**ORIGINAL PAPER**

# Design, synthesis, and antibacterial activity of novel myricetin derivatives containing sulfonate

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## Abstract

A series of myricetin derivatives containing sulfonate groups were designed and synthesized. Preliminary antibacterial activity showed that most of the target compounds exhibited significant biological activities against *Xanthomonas axonopodis pv. Citri (Xac)*, *Ralstonia solanacearum (Rs)*, and *Xanthomonas oryzae pv. Oryzae (Xoo)*. In particular, the $EC_{50}$ value of compound 3e was 13.76 µg/cm$^3$ against *Xac*, which was better than commercial reagents bismerthiazol (50.32 µg/cm$^3$) and thiodiazole copper. (83.27 µg/cm$^3$), and the $EC_{50}$ value of compound **3j** was 11.92 µg/cm$^3$ against *Xoo* in vitro, The result was better than that of bismerthiazol (72.08 µg/cm$^3$) and thiodiazole copper (99.26 µg/cm$^3$). Compound **3j** displayed the better in vivo activity against rice bacterial leaf blight than bismerthiazol and thiodiazole copper. Meanwhile, the antibacterial mechanism of compounds **3e** and **3j** was studied by scanning electron microscope (SEM). These results suggested that myricetin derivatives containing sulfonate can be considered as a new antibacterial reagents.

**Graphic abstract**
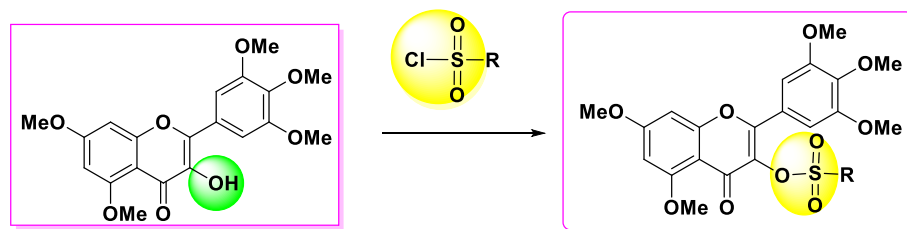


**Keywords** Myricetin derivatives · Sulfonate · Antibacterial activities · Crystal structure · Scanning electron microscopy

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# Introduction

Plant bacterial diseases are frequently encountered in agricultural production and difficult to manage, such as citrus canker, tobacco bacterial wilt and rice bacterial leaf blight, which can be caused by *Xanthomonas axonopodis pv. Citri (Xac)*, *Ralstonia solanacearum (Rs)*, and *Xanthomonas oryzae pv. oryzae (Xoo)*, respectively. Meanwhile, these bacterial diseases have a serious impact on the yield of crops every year [1–3]. Although there are many traditional agricultural fungicides on the market at present, the extensive application and abuse of antibacterial drugs have not only increased the resistance of pathogenic genes, but also caused serious environmental pollution and affect human health [4–6]. Therefore, it is of great significance to develop a new kind of antibacterial reagents with high efficiency and novel mechanism.

Myricetin, also named as 3′,4′,5′,3,5,7-hexahydroxyflavonol (Fig. 1A), is a class of flavonoids widely found in fruits, vegetables, teas, and so on [7]. Myricetin has been disclosed to display extensive biological activities, such as antibacterial [8, 9], antiviral [10, 11], antioxidant [12, 13], anti-inflammatory [14, 15], anticancer [16, 17], hypoglycemic [18] activities, and cardioprotective effects [19]. Due to

wide range of plant sources and biological activity, myricetin and its derivatives have attracted more and more attention of researchers in recent years. In our previous study, we have demonstrated that myricetin derivatives exhibited excellent antibacterial activity [20, 21] (Fig. 1B and C). Myricetin derivatives could destroy the integrity of the cell membrane and cause the death of bacteria, thus achieving the objective of bacteriostasis [22].

Sulfonate derivatives, owing to physicochemical properties, have a strong affinity for lipid phases and can cross the cuticle membrane easily to bind to target sites [23], and compounds containing aryl sulfonate moieties have received considerable attention due to extensive biological activities, and it has been proven to possess antiviral [24, 25], antibacterial [26–28], insecticidal [29, 30], anticancer [31, 32], and other biological activity [33]. They were widely used in agricultural industries, medicine researches and other fields. We theorized that introducing sulfonate groups into myricetin might generate novel lead molecules with better physicochemical properties. Therefore, a series of novel myricetin derivatives containing sulfonate were designed (Fig. 2), synthesized (Scheme 1), and their in vitro and in vivo antibacterial activity was evaluated. To the best of our knowledge, this is the first report on the synthesis and
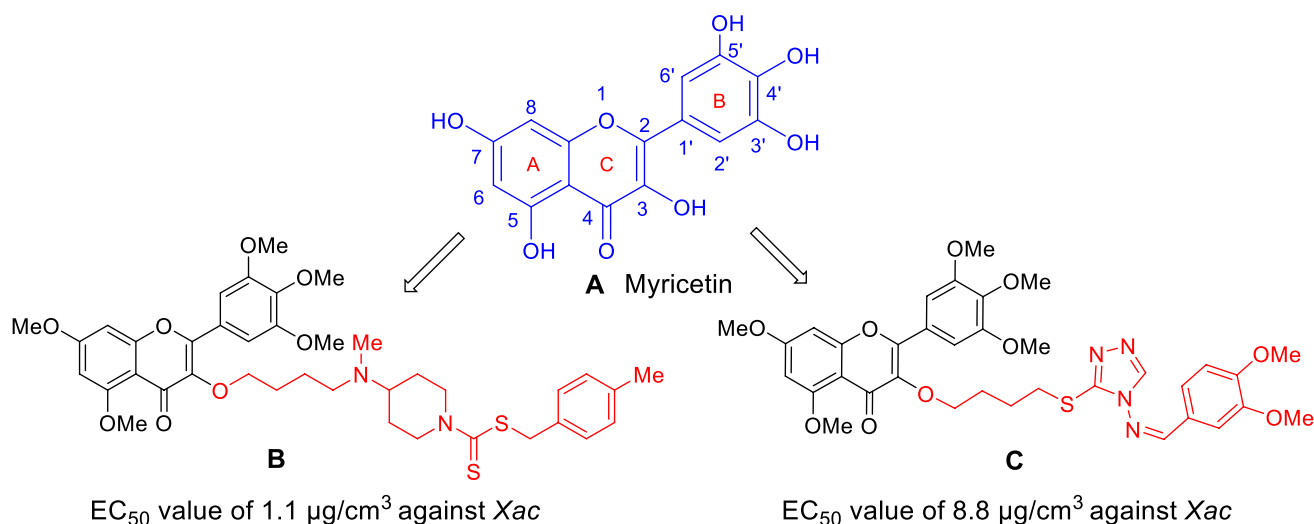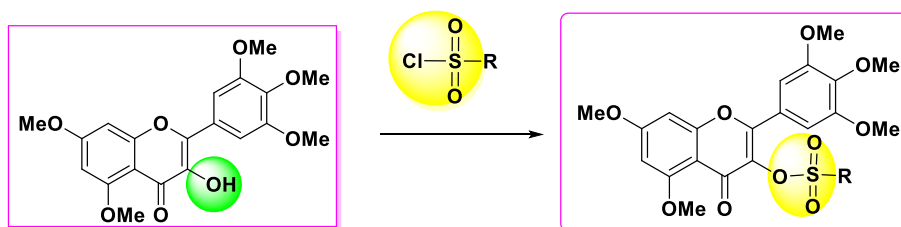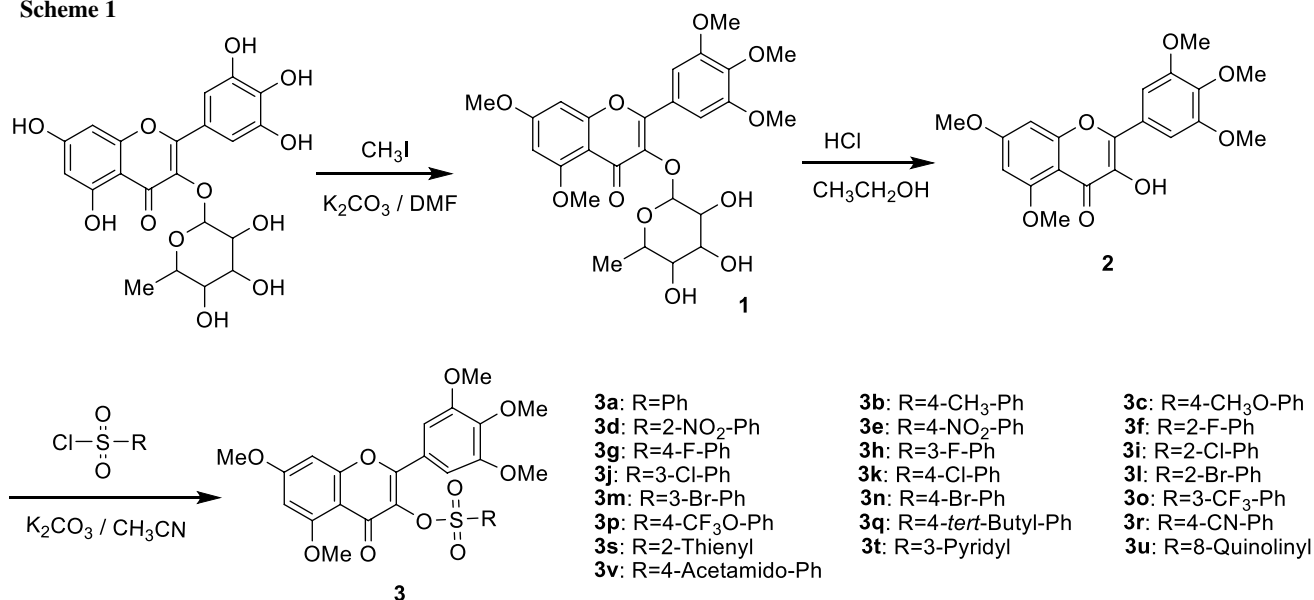


**Fig. 1** Structure of myricetin and its derivatives with antibacterial activity



**Fig. 2** Design strategy of the title compounds

**Scheme 1**



**3a**: R=Ph
**3d**: R=2-NO$_2$-Ph
**3g**: R=4-F-Ph
**3j**: R=3-Cl-Ph
**3m**: R=3-Br-Ph
**3p**: R=4-CF$_3$O-Ph
**3s**: R=2-Thienyl
**3v**: R=4-Acetamido-Ph

**3b**: R=4-CH$_3$-Ph
**3e**: R=4-NO$_2$-Ph
**3h**: R=3-F-Ph
**3k**: R=4-Cl-Ph
**3n**: R=4-Br-Ph
**3q**: R=4-*tert*-Butyl-Ph
**3t**: R=3-Pyridyl

**3c**: R=4-CH$_3$O-Ph
**3f**: R=2-F-Ph
**3i**: R=2-Cl-Ph
**3l**: R=2-Br-Ph
**3o**: R=3-CF$_3$-Ph
**3r**: R=4-CN-Ph
**3u**: R=8-Quinolinyl

antibacterial activity evaluation of myricetin derivatives containing sulfonate moiety.

# Results and discussion

The synthetic route of myricetin derivatives containing sulfonate is shown in Scheme 1. Myricetrin, methyl iodide, and potassium carbonate were mixed and stirred at room temperature to give intermediate 1 and then continued to react with concentrated hydrochloric acid to get intermediate **2**. Intermediate **2** was treated with different benzenesulfonyl chlorides in the presence of potassium carbonate to obtain

the target products **3a**–**3v** in good yields ranging from 53 to 89%.

The structures of all compounds were confirmed by ^{1}H NMR, ^{13}C NMR, ^{19}F NMR, and HRMS. The representative data of compound 3b are shown below. In the ^{1}H NMR spectrum, the multiple signal $\delta = 6.57$–$7.57$ ppm demonstrated the presence of aromatic ring protons, the singlet signal of 3.6–4.0 ppm belonged to -OCH$_3$ on myricetin, and the singlet signal of 2.34 ppm indicates the presence of –CH$_3$ group. Typical chemical shifts at $\delta = 145.45$, 133.91, and 21.56 ppm in ^{13}C NMR spectrum confirmed the existence of –O–C-, –S–C–, and –CH$_3$ groups, respectively. In ^{19}F NMR spectrum, the obvious singlets at $-109.88$, $-107.54$, $-103.47$, $-61.51$, and $-56.74$ ppm confirm,

**Table 1** Crystal data of title compound **3n**

| Crystal data | |
| --- | --- |
| C$_{26}$H$_{23}$BrO$_{10}$S | $T = 293$ K |
| FW = 607.41 | $\alpha = 90°$ |
| Monoclinic /C12/c 1 | $\beta = 107.9680(10)°$ |
| $a = 18.2079(6)$ Å | $\gamma = 90°$ |
| $b = 20.8420(6)$ Å | $V = 5117.0(3)$ Å$^3$ |
| $c = 14.1753(4)$ Å | $Z = 8$ |
| $F(000) = 2480$ | $\rho = 1.577$ mg/m$^3$ |
| Data collection | |
| $T_{min} = 0.8914$, $T_{max} = 0.9866$ | Absorption coefficient: 3.465 mm$^{-1}$ |
| 18,533 Reflections collected | $-21 < =h < =21$, $-24 < =k < =24$, $-13 < =l < =16$ |
| 4341 independent reflections | $\theta_{min} = 3.318°$, $\theta_{max} = 65.115°$ |
| Refinement | |
| 349 parameters | $R$ indices (all data) $R_1 = 0.0548$, w$R_2 = 0.1447$ |
| Goodness-of-fit: 1.052 | $R$ indices [$I > 2\sigma(I)$] $R_1 = 0.0536$, w$R_2 = 0.1440$ |
| Extinction coefficient = 0.00125(12) | $\Delta\rho_{max} = 0.818$ eÅ$^{-3}$, $\Delta\rho_{min} = -0.779$ eÅ$^{-3}$ |

**Fig. 3** Crystal structure and crystal packing diagram of compound **3n**
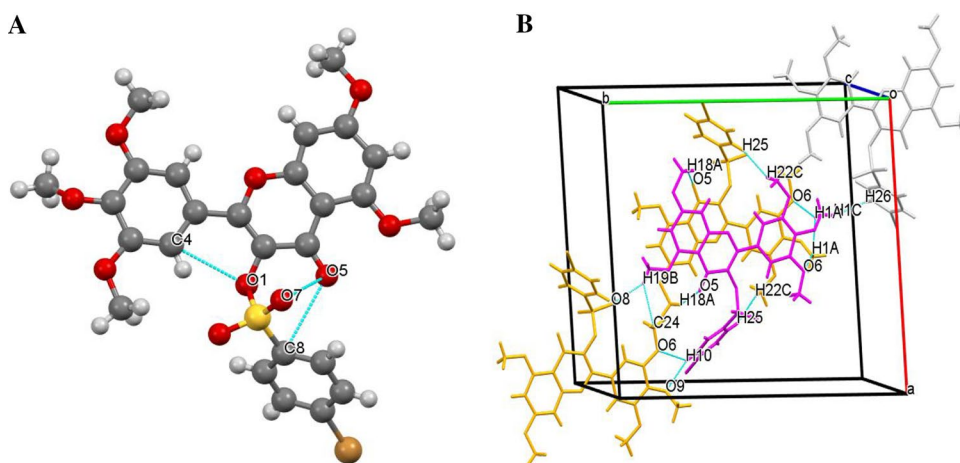


respectively, the presence of a 3-F atom, a 2-F atom, a 4-F atom, a 3-CF$_3$, and a 4-OCF$_3$ group at the benzene ring. The strong presence of [M + H]$^+$ ions indicates the stable state of the title compounds.

To further confirm the structure of synthesized compounds, the molecular structure of **3n** was studied as a representative example by single-crystal *X-ray* analysis. The tested single crystal was crystallized from the mixture of acetone and *N,N*-dimethylformamide solution under room temperature. The crystal diffraction data are presented in Table 1. Crystal structure diagram and crystal packing diagram are shown in Fig. 3A and B, respectively. Figure 3A shows that the intramolecular hydrogen bond C$_4$···O$_1$, O$_7$···O$_5$, O$_5$···C$_8$ in crystal combines with the skeleton of myricetin and sulfonate. As showed in Fig. 3B, the four intermolecular hydrogen bonds H$_{25}$···H$_{22}$–C, H$_{18}$A···O5, C–H$_1$A···O$_6$, and C–H$_1$A···H$_1$A-C constructed the three-dimensional structure of target compound **3n**. The deposition number is CCDC-2017276.

## Antibacterial activity

The in vitro antibacterial activities of the title compounds **3a–3v** against three phytopathogenic bacteria (*Xac*, *Rs*, and *Xoo*) were tested by turbidimeter [34, 35]. The commercial bactericides bismerthiazol (BT) and thiadiazole-copper (TC) were used as a positive control under the same conditions, the bioassay results showed (Table 2) that some of the compounds exhibited considerable antibacterial effects against *Xac*, *Rs*, and *Xoo*. Especially, compounds **3e, 3i, 3k, 3n, 3o**, and **3q** showed excellent antibacterial activity against *Xac* at 100 μg/cm$^3$, with the inhibition rates of 95, 82, 88, 93, 90, and 82%, respectively, which were superior to the commercial bactericides BT (66%) and TC (56%). Meanwhile, the title compounds **3d, 3h, 3j, 3m**, and **3p**

exhibited obvious antibacterial activity against *Rs* at 100 μg/cm$^3$, with the inhibition rates of 86, 87, 92, 90, and 87%, respectively, which exceeded both BT (70%) and TC (57%). And the antibacterial activity of the compounds **3b, 3c, 3h, 3j**, and **3r** against *Xoo* at 100 μg/cm$^3$ were 90%, 89%, 91%, 94%, 80%, respectively, which were better than BT (50%) and TC (47%). Obviously, most of the myricetin derivatives containing sulfonate had better inhibitory effects against bacteria than lead compound myricetin.

In order to further confirm the antibacterial activities of title compounds, their EC$_{50}$ values were determined. The results indicated that compounds **3e, 3i, 3k, 3n**, and **3o** exhibited prominent antibacterial activity against *Xac* with EC$_{50}$ values of 13.72, 23.19, 19.81, 16.89, and 19.19 μg/cm$^3$ (Table 3), which were superior to BT (50.32 μg/cm$^3$) and TC (83.27 μg/cm$^3$). Meanwhile, Table 3 indicated that compounds **3a, 3d, 3h**, and **3j** displayed excellent antibacterial activity against *Rs* with the EC$_{50}$ values of 26.66, 25.07, 21.64, and 17.11 μg/cm$^3$, respectively, which were better than BT (43.53 μg/cm$^3$) and TC (64.32 μg/cm$^3$). Compounds **3b**, **3c**, **3h**, and **3j** have fine antibacterial activity against *Xoo* with EC$_{50}$ values of 21.93, 24.98, 19.53, and 11.92 μg/cm$^3$, respectively, which were better than BT (72.08 μg/cm$^3$) and TC (99.26 μg/cm$^3$). The results showed that these compounds could be further studied as potential compounds in search of novel antibacterial agents.

## Structure–activity relationships (SAR) of antibacterial activities

It can be seen from Tables 2 and 3 that the substituents greatly impact the inhibition effects against bacteria. When the R group were 4-NO$_2$-C$_6$H$_5$ (**3e**), 4-Cl-C$_6$H$_5$ (**3k**), 4-Br-C$_6$H$_5$ (**3n**), and 3-CF$_3$-C$_6$H$_5$ (**3o**), their inhibition rates against *Xac* at 100 μg/cm$^3$ were 95, 88, 93, and

**Table 2** Inhibition rate of title compounds **3a–3v** against *Xac*, *Rs*, and *Xoo* in vitro

| Compd | R | Xac/% | | Rs/% | | Xoo/% | |
|---|---|---|---|---|---|---|---|
| | | 100 µg/cm³ | 50 µg/cm³ | 100 µg/cm³ | 50 µg/cm³ | 100 µg/cm³ | 50 µg/cm³ |
| 3a | $C_6H_5$ | 48 | 27 | 85 | 54 | 48 | 30 |
| 3b | 4-$CH_3$-$C_6H_5$ | 50 | 28 | 58 | 27 | 90 | 70 |
| 3c | 4-$CH_3O$-$C_6H_5$ | 41 | 21 | 34 | 12 | 89 | 75 |
| 3d | 2-$NO_2$-$C_6H_5$ | 79 | 59 | 86 | 56 | 54 | 30 |
| 3e | 4-$NO_2$-$C_6H_5$ | 95 | 78 | 76 | 39 | 60 | 40 |
| 3f | 2-F-$C_6H_5$ | 60 | 40 | 70 | 43 | 56 | 34 |
| 3g | 4-F-$C_6H_5$ | 43 | 27 | 71 | 43 | 37 | 17 |
| 3h | 3-F-$C_6H_5$ | 71 | 44 | 87 | 51 | 91 | 69 |
| 3i | 2-Cl-$C_6H_5$ | 82 | 41 | 75 | 32 | 73 | 48 |
| 3j | 3-Cl-$C_6H_5$ | 60 | 46 | 92 | 66 | 94 | 72 |
| 3k | 4-Cl-$C_6H_5$ | 88 | 68 | 57 | 35 | 69 | 34 |
| 3l | 2-Br-$C_6H_5$ | 75 | 49 | 65 | 37 | 33 | 17 |
| 3m | 3-Br-$C_6H_5$ | 63 | 34 | 90 | 60 | 80 | 50 |
| 3n | 4-Br-$C_6H_5$ | 93 | 72 | 67 | 41 | 55 | 29 |
| 3o | 3-$CF_3$-$C_6H_5$ | 90 | 69 | 71 | 55 | 74 | 36 |
| 3p | 4-$CF_3O$-$C_6H_5$ | 38 | 22 | 87 | 63 | 31 | 22 |
| 3q | 4-*tert*-Butyl-$C_6H_5$ | 82 | 54 | 64 | 53 | 67 | 46 |
| 3r | 4-CN-$C_6H_5$ | 64 | 55 | 55 | 38 | 78 | 57 |
| 3s | 2-Thienyl | 45 | 29 | 36 | 14 | 35 | 24 |
| 3t | 3-Pyridyl | 55 | 37 | 54 | 35 | 36 | 19 |
| 3u | 3-Quinolinyl | 38 | 21 | 40 | 16 | 23 | 13 |
| 3v | 4-Acetamido-$C_6H_5$ | 26 | 17 | 63 | 31 | 40 | 20 |
| Myr | – | 47 | 36 | 65 | 40 | 40 | 27 |
| BT | – | 66 | 42 | 70 | 44 | 50 | 31 |
| TC | – | 56 | 38 | 57 | 36 | 47 | 29 |

**Table 3** $EC_{50}$ values of some target compounds against *Xac*, *Xoo*, and *Rs*

| Compound | R | EC₅₀/µg cm⁻³ | | |
|---|---|---|---|---|
| | | *Xac* | *Xoo* | *Rs* |
| 3a | $C_6H_5$ | – | – | 26.66 |
| 3b | 4-$CH_3$-$C_6H_5$ | – | 21.93 | – |
| 3c | 4-$CH_3O$-$C_6H_5$ | – | 24.98 | – |
| 3d | 2-$NO_2$-$C_6H_5$ | – | – | 25.07 |
| 3e | 4-$NO_2$-$C_6H_5$ | 13.76 | – | – |
| 3h | 3-F-$C_6H_5$ | | 19.53 | 21.64 |
| 3i | 2-Cl-$C_6H_5$ | 23.19 | – | – |
| 3j | 3-Cl-$C_6H_5$ | – | 11.92 | 17.11 |
| 3k | 4-Cl-$C_6H_5$ | 19.81 | – | – |
| 3m | 3-Br-$C_6H_5$ | – | 35.98 | 35.04 |
| 3n | 4-Br-$C_6H_5$ | 16.89 | – | – |
| 3o | 3-$CF_3$-$C_6H_5$ | 19.19 | – | – |
| 3p | 4-$CF_3O$-$C_6H_5$ | – | – | 33.96 |
| 3q | 4-*tert*-Butyl-$C_6H_5$ | 29.67 | – | – |
| 3r | 4-CN-$C_6H_5$ | – | 29.47 | – |
| Myr | – | 92.34 | 108.43 | 68.79 |
| BT | – | 50.32 | 72.08 | 43.53 |
| TC | – | 83.27 | 99.26 | 64.32 |

90%, respectively, which were superior to the BT (66%), TC (56%), myricitin (47%), 3a (R=$C_6H_5$, 48%), **3b** (R=4-$CH_3$-$C_6H_5$, 50%), and **3c** (R=4-$OCH_3$-$C_6H_5$, 41%). The results indicated that the electron-absorbing groups on aromatic rings were favorable for the antibacterial activity against *Xac*. The designated compounds **3d** (R=2-$NO_2$-$C_6H_5$), **3h** (R=3-F-$C_6H_5$), **3j** (R=3-Cl-$C_6H_5$), **3m** (R=3-Br-$C_6H_5$), and **3p** (R=4-$OCF_3$-$C_6H_5$) also effectively enhance the antibacterial activity against *Rs* at 100 µg/cm³, with inhibition rates of 86, 87, 92, 90, and 87%, respectively, which exceeded BT (70%) and TC (57%), myricitin (65%), **3b** (R=4-$CH_3$-$C_6H_5$, 58%), and **3c** (R=4-$OCH_3$-$C_6H_5$, 34%) thus, the electron-absorbing groups on aromatic rings were favorable for the antibacterial activity against *Rs,* the electron-donating groups on the aromatic rings were not favorable the biological activity of the corresponding compounds against *Rs*. At the same time, when the R group were 4-$CH_3$-$C_6H_5$ (**3b**), 4-$OCH_3$-$C_6H_5$ (**3c**), 3-F-$C_6H_5$ (**3h**), 3-Cl-$C_6H_5$ (**3j**), and 3-Br-$C_6H_5$ (**3r**), corresponding compounds possess better antibacterial activity against *Xoo*, with inhibition rates of 90, 89, 91, 94, and 80%, respectively, which were better than that of BT (50%), TC (47%), myricitin (40%), and **3a** (R=$C_6H_5$, 48%), the results showed that

**Table 4** Curative and protection effects of compound **3j** against *Xoo* under greenhouse conditions at 200 μg/cm$^3$

| Treatment | Curative activity | | Protection activity | |
|---|---|---|---|---|
| | Disease index /% | Control efficiency /% | Disease index /% | Control efficiency /% |
| **3j** | 50 | 40 | 44 | 47 |
| Bismerthiazol | 55 | 35 | 51 | 39 |
| Thiodiazole-copper | 59 | 30 | 61 | 27 |
| Negative control | 85 | – | 85 | – |

electron-withdrawing groups on 3-position of aromatic rings and electron-donating groups on 4-position of aromatic rings were favorable for the antibacterial activity against *Xoo*.

The control effect of compound **3j** against rice bacterial leaf blight was determined by leaf-cutting method. As shown in Table 4 and Fig. 4, the effective curative activity against rice bacterial leaf blight was 40%, which was better than BT (35%) and TC (30%). Furthermore, **3j** demonstrated better protection activity (47%) against rice bacterial leaf blight

than BT (39%) and TC (27%). These results suggest that **3j** effectively inhibit the growth of rice bacterial leaf blight under greenhouse conditions.

## Scanning electron microscopy (SEM) studies

Through the analysis of antibacterial activity, the mechanism of **3e** for *Xac* and **3j** for *Xoo* were further studied via SEM. We found that the increase of concentration would lead to the deepening of cell membrane damage, in the control group without treatment with compound, the cell membrane were full and remains intact (Figs. 5A and 6D). Part of the cell membranes began to be destroyed when the concentration was 50 μg/cm$^3$ (Figs. 5B and 6E). And most of the cell membrane was destroyed when the concentration was increased to 100 μg/cm$^3$, and only a few cells were remained unaffected (Figs. 5C and 6F). These results showed that the damage of cell membrane became more and more serious with the increasing of the compound concentration. These SEM images further confirmed that 3e and 3j destroyed the bacterial cell membrane and eventually killed the bacteria.



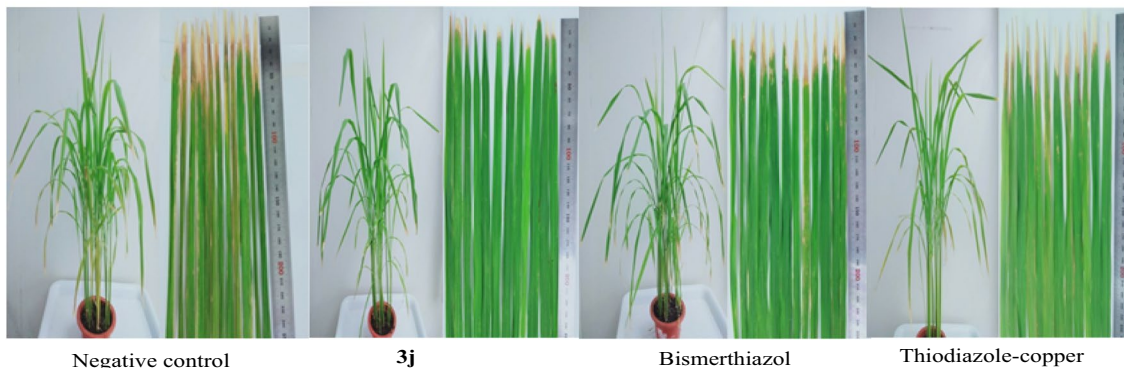**Fig. 4** Curative and protective effects of compound **3j** (200 μg/cm$^3$) against *Xoo* under greenhouse conditions. BT and TC were used as positive controls under similar experimental conditions

**Fig. 5** SEM images for *Xac* after incubated using different concentrations of compound **3e**, **a** 0 μg/cm³, **b** 50 μg/cm³, **c** 100 μg/cm³. Scale bar for **A–C** are 2 μm
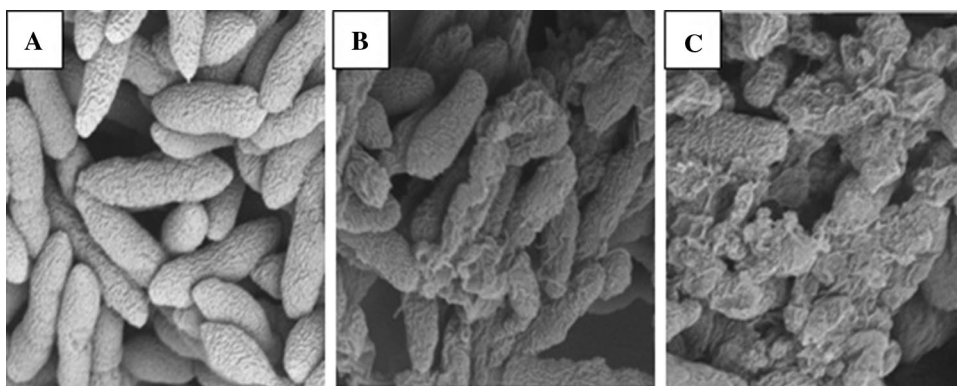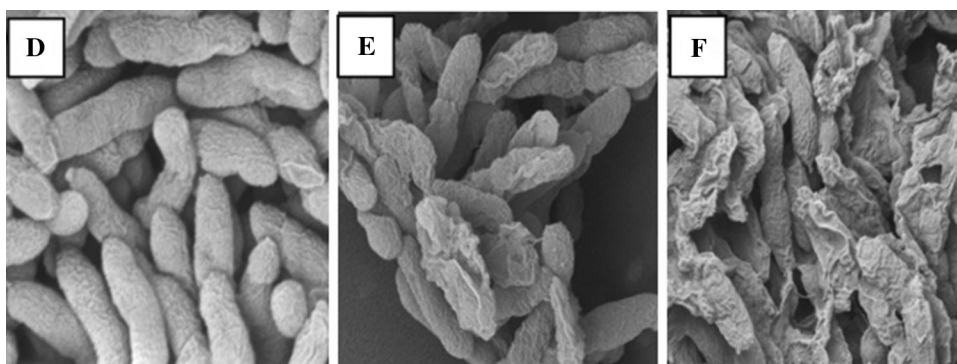


**Fig. 6** SEM images for *Xoo* after incubated using different concentrations of compound **3j**, **d** 0 μg/cm³, **e** 50 μg/cm³, and **f** 100 μg/cm³. Scale bar for **D–F** are 2 μm



## Conclusions

In conclusion, a series of myricetin derivatives containing sulfonate were designed and synthesized, the antibacterial activity of these derivatives against *Xac*, *Rs*, and *Xoo* have been tested in vitro, and the results indicated that most of compounds have good antibacterial activities. Especially compound **3e** against *Xac* and compound **3j** against *Xoo* wih the $EC_{50}$ values were 13.76, 11.92 μg/cm³, respectively, which were superior to BT (50.32 and 72.08 μg/cm³, respectively) and TC (83.2 and 99.2 μg/cm³, respectively). Compound **3j** also displayed good antibacterial activities against rice bacterial leaf blight (curative activity was 40.7% and protective activity was 47.9%), which were superior to the curative and protection activities of BT (35% and 39%) and TC (30% and 27%). The SEM images of *Xac* treated with compound **3e** and *Xoo* treated with compound **3j** revealed that the cell membranes of bacteria are deformed and broken. These results demonstrate that novel myricetin derivatives containing sulfonate could be further studied as new antibacterial compounds.

## Experimental

All reagents and solutions were purchased from Chemical Reagent Company and were analytical grade reagents. The melting point of all synthesized compounds were found by an XT-4 Binocular Microscope melting point apparatus (Beijing Tech. Instrument, China). DMSO-$d_6$ were used as a solvent and TMS as an internal standard, a Bruker Ascend-400 spectrometer (Bruker Optics, Switzerland) was used to give the ¹H NMR, ¹³C NMR, and ¹⁹F NMR spectra of title compounds. HRMS data were obtained using Thermo Scientific Q Exactive Hybrid Quadrupole Mass Spectrometer (Thermo Scientific Inc., St Louis, MO, USA). The X-ray crystal data were acquired using a Bruker D8-QUEST diffractometer (Bruker Optics, Switzerland). All ¹H NMR, ¹³C NMR, and ¹⁹F NMR spectra, and HRMS are provided in Supporting Information.

## General synthesis procedure for intermediate 1 and intermediate 2

Based on the previously reported method [36–38], the synthetic route of target compound is listed in Scheme 1. The myricetin, anhydrous potassium carbonate and *N,N*-dimethylformamide (DMF) were added to a round-bottom flask with magnetic stirring; the reaction mixture was allowed to stir for 20 min at room temperature and potassium iodide was asses dropwise slowly. After completion of the reaction, monitored by TLC plate, the reaction mixture was extracted with dichloromethane and the solvent was removed under reduced pressure to obtain 5,7-dimethoxy-3-[(3,4,5-trimethoxy-6-methyltetrahydro-2*H*-pyran-2-yl)-

oxy]-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-4-one (intermediate 1), which was used for the next step without purification.

Intermediate 1 was added in ethanol and refluxed with stirring for 2 h. Concentrated hydrochloric acid was slowly added dropwise at this temperature, continued to reflux for 2–3 h, and a large amount of solid precipitated when the reaction was cooled to ambient temperature, which was filtered and dried to obtain 3-hydroxy-5,7-dimethoxy-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-4-one (intermediate 2).

## General synthesis procedure for target compounds 3a–3v

Intermediate 2, anhydrous potassium carbonate and acetonitrile were added to round-bottom flask with magnetic stirring and reflux for 0.5–1 h.

Then substituted benzenesulfonyl chloride was added and continued to reflux for 2–3 h until completion of the reaction as determined by TLC. The mixture was cooled to room temperature and poured into ice water; the crude products were recrystallized with anhydrous ethanol and DMF to give target compounds **3a–3v**.

**5,7-Dimethoxy-4-oxo-2-(3,4,5-trimethoxyphenyl)-4***H***-chromen-3-yl benzenesulfonate (3a, $C_{26}H_{24}O_{10}S$)** Yellow solid; yield: 89%; m.p.: 194–195 °C; $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta = 7.71$ (dd, $J = 8.4, 1.1$ Hz, 2H, Ph-H), 7.64 (t, $J = 7.5$ Hz, 1H, Ph-H), 7.45 (dd, $J = 8.2, 7.6$ Hz, 2H, Ph-H), 6.95 (s, 2H, Ph-H), 6.85 (d, $J = 2.2$ Hz, 1H, Ph-H), 6.58 (d, $J = 2.2$ Hz, 1H, Ph-H), 3.91 (s, 3H, Ph-OCH$_3$), 3.87 (s, 3H, Ph-OCH$_3$), 3.75 (s, 6H, 2×Ph-OCH$_3$), 3.72 (s, 3H, Ph-OCH$_3$) ppm; $^{13}$C NMR (101 MHz, DMSO-$d_6$): $\delta = 170.08$, 164.84, 160.87, 158.69, 155.58, 152.96, 140.18, 137.13, 134.83, 133.22, 129.58, 128.89, 128.11, 127.97, 125.95, 124.22, 108.34, 106.63, 97.11, 93.99, 60.41, 56.77, 56.68, 56.42 ppm; HRMS (ESI): *m/z* calcd. [M + H]$^+$ 529.114, found 529.116.

**5,7-Dimethoxy-4-oxo-2-(3,4,5-trimethoxyphenyl)-4***H***-chromen-3-yl 4-methylbenzenesulfonate (3b, $C_{27}H_{26}O_{10}S$)** White solid; yield: 81%; m.p.: 170–171 °C; $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta = 7.56$ (d, $J = 8.3$ Hz, 2H, Ph-H), 7.23 (d, $J = 8.1$ Hz, 2H, Ph-H), 6.92 (s, 2H, Ph-H), 6.83 (d, $J = 2.2$ Hz, 1H, Ph-H), 6.57 (d, $J = 2.2$ Hz, 1H, Ph-H), 3.91 (s, 3H, Ph-OCH$_3$), 3.87 (s, 3H, Ph-OCH$_3$), 3.76 (s, 6H, 2×Ph-OCH$_3$), 3.73 (s, 3H, Ph-OCH$_3$), 2.34 (s, 3H, Ph-CH$_3$) ppm; $^{13}$C NMR (101 MHz, DMSO-$d_6$): $\delta = 170.12$, 164.80, 160.86, 158.67, 155.58, 152.95, 145.45, 140.29, 133.91, 133.07, 130.03, 128.10, 124.27, 108.40, 106.62, 97.08, 93.96, 60.55, 56.75, 56.65, 56.40, 21.49 ppm; HRMS (ESI): *m/z* calcd. [M + H]$^+$ 543.1306, found 543.1319.

**5,7-Dimethoxy-4-oxo-2-(3,4,5-trimethoxyphenyl)-4***H***-chromen-3-yl 4-methoxybenzenesulfonate (3c, $C_{27}H_{26}O_{11}S$)** White solid; yield: 73%; m.p.: 150–151 °C; $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta = 7.61$–7.57 (m, 2H, Ph-H), 6.91 (s, 2H, Ph-H), 6.89 (d, $J = 1.9$ Hz, 2H, Ph-H), 6.84 (d, $J = 2.2$ Hz, 1H, Ph-H), 6.58 (d, $J = 2.2$ Hz, 1H, Ph-H), 3.91 (s, 3H, Ph-OCH$_3$), 3.87 (s, 3H, Ph-OCH$_3$), 3.81 (s, 3H, Ph-OCH$_3$), 3.77 (s, 6H, 2×Ph-OCH$_3$), 3.72 (s, 3H, Ph-OCH$_3$) ppm; $^{13}$C NMR (101 MHz, DMSO-$d_6$): $\delta = 170.20$, 164.78, 163.93, 160.87, 158.68, 155.58, 152.94, 140.16, 133.00, 130.52, 127.92, 124.35, 114.79, 108.46, 106.60, 97.09, 93.97, 60.45, 56.77, 56.66, 56.41, 56.20 ppm; HRMS (ESI): *m/z* calcd. [M + H]$^+$ 559.1256, found 559.1268.

**5,7-Dimethoxy-4-oxo-2-(3,4,5-trimethoxyphenyl)-4***H***-chromen-3-yl 2-nitrobenzenesulfonate (3d, $C_{26}H_{23}NO_{12}S$)** Yellow solid; yield: 74%; m.p.: 239–241 °C; $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta = 8.06$ (d, $J = 8.1$ Hz, 1H, Ph-H), 7.92 (dd, $J = 12.0, 4.4$ Hz, 2H, Ph-H), 7.76–7.70 (m, 1H, Ph-H), 7.06 (s, 2H, Ph-H), 6.88 (d, $J = 1.9$ Hz, 1H, Ph-H), 6.59 (d, $J = 2.1$ Hz, 1H, Ph-H), 3.92 (s, 3H, Ph-OCH$_3$), 3.86 (s, 3H, Ph-OCH$_3$), 3.80 (s, 6H, 2×Ph-OCH$_3$), 3.69 (s, 3H, Ph-OCH$_3$) ppm; $^{13}$C NMR (101 MHz, DMSO-$d_6$): $\delta = 169.77$, 165.00, 160.91, 158.80, 155.85, 153.00, 147.49, 140.25, 136.58, 133.60, 133.28, 131.36, 129.64, 125.14, 123.86, 108.21, 106.68, 97.23, 94.07, 60.43, 56.82, 56.72, 56.40 ppm; HRMS (ESI): *m/z* calcd. [M + H]$^+$ 574.0999, found 574.1013.

**5,7-Dimethoxy-4-oxo-2-(3,4,5-trimethoxyphenyl)-4***H***-chromen-3-yl 4-nitrobenzenesulfonate (3e, $C_{26}H_{23}NO_{12}S$)** Yellow solid; yield: 71%; m.p.: 220–221 °C; $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta = 8.27$–8.23 (m, 2H, Ph-H), 8.03–7.99 (m, 2H, Ph-H), 6.93 (s, 2H, Ph-H), 6.86 (d, $J = 2.2$ Hz, 1H, Ph-H), 6.59 (d, $J = 2.2$ Hz, 1H, Ph-H), 3.91 (s, 3H, Ph-OCH$_3$), 3.86 (s, 3H, Ph-OCH$_3$), 3.77 (s, 6H, 2×Ph-OCH$_3$), 3.67 (s, 3H, Ph-OCH$_3$) ppm; $^{13}$C NMR (101 MHz, DMSO-$d_6$): $\delta = 169.82$, 164.97, 160.88, 158.75, 155.82, 152.99, 150.60, 142.21, 140.32, 133.15, 129.88, 124.73, 123.91, 108.28, 106.69, 97.21, 94.05, 60.37, 56.80, 56.71, 56.49 ppm; HRMS (ESI): *m/z* calcd. [M + H]$^+$ 574.0999, found 574.1013.

**5,7-Dimethoxy-4-oxo-2-(3,4,5-trimethoxyphenyl)-4***H***-chromen-3-yl 2-fluorobenzenesulfonate (3f, $C_{26}H_{23}FO_{10}S$)** White solid; yield: 83%; m.p.: 196–198 °C; $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta = 7.74$–7.65 (m, 2H, Ph-H), 7.33–7.26 (m, 2H, Ph-H), 6.98 (s, 2H, Ph-H), 6.83 (d, $J = 2.2$ Hz, 1H, Ph-H), 6.57 (d, $J = 2.2$ Hz, 1H, Ph-H), 3.90 (s, 3H, Ph-OCH$_3$), 3.85 (s, 3H, Ph-OCH$_3$), 3.79 (s, 6H, 2×Ph-OCH$_3$), 3.73 (s, 3H, Ph-OCH$_3$) ppm; $^{13}$C NMR (101 MHz, DMSO): $\delta = 169.82$, 164.89, 160.86, 158.69, 155.78, 153.02, 140.13, 137.78 (d, $J = 8.7$ Hz), 133.21, 130.41, 125.26 (d, $J = 13.9$ Hz),

124.12, 117.85, 117.74 (d, $J = 20.4$ Hz), 108.29, 106.39, 97.14, 94.00, 60.41, 56.71, 56.39 ppm; $^{19}$F NMR (376 MHz, DMSO-$d_6$): $\delta = $ -107.54 ppm; HRMS (ESI): $m/z$ calcd. [M + H]$^+$ 547.1056, found 547.1068.

**5,7-Dimethoxy-4-oxo-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-3-yl 4-fluorobenzenesulfonate (3g, C$_{26}$H$_{23}$FO$_{10}$S)** White solid; yield: 72%; m.p.: 195–197 °C; $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta = $ 7.80 (dd, $J = 8.9$, 5.0 Hz, 2H, Ph-H), 7.27 (t, $J = 8.8$ Hz, 2H, Ph-H), 6.94 (s, 2H, Ph-H), 6.85 (d, $J = 2.2$ Hz, 1H, Ph-H), 6.59 (d, $J = 2.2$ Hz, 1H, Ph-H), 3.91 (s, 3H, Ph-OCH$_3$), 3.87 (s, 3H, Ph-OCH$_3$), 3.78 (s, 6H, 2×Ph-OCH$_3$), 3.72 (s, 3H, Ph-OCH$_3$) ppm; $^{13}$C NMR (101 MHz, DMSO-$d_6$): $\delta = $ 170.06, 164.87, 160.88, 158.72, 155.62, 152.99, 140.22, 133.21 (d, $J = 15.4$ Hz), 131.42 (d, $J = 10.1$ Hz), 124.21, 117.03, 116.81, 108.36, 106.64, 97.13, 94.00, 60.42, 56.73, 56.46 ppm; $^{19}$F NMR (376 MHz, DMSO-$d_6$): $\delta = $ -103.47 ppm; HRMS (ESI): $m/z$ calcd. [M + H]$^+$ 547.1057, found 547.1068.

**5,7-Dimethoxy-4-oxo-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-3-yl 3-fluorobenzenesulfonate (3h, C$_{26}$H$_{23}$FO$_{10}$S)** Yellow solid; yield: 68%; m.p.: 195–196 °C; $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta = $ 7.64–7.59 (m, 1H, Ph-H), 7.55–7.49 (m, 3H, Ph-H), 6.95 (s, 2H, Ph-H), 6.85 (d, $J = 2.2$ Hz, 1H, Ph-H), 6.58 (d, $J = 2.2$ Hz, 1H, Ph-H), 3.91 (s, 3H, Ph-OCH$_3$), 3.87 (s, 3H, Ph-OCH$_3$), 3.77 (s, 6H, 2×Ph-OCH$_3$), 3.72 (s, 3H, Ph-OCH$_3$) ppm; $^{13}$C NMR (101 MHz, DMSO-$d_6$): $\delta = $ 170.03, 164.88, 162.99, 160.88, 160.52, 158.74, 155.61, 152.97, 140.14, 139.13 (d, $J = 7.5$ Hz), 133.27, 131.97 (d, $J = 8.1$ Hz), 124.22 (d, $J = 18.1$ Hz), 122.29, 122.08, 115.18, 114.93, 108.32, 106.59, 97.13, 94.01, 60.29, 56.73, 56.41 ppm; $^{19}$F NMR (376 MHz, DMSO-$d_6$): $\delta = $ -109.88 ppm; HRMS (ESI): $m/z$ calcd. [M + H]$^+$ 547.1051, found 547.1068.

**5,7-Dimethoxy-4-oxo-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-3-yl 2-chlorobenzenesulfonate (3i, C$_{26}$H$_{23}$ClO$_{10}$S)** White solid; yield: 65%; m.p.: 227–229 °C; $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta = $ 7.83 (dd, $J = 7.4$, 2.1 Hz, 1H, Ph-H), 7.77 (dd, $J = 7.5$, 1.5 Hz, 1H, Ph-H), 7.57–7.47 (m, 2H, Ph-H), 7.01 (s, 2H, Ph-H), 6.83 (d, $J = 2.1$ Hz, 1H, Ph-H), 6.57 (d, $J = 2.1$ Hz, 1H, Ph-H), 3.90 (s, 3H, Ph-OCH$_3$), 3.84 (s, 3H, Ph-OCH$_3$), 3.82 (s, 6H, 2×Ph-OCH$_3$), 3.73 (s, 3H, Ph-OCH$_3$) ppm; $^{13}$C NMR (101 MHz, DMSO-$d_6$): $\delta = $ 169.85, 164.92, 160.92, 158.75, 155.93, 153.02, 140.15, 137.63, 135.84, 135.76, 133.58, 131.39, 128.44, 124.03, 120.11, 108.31, 106.57, 97.16, 94.04, 60.41, 56.79, 56.68, 56.49 ppm; HRMS (ESI): $m/z$ calcd. [M + H]$^+$ 563.0762, found 563.0773.

**5,7-Dimethoxy-4-oxo-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-3-yl 3-chlorobenzenesulfonate (3j, C$_{26}$H$_{23}$ClO$_{10}$S)** White

solid; yield: 83%; m.p.: 182–183 °C; $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta = $ 7.84–7.75 (m, 3H, Ph-H), 7.41 (t, $J = 7.9$ Hz, 1H, Ph-H), 6.96 (s, 2H, Ph-H), 6.85 (d, $J = 2.2$ Hz, 1H, Ph-H), 6.58 (d, $J = 2.2$ Hz, 1H, Ph-H), 3.92 (s, 3H, Ph-OCH$_3$), 3.88 (s, 3H, Ph-OCH$_3$), 3.78 (s, 6H, 2×Ph-OCH$_3$), 3.73 (s, 3H, Ph-OCH$_3$) ppm; $^{13}$C NMR (101 MHz, DMSO-$d_6$): $\delta = $ 170.03, 164.92, 160.92, 158.75, 155.46, 153.02, 140.20, 139.35, 137.76, 133.30, 131.74, 130.03, 126.94, 124.08, 122.49, 108.34, 106.51, 97.16, 94.09, 60.22, 56.81, 56.69, 56.44 ppm; HRMS (ESI): $m/z$ calcd. [M + H]$^+$ 563.0761, found 563.0773.

**5,7-Dimethoxy-4-oxo-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-3-yl 4-chlorobenzenesulfonate (3k, C$_{26}$H$_{23}$ClO$_{10}$S)** Yellow solid; yield: 88%; m.p.: 102–103 °C; $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta = $ 7.74–7.69 (m, 2H, Ph-H), 7.55–7.49 (m, 2H, Ph-H), 6.94 (s, 2H, PH-H), 6.84 (d, $J = 2.1$ Hz, 1H, Ph-H), 6.58 (s, 1H, Ph-H), 3.91 (s, 3H, Ph-OCH$_3$), 3.87 (s, 3H, Ph-OCH$_3$), 3.78 (s, 6H, 2×Ph-OCH$_3$), 3.75 (s, 3H, Ph-OCH$_3$) ppm; $^{13}$C NMR (101 MHz, DMSO-$d_6$): $\delta = $ 169.97, 164.87, 160.87, 158.70, 155.68, 153.04, 140.37, 139.87, 135.55, 133.05, 130.04, 129.79, 124.10, 108.36, 106.66, 97.13, 94.01, 60.58, 56.77, 56.67, 56.47 ppm; HRMS (ESI): $m/z$ calcd. [M + H]$^+$ 563.0764, found 563.0773.

**5,7-Dimethoxy-4-oxo-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-3-yl 2-bromobenzenesulfonate (3l, C$_{26}$H$_{23}$BrO$_{10}$S)** White solid; yield: 82%; m.p.: 232–233 °C; $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta = $ 7.83 (dd, $J = 7.4$, 2.1 Hz, 1H, Ph-H), 7.79–7.73 (m, 1H, Ph-H), 7.56–7.47 (m, 2H, Ph-H), 7.00 (s, 2H, Ph-H), 6.83 (d, $J = 2.1$ Hz, 1H, Ph-H), 6.57 (d, $J = 2.1$ Hz, 1H, Ph-H), 3.90 (s, 3H, Ph-OCH$_3$), 3.84 (s, 3H, Ph-OCH$_3$), 3.82 (s, 6H, 2×Ph-OCH$_3$), 3.72 (s, 3H, Ph-OCH$_3$) ppm; $^{13}$C NMR (101 MHz, DMSO-$d_6$): $\delta = $ 169.87, 164.90, 160.87, 158.74, 155.93, 152.99, 140.03, 137.56, 135.84, 135.78, 133.55, 131.39, 128.45, 124.02, 120.12, 108.26, 106.46, 97.13, 93.99, 60.40, 56.77, 56.68, 56.44 ppm; HRMS (ESI): $m/z$ calcd. [M + H]$^+$ 607.0252, found 607.0268.

**5,7-Dimethoxy-4-oxo-2-(3,4,5-trimethoxyphenyl)-4*H*-chromen-3-yl 3-bromobenzenesulfonate (3m, C$_{26}$H$_{23}$BrO$_{10}$S)** Yellow solid; yield: 71%; m.p.: 193–194 °C; $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta = $ 7.70 (dd, $J = 16.1$, 6.7, 1.5 Hz, 2H, Ph-H), 7.29 (dd, $J = 13.2$, 5.1 Hz, 2H, Ph-H), 6.98 (s, 2H, Ph-H), 6.83 (d, $J = 2.2$ Hz, 1H, Ph-H), 6.57 (d, $J = 2.2$ Hz, 1H, Ph-H), 3.90 (s, 3H, Ph-OCH$_3$), 3.85 (s, 3H, Ph-OCH$_3$), 3.79 (s, 6H, 2×Ph-OCH$_3$), 3.73 (s, 3H, Ph-OCH$_3$) ppm; $^{13}$C NMR (101 MHz, DMSO-$d_6$): $\delta = $ 169.83, 164.90, 160.87, 158.70, 155.80, 153.02, 140.14, 137.83, 137.74, 133.21, 130.42, 125.32, 124.12, 117.85, 117.64, 108.30, 106.40, 97.16, 94.02, 60.42, 56.78, 56.67, 56.40 ppm; HRMS (ESI): $m/z$ calcd. [M + H]$^+$ 607.0255, found 607.0268.

**5,7-Dimethoxy-4-oxo-2-(3,4,5-trimethoxyphenyl)-4H-chromen-3-yl 4-bromobenzenesulfonate (3n, $C_{26}H_{23}BrO_{10}S$)** White solid; yield: 73%; m.p.: 131–133 °C; $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ = 7.68–7.61 (m, 4H, Ph-H), 6.95 (s, 2H, Ph-H), 6.85 (d, $J$ = 2.2 Hz, 1H, Ph-H), 6.58 (d, $J$ = 2.2 Hz, 1H, Ph-H), 3.91 (s, 3H, Ph-OCH$_3$), 3.87 (s, 3H, Ph-OCH$_3$), 3.79 (s, 6H, 2 × Ph-OCH$_3$), 3.77 (s, 3H, Ph-OCH$_3$) ppm; $^{13}$C NMR (101 MHz, DMSO-$d_6$): $\delta$ = 169.96, 164.89, 160.89, 158.70, 155.70, 153.06, 140.44, 135.93, 133.03, 132.75, 130.04, 129.09, 124.10, 108.37, 106.71, 97.15, 94.03, 60.66, 56.79, 56.68, 56.51 ppm; HRMS (ESI): *m/z* calcd. [M + H]$^+$ 607.0255, found 607.0268.

**5,7-Dimethoxy-4-oxo-2-(3,4,5-trimethoxyphenyl)-4H-chromen-3-yl 3-(trifluoromethyl)benzenesulfonate (3o, $C_{27}H_{23}F_3O_{10}S$)** White solid; yield: 89%; m.p.: 171–172 °C; $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ = 8.11 (d, $J$ = 8.1 Hz, 1H, Ph-H), 8.05 (d, $J$ = 7.9 Hz, 1H, Ph-H), 7.98 (s, 1H, Ph-H), 7.72 (t, $J$ = 7.9 Hz, 1H, Ph-H), 6.97 (s, 2H, Ph-H), 6.86 (d, $J$ = 2.2 Hz, 1H, Ph-H), 6.59 (d, $J$ = 2.2 Hz, 1H, Ph-H), 3.92 (s, 3H, Ph-OCH$_3$), 3.87 (s, 3H, Ph-OCH$_3$), 3.76 (s, 6H, 2 × Ph-OCH$_3$), 3.69 (s, 3H, Ph-OCH$_3$) ppm; $^{13}$C NMR (101 MHz, DMSO-$d_6$): $\delta$ = 169.99, 164.94, 160.88, 158.74, 155.45, 152.97, 140.14, 138.72, 133.35, 132.08, 131.51 (d, $J$ = 29.7 Hz), 130.32, 124.32, 123.96, 108.26, 106.44, 97.16, 94.04, 60.26, 56.73, 56.35 ppm; $^{19}$F NMR (376 MHz, DMSO-$d_6$): $\delta$ = -61.51 ppm; HRMS (ESI): *m/z* calcd. [M + H]$^+$ 597.1029, found 597.1036.

**5,7-Dimethoxy-4-oxo-2-(3,4,5-trimethoxyphenyl)-4H-chromen-3-yl 4-(trifluoromethoxy)benzenesulfonate (3p, $C_{27}H_{23}F_3O_{11}S$)** White solid; yield: 81%; m.p.: 189–191 °C; $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ = 7.81 (dd, $J$ = 7.9, 1.2 Hz, 1H, Ph-H), 7.66–7.60 (m, 1H, Ph-H), 7.60–7.53 (m, 1H, Ph-H), 7.46 (dd, $J$ = 11.0, 4.2 Hz, 1H, Ph-H), 6.99 (s, 2H, Ph-H), 6.82 (d, $J$ = 2.1 Hz, 1H, Ph-H), 6.56 (d, $J$ = 2.0 Hz, 1H, Ph-H), 3.90 (s, 3H, Ph-OCH$_3$), 3.84 (s, 3H, Ph-OCH$_3$), 3.81 (s, 6H, 2 × Ph-OCH$_3$), 3.73 (s, 3H, Ph-OCH$_3$) ppm; $^{13}$C NMR (101 MHz, DMSO-$d_6$): $\delta$ = 169.84, 164.91, 160.91, 158.74, 155.94, 153.01, 140.15, 135.92 (d, $J$ = 9.09 Hz), 135.67, 133.52, 132.36, 131.61, 131.17, 128.03, 124.05, 108.31, 106.53, 97.16, 94.04, 60.42, 56.73, 56.45 ppm; $^{19}$F NMR (376 MHz, DMSO-$d_6$): $\delta$ = -56.74 ppm; HRMS (ESI): *m/z* calcd. [M + H]$^+$ 613.097, found 613.0985.

**5,7-Dimethoxy-4-oxo-2-(3,4,5-trimethoxyphenyl)-4H-chromen-3-yl 4-(tert-butyl)benzenesulfonate (3q, $C_{30}H_{32}O_{10}S$)** Yellow solid; yield: 70%; m.p.: 184–185 °C; $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ = 7.63 (d, $J$ = 8.6 Hz, 2H, Ph-H), 7.46 (d, $J$ = 8.6 Hz, 2H, Ph-H), 7.01 (s, 2H, Ph-H), 6.86 (d, $J$ = 2.2 Hz, 1H, Ph-H), 6.58 (d, $J$ = 2.2 Hz, 1H, Ph-H), 3.92 (s, 3H, Ph-OCH$_3$), 3.87 (s, 3H, Ph-OCH$_3$), 3.73 (s, 6H, 2 × Ph-OCH$_3$), 3.72 (s, 3H, Ph-OCH$_3$), 1.27 (s, 9H, Ph-C(CH$_3$)$_3$) ppm; $^{13}$C NMR (101 MHz, DMSO-$d_6$): $\delta$ = 170.12, 164.83, 160.88, 158.66, 158.07, 155.35, 152.97, 140.49, 134.12, 133.24, 128.01, 126.43, 125.77, 124.77, 124.17, 108.35, 106.70, 97.09, 94.01, 60.64, 56.77, 56.66, 56.43, 35.43, 31.01 ppm; HRMS (ESI): *m/z* calcd. [M + H]$^+$ 585.1776, found 585.1788.

**5,7-Dimethoxy-4-oxo-2-(3,4,5-trimethoxyphenyl)-4H-chromen-3-yl 4-cyanobenzenesulfonate (3r, $C_{27}H_{23}NO_{10}S$)** Yellow solid; yield: 63%; m.p.: 237–238 °C; $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ = 7.96–7.89 (m, 4H, Ph-H), 6.94 (s, 2H, Ph-H), 6.84 (d, $J$ = 2.0 Hz, 1H, Ph-H), 6.57 (d, $J$ = 2.1 Hz, 1H, Ph-H), 3.91 (s, 3H, Ph-OCH$_3$), 3.87 (s, 3H, Ph-OCH$_3$), 3.79 (s, 6H, 2 × Ph-OCH$_3$), 3.76 (s, 3H, Ph-OCH$_3$) ppm; $^{13}$C NMR (101 MHz, DMSO-$d_6$): $\delta$ = 167.74, 162.83, 158.78, 156.62, 153.63, 150.91, 138.87, 138.24, 131.49, 131.08, 126.68, 121.85, 115.65, 114.84, 106.18, 104.60, 95.05, 91.94, 58.40, 54.67, 54.57, 54.41 ppm; HRMS (ESI): *m/z* calcd. [M + H]$^+$ 554.1102, found 554.1115.

**5,7-Dimethoxy-4-oxo-2-(3,4,5-trimethoxyphenyl)-4H-chromen-3-yl thiophene-2-sulfonate (3 s, $C_{24}H_{22}O_{10}S_2$)** White solid; yield: 88%; m.p.: 102–103 °C; $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ = 8.02 (dd, $J$ = 5.0, 1.3 Hz, 1H, thienyl-H), 7.62 (dd, $J$ = 3.8, 1.3 Hz, 1H, thienyl-H), 7.04 (dd, $J$ = 4.9, 4.0 Hz, 1H, thienyl-H), 7.01 (s, 2H, Ph-H), 6.87 (d, $J$ = 2.2 Hz, 1H, Ph-H), 6.59 (d, $J$ = 2.2 Hz, 1H, Ph-H), 3.92 (s, 3H, Ph-OCH$_3$), 3.88 (s, 3H, Ph-OCH$_3$), 3.80 (s, 6H, 2 × Ph-OCH$_3$), 3.74 (s, 3H, Ph-OCH$_3$) ppm; $^{13}$C NMR (101 MHz, DMSO-$d_6$): $\delta$ = 169.95, 164.87, 160.89, 158.68, 155.73, 153.04, 140.29, 137.09, 136.19, 135.83, 133.16, 128.43, 124.30, 108.38, 106.66, 97.15, 94.02, 60.49, 56.79, 56.68, 56.50 ppm; HRMS (ESI): *m/z* calcd. [M + H]$^+$ 536.0719, found 536.0727.

**5,7-Dimethoxy-4-oxo-2-(3,4,5-trimethoxyphenyl)-4H-chromen-3-yl pyridine-3-sulfonate (3t, $C_{25}H_{23}NO_{10}S$)** Brown solid; yield: 87%; m.p.: 141–143 °C; $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta$ = 8.84 (dd, $J$ = 24.8, 3.0 Hz, 2H, Py-H), 8.18 (d, $J$ = 8.1 Hz, 1H, Py-H), 7.51 (dd, $J$ = 8.0, 4.8 Hz, 1H, Py-H), 7.01 (s, 2H, Ph-H), 6.87 (s, 1H, Ph-H), 6.59 (s, 1H, Ph-H), 3.90 (d, $J$ = 14.5 Hz, 3H, Ph-OCH$_3$), 3.87 (s, 3H, Ph-OCH$_3$), 3.77 (d, $J$ = 17.6 Hz, 6H, 2 × Ph-OCH$_3$), 3.74 (s, 3H, Ph-OCH$_3$) ppm; $^{13}$C NMR (101 MHz, DMSO-$d_6$): $\delta$ = 169.93, 164.95, 160.90, 158.75, 155.81, 155.09, 153.08, 148.13, 140.32, 136.09, 134.12, 133.26, 124.53, 124.01, 108.29, 106.65, 97.20, 94.05, 60.46, 56.81, 56.70, 56.51 ppm; HRMS (ESI): *m/z* calcd. [M + H]$^+$ 530.1099, found 530.1115.

**5,7-Dimethoxy-4-oxo-2-(3,4,5-trimethoxyphenyl)-4H-chromen-3-yl quinoline-8-sulfonate (3u, $C_{29}H_{253}NO_{10}S$)** White solid; yield: 53%; m.p.: 259–260 °C; $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta = 8.99$ (d, $J = 4.2$ Hz, 1H, quinoline-H), 8.51–8.43 (m, 1H, quinoline-H), 8.25 (dd, $J = 13.6$, 6.2 Hz, 2H, quinoline-H), 7.66 (dd, $J = 7.1$, 4.4 Hz, 2H, quinoline-H), 6.83 (s, 1H, Ph-H), 6.82 (d, $J = 2.5$ Hz, 2H, Ph-H), 6.58–6.53 (m, 1H, Ph-H), 3.90 (s, 3H, Ph-OCH$_3$), 3.84 (s, 3H, Ph-OCH$_3$), 3.64 (d, $J = 4.1$ Hz, 6H, $2 \times$ Ph-OCH$_3$), 3.61 (s, 3H, Ph-OCH$_3$) ppm; $^{13}$C NMR (101 MHz, DMSO-$d_6$): $\delta = 170.20$, 164.78, 160.86, 158.71, 155.49, 152.50, 152.18, 143.19, 139.61, 137.17, 135.95, 134.71, 133.81, 132.48, 128.96, 125.72, 124.20, 123.09, 108.39, 106.28, 97.02, 93.94, 60.30, 56.73, 56.66, 56.18 ppm; HRMS (ESI): *m/z* calcd. [M + H]$^+$ 580.1253, found 580.1271.

**5,7-Dimethoxy-4-oxo-2-(3,4,5-trimethoxyphenyl)-4H-chromen-3-yl 4-acetamidobenzenesulfonate (3v, $C_{287}H_{27}NO_{11}S$)** White solid; yield: 65%; m.p.: 260–261 °C; $^1$H NMR (400 MHz, DMSO-$d_6$): $\delta = 10.40$ (s, 1H, Ph-NH-), 7.64–7.57 (m, 4H, Ph-H), 6.93 (s, 2H, Ph-H), 6.84 (d, $J = 1.5$ Hz, 1H, Ph-H), 6.57 (d, $J = 2.1$ Hz, 1H, Ph-H), 3.91 (s, 3H, Ph-OCH$_3$), 3.87 (s, 3H, Ph-OCH$_3$), 3.76 (s, 6H, $2 \times$ Ph-OCH$_3$), 3.70 (s, 3H, Ph-OCH$_3$), 2.09 (s, 3H, -CH$_3$) ppm; $^{13}$C NMR (101 MHz, DMSO-$d_6$): $\delta = 170.15$, 169.67, 164.77, 160.86, 158.66, 155.57, 152.98, 144.89, 140.27, 132.99, 129.58, 124.30, 118.45, 108.45, 106.65, 97.06, 93.97, 60.44, 56.74, 56.64, 56.42, 24.64 ppm; HRMS (ESI): *m/z* calcd. [M + H]$^+$ 586.1369, found 586.1377.

## Evaluation of the antibacterial activity

Antibacterial activities of the title compounds against *Xanthomonas axonopodispv. citri (Xac)*, *Ralstonia solanacearum* (*Rs*), and *Xanthomonas oryzaepv. oryzae (Xoo)* were evaluated using the turbidimeter in vitro; commercial agricultural antibacterial bismerthiazol and thiodiazole-copper were used as control. This test method is provided in "Supporting Information".

The protection and curative activities of compound **3j** against rice bacterial leaf blight were determined in potted plants using a complete randomized block design. According to the previously reported method [38], we used Hu you ming zhan as the experimental seed; this variety is susceptible to rice bacterial blight in recent years. Commercial bactericides BT and TC were used as the positive control samples. This test method is provided in "Supporting Information".

## Scanning electron microscope sample preparation

According to the previously reported method [39], *Xac* and *Xoo* were provided with scanning electron microscopy to observe the changes of their cell structure after being treated with different concentrations of drugs. All the bacteria were cultured in NA medium at 28 °C for 12 h with active growth. Detailed operating procedures are provided in "Supporting Information".

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