



Synthesis of 2-[2-(4-Substituted-1,3,5-triazin-2-yl)oxy]phenyl]-3,3-dimethoxypropanoate

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In this article, the synthesis of a series of novel compounds, methyl 2-[2-(4-substituted-1,3,5-triazin-2-yl)oxy]phenyl]-3,3-dimethoxypropanoate is reported. 4,6-Dichloro-*N,N*-diethyl-1,3,5-triazin-2-amine reacted with methyl 2-(2-hydroxyphenyl)-3,3-dimethoxypropanoate to give methyl 2-[2-(4-chloro-6-(diethylamino)-1,3,5-triazin-2-yl)oxy]phenyl]-3,3-dimethoxypropanoate, which then reacted with phenols or thiophenols to give nine novel target compounds. The structures of target compounds had been characterized by IR, ¹H NMR and HRMS.

Keywords: Methoxyacrylate, 3,3-Dimethoxypropanoate, Synthesis.

INTRODUCTION

The naturally-occurring derivatives of β -methoxyacrylic acid, such as strobilurin A (Fig. 1) has wide range of biological activities and serve as important lead compounds for the development of a new class of fungicides for crop protection¹⁻³.

In past decades, structural modification and optimization about strobilurin A had been carried out and produced large quantities of methoxyacrylate derivatives. Research showed that the introduction of heterocyclic structure would help to improve bioactivity of compounds. Many methoxyacrylate derivatives containing nitrogenous heterocycle, such as pyrimidinyl and pyrazolyl had been synthesized⁴⁻¹³. Some of these compounds showed good fungicidal activity on a wide range of crops and was successfully commercialized. For example, azoxystrobin and pyraoxystrobin (Fig. 1) had been widely sold as the most significant examples among the structural analogues of methoxyacrylate derivatives.

In our previous research on methoxyacrylates fungicide, methyl 2-[2-(4-chloro-6-(diethylamino)-1,3,5-triazin-2-yl)oxy]phenyl]-3,3-dimethoxypropanoate (**3**, Fig. 1) was found to exhibit antibacterial activity and compound **3** had a certain structural similarity to methoxyacrylates.

It can be expected that the compound **3** analogues was one kind of novel compound with potential bioactivity. In this study a series of novel compounds were designed and synthesized on the basic moiety of **3**. The synthetic route is outlined in **Scheme-I**. 4,6-Dichloro-*N,N*-diethyl-1,3,5-triazin-2-amine (**1**) reacted with methyl 2-(2-hydroxyphenyl)-3,3-dimethoxypropanoate (**2**) to give compound **3**, then phenols or thiophenols,

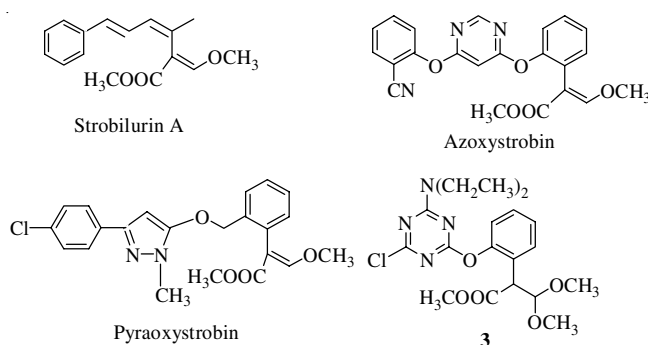


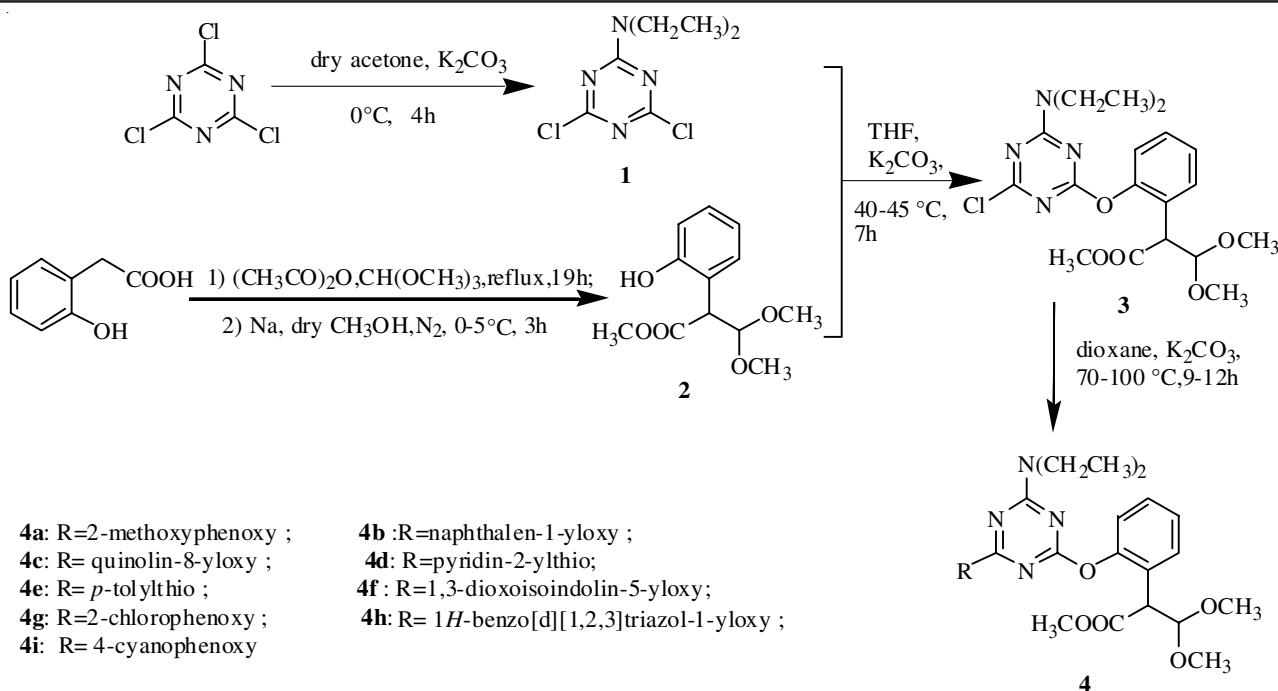
Fig. 1. Structure of strobilurin A, azoxystrobin, pyraoxystrobin and compound **3**

with different substituted groups or heteroatom, were linked to compound **3** to give nine novel target compounds, methyl 2-[2-(4-substituted-1,3,5-triazin-2-yl)oxy]phenyl]-3,3-dimethoxypropanoate (**4**).

EXPERIMENTAL

4,6-Dichloro-*N,N*-diethyl-1,3,5-triazin-2-amine (**1**) was prepared according to literature¹³. Methyl 2-(2-hydroxyphenyl)-3,3-dimethoxypropanoate (**2**) was prepared according to literature¹⁴. All the reagents were analytically pure. All of the organic solvents used in this study were dried over appropriate drying agents.

Melting points (m.p.) were determined with XRC-1 melting point apparatus without correction. TLC was performed on silica gel GF254 and spots were visualized with ultraviolet (UV) light. IR spectra were recorded with a Perkin-Elmer 16PC-FT spectrometer as pellets (KBr). Mass spectra were



Scheme-I: Synthetic route of compound 4a-4i

recorded with Agilent 6210 (DOF-MAS) spectrometer (Agilent Inc., Santa Clara, CA, USA) using the electrospray ionization (ESI⁺) method. ¹H NMR spectra were recorded with a Varian INVOA-400 spectrometer using TMS as internal standard. The chemical shift values (δ) were given in ppm and coupling constants were given in Hz.

Preparation of methyl 2-[2-(4-chloro-6-(diethylamino)-1,3,5-triazin-2-yloxy)phenyl]-3,3-dimethoxypropanoate (3): Compound **1** (4.86 g, 22 mmol), K₂CO₃ (2.76, 20 mmol) and dry acetone (30 mL) were added in a flask. Then the compound **2** (4.76 g, 20 mmol) in dry THF (20 mL) was added dropwise to the solution slowly at room temperature. After dropping was finished, the mixture was warmed to 35-40 °C and stirred until completion of the reaction (monitored with TLC, petroleum ether/ethyl acetate, 2:1, v/v). The mixture was filtered and concentrated under reduced pressure. The residue was dissolved in ethyl acetate (20 mL), washed with water (10 mL × 3). The combined organic layer was dried with anhydrous Na₂SO₄, filtered and concentrated in vacuo to give crude product. The crude product was purified by column chromatography (silica gel; petroleum ether/ethyl acetate, 2:1, v/v) gave compound **3** as light yellow solid.

Typical procedure for the preparation of compound 4a-4i: Substituted phenols or thiophenols (20 mmol), K₂CO₃ (2.76, 20 mmol) and dry dioxane (30 mL), KI (5 % wt) were added in a single-necked round bottom flask. Then the compound **3** (4.86 g, 22 mmol) in dry dioxane (20 mL) was added dropwise to the suspension slowly at room temperature. After dropping was finished, the mixture was warmed to 65-100 °C and stirred. The end-point of the reaction was monitored with TLC (petroleum ether/ethyl acetate = 1:1-4:1, v/v). Then the mixture was filtered and evaporated under reduced pressure. The residue was dissolved in ethyl acetate (20 mL), washed with water (10 mL × 3). The combined organic layer was dried with anhydrous Na₂SO₄, filtered and concentrated *in vacuo*.

The residue was purified with column chromatography on silica with mixture of petroleum ether and ethyl acetate (v/v) to afford product **4**.

Methyl 2-[2-(4-chloro-6-(diethylamino)-1,3,5-triazin-2-yloxy)phenyl]-3,3-dimethoxypropanoate (3): Light yellow solid, yield 64 %. IR (KBr, ν_{\max} , cm⁻¹) 2972 (Ar-H), 1728 (C=O), 1581 (Ar-N), 1500 (Ph), 1293 (C-N), 1259 (Ar-O-O), 1209 (C-O), 1121 (C-O-C), 807 (Ar), 769 (C-Cl); ¹H NMR (CDCl₃, 400 MHz) δ: 0.99 (t, *J* = 7.2, 6.8 Hz, 3 H, -NCH₂CH₃), 1.14 (t, *J* = 7.2, 6.8 Hz, 3 H, -NCH₂CH₃), 3.16 (s, 3H, -OCH₃), 3.40 (s, 3H, -OCH₃), 3.51 (s, 3 H, -COOCH₃), 3.34 (m, 4H, -NCH₂CH₃), 4.26 (d, *J* = 8.4 Hz, 1H, -CHCOOCH₃), 5.04 (d, *J* = 8.8 Hz, 1H, -CH(OCH₃)₂), 7.07-7.63 (m, 4 H, Ph-H); HR-MS (+ESI): Calcd. for C₁₉H₂₅ClN₄O₅Na [M + Na]⁺: 447.1411, found: 447.1397.

Methyl 2-[2-(4-(diethylamino)-6-(2-methoxyphenoxy)-1,3,5-triazin-2-yloxy)phenyl]-3,3-dimethoxypropanoate (4a): The crude product was prepared by the reaction of *o*-methoxyphenol with compound **3** and was purified by TLC on silica gel with petroleum ether and ethyl acetate (4:1, v/v) as a viscous brown liquid. IR (KBr, ν_{\max} , cm⁻¹) 3069 (Ar-H), 1738 (C=O), 1605 (Ar-N), 1528 (Ph), 1316 (C-N), 1259 (Ar-O-Ar), 1215 (C-O), 1112 (C-O-C), 810 (Ar-H); ¹H NMR (CDCl₃, 400 Hz): 0.89-1.07 (m, 6H, -NCH₂CH₃), 3.14 (s, 3H, -OCH₃), 3.26-3.44 (m, 7H, -OCH₃, -NCH₂CH₃), 3.55 (s, 3H, -COOCH₃), 3.77 (d, *J* = 8.5 Hz, 3H, -OCH₃Ph), 4.31 (d, *J* = 8.5 Hz, 1H, -CHCO-OCH₃), 5.04 (d, *J* = 8.5 Hz, 1H, -CH(OCH₃)₂), 6.87-6.93 (m, 2H, Ph-H), 7.04-7.24 (m, 5H, Ph-H), 7.55 (d, *J* = 12.1 Hz, 1 H, Ph-H); HR-MS (+ESI): Calcd. for C₂₆H₃₂N₄O₇Na [M + Na]⁺: 535.2169, found: 535.2160.

Methyl 2-[2-(4-(diethylamino)-6-(naphthalen-1-yloxy)-1,3,5-triazin-2-yloxy)phenyl]-3,3-dimethoxypropanoate (4b): The crude product was prepared by the reaction of α -naphthol with compound **3** and was purified by TLC on silica gel with petroleum ether and ethyl acetate (4:1, v/v) as a

viscous brown liquid. IR (KBr, ν_{\max} , cm^{-1}) 3061 (Ar-H), 1738 (C=O), 1589 (Ar-N), 1527 (ph), 1317 (C-N), 1257 (Ar-O-Ar), 1222 (C-O), 1105 (C-O-C), 807 (Ar-H); ^1H NMR (CDCl_3 , 400 Hz): 0.99-0.71 (m, 6H, $-\text{NCH}_2\text{CH}_3$), 3.12 (s, 3H, $-\text{OCH}_3$), 3.13-3.34 (m, 4H, $-\text{NCH}_2\text{CH}_3$), 3.40 (s, 3H, $-\text{OCH}_3$), 3.53 (s, 3H, $-\text{COOCH}_3$), 4.30 (d, 1H, $J = 8.5$ Hz, $-\text{CHCOOCH}_3$), 5.03 (d, 1H, $J = 8.5$ Hz, $-\text{CH}(\text{OCH}_3)_2$), 7.06 (m, 1H, Ph-H), 7.16-7.29 (m, 3H, Ph-H), 7.37-7.51 (m, 3H, Naphth-H), 7.54-7.60 (m, 1H, Naphth-H), 7.71 (d, 1H, $J = 2$ Hz, Naphth-H), 7.84-7.87 (m, 1H, Naphth-H), 7.90-7.98 (m, 1H, Naphth-H); HR-MS (+ESI): Calcd. for $\text{C}_{29}\text{H}_{32}\text{N}_4\text{O}_6\text{Na}$ [$\text{M} + \text{Na}$] $^+$: 555.2220, found: 555.2212.

Methyl 2-[2-{4-(diethylamino)-6-(quinolin-8-yloxy)-1,3,5-triazin-2-yloxy}phenyl]-3,3-dimethoxypropanoate (4c): The crude product was prepared by the reaction of 8-hydroxyquinoline with compound **3** and was purified by TLC on silica gel with petroleum ether and ethyl acetate (1:1, v/v) as a yellow solid, m.p. 95 °C. IR (KBr, ν_{\max} , cm^{-1}) 3064 (Ar-H), 1740 (C=O), 1591 (Ar-N), 1527 (Ph), 1316 (C-N), 1212 (C-O), 1105 (C-O-C), 791 (Ar-H); ^1H NMR (CDCl_3 , 400 Hz): 1.24-1.27 (m, 6H, $-\text{NCH}_2\text{CH}_3$), 3.56 (s, 3H, $-\text{COOCH}_3$), 3.38 (s, 3H, $-\text{OCH}_3$), 3.25-3.35 (m, 4H, $-\text{NCH}_2\text{CH}_3$), 3.07 (s, 3H, $-\text{OCH}_3$), 4.27 (d, $J = 8.4$ Hz, 1H, $-\text{CHCOOCH}_3$), 4.99 (d, $J = 8.4$ Hz, 1H, $-\text{CH}(\text{OCH}_3)_2$), 6.96 (t, $J = 6.8$, 2 Hz, 1H, Ph-H), 7.10-7.15 (m, 2H, Ph-H), 7.42-7.43 (m, 1H, Ph-H), 7.51-7.52 (m, 3H, quinolin-H), 7.70 (t, $J = 4.4$, 4.8 Hz, 1H, quinolin-H), 8.19 (d, $J = 8$ Hz, 1H, quinolin-H), 8.89 (s, 1H, quinolin-H); HR-MS (+ESI): Calcd. for $\text{C}_{28}\text{H}_{32}\text{N}_5\text{O}_6$ [$\text{M} + \text{H}$] $^+$: 534.2352, found: 534.2352.

Methyl 2-[2-{4-(diethylamino)-6-(pyridin-2-ylthio)-1,3,5-triazin-2-yloxy}phenyl]-3,3-dimethoxypropanoate (4d): The crude product was prepared by the reaction of 2-mercaptopyridine with **3** and was purified by TLC on silica gel with petroleum ether and ethyl acetate (4:1, v/v) as a yellow solid, m.p. 85 °C. IR (KBr, ν_{\max} , cm^{-1}) 3071 (Ar-H), 1734 (C=O), 1573 (Ar-N), 1504 (Ph), 1295 (C-N), 1206 (C-O), 1117 (C-O-C), 807 (Ar-H); ^1H NMR (CDCl_3 , 400 Hz): 0.98-1.05 (m, 6H, $-\text{NCH}_2\text{CH}_3$), 3.54 (s, 3H, $-\text{COOCH}_3$), 3.38 (s, 3H, $-\text{OCH}_3$), 3.35-3.37 (m, 4H, $-\text{NCH}_2\text{CH}_3$), 3.13 (s, 3H, $-\text{OCH}_3$), 4.25 (d, $J = 8.4$ Hz, 1H, $-\text{CHCOOCH}_3$), 5.01 (d, $J = 8.8$ Hz, 1H, $-\text{CH}(\text{OCH}_3)_2$), 7.04 (m, 1H, Ph-H), 7.22 (m, 3H, Ph-H), 7.55 (m, 3H, py-H), 8.53 (d, $J = 4.0$ Hz, 1H, py-H); HR-MS (+ESI): Calcd. for $\text{C}_{24}\text{H}_{30}\text{N}_5\text{O}_5\text{S}$ [$\text{M} + \text{H}$] $^+$: 500.1967, found: 500.1966.

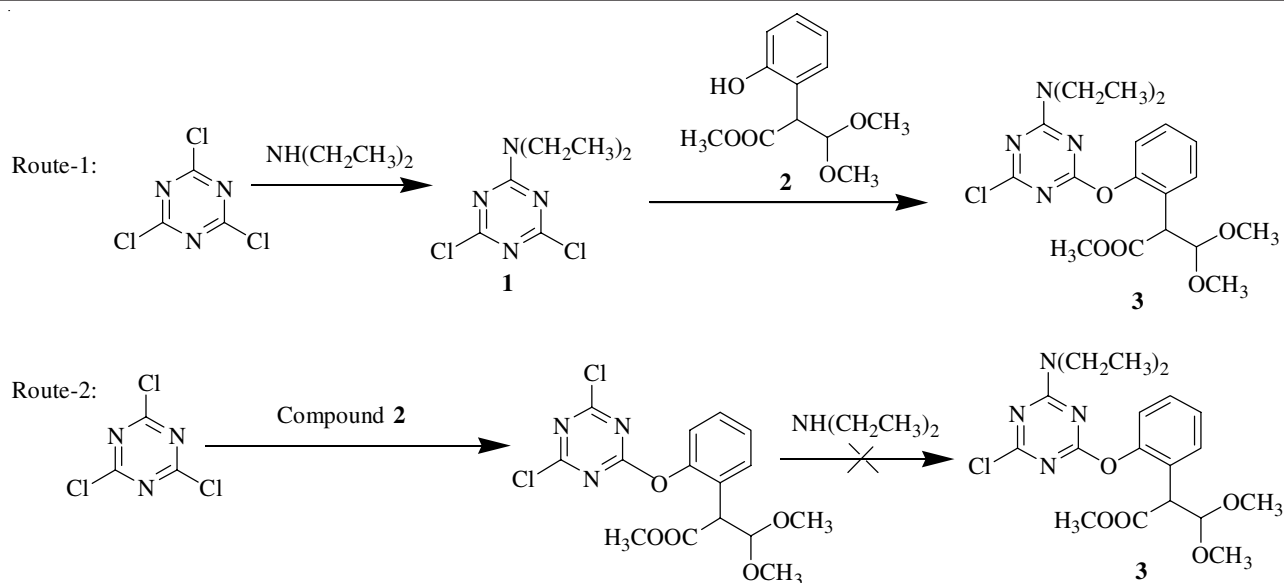
Methyl 2-[2-{4-(diethylamino)-6-(*p*-tolylthio)-1,3,5-triazin-2-yloxy}phenyl]-3,3-dimethoxypropanoate (4e): The crude product was prepared by the reaction of *p*-methyl thiophenol with **3** and was purified by TLC on silica gel with petroleum ether and ethyl acetate (4:1, v/v) as a yellow solid, m.p. 42 °C. IR (KBr, ν_{\max} , cm^{-1}) 3063 (Ar-H), 1737 (C=O), 1563 (Ar-H), 1487 (Ph), 1294 (C-N), 1206 (C-O), 1107 (C-O-C), 803 (Ar-H); ^1H NMR (CDCl_3 , 400 Hz): 0.97-0.99 (m, 6H, $-\text{NCH}_2\text{CH}_3$), 2.36 (s, 3H, $-\text{CH}_3$), 3.14 (s, 3H, $-\text{OCH}_3$), 3.25-3.32 (m, 4H, $-\text{NCH}_2\text{CH}_3$), 3.41 (s, 3H, $-\text{OCH}_3$), 3.54 (s, 3H, $-\text{COOCH}_3$), 4.27 (d, $J = 8.8$ Hz, 1H, $-\text{CHCOOCH}_3$), 5.03 (d, $J = 10.8$ Hz, 1H, $-\text{CH}(\text{OCH}_3)_2$), 7.02-7.05 (m, 1H, Ph-H), 7.11 (d, $J = 7.2$ Hz, 2H, Ph-H), 7.21-7.26 (m, 2H, Ph-H), 7.38 (d, $J = 8$ Hz, 2H, Ph-H), 7.56-7.59 (m, 1H, Ph-H); HR-MS (+ESI): Calcd. for $\text{C}_{26}\text{H}_{33}\text{N}_4\text{O}_5\text{S}$ [$\text{M} + \text{H}$] $^+$: 513.2171; found: 513.2178.

Methyl 2-[2-{4-(diethylamino)-6-(1,3-dioxoisindolin-5-yloxy)-1,3,5-triazin-2-yloxy}phenyl]-3,3-dimethoxypropanoate (4f): The crude product was prepared by the reaction of 5-hydroxy-isindole-1,3-dione and **3** and was purified by TLC on silica gel with petroleum ether and ethyl acetate (2:1, v/v) as a yellow solid, m.p. 117 °C. IR (KBr, ν_{\max} , cm^{-1}) 3113 (N-H), 3062 (Ar-H), 1736 (C=O), 1589 (Ar-H), 1483 (Ph), 1307 (C-N), 1215 (C-O), 1100 (C-O-C), 809 (Ar-H); ^1H NMR (CDCl_3 , 400 Hz): 0.99 (t, $J = 7.2, 7.2$ Hz, 3H, $-\text{NCH}_2\text{CH}_3$), 1.09 (t, $J = 7.2$, 6.8 Hz, 3H, $-\text{NCH}_2\text{CH}_3$), 3.15 (s, 3H, $-\text{OCH}_3$), 3.34-3.36 (m, 4H, $-\text{NCH}_2\text{CH}_3$), 3.46 (s, 3H, $-\text{OCH}_3$), 3.53 (s, 3H, $-\text{COOCH}_3$), 4.26 (d, $J = 8.4$ Hz, 1H, $-\text{CHCOOCH}_3$), 5.03 (d, $J = 8.4$ Hz, 1H, $-\text{CH}(\text{OCH}_3)_2$), 7.11 (d, $J = 9.2$ Hz, 1H, Ph-H), 7.27 (m, 2H, Ph-H), 7.51-7.60 (m, 2H, Ph-H), 7.69 (s, 1H, NH), 7.85 (d, $J = 8.4$ Hz, 1H, Ph-H); HR-MS (+ESI): Calcd. for $\text{C}_{27}\text{H}_{29}\text{N}_5\text{O}_8\text{Na}$ [$\text{M} + \text{Na}$] $^+$: 574.1914; found: 574.1920.

Methyl 2-[2-{4-(2-chlorophenoxy)-6-(diethylamino)-1,3,5-triazin-2-yloxy}phenyl]-3,3-dimethoxypropanoate (4g): The crude product was prepared by the reaction of 2-chlorophenol with compound **3** and was purified by TLC on silica gel with petroleum ether and ethyl acetate (4:1, v/v) as a viscous yellow liquid. IR (KBr, ν_{\max} , cm^{-1}) 3068 (Ar-H), 1739 (C=O), 1589 (Ar-H), 1482 (Ph), 1318 (C-N), 1223 (C-O), 1110 (C-O-C), 810 (Ar-H), 766 (C-Cl); ^1H NMR (CDCl_3 , 400 Hz): 0.94-1.01 (m, 6H, $-\text{NCH}_2\text{CH}_3$), 3.15 (s, 3H, $-\text{OCH}_3$), 3.28-3.29 (m, 4H, $-\text{NCH}_2\text{CH}_3$), 3.41 (s, 3H, $-\text{OCH}_3$), 3.55 (s, 3H, $-\text{COOCH}_3$), 4.32 (d, $J = 8.4$ Hz, 1H, $-\text{CHCOOCH}_3$), 5.05 (d, $J = 8.4$ Hz, 1H, $-\text{CH}(\text{OCH}_3)_2$), 7.20 (m, 6H, Ph-H), 7.41 (dd, $J = 1.2$, 1.2 Hz, 1H, Ph-H), 7.58 (dd, $J = 1.6$, 1.2 Hz, 1H, Ph-H). HR-MS (+ESI): Calcd. for $\text{C}_{25}\text{H}_{29}\text{ClN}_4\text{O}_6\text{Na}$ [$\text{M} + \text{Na}$] $^+$: 539.1674; found: 539.1979.

Methyl 2-[2-{4-(1*H*-benzo[d][1,2,3]triazol-1-yloxy)-6-(diethylamino)-1,3,5-triazin-2-yloxy}phenyl]-3,3-dimethoxypropanoate (4h): The crude product was prepared by the reaction of benzotriazol-1-ol with compound **3** and was purified by TLC on silica gel with petroleum ether and ethyl acetate (1:1, v/v) as a yellow solid, m.p. 150 °C. IR (KBr, ν_{\max} , cm^{-1}) 2976 (Ar-H), 1740 (C=O), 1599 (Ar-H), 1489 (Ph), 1316 (C-N), 1212 (C-O), 1100 (C-O-C), 800 (Ar-H)-1; ^1H NMR (CDCl_3 , 400 Hz): 1.17-1.20 (t, $J = 7.2$, 7.2 Hz, 3H, $-\text{NCH}_2\text{CH}_3$), 1.26-1.30 (t, $J = 7.6$, 6.8 Hz, 3H, $-\text{NCH}_2\text{CH}_3$), 3.15 (s, 3H, $-\text{OCH}_3$), 3.28 (s, 3H, $-\text{OCH}_3$), 3.40 (s, 3H, $-\text{COOCH}_3$), 3.59 (q, $J = 6.8$, 7.6, 7.6 Hz, 2H, $-\text{NCH}_2\text{CH}_3$), 3.77 (q, $J = 7.2$, 6.8, 7.2 Hz, 2H, $-\text{NCH}_2\text{CH}_3$), 4.29 (d, $J = 8.4$ Hz, 1H, $-\text{CHCOOCH}_3$), 5.05 (d, $J = 8.8$ Hz, 1H, $-\text{CH}(\text{OCH}_3)_2$), 7.20-7.21 (m, 1H, Ph-H), 7.38-7.43 (m, 4H, benzotriazol-H, Ph-H), 7.68-7.74 (m, 2H, benzotriazol-H), 7.95-7.98 (m, 1H, benzotriazol-H). HR-MS (+ESI): Calcd. for $\text{C}_{25}\text{H}_{29}\text{N}_7\text{O}_6\text{Na}$ [$\text{M} + \text{Na}$] $^+$: 546.2077; found: 546.2079.

Methyl 2-[2-{4-(4-cyanophenoxy)-6-(diethylamino)-1,3,5-triazin-2-yloxy}phenyl]-3,3-dimethoxypropanoate (4i): The crude product was prepared by the reaction of 4-cyanophenol and compound **3** and was purified by TLC on silica gel with petroleum ether and ethyl acetate (4:1, v/v) as a pale yellow solid, m.p. 138 °C. IR (KBr, ν_{\max} , cm^{-1}) 3068 (Ar-H), 2233 (CN), 1743 (C=O), 1584 (Ar-H), 1496 (Ph), 1320 (C-N), 1229 (C-O), 1106 (C-O-C), 808 (Ar-H). ^1H NMR (CDCl_3 , 400 Hz): 0.99 (t, $J = 6.8$, 7.2 Hz, 3H, (s, 3H, $-\text{OCH}_3$), 3.55 (s, 3H, $-\text{COOCH}_3$), $-\text{NCH}_2\text{CH}_3$), 1.07 (t, $J = 7.2$, 6.8 Hz,



Scheme-II: Two designed synthetic route for compound 3

3H, -NCH₂CH₃), 3.14 (s, 3H, -OCH₃), 3.33-3.39 (m, 4H, -NCH₂CH₃), 3.41 4.27 (d, *J* = 8.8 Hz, 1H, -CHCOOCH₃), 5.04 (d, *J* = 8.8 Hz, 1H, -CH(OCH₃)₂), 7.10 (d, *J* = 9.2 Hz, 1H, Ph-H), 7.25-7.30 (m, 5H, Ph-H), 7.60 (d, *J* = 7.6 Hz, 1H, Ar-H), 7.65 (d, *J* = 8.4 Hz, 1H, Ph-H). HR-MS (+ESI): Calcd. for C₂₆H₂₉N₅O₆Na [M + Na]⁺: 530.2016; found: 530.2017.

RESULTS AND DISCUSSION





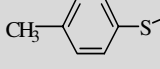
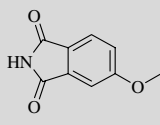

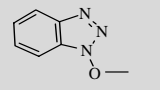

Synthesis of compound 3: In the synthesis of compound 3, two possible synthetic route were designed (Scheme-II). Experiment showed that no compound 3 was produced when route 2 was taken. The proper synthetic route for compound 3 should be route 1. When the ratio of compound 1, 2 and K₂CO₃ was 1.1:1:1 (molar ratio) and temperature was kept between 40-45 °C, the best yield of compound 3 was observed.

In order to find better base used in the synthesis of compound 3, NaH, KOH, pyridine, K₂CO₃ were tested. Experiment showed that when NaH was used, more by-products were produced. When pyridine was used, the color of products was darker. When KOH was used, the yield was rather poor. When K₂CO₃ was used, the yield and color of products was better than others. So K₂CO₃ was used in synthesis of compound 3.

Synthesis of compound 4: The synthesis of compound 4a was chosen as model to optimize the reaction conditions of target compounds. Dioxane was used as solvent and K₂CO₃ was chosen as base. Better yield of compound 4a was observed when the ratio of compound 3, phenol and K₂CO₃ was 1.1:1:1 (molar ratio) and the dosage of catalyst KI (if used) was 5 % (wt %) of compound 3. Different phenol exhibited different reactivity and required different reaction temperature and time (Table-1). The results showed that thiophenols was more reactive than phenols. Pyridine-2-thiol and 4-methylbenzenethiol reacted with compound 3 at 65 °C for 5 h to give better yield without catalyst KI. But for other phenols, the reaction temperature was always higher than 90 °C, required catalyst KI and longer time. For phenols containing strong electron-withdrawing groups, such as 4-fluorophenol, 4-trifluoromethyl-phenol, 4-nitrophenol, the reaction was difficult to take place. Even after

12 h at 110-120 °C, only trace of product or no product were observed. The steric hindrance was unfavorable to reaction. The reaction between 5-hydroxyisoindoline-1,3-dione and compound 3 required higher temperature (100 °C) and longer time (9 h). The reaction condition for compounds 4a-4i were listed in Table-1.

TABLE-1
REACTION CONDITION OF THE COMPOUNDS 4a-4i

Compound	R	Temp. (°C)	Time (h)	KI (wt %)	Yield (%)
4a		90	7	5	56
4b		90	7	5	70
4c		90	7	5	67
4d		65	5	0	73
4e		65	5	0	68
4f		100	9	5	51
4g		90	7	5	40
4h		90	7	5	48
4i		90	7	5	53

Conclusion

A series of novel 2-[2-(4-substituted-1,3,5-triazin-2-yloxy)phenyl]-3,3-dimethoxypropanoate compounds were synthesized. The structure of all target compounds were identified by ¹H NMR, IR and high resolution mass spectrum (HR-MS).

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REFERENCES

1. J.C. Yang, Q. Wu, R.L. Liu, S.C. Ma and C.L. Liu, *Agrochemicals*, **47**, 402 (2008).
2. G.S. Zhang, *Pesticides Sci. Admin.*, **24**, 30 (2003).
3. S. Kroiß and W. Steglich, *Tetrahedron*, **60**, 4921 (2004).
4. D.G. Brooke and J.C. Morris, *Tetrahedron Lett.*, **49**, 2414 (2008).
5. B. Chai, S.Y. Wang, W.Q. Yu, H.C. Li, C.J. Song, Y. Xu, C.L. Liu and J.B. Chang, *Bioorg. Med. Chem. Lett.*, **23**, 3505 (2013).
6. G.H. Lu, H.B. Chu, M. Chen and C.L. Yang, *Chin. Chem. Lett.*, **25**, 61 (2014).
7. H.C. Li, B.S. Chai, Z.N. Li, J.C. Yang and C.L. Liu, *Chin. Chem. Lett.*, **20**, 1287 (2009).
8. B.S. Chai, C.L. Liu, H.C. Li, S.W. Liu, Y. Xu, Y.Q. Song and J.B. Chang, *Chin. Chem. Lett.*, **25**, 137 (2014).
9. M. Li, R.L. Liu, Z.N. Li, C.L. Liu and Z.M. Li, *Agrochemicals*, **48**, 405 (2009).
10. K. Sun, H.F. Wu, H. Zhang, F.R. Wang, W. Cao, J. Zhao, H. Yang and J.B. Xu, *Modern Agrochem.*, **12**, 17 (2013).
11. H.Y. Wang, S.Q. Li, Z.J. Fan, J.Y. Chen, F. Chai, S. Li and C.L. Liu, *Fine Chem. Intermed.*, **40**, 66 (2010).
12. A.Y. Guan, C.L. Liu, Z.N. Li and M.X. Zhang, *Chin. Chem. Lett.*, **22**, 663 (2011).
13. T. Hermon and E.Y. Tshuva, *J. Org. Chem.*, **73**, 5953 (2008).
14. J. Dong, D.H. Liao, J.S. Lou and H.J. Pi, *Fine Chem. Intermed.*, **37**, 25 (2007).