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ORIGINAL PAPER

Synthesis, antifungal and insecticidal activity of novel [1,2,4]triazolo[4,3-*a*]pyridine derivatives containing a sulfide substructure

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Abstract A series of [1,2,4]triazolo[4,3-*a*]pyridine derivatives bearing a sulfide substructure was designed, synthesized and characterized via ^{1}H·NMR, ^{13}C·NMR, IR and elemental analyses. Bioassay Results indicated some of the derivatives displayed good fungicidal activity on *Rhizoctonia cerealis*, moderated insecticidal activity against *Plutella xylostella* and good insecticidal activity on *Helicoverpa armigera.* The inhibitory effects of compounds **4g** and **4u** against *Rhizotonia cerealis* were 70.9% at 50 μg mL^{-1}; the IC_{50} values of compounds **4d** and **4s** against *Plutella xylostella* were 43.87 and 50.75 μg mL^{-1}, respectively. And the IC_{50} values of compounds **4d**, **4q**, and **4s** on *Helicoverpa armigera* were 58.3, 77.14 and 65.31 μg mL^{-1}, respectively, which were better than that of commercial chlorpyrifos (103.77 μg mL^{-1}).

Keywords [1,2,4]Triazolo[4,3-*a*]pyridine · Sulfide · Synthesis · Antifungal activity · Insecticidal activity

Introduction

The triazolopyridine is an important class of fused heterocyclic compound that possesses broad spectrum of biological activities (Bell et al. 2012; Ferguson et al. 2016; Jerome et al. 2010; McClure et al. 2005; Tresadern et al. 2014; Zhang et al. 2015; Mu et al. 2015). As an integral part of triazolopyridines, [1,2,4]triazolo[4,3-*a*]pyridines attracted more attentions due to their broad spectrum of biological activities (Liu et al. 2014, 2015; Schmidt and Qian 2013; Shen et al. 2016; Vadagaonkar et al. 2014; Wang et al. 2016), such as herbicidal activity (Liu et al. 2015), antifungal activity (Shen et al. 2016; Wang et al. 2016; Yang et al. 2015; Zhai et al. 2016; Mu et al. 2016), anticonvulsant activity (Guan et al. 2012), and antibacterial activity (Prakash et al. 2011; Sadana et al. 2003), etc. In 2014, several new [1,2,4]triazolo[4,3-*a*]pyridines have been found to show excellent antifungal activities against *Phyllosticta Pirina*, *Sclerotinia sclerotiorum*, *Rhizoctonia solanii, Fusarium oxysporum, Fusarium nivale, Aspergillus fumigatus* and *Candida albicans* (Liu et al. 2014), and more recently, [1,2,4] triazolo[4,3-*a*]pyridines containing a Schiff base were also found to show excellent antifungal activity (Shen et al. 2016).

Sulfide substructure is an important moiety and attracts more and more attentions in the development of pesticide in recent years. Many derivatives containing a sulfide substructure with good antifungal activity (Hua et al. 2016;

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Wang et al. 2016;) and good marketing perspective have been discovered (Xu et al. 2011), some of them containing both [1,2,4]triazolo[4,3-*a*]pyridine and sulfide structures, simultaneously (Wang et al. 2016). And recently, Fan and co-workers reported anthranilic diamides containing a sulfide substructure showed good fungicidal activity (Hua et al. 2016). Moreover, many insecticidal molecules containing a sulfide substructure have also been identified (Chen et al. 2013; Ghorab et al. 1996; Hua et al. 2014, 2016; Shang et al. 2010; Wu et al. 2014). In our previous work (Wu et al. 2014), a series of 6,8-dichloro-quinazolines containing a sulfide substructure has been reported to display good insecticidal activity against *Plutella xylostella*.

Encouraged by those descriptions above, in continuation works on sulfide derivatives (Wu et al. 2014) and interesting in sulfides, we sought to carry out some [1,2,4]triazolo[4,3-*a*]pyridine derivatives containing a sulfide substructure, which may result in new [1,2,4]triazolo[4,3-*a*]pyridine derivatives with good biological activity. Accordingly, in this work, an attempt was made by linking the structures of [1,2,4]triazolo[4,3-*a*]pyridine and aromatic rings via a sulfide bond, the synthetic route was shown in Scheme 1. Results of bioassays indicate that some of the synthesized [1,2,4]triazolo[4,3-*a*]pyridine derivatives displayed good fungicidal activity on *Rhizotonia cerealis*. And some of them showed moderated to good insecticidal activity against both *Plutella xylostella* and *Helicoverpa armigera*.

Experimental

Materials

All reagents were purchased from Accela ChemBio Co., Ltd (Shanghai, China); The melting points of the newly synthesized compounds were tested on a WRX-4 monocular microscope (Shanghai Yice Apparatus & Equipment Co., Ltd, Shang Hai, China). The ^{1}H-NMR and ^{13}C-NMR spectra were recorded on a JEOL ECX 500 NMR spectrometer (JEOL Ltd., Tokyo, Japan), operating at 500 MHz for ^{1}H-NMR and 125 MHz for ^{13}C-NMR, and using $CDCl_3$ as solvents; infrared spectra were analyzed in KBr pellets on a IR Pristige-21 spectrometer (Shimadzu corporation, Kyoto, Japan); elemental analysis was performed on an Elemental Vario-III CHN analyzer (Elementar, Hanau, German). The proceeding of the reaction was monitored by TLC.

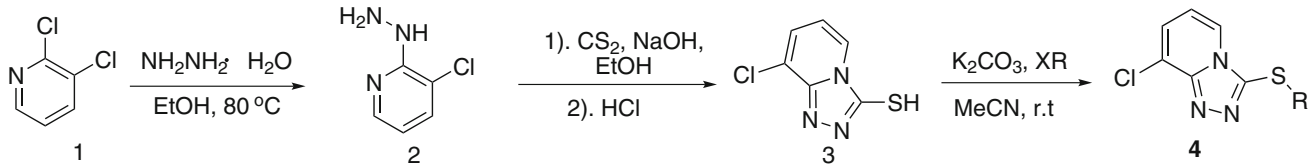
All fungal strains species and insects were provided by the Yun-long Agricultural Science & Technology Co., Ltd (Wuhan, China), which were conserved and breed in our laboratory. The commercial chlorpyrifos and carbendazim were purchased from Guangxi Tianyuan Biochemistry Co., Ltd (Nanning, China) and used as comparisons.

Chemicals

Synthesis of intermediate **2**: A mixture of 2,3-dichloropyridine (25.0 g), 80% hydrazine hydrate (12.69 g) was stirred in refluxing EtOH (40 mL), the reaction proceeding was monitored by TLC. After complication of the reaction, the resulting mixture was cooled to room temperature to get white needle crystal (20.76 g), yield, 85.59%, m.p.163–164 °C.

The procedures for the preparation of intermediate **2** (Mokrushina et al. 1977): 3-chloro-2-hydrazinylpyridine (12.0 g, 83.58 mmol) was reacted with carbon disulfide (7.64 g, 100 mmol) in the present of NaOH in ethanol at room temperature for 24 h, after complication of the reaction, the ethanol was evaporated, the residues were poured into 50 mL water, and acidized (pH = 4–5) to obtain intermediates 3 (10.31 g), yield, 66.5%, m.p. 298–299 °C.

General synthetic procedures for compounds **4a–4v**: A mixture of intermediate **3** (1 mmol), halogenated



4a: R = 2,4-dichlorobenzyl; **4b**: R = 4-fluorobenzyl; **4c**: R = 4-methoxybenzyl;
4d: R = 6-chloropyridin-3-ylmethyl; **4e**: R = Methyl; **4f**: R = Ethyl;
4g: R = 2-methylbenzyl; **4h**: R = 4-(trifluoromethoxy)benzyl; **4i**: R = 4-(trifluoromethyl)benzyl;
4j: R = 2-(trifluoromethyl)benzyl; **4k**: R = 2,4-difluorobenzyl; **4l**: R = 2,5-difluorobenzyl;
4m: R = 2,6-difluorobenzyl; **4n**: R = 4-bromo-2-fluorobenzyl; **4o**: R = 2-chloro-4-fluorobenzyl;
4p: R = 3-chloro-2-fluorobenzyl; **4q**: R = 2-bromo-5-fluorobenzyl; **4r**: R = 2-bromo-4-fluorobenzyl;
4s: R = (5-(trifluoromethyl)-1,3,4-oxadiazol-2-yl)methyl; **4t**: R = 3-methyl-4-(2,2,2-trifluoroethoxy)pyridin-2-yl)methyl;
4u: R = 2-fluoro-5-(trifluoromethyl)benzyl; **4v**: R = 3,4,4-trifluorobut-3-en-1-yl.

Scheme 1 Synthesis of compounds **4a–4v**

hydrocarbon (1.1 mmol), and K_2CO_3 (0.5 mmol) in acetonitrile was stirred under reflux for 2 h and concentrated in vacuum. The residue was poured into 50 mL water, filtered and dried to obtain the [1,2,4]triazolo[4,3-*a*]pyridine derivatives with a sulfide substructure. The properties and analytical data for the compounds are listed in Table 1, and the spectral data are shown in Table 2.

Bioassays

Antifungal biological assay: Compounds **4a–4v** were evaluated for their antifungal activities against *Rhizoctonia cerealis*, *Helminthosporium sativum*, and *Fusarium graminearum* in vitro as described in literature (Wu et al. 2012b) at a concentration of 50 mg/L. All the synthesized compounds were dissolved in dimethyl sulfoxide (10 mL) and then mixed with potato dextrose agar (PDA, 90 mL). All fungal species were incubated in PDA at 27 ± 1 °C for 5 days to obtain new mycelium for antifungal assay; then mycelia dishes were cut from the culture medium in approximately 4 mm diameter. One of the specimens was picked up with a sterilized inoculation needle and then inoculated in the center of the PDA plate aseptically. The inoculated plates were incubated at 27 ± 1 °C for 5 days. DMSO in sterile distilled water served as the control, whereas carbendazim acted as the positive control. Three replicates were carried out for each treatment. The radial growth of the fungal colonies was measured on the sixth day and the data were statistically analyzed. The in vitro inhibiting effects of the test compounds on the fungi were calculated by the formula:

$$I(\%) = [(C - T)/(C - 0.4)] \times 100,$$

where C represents the diameter of fungal growth on untreated PDA, T represents the diameter of fungi on treated PDA, and I is the inhibitory rate.

Insecticidal bioassays against Plutella xylostella: Previously reported protocols (Wu et al. 2012a, 2014) were used to test insecticidal activities against *Plutella xylostella*. Fresh cabbage discs (diameter of 2 cm) were dipped in the prepared solutions containing compounds **4a–4v** for 10 s, dried in air and placed in a Petri dish (diameter of 9 cm) lined with filter paper. Ten larvae of secondinstar of *Plutella xylostella* were carefully transferred to the Petri dishes. Chlorpyrifos was used as positive control; three replicates were performed for each experiment. Mortality was calculated after 72 h. Evaluations of mortality were calculated in a percentage scale (0 = no activity and 100 = complete eradication) at 5% intervals. The results are summarized in Table 4.

Insecticidal activity against Helicoverpa armigera: The insecticidal activities of compounds **4a–4v** against *Helicoverpa armigera* were tested by the diet-incorporated method (Wu et al. 2012a). A quantity of 3 mL of prepared solutions containing the compounds was added to the forage (27 g), subsequently diluted to different concentrations and then placed in a 24-pore plate. One larva was placed in each of the wells on the plate. Mortalities were determined after 72–96 h, Evaluations were based on a percentage scale (0 = no activity and 100 = complete eradication) at 5% intervals and the results are given in Table 4.

Results and discussion

Synthesis

The synthetic protocols of the [1,2,4]triazolo[4,3-*a*]pyridine derivatives bearing a sulfide are depicted in Scheme 1. Firstly, 3-chloro-2-hydrazinylpyridine, **2**, was obtained in excelent yield (90%) by treatment of 2,3-dichloropyridine (**1**) with hydrazine hydrate (80%) in refluxing EtOH for 20 h. Subsequently, key intermediate 8-chloro-[1,2,4]triazolo[4,3-*a*]pyridine-3-thiol (**3**) was then synthesized by reacting **3** with CS_2 in the present of base (NaOH) in EtOH under room temperature for 24 h and acidification with 5% HCl in good yield (Mokrushina et al. 1977). Finally, the title compounds **4a–4v** were synthesized in good yields via reaction in the presence of potassium carbonate in acetonitrile by the treatment of intermediate **3** with different halogenated hydrocarbon.

The structures of **4a–4v** were confirmed based on their spectroscopic data. The IR spectra showed absorption bands near 3052 cm^{-1} are the stretching vibrations of Ar–H. Absorption bands between 2940 and 2860 cm^{-1} belong to stretching vibrations of methylene (–CH_2–); the absorption zones between 1420 and 1650 cm^{-1} correspond to the skeleton vibration of aromatic ring. In the ^{1}H·NMR spectra, take compound **4s** as an example, the proton at *o*-position of "*N*" was shown at δ_H 8.08 ppm as a doublet and with coupling constant of 6.9 Hz, the proton adjacent the "Cl" was at δ_H 7.41 ppm, and the coupling constant is 7.2 Hz; the proton at *m*-position of "Cl" resonance frequency is at δ_H 7.41 ppm as a triplet and with "J = 7.1 Hz". The main characteristic of the ^{1}H NMR spectra for the compound was the presence of a singlet near δ_H 4.4 ppm for –CH_2–S– proton. In ^{13}C NMR spectra of the "F" contained compounds, the carbons were split into multiplet, for instance, in the ^{13}C NMR spectra of compound **4s**, the carbon of "–CF_3" resonance frequency is near δ_C 155.59 ppm as a quartet, the coupling constant ($^1J_{C\text{-}F}$) was 44.8 Hz; and in ^{13}C NMR spectra of two fluorines contained compounds (**4k**, **4l** and **4m**), the carbon resonance frequencies are near δ_C 155-163 ppm as a doublet with coupling constant ($^1J_{C\text{–}F}$) 213–257 Hz.

Table 1 Physical properties and analytical data for newly synthesized compounds

Com.	Formula	Appearance	M_r	w_i(Calc.)/% w_i(Found)/%			Yield	M.p.
				C	H	N	%	°C
4a	$C_{13}H_8Cl_3N_3S$	Yellow solid	344.64	45.30	2.34	12.19	94.8	114–116
				45.32	2.36	12.17		
4b	$C_{13}H_9ClFN_3S$	Yellow solid	293.02	53.15	3.09	14.30	84.7	88–90
				53.17	3.19	14.33		
4c	$C_{14}H_{12}ClN_3OS$	Yellow solid	305.78	54.99	3.96	13.74	92.5	76–78
				54.86	3.97	13.84		
4d	$C_{12}H_8Cl_2N_4S$	Yellow solid	311.19	46.32	2.59 2.60	18.00	67.8	108–109
				46.34		18.02		
4e	$C_7H_6ClN_3S$	Brown solid	351.25	42.11	3.03	21.05	77.9	68–69
				42.16	3.13	21.15		
4f	$C_8H_8ClN_3S$	Yellow solid	245.13	44.97	3.77 3.79	19.66	76.8	97–98
				44.92		19.68		
4g	$C_{14}H_{12}ClN_3S$	Yellow solid	289.78	58.03	4.17	14.50	93.3	90–81
				58.13	4.13	14.52		
4h	$C_{14}H_{12}ClN_3OS$	Yellow solid	359.75	46.74	2.52	11.68	79.5	90–91
				46.72	2.53	11.78		
4i	$C_{14}H_9ClF_3N_3S$	White solid	343.75	48.92	2.57	12.22	58.9	101–102
				48.82	2.56	12.24		
4j	$C_{14}H_9ClF_3N_3S$	Brown solid	343.75	48.92	2.57	12.22	89.2	109–111
				48.85	2.64	12.18		
4k	$C_{13}H_8ClF_2N_3S$	White solid	311.74	50.09	2.59	13.48	90.5	100–102
				50.10	2.62	13.47		
4l	$C_{13}H_8ClF_2N_3S$	Yellow solid	311.74	50.09	2.59	13.48	84.6	90–91
				50.11	2.61	13.50		
4m	$C_{13}H_8ClF_2N_3S$	Brown solid	311.74	50.09	2.59	13.48	88	145–146
				50.12	2.63	13.51		
4n	$C_{13}H_8BrClFN_3S$	White solid	372.64	41.90	2.16	11.28	95.7	113–114
				41.95	2.23	11.25		
4o	$C_{13}H_8Cl_2FN_3S$	Yellow solid	328.19	47.58	2.46	11.80	99.1	121–123
				47.54	2.43	11.88		
4p	$C_{13}H_8Cl_2FN_3S$	Yellow solid	328.19	47.58	2.46	11.80	82.8	105–107
				47.49	2.51	11.85		
4q	$C_{13}H_8BrClFN_3S$	White solid	372.64	41.90	2.16	11.28	88.2	169–170
				41.93	2.17	11.31		
4r	$C_{13}H_8BrClFN_3S$	White solid	372.64	41.90	2.16	11.28	96.5	168–169
				41.95	2.14	11.33		
4s	$C_{10}H_5ClF_3N_5OS$	Yellow solid	355.69	35.78	1.50	20.86	56.1	90–91
				35.85	1.52	20.87		
4t	$C_{15}H_{12}ClF_3N_4OS$	Gray solid	388.79	46.34	3.11	14.41	57.1	110–112
				46.41	3.16	14.43		
4u	$C_{14}H_8BrClF_4N_3S$	White solid	361.75	46.48	2.23	11.62	76.8	92–93
				46.53	2.27	11.64		
4v	$C_{10}H_7ClF_3N_3S$	Yellow solid	293.69	40.90	2.40	14.31	76.4	47–48
				40.87	2.43	14.34		

Table 2 Spectral data of newly prepared compounds

Comp.	Spectral data
4a	IR, $\tilde{\nu}$/cm^{-1}: 3062.7 (Ar–H), 2940, 3915, 2860 (stretching vibration of –CH_2–), 1544.5, 1531.3, 1506.8, 1456.2 (skeleton vibration of aromatic ring)
	^{1}H NMR ($CDCl_3$) δ 7.73 (dt, ^3J = 8.6 Hz, ^4J = 4.3 Hz, 1H, [1,2,4]triazolo[4,3-*a*]pyridine-H), 7.33 (d, ^3J = 1.8 Hz, 1H [1,2,4]triazolo[4,3-*a*]pyridine-H), 7.29 (dd, ^3J = 7.2, ^4J = 0.7 Hz, 1H [1,2,4]triazolo[4,3-*a*]pyridine-H), 7.00–6.93 (m, 2H, Ph-H), 6.72 (t, ^3J = 7.0 Hz, 1H, Ph-H), 4.38 (s, 2H, –CH_2–)
	^{13}C NMR (125 MHz, $CDCl_3$) δ 149.19, 141.95, 134.76, 134.71, 133.18, 131.72, 129.73, 127.38, 126.53, 122.75, 121.39, 113.92, 37.07
4b	IR, $\tilde{\nu}$/cm^{-1}: 3042.7 (Ar–H), 2921.2, 2910.5, 2879.4 (stretching vibration of –CH_2–), 1544.8, 1530.5, 1456.4 (skeleton vibration of aromatic ring)
	^{1}H NMR ($CDCl_3$) δ 7.67 (d, ^3J = 6.9 Hz, 1H, Ar–H), 7.26 (d, ^3J = 9.4 Hz, 1H, Ar–H), 7.09 (dd, ^3J = 8.5 Hz, ^3J = 5.3 Hz, 2H, Ar–H), 6.87–6.79 (m, 2H, Ph-H), 6.68 (t, ^3J = 7.0 Hz, 1H, Ar–H), 4.27 (s, 2H, –CH_2–)
	^{13}C NMR ($CDCl_3$) δ 162.42 (d, $^1J_{C-F}$ = 247.6 Hz), 149.06, 142.24, 132.62, 130.56 (d, $^2J_{C-F}$ = 21.6 Hz), 126.47, 122.62, 121.46, 115.75 (d, $^2J_{C-F}$ 21.6 Hz), 113.77, 39.39
4c	IR, $\tilde{\nu}$/cm^{-1}: 3034.8 (Ar–H), 2927.3, 2911.5, 2880.3 (stretching vibration of –CH_2–), 1532.4, 1453.2, 1419.1 (skeleton vibration of aromatic ring)
	^{1}H NMR ($CDCl_3$) δ 7.67 (d, ^3J = 6.9 Hz, 1H, [1,2,4]triazolo[4,3-*a*]pyridine-H), 7.25 (d, ^3J = 7.0 Hz, 1H, [1,2,4]triazolo[4,3-*a*]pyridine-H), 7.02 (d, ^3J = 8.6 Hz, 1H, Ph-H), 6.67 (d, ^3J = 8.6 Hz, 1H, Ph-H), 6.64 (t, ^3J = 7.0 Hz, 1H, [1,2,4]triazolo [4,3-*a*]pyridine-H), 4.26 (s, 2H, –CH_2–), 3.71 (s, 3H, –CH_3)
	^{13}C NMR ($CDCl_3$) δ 159.38, 154.10, 149.01, 143.47, 130.06, 128.66, 126.37, 123.14, 122.48, 121.69, 115.12, 114.18, 113.56, 55.39, 39.98
4d	IR, $\tilde{\nu}$/cm^{-1}: 3048.5 (Ar–H); 2928.3, 2913.5, 2882.3 (stretching vibration of –CH_2–), 1542.1, 1532.3, 1507.4, 1466.2 (skeleton vibration of aromatic ring)
	^{1}H NMR ($CDCl_3$) δ 8.26 (d, ^3J = 2.5 Hz, 1H), 7.77 (d, ^3J = 6.9 Hz, 1H), 7.53 (dd, ^3J = 8.2, ^4J = 2.5 Hz, 1H), 7.30 (d, ^3J = 7.2 Hz, 1H), 7.13 (d, ^3J = 8.2 Hz, 1H), 6.77 (t, ^3J = 7.0 Hz, 1H), 4.35 (s, 2H, –CH_2–)
	^{13}C NMR ($CDCl_3$) δ 151.03, 149.81, 149.20, 141.61, 139.29, 131.80, 126.58, 124.26, 122.90, 121.21, 114.21, 35.63
4e	IR, $\tilde{\nu}$/cm^{-1}: 3045.9 (Ar–H), 2979.1, 2935.2, 2910.8 (stretching vibration of CH_3)
	^{1}H NMR ($CDCl_3$) δ 8.27 (d, ^3J = 7.1 Hz, 1H, [1,2,4]triazolo[4,3-*a*]pyridine-H), 7.38 (d, ^3J = 7.2 Hz, 1H, [1,2,4]triazolo[4,3-*a*]pyridine-H), 6.78 (t, ^3J = 7.1 Hz, 1H [1,2,4]triazolo [4,3-*a*]pyridine-H), 4.06 (s, 3H, –CH_3)
	^{13}C NMR ($CDCl_3$) δ 149.06, 144.30, 126.19, 122.81, 121.54, 113.82, 16.61
4f	IR, $\tilde{\nu}$/cm^{-1}: 3045.9 (Ar–H), 2938.1, 2935.2, 2910.8, 2865.7 (stretching vibration of –CH_2CH_3)
	^{1}H NMR ($CDCl_3$) δ 8.04 (d, ^3J = 6.8 Hz, 1H, [1,2,4]triazolo[4,3-*a*]pyridine-H), 7.32 (d, ^3J = 7.8 Hz, 1H, Ar–H), 6.85 (t, ^3J = 7.0 Hz, 1H, Ar–H), 3.16 (q, ^3J = 7.3 Hz, 2H, –CH_2–), 1.34 (t, ^3J = 7.2 Hz, 3H, –CH_3)
	^{13}C NMR ($CDCl_3$) δ 145.78, 136.39, 126.32, 122.80, 121.73, 113.90, 29.33, 15.38
4g	IR, $\tilde{\nu}$/cm^{-1}: 3048.8(Ar–H), 2924.2, 2912.5, 2878.4 (stretching vibration of –CH_2–), 1533.4, 1458.1 (skeleton vibration of aromatic ring)
	^{1}H NMR ($CDCl_3$) δ 7.51 (d, J = 6.9 Hz, 1H, Ar–H), 7.25 (d, ^3J = 6.3 Hz, 1H, Ar–H), 7.11–7.04 (m, 2H, Ar–H), 6.85 (t, ^3J = 7.2 Hz, 1H, Ar–H), 6.76 (d, ^3J = 7.5 Hz, 1H, Ar–H), 6.58 (t, ^3J = 7.0 Hz, 1H, Ar–H), 4.28 (s, 2H, –CH_2–), 2.39 (s, 3H, –CH_3)
	^{13}C NMR ($CDCl_3$) δ 149.05, 142.47, 136.53, 134.58, 130.80, 129.60, 128.37, 126.44, 126.33, 122.43, 121.49, 113.59, 38.58, 19.18
4h	IR, $\tilde{\nu}$/cm^{-1}: 3052.8 (Ar–H), 2925.2, 2912.5, 2874.4 (stretching vibration of –CH_2–), 1533.4, 1458.1 (skeleton vibration of aromatic ring)
	^{1}H NMR ($CDCl_3$) δ 7.62 (dd, ^3J = 6.9 Hz, ^4J = 0.7 Hz, 1H, [1,2,4]triazolo[4,3-*a*]pyridine-H), 7.27 (d, ^4J = 0.8 Hz, 1H, [1,2,4]triazolo[4,3-*a*]pyridine-H), 7.15 (d, 2H, Ph-H), 6.99 (d, J = 8.1 Hz, 2H, Ph-H), 6.64 (t, ^3J = 7.1 Hz, 1H, [1,2,4]triazolo[4,3-*a*]pyridine-H), 4.28 (s, 2H, –CH_2–)
	^{13}C NMR ($CDCl_3$) δ 149.12, 148.82, 141.94, 135.76, 130.30, 126.48, 122.65, 121.42, 121.31, 119.35, 113.80, 77.38, 77.13, 76.87, 39.40
4i	IR, $\tilde{\nu}$/cm^{-1}: 3068.7 (Ar–H), 2925.2, 2912.5, 2873.4 (stretching vibration of –CH_2–), 1647.2, 1533.4, 1458.1 (skeleton vibration of aromatic ring)
	^{1}H NMR ($CDCl_3$) δ 7.63 (d, ^3J = 6.9 Hz, 1H, [1,2,4]triazolo[4,3-*a*]pyridine-H), 7.41 (d, ^3J = 7.9 Hz, 2H, Ph-H), 7.27 (d, ^3J = 7.7 Hz, 2H, Ph-H), 7.25 (d, ^3J = 6.9 Hz, 1H, [1,2,4]triazolo[4,3-*a*]pyridine-H), 6.66 (t, ^3J = 7.1 Hz, 1H), 4.35 (s, 2H, –CH_2–)
	^{13}C NMR ($CDCl_3$) δ 149.12, 148.82, 141.94, 135.76, 130.30, 126.48 (q, $^1J_{C-F}$ = 129.1 Hz), 123.45, 122.65, 121.42, 121.31, 119.35, 117.31, 113.80, 77.38, 77.13, 76.87, 39.40, 0.09
4j	IR, $\tilde{\nu}$/cm^{-1}: 3054.2 (Ar–H), 2921.2, 2914.5, 2864.4 (stretching vibration of –CH_2–), 1647.2, 1533.4, 1458.1 (skeleton vibration of aromatic ring)
	^{1}H NMR ($CDCl_3$) δ 7.73 (d, ^3J = 6.9 Hz, 1H, [1,2,4]triazolo[4,3-*a*]pyridine-H), 7.60 (d, ^3J = 7.6 Hz, 1H, [1,2,4]triazolo[4,3-*a*]pyridine-H), 7.33–7.20 (m, 3H, Ph-H), 7.10 (d, ^3J = 7.5 Hz, 1H), 6.70 (dd, ^3J = 9.0, ^3J = 5.0 Hz, 1H, Ph-H), 4.46 (s, 2H, –CH_2–)
	^{13}C NMR ($CDCl_3$) δ 149.20, 142.14, 135.08, 132.20, 131.72, 128.67 (q, $^1J_{C-F}$ = 129.4 Hz), 127.95, 127.56, 126.61, 125.38, 123.20, 122.67, 121.47, 113.97, 77.40, 77.15, 76.89, 36.59

Table 2 continued

Comp.	Spectral data
4k	IR, $\tilde{\nu}$/cm^{-1}: 3051.9 (Ar–H), 2922.3, 2914.3, 2864.2 (stretching vibration of –CH_2–), 1545.4, 1456.2, 1459.9 (skeleton vibration of aromatic ring).
	^{1}H NMR ($CDCl_3$) δ 7.80 (dd, ^3J = 6.9 Hz, ^4J = 0.6 Hz, 1H), 7.30 (dd, ^3J = 7.2 Hz, ^4J = 0.7 Hz, 1H), 7.02 (td, ^3J = 8.6, ^3J = 6.3 Hz, 1H), 6.77–6.70 (m, 2H, Ph-H), 6.62 (dd, J = 7.1, 1.6 Hz, 1H), 4.30 (s, 2H)
	^{13}C NMR ($CDCl_3$) δ 162.86 (d, $^1J_{C–F}$ = 257.1 Hz), 160.59 (d, $^1J_{C–F}$ = 213.4 Hz), 152.33, 149.19, 142.04, 131.75 (d, $^2J_{C–F}$ = 9.7 Hz), 126.54, 122.78, 121.40, 120.00, 111.54 (d, $^2J_{C–F}$ = 21.2 Hz), 104.25 (t, $^2J_{C–F}$ = 25.3 Hz), 32.64
4l	IR, $\tilde{\nu}$/cm^{-1}: 3056.3 (Ar–H), 2934.1, 2912.3, 2865.2 (stretching vibration of –CH_2–), 1568.4, 1458.2, 1448.9 (skeleton vibration of aromatic ring)
	^{1}H NMR ($CDCl_3$) δ 7.82 (dd, ^3J = 6.9, 0.8 Hz, 1H, [1,2,4]triazolo[4,3-*a*] pyridine-H), 7.33–7.29 (m, 1H, Ar–H), 6.93 (td, ^3J = 8.9 Hz, ^4J = 4.5 Hz, 1H, [1,2,4]triazolo[4,3-*a*]pyridine-H), 6.86 (m, 2H, Ar–H), 6.75 (t, ^3J = 7.0 Hz, 1H, ArH), 4.30 (s, 2H, –CH_2–)
	^{13}C NMR ($CDCl_3$) δ 158.39 (d, $^1J_{C–F}$ = 241.9 Hz), 156.70 (d, $^1J_{C–F}$ = 244.9 Hz), 149.25, 141.89, 126.55, 122.85, 121.40, 117.39, 116.83 (d, $^2J_{C–F}$ = 8.6 Hz), 116.64 (d, $^2J_{C–F}$ = 8.5 Hz), 116.48 (d, $^2J_{C–F}$ = 8.5 Hz), 116.29 (d, $^2J_{C–F}$ = 8.4 Hz), 114.00, 32.75
4m	IR, $\tilde{\nu}$/cm^{-1}: 3074.3 (Ar–H), 2932.3, 2902.8, 2875.4 (stretching vibration of –CH_2–),1556.4, 1467.7, 1438.9 (skeleton vibration of aromatic ring)
	^{1}H NMR ($CDCl_3$) δ 7.95 (dd, ^3J = 6.9, ^4J = 0.6 Hz, 1H, [1,2,4]triazolo[4,3-*a*]pyridine-H), 7.33 (dd, ^3J = 7.2, ^4J = 0.8 Hz, 1H, [1,2,4]triazolo[4,3-*a*]pyridine-H), 7.21 (dd, ^3J = 7.2, ^4J = 4.5, 1H, [1,2,4]triazolo[4,3-*a*]pyridine-H), 6.77 (m, 3H, PH-H), 4.25 (s, 2H)
	^{13}C NMR ($CDCl_3$) δ 161.03 (d, $^1J_{C–F}$ = 250.5 Hz), 160.97 (d, $^1J_{C–F}$ = 250.4 Hz), 149.34, 141.58, 130.09, 130.01, 129.93, 126.67, 122.92, 121.58, 114.04, 113.31, 113.16 (t, J = 19.0 Hz), 111.54 (d, $^2J_{C–F}$ = 20.4 Hz), 111.51 (d, $^2J_{C–F}$ = 20.3 Hz), 26.85
4n	IR, $\tilde{\nu}$/cm^{-1}: 3041.3 (Ar–H), 2934.6, 2932.3, 2870.2 (stretching vibration of –CH_2–), 1555.3, 1467.7, 1433.7 (skeleton vibration of aromatic ring)
	^{1}H NMR ($CDCl_3$) δ 7.78 (dd, ^3J = 6.85 Hz, ^4J = 1.8 Hz, 1H, [1,2,4]triazolo[4,3-*a*]pyridine-H), 7.31 (dd, ^3J = 6.8 Hz, ^4J = 0.85 Hz, 1H, [1,2,4]triazolo[4,3-*a*]pyridine-H), 7.15 (dd, ^3J = 9.3 Hz, ^4J = 1.8 Hz, 1H, Ar–H), 7.02 (dd, ^3J = 8.3 Hz, ^4J = 1.8 Hz, 1H, Ar–H), 6.92 (t, J = 8.1 Hz, 1H, Ar–H), 6.75 (t, J = 7.1 Hz, 1H, Ar–H), 4.27 (s, 2H, –CH_2)
	^{113}C NMR ($CDCl_3$) δ 160.44 (d, $^1J_{C–F}$ = 253.0 Hz), 149.20, 141.90, 131.96, 131.93, 127.70, 126.59, 123.34 (d, $^2J_{C–F}$ = 14.7 Hz), 122.47 (d, $^2J_{C–F}$ = 9.6 Hz), 122.43, 121.40, 119.47, 119.28, 114.03, 32.64
4o	IR, $\tilde{\nu}$/cm^{-1}: 3054.3 (Ar–H), 2931.1, 2911.3, 2867.2 (stretching vibration of –CH_2–), 1556.4, 1467.7, 1438.9 (skeleton vibration of aromatic ring)
	^{1}H NMR ($CDCl_3$) δ 7.74 (dd, ^3J = 6.9, ^4J = 0.9 Hz, 1H, [1,2,4]triazolo[4,3-*a*]pyridine-H), 7.29 (dd, ^3J = 7.2, ^4J = 0.9 Hz, 1H, [1,2,4]triazolo[4,3-*a*]pyridine-H), 7.07 (dd, ^3J = 8.4, ^4J = 2.6 Hz, 1H, Ph-H), 7.00 (dd, J = 8.6, 6.0 Hz, 1H, [1,2,4]triazolo[4,3-*a*]pyridine-H), 6.73–6.67 (m, 2H, Ph-H), 4.38 (s, 2H, –CH_2)
	^{13}C NMR ($CDCl_3$) δ 162.22 (d, $^1J_{C–F}$ = 251.4 Hz), 149.17, 142.03, 134.81, 132.05, 131.98, 130.56, 126.53, 122.71, 121.40, 117.34 (d, $^2J_{C–F}$ = 25.0 Hz), 114.34 (d, $^2J_{C–F}$ = 20.9 Hz), 113.89, 37.05
4p	IR, $\tilde{\nu}$/cm^{-1}: 3048.3 (Ar–H), 2932.1, 2915.3, 2865.2 (stretching vibration of –CH_2–), 1553.4, 1466.7, 1432.9 (skeleton vibration of aromatic ring)
	^{1}H NMR ($CDCl_3$) δ 7.79 (d, ^3J = 6.9 Hz, 1H, [1,2,4]triazolo [4,3-*a*]pyridine-H), 7.29 (d, ^3J = 7.1 Hz, 1H, Ar–H), 7.23–7.18 (m, 1H, Ar–H), 6.90 (dd, ^3J = 10.3 Hz, ^4J = 3.8 Hz, 1H), 6.80 (t, ^3J = 7.8 Hz, 1H, Ar–H), 6.74 (t, ^3J = 7.0 Hz, 1H, Ar–H), 4.33 (s, 2H, –CH_2–)
	^{13}C NMR ($CDCl_3$) δ 156.19 (d, $^1J_{C–F}$ = 250.6 Hz), 149.19, 141.82, 130.55, 129.21, 126.58, 125.80 (d, $^2J_{C–F}$ = 14.5 Hz), 124.74, 124.71,122.72, 121.40, 113.95, 33.21
4q	IR, $\tilde{\nu}$/cm^{-1}: 3038.3 (Ar–H), 2931.1, 2912.3, 2868.1 (stretching vibration of –CH_2–), 1556.4, 1467.7, 1438.9 (skeleton vibration of aromatic ring)
	^{1}H NMR ($CDCl_3$) δ 7.75 (d, ^3J = 6.9 Hz, 1H, ArH), 7.45 (dd, ^3J = 8.8, ^3J = 5.2 Hz, 1H, [1,2,4]triazolo[4,3-*a*]pyridine-H), 7.29 (d, ^3J = 7.2 Hz, 1H, Ar–H), 6.86 (dd, ^3J = 8.7 Hz, ^4J = 2.9 Hz, 1H, ArH), 6.80 (td, ^3J = 8.4 Hz, ^4J = 3.0 Hz, 1H, ArH), 6.72 (t, ^3J = 7.0 Hz, 1H, ArH), 4.39 (s, 2H, –CH_2–)
	^{13}C NMR ($CDCl_3$) δ 161.71 (d, $^1J_{C–F}$ = 248.8 Hz), 149.26, 141.85, 138.22, 126.53, 122.80, 121.42, 118.48, 118.03 (d, J = 23.5 Hz), 116.89 (d, J = 22.5 Hz), 113.92, 39.99
4r	IR, $\tilde{\nu}$/cm^{-1}: 3051.2 (Ar–H), 2932.1, 2915.3, 2862.1 (stretching vibration of –CH_2–), 1559.4, 1468.7, 1458.9 (skeleton vibration of aromatic ring)
	^{1}H NMR ($CDCl_3$) δ 7.74 (d, ^3J = 6.9 Hz, 1H, [1,2,4]triazolo[4,3-*a*]pyridine-H), 7.74 (d, ^3J = 6.9 Hz, 1H, Ar–H), 7.30–7.23 (m, 3H, Ar–H), 7.01 (dd, ^3J = 8.5, ^3J = 5.9 Hz, 1H, Ar–H), 6.73 (dd, ^3J = 11.2, ^3J = 4.8 Hz, 2H, Ar–H), 4.40 (s, 2H, –CH_2–)
	^{13}C NMR ($CDCl_3$) δ 161.99 (d, $^1J_{C–F}$ = 252.4 Hz), 149.18, 141.98, 132.25, 131.98, 131.91, 126.5, 124.53, 122.70, 121.44, 120.52 (d, $^2J_{C–F}$ = 24.9 Hz), 114.88 (d, $^2J_{C–F}$ = 20.8 Hz), 113.88, 39.65

Table 2 continued

Comp.	Spectral data
4s	IR, $\tilde{\nu}$/cm^{-1}: 3036.3 (Ar–H), 2931.1, 2916.3, 2865.1 (stretching vibration of –CH_2–), 1590.1, 1458.7, 1448.9 (skeleton vibration of aromatic ring)
	^{1}H NMR ($CDCl_3$) δ 8.08 (d,^3J = 6.9 Hz, 1H, [1,2,4]triazolo[4,3-*a*]pyridine-H), 7.41 (d, ^3J = 7.2 Hz, 1H, [1,2,4]triazolo[4,3-*a*]pyridine-H), 6.93 (t, ^3J = 7.1 Hz, 1H, [1,2,4]triazolo[4,3-*a*]pyridine-H), 4.55 (s, 2H, –CH_2–)
	^{13}C NMR ($CDCl_3$) δ 165.30, 155.95 (q, $^1J_{C-F}$ = 44.8 Hz), 149.62, 139.74, 127.13, 123.18, 121.57, 117.00, 114.82, 28.82
4t	IR, $\tilde{\nu}$/cm^{-1}: 3052.3 (Ar–H), 2933.3, 2916.2, 2866.1 (stretching vibration of –CH_2–), 1576.4, 1527.7, 1438.9 (skeleton vibration of aromatic ring)
	^{1}H NMR ($CDCl_3$) δ 8.18 (d, ^3J = 5.6 Hz, 1H, pyridine-H), 7.95 (d, ^3J = 6.6 Hz, 1H, [1,2,4]triazolo[4,3-*a*]pyridine-H), 7.31 (d, ^3J = 7.1 Hz, 1H, pyridine-H), 6.78 (t, ^3J = 7.0 Hz, 1H, [1,2,4]triazolo[4,3-*a*]pyridine-H), 6.60 (d, ^3J = 5.6 Hz, 1H, [1,2,4]triazolo[4,3-*a*]pyridine-H), 4.51 (s, 2H, –CH_2–), 4.37 (q, ^3J = 7.8 Hz, 2H, -CH_2-CF_3), 2.21 (s, 3H)
	^{13}C NMR ($CDCl_3$) δ 161.70, 155.54, 149.14, 148.12, 142.54, 126.40, 122.74, 121.89, 121.48, 113.75, 105.70, 65.43 (q, $^1J_{C-F}$ = 36.7 Hz), 39.13, 10.68
4u	IR, $\tilde{\nu}$/cm^{-1}: 3051.8 (Ar–H), 2930.3, 2918.2, 2868.1 (stretching vibration of –CH_2–), 1557.8, 1468.3, 1436.2 (skeleton vibration of aromatic ring)
	^{1}H NMR ($CDCl_3$) δ 7.76 (d, ^3J = 6.9 Hz, 1H, [1,2,4]triazolo[4,3-*a*]pyridine-H), 7.48–7.42 (m, 1H, Ar–H), 7.31–7.26 (m, 2H, Ph-H), 7.09 (t, ^3J = 8.9 Hz, 1H, Ph-H), 6.73 (t, ^3J = 7.0 Hz, 1H), 4.34 (s, 2H, –CH_2–)
	^{13}C NMR ($CDCl_3$) δ 162.41 (d, $^1J_{C-F}$ = 254.4 Hz), 128.21, 127.32, 125.31 (d, $^2J_{C-F}$ = 15.9 Hz), 124.35, 122.91, 122.19, 121.19, 116.42 (d, $^2J_{C-F}$ = 22.8 Hz), 114.13, 32.83
4v	IR, $\tilde{\nu}$/cm^{-1}: 3068.3 (Ar–H), 2931.3, 2926.4, 2870.1 (stretching vibration of –CH_2–), 1578.4, 1457.2, 1445.2 (skeleton vibration of aromatic ring)
	^{1}H NMR ($CDCl_3$) δ 8.28 (d, ^3J = 7.2 Hz, 1H, [1,2,4]triazolo[4,3-*a*]pyridine-H), 7.40 (d, ^3J = 7.0 Hz, 1H, [1,2,4]triazolo[4,3-*a*]pyridine-H), 6.80 (t, ^3J = 7.1 Hz, 1H, [1,2,4]triazolo[4,3-*a*]pyridine-H), 4.67 (t, ^3J = 7.2 Hz, 2H, –CH_2–), 3.03–2.95 (m, 2H, –$CH_2CF{=}CF_2$)
	^{13}C NMR ($CDCl_3$) δ 153.76 (ddd, $^1J_{C-F}$ = 287.8, $^1J_{C-F}$ = 274.6, $^2J_{C-F}$ = 45.7 Hz), 149.17, 142.21, 127.60 (ddd, $^1J_{C-F}$ = 234.9 Hz, J = 53.3 Hz, $^2J_{C-F}$ = 16.9 Hz), 126.43, 122.92, 121.47, 114.12, 30.22, 26.62 (d, $^2J_{C-F}$ = 21.6 Hz).

Biological activity

The inhibitory effects of the [1,2,4]triazolo[4,3-*a*]pyridine derivatives on *Rhizoctonia cerealis*, *Helminthosporium sativum*, and *Fusarium graminearum* were evaluated and summarized in Table 3. The results indicated that except for compounds **4s**, the rest of compounds displayed weak to good antifungal activities against *Rhizoctonia cerealis*, which with inhibitory rates ranging from 20.5 to 70.9%. Particularly, both compounds **4g** and **4u** showed 70.9% inhibitory effects at 50 μg mL^{-1}; and compounds **4b**, **4f**, **4k**, **4l** showed moderated activities on *Rhizoctonia cerealis*. As well as some of the synthesized compounds showed moderated inhibitory rates against *Helminthosporium sativum*, such as compounds **4b**, **4g**, **4k**, and **4u** showed >50% activities on *Helminthosporium sativum*, and the activity of **4u** was 67.3%; Unfortunately, most of the [1,2,4]triazolo[4,3-*a*]pyridine derivatives show no activity against *Fusarium graminearum*, only compounds **4g** and **4u** displayed certain activity. From these data it can be concluded that the antifungal activities could be decreased by introduction of pyridine and 1,3,4-oxadiazole (such as compounds **4d**, **4s**, and **4t**). As well as the introductions of bromine were disfavored by antifungal activities (compounds **4n**, **4q**, and **4r**). However, the introduction of trifluoromethyl (compounds **4i**, **4j**) and trifluoromethoxy (**4h**) can little improve the antifungal activity against both *Rhizoctonia cerealis* and *Helminthosporium sativum*, and the introduction of fluorine atom at benzene ring (compounds **4b**, **4k**, **4l** and **4u**) could enhance the antifungal activities. Moreover, the compound with a methyl (**4g**) also showed good antifungal activity. However, further structure–activity relationship (SAR) is not obvious due to limited active data and substituents on benzene.

Insecticidal activities against *Plutella xylostella* and *Helicoverpa armigera* of [1,2,4]triazolo[4,3-*a*]pyridine derivatives were also evaluated. The results listed in Table 4 indicated that most of the title compounds showed weakly insecticidal activity against the two pests. However, some of the compounds displayed good insecticidal activities. For example, compounds **4d** and **4s** showed 100% activities at 500 μg mL^{-1} and >50% activities at 50 μg mL^{-1} against both *Plutella xylostella* and *Helicoverpa armigera*; the activities of compounds **4d** and **4s** against *Helicoverpa armigera* were better than these of chlorpyrifos at 200 μg mL^{-1}; compound **4s** showed 86.7% activity against *Plutella xylostella* at 200 μg mL^{-1}. In addition, compounds **4p** and **4q** also showed good insecticidal activities, the mortalities of them against *Plutella*

Table 3 Antifungal effects of [1,2,4]triazolo[4,3-*a*]pyridine derivatives in vitro (50 μg mL^{-1})

Compounds	Antifungal effects/%		
	Rhizoctonia cerealis	*Helminthosporium sativum*	*Fusarium graminearum*
4a	36.4	38.2	9.1
4b	49.1	52.7	18.2
4c	40.0	30.9	7.3
4d	28.2	10.9	1.8
4e	30.9	18.2	10.9
4f	49.1	43.6	27.3
4 g	70.9	53.6	30.9
4 h	36.4	30.9	10.9
4i	34.5	34.5	9.1
4j	34.5	36.4	18.2
4 k	54.5	51.8	16.4
4l	45.5	49.1	18.2
4m	28.2	23.6	0.0
4n	28.2	30.9	0.0
4o	27.3	21.8	0.0
4p	36.4	25.5	9.1
4q	28.2	1.8	0.0
4r	28.2	18.2	0.0
4s	0.0	0.0	0.0
4t	20.5	25.5	0.0
4u	70.9	67.3	32.7
4v	25.5	36.4	9.1
Carbendazim	100	100	100

xylostella were 90 and 73.3%, respectively (500 μg mL^{-1}), and when the concentration was 200 μg mL^{-1}, the activity of **4p** against *Plutella xylostella* still >60%; furthermore, the activities of compounds **4p** and **4q** against *Helicoverpa armigera* at 200 μg mL^{-1} were 60%. Moreover, compound **4g** processed 55.6% and 46.6% activities on *Plutella xylostella* and *Helicoverpa armigera* at 500 μg mL^{-1}, respectively. Preliminary SAR studies indicated these compounds containing a substituent at 4 position of benzene (e.g., compounds **4h**, **4i**, **4k**, **4n**, **4o**, **4r**, etc.) showed very low insecticidal activities, and the introduction of trifluoromethyl at 2 or 5 position of benzene (compounds **4j** and **4u**) could little increase their insecticidal activities, these compounds with 3-chloro-2-fluorobenzyl (**4p**) and 2-bromo-5-fluorobenzyl (**4q**) also showed good insecticidal activity, and interestingly, in contrast to the above antifungal activity, these compounds containing 6-chloropyridin-3-ylmethyl (**4d**) and (5-(trifluoromethyl)-1,3,4-oxadiazol-2-yl)methyl (**4s**) showed good insecticidal activities. The IC_{50} of compounds **4d**, **4p**, **4q**, and **4s** were further evaluated. The results listed in Table 5 indicated that these compounds showed good insecticidal activity against *Plutella xylostella* and *Helicoverpa armigera*. Especially, the IC_{50} values of **4d**, **4q**, and **4s** on *Helicoverpa armigera* were much lower than that of chlorpyrifos, which indicated that the activities of these compounds on *Helicoverpa armigera* were better than that of chlorpyrifos.

Conclusions

In conclusion, a series of novel [1,2,4]triazolo[4,3-*a*]pyridine derivatives with a sulfide substructure was synthesized and characterized by spectral data and elemental analyses. Results from bioassays indicated that the synthesized compounds showed good fungicidal activities and insecticidal activities. The antifungal activities of compounds **4g** and **4u** against *Rhizoctonia cerealis* were 70.9% at 50 μg mL^{-1} and were much better than these of the rest of the synthesized compounds; and some of the synthesized compounds (e.g.: **4d**, **4q**, and **4s**) displayed good insecticidal activities against both *Plutella xylostella* and *Helicoverpa armigera*, the activities of compounds **4d**, **4q**, and **4s** on *Helicoverpa armigera* were better than that of chlorpyrifos. Preliminary structure activity relationship indicated that introduction of 6-chloropyridin-3-ylmethyl

Table 4 Insecticidal activity of the synthesized compounds against *Plutella xylostella* and *Helicoverpa armigera*

Comp.	Insecticidal activity (%) at different concentrations (μg mL^{-1})									
	Plutella xylostella					*Helicoverpa armigera*				
	500	200	100	50	25	500	200	100	50	25
4a	35.6	6.8	/	/	/	34.0	18.7	5.5	/	/
4b	38.6	7.8	/	/	/	36.0	11.7	/	/	/
4c	32.0	6.0	/	/	/	34.8	11.4	/	/	/
4d	100	80.0	60.8	53.3	36.7	100	80.0	60.0	50.0	26.7
4e	13.6	3.6	/	/	/	34.0	13.3	/	/	/
4f	10.0	7.3	/	/	/	36.7	15.8	/	/	/
4g	8.6	5.5	/	/	/	33.3	14.2	/	/	//
4h	6.6	3.6	/	/	/	10.6	/	/	/	/
4i	18.6	7.3	/	/	/	8.6	/	/	/	/
4j	55.6	23.8	6.0	/	/	46.6	27.8	10.0	/	/
4k	22.6	5.5	/	/	/	18.6	/	/	/	/
4l	15.6	6.8	/	/	/	25.6	/	/	/	/
4m	14.0	7.8	/	/	/	22.6	/	/	/	/
4n	16.0	6.0	/	/	/	15.6	/	/	/	/
4o	14.8	8.0	/	/	/	14.0	/	/	/	/
4p	90.0	63.3	43.3	33.3	23.3	76.7	60.0	50.0	33.3	23.3
4q	73.3	56.7	33.3	23.3	16.7	76.7	60.0	53.3	46.7	33.3
4r	8.0	/	/	/	/	23	13.1	/	/	/
4s	100	86.7	63.3	53.3	26.7	100	80.0	53.3	46.7	23.3
4t	40.5	10.6	/	/	/	24.0	12.5	/	/	/
4u	46.7	8.4	/	/	/	36.0	12.4	/	/	/
4v	35.1	5.5	/	/	/	25.6	7.3	/	/	/
Chlorpyrifos	100	100	100	90	83	83.3	60	56.7	30	20

Table 5 IC_{50} values of **4d**, **4p**, **4q**, **4s** and chlorpyrifos against *Plutella xylostella* and *Helicoverpa armigera*

Insects	Comp.	IC_{50}	$y = a + bx$	r	95% Confidence limits
Plutella xylostella	**4d**	43.87	$y = 1.10490x + 3.1855$	0.98	28.2708–68.0924
	4p	95.57	$y = 1.59132x + 2.35537$	0.98	68.5429–133.2597
	4q	169.4	$y = 1.2746x + 2.15894$	0.99	109.88–261.1351
	4s	50.75	$y = 1.70083x + 2.09929$	0.98	37.6834–68.35623
	Chlorpyrifos	7.61	$y = 1.44x + 3.730$	0.98	5.2700–9.5400
Helicoverpa armigera	**4d**	58.3	$y = 1.4930x + 2.3644$	0.98	41.5738–81.6283
	4p	112.46	$y = 1.1223x + 2.6982$	0.99	72.9958–173.2556
	4q	77.14	$y = 0.8335x + 3.4268$	0.98	42.57697–139.7665
	4s	65.31	$y = 1.4715x + 2.3292$	0.98	45.90219–92.93366
	Chlorpyrifos	103.77	$y = 1.3748x + 2.2283$	0.97	72.3783–148.7882

and (5-(trifluoromethyl)-1,3,4-oxadiazol-2-yl)methyl were disfavored by fungicidal activity but favored by insecticidal activities, and these compounds containing 3-chloro-2-fluorobenzyl and 2-bromo-5-fluorobenzyl also showed good insecticidal activity. Moreover, the introduction of fluorine atom could enhance their bio-activities. The present report is the first study of the synthesis, fungicidal and insecticidal activities of [1,2,4]triazolo[4,3-*a*]pyridine derivatives with a sulfide. However, the structures of the synthesized compounds need to be optimized. Future structural modification and biological evaluation are currently underway to explore the full potential of this kind of [1,2,4]triazolo[4,3-*a*]pyridine derivatives with a sulfide group based on these findings.

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