-enhancing agent, and also in pharmaceutical and cosmetic formulations. More recently, we have investigated the antifungal activities against *Botrytis cinerea* and *Fusarium oxysporum* of compound containing hydroxyl of maltol [18]. In the meantime, the sulfonyl group introduced at the skeletons of different natural products was necessary for obtaining the potent compounds [11, 14, 24]. For example, aminoguanidine derivatives of *N*-arylsulfonyl-3-acylindoles (**I**, Figure 1) exhibited the promising and pronounced antifungal activity [24]; and *N*-arylsulfonyl-3-acylindole arylcarbonyl hydrazine derivatives (**II**, Figure 1) showed significant nematicidal activity [11]. Inspired by the above-mentioned interesting results, and the aim in our continuing endeavor to find more active natural



Scheme 1. The synthetic route of sulfonate derivatives of maltol (**3a–p**).

product-based antifungal hits [25], we herein designed and synthesized of three-substituted sulfonate derivatives of maltol, and first report the results of the antifungal activity of 16 sulfonate derivatives of maltol against *P. capsici* and *B. xylophilus in vitro*, respectively. Additionally, their structure–activity relationship (SAR) studies were also described.

2. Results and discussion

2.1. Chemistry

As depicted in Scheme 1, maltol (**1**) reacted with 1.2 equiv. of ethanesulfonyl chloride/arylsulfonyl chloride (**2a–p**) in the presence of 1.5 equiv. of triethylamine to afford 3-substituted sulfonate derivatives of maltol (**3a–p**) in relatively good yields.

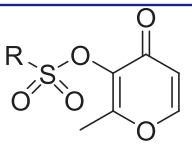
2.2. Antioomycete activity

Sixteen sulfonate derivatives of maltol (**3a–p**) were screened *in vitro* for their antioomycete activities against *P. capsici* [6]. Zoxamide, a commercially available agricultural fungicide, was used as a positive control. And the inhibitory effects showed an obviously dose-dependent manner that with the concentration of compound increased, the colony diameter decreased.

As shown in Table 1, among all of the title derivatives, compounds **3e**, **3m**, and **3p** exhibited the most promising and pronounced anti-oomycete activity against *P. capsici* than zoxamide. The EC_{50} values of **3e**, **3m**, **3p** and zoxamide against *P. capsici* were 25.42, 18.44, 23.69, and 27.99 mg/L, respectively. Generally, the introduction of different substitutions at the hydroxyl position of maltol has remarkable effect on antioomycete activity.

Through a comparative study on the relationship between the chemical structures and antioomycete activity of **3a–p** (SAR), some interesting results were found as follows: (1) The introduction of 4-tert-butylphenylsulfonyl at the hydroxyl position of maltol could lead to more potent compound than possessing tosyl group, 4-methoxyphenylsulfonyl group and phenylsulfonyl group (**3e** versus **3c**, **3d,** and **3b**). For example, the EC_{50} values of **3e**, **3c**, **3d**, and **3b** against *P. capsici* were 25.42, 115.39, 151.88, and 196.69 mg/L, respectively, that is, the EC_{50} values of **3b** was close to eight

Table 1. Anti-oomycete and nematicidal activities of compounds **3a–p** against *P. capsici* and *B. xylophilus*, respectively.



3a-p

Compounds	R	*P. capsici* EC_{50} (mg/L)	*B. xylophilus* LC_{50} (mg/L)
Maltol		89.56	20.2237
3a	Et	126.33	5.5102
3b	Ph	196.69	2.3956
3c	(*p*-Me)Ph	115.39	5.5709
3d	(*p*-OMe)Ph	151.88	6.7881
3e	(*p*-tert-butyl)Ph	25.42	1.5902
3f	(2,4,6-trimethyl)Ph	73.62	3.3387
3g	(2,4,6-triisopropyl)Ph	102.56	4.0221
3h	(*p*-F)Ph	91.61	10.2235
3i	(*p*-Br)Ph	70.18	12.3741
3j	(*o*-NO_2)Ph	82.20	5.7106
3k	(*m*-NO_2)Ph	148.15	2.3341
3l	(*p*-NO_2)Ph	92.59	8.9812
3m	(*p*-Cl, *m*-NO_2)Ph	18.44	1.1762
3n	2-thienyl	119.05	1.2384
3o	1-naphthyl	83.33	3.8751
3p	8-quinolyl	23.69	1.5624
Zoxamide		27.99	
Emamectin benzoate			0.5603

times of that of **3e**. Similarly, comparing the EC_{50} value of R = 2,4,6-trimethylphenyl derivative, it exhibited more potent anti-oomycete activity than R = 2,4,6-triisopropylphenyl derivative. (2) Interestingly, we found that the introduction of nitrophenylsulfonyl at the hydroxyl position of maltol, and the nitro group at different position of the benzene ring, could lead to derivatives with different antioomycete activity. For example, the EC_{50} values of **3j**, **3l**, and **3k** against *P. capsici* were 82.20, 92.59, and 148.15 mg/L, respectively. In addition, the introduction of 4-bromophenylsulfonyl to the hydroxyl position of maltol could lead to more potent compound than possessing 4-fluorophenylsulfonyl group (e.g. 70.18 mg/L for **3i** and 91.61 mg/L for **3h**). It is noteworthy that the introduction of 4-chloro-3-nitrophenylsulfonyl as a two-electron-withdrawing substituent (such as NO_2 and Cl) could result in more potent compound **3m** relative to those containing phenylsulfonyl as a one-electron-withdrawing substituent (e.g. **3h-l**). For example, the EC_{50} values of **3h–m** against *P. capsici* were 91.61, 70.18, 82.20, 148.15, 92.59, and 18.44 mg/L, respectively. (3) As compared with 2-thiophenesulfonyl and 1-naphthalensulyonyl derivatives, 8-quinolinesulfonyl derivative exhibited more potent anti-oomycete activity (**3n** and **3o** versus **3p**). For example, the EC_{50} values of **3n–p** against *P. capsici* were 119.05, 83.33, and 23.69 mg/L, respectively.

2.3. Nematicidal activity

Maltol, compounds **3a–p** and emamectin benzoate (used as a positive control) were screened *in vitro* for their nematicidal activities against *B. xylophilus* [11]. As outlined

in Table 1, among all of the derivatives, compounds **3e**, **3m**, **3n**, and **3p** exhibited potent nematicidal activity with LC_{50} values ranging from 1 to 2 mg/L. Especially **3m** and **3n** showed the best promising and pronounced nematicidal activity, with LC_{50} values of 1.1762 and 1.2384 mg/L, respectively.

Consequently, based upon the above investigation, when the sulfonyl moieties were introduced on the 3-position of the maltol, the nematicidal activity of the corresponding compounds were significantly increased (**1** versus **3a–p**). Finally, some interesting results of the structure-activity relationships of **3a–p** were also observed: (1) The introduction of 4-tert-butylphenylsulfonyl at the hydroxyl position of maltol could lead to more potent compound than possessing phenylsulfonyl group, tosyl group, and 4-methoxyphenylsulfonyl group (**3e** versus **3b**, **3c**, and **3d**). The LC_{50} values of **3b-e** against *B. xylophilus* were 2.3956, 5.5709, 6.7881, and 1.5902 mg/L, respectively. (2) It is interesting that the introduction of 4-chloro-3-nitrophenylsulfonyl as a two-electron-withdrawing substituent (such as NO_2 and Cl) could result in more potent compound **3m** relative to those containing phenylsulfonyl as a one-electron-withdrawing substituent (e.g. **3h–l**, the LC_{50} values ranging from 2.3341 to 12.3741 mg/L). On the other hand, we found that the introduction of nitrophenylsulfonyl at the hydroxyl position of maltol, and the nitro group at different position of the benzene ring, could lead to derivatives with different nematicidal activity (**3k** versus **3j** and **3l**). (3) The introduction of the sulfonyl containing heterocyclic ring moieties can significantly improve the nematicidal activity. As compared with 1-naphthalensulyonyl derivative, 2-thiophenesulfonyl and 8-quinolinesulfonyl derivative exhibited more potent nematicidal activity (**3n** and **3p** versus **3o**). For example, the LC_{50} values of **3n-p** against *B. xylophilus* were 1.2384, 3.8751, and 1.5624 mg/L, respectively.

This suggested that a 4-chloro-3-nitrophenylsulfonyl group (two-electron-withdrawing substituent) introduced at the hydroxyl position of maltol was necessary for obtaining the most potent compound.

3. Experimental

3.1. General experimental procedures

Maltol, triethylamine, ethanesulfonyl chloride, and arylsulfonyl chloride were purchased from Aladdin Chemistry Co., Ltd. (Shanghai, China). Ethyl acetate, dichloromethane and petroleum ether were purchased from Beichen Fangzheng Reagent Factory (Tianjin, China). Analytical thin-layer chromatography (TLC) was performed with silica gel plate using silica gel 60 GF_{254} (Qingdao Haiyang Chemical Co., Ltd., Shandong, China). Silica gel column chromatography was performed with silica gel 200–300 mesh (Qingdao Haiyang Chemical Co., Ltd., Shandong, China). Melting points were taken on a X-6 microscopic melting point apparatus (Beijing Tech instrument Co., Ltd., Beijing, China) and are uncorrected. Nuclear magnetic resonance spectra (NMR) were recorded on a Bruker Avance DMX 400 MHz instrument (Bruker Daltonik, Bremen, Germany) in $CDCl_3$ (^1H at 400 MHz) using TMS (tetramethylsilane) as the internal standard. Electrospray ion trap mass spectrometry (ESI-

TRAP-MS) was carried out with a Bruker ESI-TRAP Esquire 6000 plus mass spectrometry instrument (Bruker, Germany).

3.2. General procedure for the synthesis of sulfonate derivatives of maltol (3a–p)

To a solution of maltol (**1**, 1.0 mmol) and ethanesulfonyl chloride/arylsulfonyl chloride (**2**, 1.2 mmol) in dry dichloromethane (DCM, 10 ml) at room temperature, a solution of triethylamine (Et_3N) (1.5 mmol) in dry DCM (5 ml) was added dropwise for 10 min. When the reaction was completed by TLC analysis, the reaction mixture was diluted with water (15 ml), and extracted with DCM (30 ml × 3). Subsequently, the combined organic phase was washed by saturated aq. brine (30 ml), dried over anhydrous Na_2SO_4, concentrated *in vacuo*, and purified by silica gel column chromatography to obtain in 28–97% yields. The data for **3a**–**p** are shown as follows.

3.2.1. Data for 3a

Yield = 66%, Yellow oily liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.70 (d, J = 5.6 Hz, 1H), 6.42 (d, J = 5.6 Hz, 1H), 3.72 (q, J = 7.6 Hz, 2H), 2.46 (s, 3H), 1.60 (t, J = 7.6 Hz, 3H). HRESIMS: *m/z* 219.0325 $[M+H]^+$ (calcd for $C_8H_{11}O_5S$, 219.0322).

3.2.2. Data for 3b

Yield = 78%, White solid, m.p. 106-107 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.10–8.13 (m, 2H), 7.68–7.72 (m, 1H), 7.66 (d, J = 5.6 Hz, 1H), 7.56–7.60 (m, 2H), 6.34 (d, J = 5.6 Hz, 1H), 2.46 (s, 3H). HRESIMS: *m/z* 267.0321 $[M+H]^+$ (calcd for $C_{12}H_{11}O_5S$, 267.0322).

3.2.3. Data for 3c

Yield = 31%, White solid, m.p. 96-97 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.96–7.99 (m, 2H), 7.65 (d, J = 5.6 Hz, 1H), 7.35–7.38 (m, 2H), 6.34 (d, J = 5.6 Hz, 1H), 2.46 (s, 6H). HRESIMS: *m/z* 281.0481 $[M+H]^+$ (calcd for $C_{13}H_{13}O_5S$, 281.0478).

3.2.4. Data for 3d

Yield = 97%, White solid, m.p. 87–88 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.02–8.05 (m, 2H), 7.65 (d, J = 5.6 Hz, 1H), 7.00–7.04 (m, 2H), 6.34 (d, J = 5.6 Hz, 1H), 3.89 (s, 3H), 2.47 (s, 3H). HRESIMS: *m/z* 297.0427 $[M+H]^+$ (calcd for $C_{13}H_{13}O_6S$, 297.0427).

3.2.5. Data for 3e

Yield = 49%, White solid, m.p. 121–122 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.03–8.07 (m, 2H), 7.66 (d, J = 5.6 Hz, 1H), 7.57–7.60 (m, 2H), 6.38 (d, J = 5.6 Hz, 1H), 2.46 (s, 3H), 1.36 (s, 9H). HRESIMS: *m/z* 323.0949 $[M+H]^+$ (calcd for $C_{16}H_{19}O_5S$, 323.0948).

3.2.6. Data for 3f

Yield = 28%, Yellow solid, m.p. 97-98 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.62 (d, J = 5.6 Hz, 1H), 6.99 (s, 2H), 6.29 (d, J = 5.6 Hz, 1H), 2.66 (s, 6H), 2.45 (s, 3H), 2.32 (s, 3H). HRESIMS: m/z 309.0789 $[M+H]^+$ (calcd for $C_{15}H_{17}O_5S$, 309.0791).

3.2.7. Data for 3g

Yield = 59%, White solid, m.p. 82-83 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.62 (d, J = 5.6 Hz, 1H), 7.19 (s, 2H), 6.32 (d, J = 5.6 Hz, 1H), 4.09–4.15 (m, 2H), 2.88–2.95 (m, 1H), 2.41 (s, 3H), 1.25–1.28 (m, 18H). HRESIMS: m/z 393.1731 $[M+H]^+$ (calcd for $C_{21}H_{29}O_5S$, 393.1730).

3.2.8. Data for 3h

Yield = 85%, White solid, m.p. 146–147 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.12–8.17 (m, 2H), 7.67 (d, J = 5.6 Hz, 1H), 7.22–7.28 (m, 2H), 6.35 (d, J = 5.6 Hz, 1H), 2.50 (s, 3H). HRESIMS: m/z 285.0230 $[M+H]^+$ (calcd for $C_{12}H_{10}FO_5S$, 285.0227).

3.2.9. Data for 3i

Yield = 93%, White solid, m.p. 151–152 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.96–8.00 (m, 2H), 7.70-7.73 (m, 2H), 7.67 (d, J = 5.6 Hz, 1H), 6.35 (d, J = 5.6 Hz, 1H), 2.49 (s, 3H). HRESIMS: m/z 344.9429 $[M+H]^+$ (calcd for $C_{12}H_{10}BrO_5S$, 344.9427).

3.2.10. Data for 3j

Yield = 84%, Pale yellow solid, m.p. 148–149 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.27 (dd, J = 8.0, 1.6 Hz, 1H), 7.90 (dd, J = 7.6, 1.6 Hz, 1H), 7.67–7.85 (m, 2H), 7.68 (d, J = 5.6 Hz, 1H), 6.33 (d, J = 5.6 Hz, 1H), 2.51 (s, 3H). HRESIMS: m/z 312.0175 $[M+H]^+$ (calcd for $C_{12}H_{10}NO_7S$, 312.0172).

3.2.11. Data for 3k

Yield = 56%, White solid, m.p. 105–106 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.94 (t, J = 2.0 Hz, 1H), 8.53–8.56 (m, 1H), 8.45–8.48 (m, 1H), 7.83 (t, J = 8.0 Hz, 1H), 7.70 (d, J = 5.6 Hz, 1H), 6.34 (d, J = 5.6 Hz, 1H), 2.54 (s, 3H). HRESIMS: m/z 312.0173 $[M+H]^+$ (calcd for $C_{12}H_{10}NO_7S$, 312.0172).

3.2.12. Data for 3l

Yield = 49%, White solid, m.p. 132–133 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.39–8.43 (m, 2H), 8.29-8.32 (m, 2H), 7.70 (d, J = 5.6 Hz, 1H), 6.35 (d, J = 5.6 Hz, 1H), 2.53 (s, 3H). HRESIMS: m/z 312.0172 $[M+H]^+$ (calcd for $C_{12}H_{10}NO_7S$, 312.0172).

3.2.13. Data for 3m

Yield = 42%, White solid, m.p. 140–141 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.63 (d, J = 2.0 Hz, 1H), 8.28 (dd, J = 8.4, 2.0 Hz, 1H), 7.79 (d, J = 8.4 Hz, 1H), 7.70 (d, J = 5.6 Hz, 1H), 6.37 (d, J = 5.6 Hz, 1H), 2.53 (s, 3H). HRESIMS: m/z 345.9785 $[M+H]^+$ (calcd for $C_{12}H_9ClNO_7S$, 345.9783).

3.2.14. Data for 3n

Yield = 29%, White solid, m.p. 94–95 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.93 (dd, J = 4.0, 1.2 Hz, 1H), 7.78 (dd, J = 5.2, 1.6 Hz, 1H), 7.66 (d, J = 5.6 Hz, 1H), 7.18 (dd, J = 5.2, 4.0 Hz, 1H), 6.36 (d, J = 5.6 Hz, 1H), 2.45 (s, 3H). HRESIMS: m/z 272.9888 $[M+H]^+$ (calcd for $C_{10}H_9O_5S_2$, 272.9886).

3.2.15. Data for 3o

Yield = 42%, White solid, m.p. 124-125 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.86–8.89 (m, 1H), 8.26 (dd, J = 7.6, 1.6 Hz, 1H), 8.15–8.17 (m, 1H), 7.95-7.98 (m, 1H), 7.73-7.77 (m, 1H), 7.61–7.65 (m, 1H), 7.60 (d, J = 6.0 Hz, 1H), 7.57 (dd, J = 8.4, 7.6 Hz, 1H), 6.26 (d, J = 6.0 Hz, 1H), 2.39 (s, 3H). HRESIMS: m/z 317.0477 $[M+H]^+$ (calcd for $C_{16}H_{13}O_5S$, 317.0478).

3.2.16. Data for 3p

Yield = 31%, White solid, m.p. 247–248 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.19 (dd, J = 4.4, 2.0 Hz, 1H), 8.50 (dd, J = 7.6, 1.6 Hz, 1H), 8.30 (dd, J = 8.4, 2.0 Hz, 1H), 8.16 (dd, J = 8.4, 1.6 Hz, 1H), 7.67 (dd, J = 8.4, 7.6 Hz, 1H), 7.61 (d, J = 6.0 Hz, 1H), 7.58 (q, J = 4.0 Hz, 1H), 6.19 (d, J = 6.0 Hz, 1H), 2.57 (s, 3H). HRESIMS: m/z 318.0430 $[M+H]^+$ (calcd for $C_{15}H_{12}NO_5S$, 318.0431).

3.3. Biological assay

3.3.1. Anti-oomycete activity of compounds 3a–p against P. capsici

Sixteen sulfonate derivatives of maltol (**3a**–**p**) were screened *in vitro* for their anti-oomycete activity against *P. capsici*. Potato dextrose agar (PDA) medium was prepared in the flasks and sterilized. Maltol, compounds **3a**–**p** and zoxamide (used as a positive control) were dissolved in acetone before mixing with PDA. The ranges of maltol, compounds **3a**–**p** and zoxamide concentrations for the assays were defined in preliminary experiments, and the final concentrations in medium were 5, 25, 50, 75, and 100 mg/L. Acetone without any compounds mixed with PDA was served as the control. The medium was then poured into sterilized Petri dishes. Mycelial plugs (5-mm diameter) were cut from the growing edge of a 7-day-old colony and then placed on the PDA plates, and incubated at 28 °C in the dark, respectively. Colony growth rate (mm/7 days) was determined on PDA medium. Three plates were evaluated for each compounds and an average colony diameter was calculated. The radial growths of the colonies were measured and the data were statistically analyzed. Mean colony diameter (minus the diameter of the plug) was measured for each treatment and expressed as a percentage of growth inhibition. The median effective concentration (EC_{50}) of maltol, compounds **3a**–**p** and zoxamide for *P. capsici* isolate was calculated by linear regression of relative percentage of growth inhibition against logtransformed samples concentration.

3.3.2. Nematicidal activity of compounds 3a–p against B. xylophilus

Sixteen sulfonate derivatives of maltol (**3a**–**p**) were screened *in vitro* for their nematicidal activity against *B. xylophilus*. The ranges of maltol, compounds **3a**–**p** and

emamectin benzoate (used as a positive control) concentrations for the assays were defined in preliminary experiments. Acetone solutions of maltol, compounds **3a**–**p** and emamectin benzoate were first prepared at concentrations of 5, 10, 25, 50, and 100 mg/L, respectively. Then 10 μl of the above solutions was added to the aqueous suspension (90 μl) containing approximate 1000 living nematodes (third-instar and fourth-instar larvae of *B. xylophilus*) per milliliter. Acetone without any compounds mixed was served as the control. Three replicates in each trial were made and kept at 28 °C for 24 h. The activities of five concentrations of the tested compounds were monitored under a microscope by recording the death rate of the tested nematodes. Nematodes that did not move when prodded with a needle were considered to be dead. The median lethal concentration (LC_{50}) values of maltol, compounds **3a**–**p** and emamectin benzoate were calculated using the probit method.

Disclosure statement

No potential conflict of interest was reported by the authors.

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